2020 | Report

International Evaluation of the SciLifeLab Infrastructure

SciLifeLab

Karolinska Institutet

KTH Vetenskap och konst

Stockholms universitet

Uppsala universitet

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Welcome to the International Evaluation of the SciLifeLab Infrastructure 2020

Thank you for agreeing to take part in the evaluation of the SciLifeLab National Infrastructure, including the panel meeting on April 20–22, 2020 in Stockholm.

This evaluation is of key importance and will define the optimal spending of about 1 billion SEK (about 100 million EUR) of government funding for our life science infrastructure over the next four years.

SciLifeLab was launched almost ten years ago as a collaboration between the four host universities, and has since 2013 also served as a national research infrastructure for molecular biosciences in Sweden. In our strategy work for SciLifeLab for 2020–2030, we have emphasized how the need for a national collaborative organization that promotes research and infrastructure in life sciences is critically important today and in the future. It is our wish to keep the infrastructure at the cutting edge given the rapid technology evolution underway in life science.

The first international evaluation of SciLifeLab infrastructure was conducted in 2016, and evaluations will be held every four years, i.e. 2020, 2024 etc. Guided by recommendations from these evaluations, SciLifeLab will implement new facilities or technology areas, revise facility and platform structure as well as phase-down facilities or technologies that are regarded not as significant or suitable at a national level or that would be more suitable as local core facilities.

In this evaluation, many new potential candidate facilities from across the country are now being competitively evaluated along with all of our existing facilities. If the annual government funding to SciLifeLab will not increase in 2021, difficult prioritizations will have to be made to sustain the continuity of the best existing facilities, but also the entry of new facilities and technologies. We look forward to your expert advice and global perspectives, as to what we should do to make sure SciLifeLab serves its national infrastructure mandate in the best possible way from 2021 onwards. We also do understand that you may not be an expert in all technologies, but we ask you to evaluate them if you just possibly can, but then indicate your level of familiarity with the topic (see instructions).

In the evaluation web portal you have the possibility to indicate if you have direct formal conflicts with any of the platforms or facilities (personal, collaborative, or shared publications or joint grants) with any of the facility and platform directors.

We look forward to your initial grading by March 30, and then welcoming you to the actual site visit in Stockholm on April 20–22, 2020.

Olli Kallioniemi, SciLifeLab Director

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Appendices (separate documents)

I. Terms and Conditions for Funding

II. SciLifeLab Roadmap 2020-2030

Abbreviations

AIDA	Analytic imaging diagnostics arena (Swedish arena for research and innovation on artificial intelligence, AI, for medical image analysis)
Akademiska sjukhuset	University Hospital Uppsala
ALF	County Council funding
Chalmers	Chalmers University of Technology
DC	SciLifeLab Data Centre
DD	Diagnostics Development Platform
DDD	Drug Discovery and Development Platform
EMBL	European Molecular Biology Laboratory
EMBL-EBI	European Molecular Biology Laboratory, European Bioinformatics Institute
FD	Facility Director
FTE	Full time equivalent
GDPR	The General Data Protection Regulation
GMS	Genomic Medicine Sweden
GU	University of Gothenburg
HF	Head of Facility
HPA	Human Protein Atlas
IAB	SciLifeLab International Advisory board
IEC	SciLifeLab International Evaluation Committee
JIF	Journal Impact Factor
KAW	Knut and Alice Wallenberg Foundation
KI	Karolinska Institutet
KTH	Kungliga tekniska högskolan (Royal Institute of Technology)
LiU	Linköping University
LU	Lund University
MAX-IV	The Swedish national synchrotron light laboratory
MG	SciLifeLab Management Group
NBIS	National Bioinformatics Infrastructure Sweden
NRM	Naturhistoriska riksmuseet (Swedish Museum of Natural History)
NSC	The National SciLifeLab Committee
PD	Platform Director
PI	Principal Investigator
RCP	SciLifeLab Research Community Programs
RISE	Research Institutes of Sweden
Sahlgrenska	Sahlgrenska University Hospital, Gothenburg
SEK	Swedish Krona (currency: 100 SEK = 9,49 EUR / 10,28 USD)
SFO	Strategiska forskningsområden (Strategic research area)
SLL	Stockholms läns landsting (Stockholm County Council)
SLU	Swedish University of Agricultural Sciences
SME	Small and medium-sized enterprises
SNIC	Swedish National Infrastructure for Computing
SSF	Swedish Foundation for Strategic Research
SU	Stockholm University
TDP	SciLifeLab Technology Development Project
UmU	Umeå University
UPPMAX	Uppsala multidisciplinary center for advanced computational science
UU	Uppsala University
VR	Vetenskapsrådet (Swedish National Research Council)
VINNOVA	Sweden's Innovation Agency
ÖRU	Örebro University

The International Evaluation Committee (IEC)

Geert Van Minnebruggen (Chair)
Head of Vlaams Interuniversitair Instituut voor Biotechnologie (VIB) Core Facilities | Head of VIB Science & Technology Unit
Belgium

Rolf Apweiler
Director of European Molecular Biology Laboratory, European Bioinformatics Institute (EMBL-EBI)
United Kingdom

Ellen Berg
Chief Scientific Officer, Translational Biology at Eurofins Discovery
United States

Justin Bryans
Executive Director, Drug Discovery at LifeArc
United Kingdom

Rainer Pepperkok
Director of Scientific Core Facilities and Scientific Services, European Molecular Biology Laboratory (EMBL)
Germany

Janna Saarela
Professor of Medicine at University of Oslo | Director of the Centre for Molecular Medicine Norway (NCMM)
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Michael Sattler
Professor of Biomolecular NMR, Dept of Chemistry, Technical University of Munich | Head of Institute of Structural Biology, Helmholtz Center Munich
Germany

Hanno Steen
Associate Professor of Pathology at Harvard Medical School | Director of Proteomics at Boston Children's Hospital
United States

Clare Turnbull
Professor of Medical Genomics | Clinical Lead for Cancer Genomics, 100,000 Genomes Project | Honorary NHS Consultant in Clinical Cancer Genetics | Honorary Consultant in Public Health
United Kingdom

More information about the IEC members can be found on the SciLifeLab website.

Part I. Background and Instructions to the Evaluators

Introduction to the International Evaluation of the SciLifeLab Infrastructure 2020
Instructions to the International Evaluation Committee (IEC)
Background Information about SciLifeLab

Introduction to the International Evaluation of the SciLifeLab Infrastructure 2020

Objectives

The mission of the SciLifeLab infrastructure is to provide a broad spectrum of cutting-edge, unique and enabling molecular technologies to the life science research community across Sweden. The infrastructure is currently organized into seven platforms, of which each comprises a number of facilities offering specialized technologies, instrumentation and dedicated expert resources (Figure 1). The facilities are arranged into platforms mainly based on technological synergies. Most platforms are to be evaluated primarily based on their impact on enabling basic research, but we also have two translational medical platforms, the Diagnostics Development (DD) and the Drug Discovery and Development (DDD) platforms, providing an integrated national capability and a link to healthcare and industry. Moreover, as a central support function for the infrastructure, Data Centre (DC) provides services and resources for handing the data production at the platforms and facilities. We also wish feedback from the evaluators on the operations and future plans of Data Centre.

The overall scope of the SciLifeLab infrastructure is to give users access to a range of complementary life science technologies, including a multiplatform holistic view of life science.

A more detailed presentation of the SciLifeLab infrastructure is given in the *Background Information about SciLifeLab* section in this report.

To ensure that SciLifeLab provides an up-to-date infrastructure with cutting-edge technologies for Swedish researchers, international evaluations are performed every fourth year. The current international evaluation is the second of its kind (the first one was carried out in 2016).

Guided by recommendations from the international evaluation, SciLifeLab will decide on implementation of new facilities or technology areas, and in parallel, if necessary, phase-down of facilities or technologies that are regarded as not as current, broadly available through other means, or if they otherwise no longer fulfil the criteria to serve as national SciLifeLab facilities.

The international evaluation is followed by a national ranking of the infrastructure, including input from universities, the National SciLifeLab Committee (NSC) and the platforms. A final decision on organization and funding of the infrastructure for the years 2021–2024 (2 + 2 year funding) will be taken by the SciLifeLab Board in November 2020.

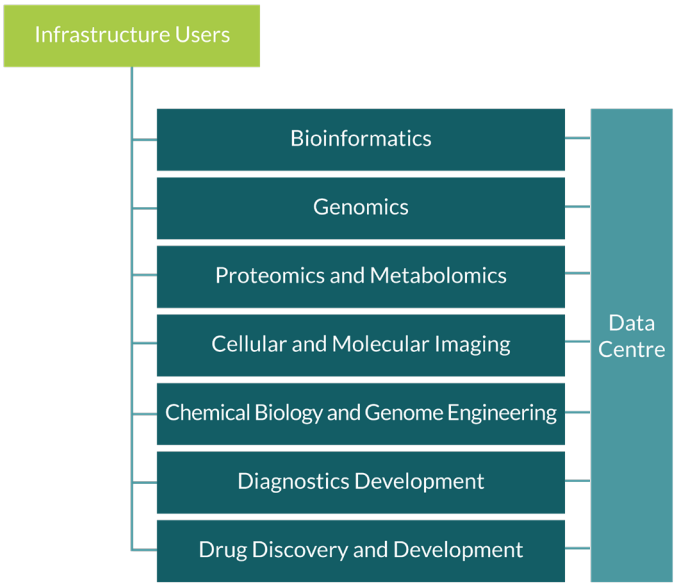


Figure 1. The organization of the SciLifeLab infrastructure platforms and Data Centre as of February 2020

Preparation of the SciLifeLab infrastructure plans 2021–2024

The platform and facility plans 2021–2024 (presented in Part II of this report) arise from an extensive and proactive strategic planning, carried out by dedicated Platform Planning Groups during 2019. The planning process engaged relevant national stakeholders and external international experts, aiming at assessing the existing state of the platforms. Through the planning process, platforms were also encouraged to suggest new facilities and/or perform changes in platform and facility organization. The aim was to arrange the platform and facilities in an improved way and to present the international evaluators with a logical new platform organization.

In addition to the internal platform planning process, SciLifeLab carried out two nation-wide surveys in May–June 2019 in an effort to engage the whole Swedish life science community in the future development of the infrastructure:

In the *Technology Needs Inventory*, we asked the community for proposals on new cutting-edge life science technologies, matching nation-wide scientific needs, currently not provided as a service by any facility in Sweden. In total, we received 73 proposals.

In the *Suggestions on New Facilities* survey, we asked the community for suggestions on existing facilities, currently not funded by SciLifeLab, for incorporation into the SciLifeLab infrastructure from 2021. The survey resulted in 32 suggestions on (unique) new facilities. In the assessment, it was emphasized that facilities to be selected should be

a) nationally unique and internationally competitive in the field of biomolecular life sciences,

b) have a potential to reach a large national user base, and

c) provide complementary and synergistic opportunities within and across SciLifeLab platforms.

As a result of the review process, 10 of the proposed facilities from the survey were approved for inclusion in the platform strategy plans for the international evaluation. The new candidate facilities are described in Part II of this report together with the current SciLifeLab facilities under the respective platform for which they have been incorporated in the 2021–2024 plans.

Instructions to the International Evaluation Committee (IEC)

The process and timelines for the International Evaluation Committee (IEC) are as follows:

Feb 24	*Infrastructure Report* and *Evaluation Portal* (*Anubis*) made available to evaluators
March 30	*Deadline* for submission of individual *pre-evaluation* via our Evaluation Portal (Anubis)
April 2	*Pre-evaluation Report* made available to evaluators and platforms
April 20–22	*Panel Meeting* in Stockholm
May 8	*Deadline* for the *IEC Report* to be submitted to SciLifeLab

Individual Pre-evaluation (deadline March 30)

As the first step in the international evaluation, each member of IEC is asked to perform an individual pre-evaluation for submission by March 30. A web-based Evaluation Portal (Anubis) is provided for the purpose:

https://anubis.scilifelab.se

In the evaluation we will refer to the term *unit*, which is defined as a SciLifeLab entity that is the subject to a separate evaluation. We ask the evaluators to assess the SciLifeLab infrastructure at both *platform* and *facility* unit level. Exceptions to this are the integrated capability platforms Diagnostics Development (DD) and Drug Discovery and Development (DDD) that will be evaluated only at platform unit level. In addition, we would also like the evaluators to assess the operations and plans for the *Data Centre* unit.

All *material for the evaluation* is given in Part II of this report, and consists of the platform and facility descriptions and plans, as well as the description and plan for Data Centre. The infrastructure steering document *Terms and Conditions for Funding*, and the *SciLifeLab Roadmap 2020–2030* are also available as background information (Appendices I and II, available through the Evaluation Portal, Anubis).

Platform and Facility Units

An overview of the units to be evaluated, in the order presented in the Platform and Facility plans section (Part II of this report) as well as in the Evaluation Portal (Anubis), is shown in Table 1. The table specifically highlights the *modifications of platforms and facilities* as a result of the internal planning process described above (orange), and the *new candidate facilities* included for evaluation (green).

Table 1. Overview of the SciLifeLab infrastructure units for evaluation. Suggested modifications of current SciLifeLab platform and facilities as result of the internal planning process are marked in red and new candidate facilities for evaluation are shown in green.

Platform	Unit	Order in Report and Evaluation Portal
Bioinformatics	**Bioinformatics Platform**	**1**
	Support, Infrastructure and Training [1]	2
	Compute and Storage	3
	BioImage Informatics [2]	4
	AIDA Data Hub *(candidate)*	5
Cellular and Molecular Imaging	**Cellular and Molecular Imaging Platform**	**6**
	Advanced Light Microscopy	7
	Biochemical Imaging Centre Umeå *(candidate)*	8
	Centre for Cellular Imaging *(candidate)*	9
	Intravital Microscopy Facility *(candidate)*	10
	Cryo-EM [3]	11
	Cell Profiling	12
	In Situ Sequencing [4]	13
	Advanced FISH Technologies *(candidate)*	14
	Gothenburg Imaging Mass Spectrometry *(candidate)*	15
	National Resource for Mass Spectrometry Imaging *(candidate)*	16
Chemical Biology and Genome Engineering	**Chemical Biology and Genome Engineering Platform**	**17**
	Chemical Biology Consortium Sweden	18
	Chemical Proteomics [5]	19
	High Throughput Genome Engineering	20
	Genome Engineering Zebrafish	21
Genomics	**Genomics Platform**	**22**
	National Genomics Infrastructure	23
	Ancient DNA	24
	Eukaryotic Single Cell Genomics	25
	Microbial Single Cell Genomics	26
Proteomics and Metabolomics	**Proteomics and Metabolomics Platform**	**27**
	Autoimmunity Profiling	28
	Plasma Profiling	29
	Proximity Proteomics [6]	30
	Mass Cytometry	31
	Proteogenomics [5]	32
	Glycoproteomics *(candidate)*	33
	Targeted and Structural Proteomics *(candidate)*	34
	Swedish Metabolomics Centre	35
	Exposomics *(candidate)*	36
Integrated Structural Biology	**Swedish NMR Centre [7]**	**37**
Diagnostics Development	**Diagnostics Development Platform**	**38**
Drug Discovery and Development	**Drug Discovery and Development Platform**	**39**
	Data Centre	**40**

[1] Facility a suggested merger of the three current facilities Long-term Support, Support and Infrastructure, and Systems Biology
[2] Previously at the Cellular and Imaging Platform
[3] Hubs and nodes facility. Hubs at SU and UmU; new candidate nodes at GU, KI, LU and UU.
[4] Currently part of the facility Eukaryotic Single Cell Genomics at the Genomics Platform
[5] Currently part of the facility Chemical Proteomics and Proteogenomics at the Proteomics and Metabolomics platform.
[6] Facility a suggested merger between the current SciLifeLab facility PLA and Single Cell Proteomics, and the UU core facillty Clinical Biomarkers
[7] Facility currently at the Cellular and Molecular Imaging platform. For the evaluation temporarily described within the virtual platform Integrated Structural Biology.

Evaluation criteria and grading of units

In the pre-evaluation, we ask the evaluators to:

1. *grade each platform and facility unit* on a scale from 1 to 9 in terms of estimated *importance for and impact on Swedish life science in* 2021–2024, and
2. provide a short *text with motivation* for the grade.

For each unit, please choose one of these four options:

- I have evaluated/graded the unit, and consider myself an expert in the technology field
- I have evaluated/graded the unit, however, I do not consider myself an expert in the technology field
- I have not evaluated/graded the unit since the technology field is far beyond my expertise
- I have not evaluated/graded the unit since I have a conflict of interest

In the comment field, give a short motivation for the grade for each unit, or why grading of the unit was not performed. It is here also possible to add general comments or address specific questions on issues that need further clarification.

The key criteria for evaluation of the SciLifeLab infrastructure technologies and operations were defined during the last international evaluation in 2016. According to these, SciLifeLab platforms and facilities should ideally:

- Facilitate world-leading research in molecular life sciences.
- Enable research that otherwise would not be possible in Sweden.
- Provide high-quality services to academic researchers, industry, healthcare and other organizations in Sweden.
- Be utilized by multiple research groups for high-quality research projects across the nation.
- Be associated with a high-quality research environment.
- Provide internationally competitive services.
- Have a long-term plan for instrumentation renewal, technology development, data management and sharing, scientific domains and user communities being served, as well as for a sustainable and versatile funding base.
- Have complementary and synergistic capabilities within and across SciLifeLab platforms.
- Participate in national coordination of similar platforms and facilities at other universities in Sweden.
- Promote translational implementation of research findings into healthcare and industry.

In addition to the criteria above, we would like the evaluators to also consider the following aspects in the evaluation:

- Quality of current technologies and services provided by the unit (national uniqueness and international competitiveness)
- Plans and impact of new technologies described for 2021–2024
- Past performance and user statistics (if applicable).
- Fit within the SciLifeLab infrastructure, and importance of the technologies and services as complement to other platforms and facilities.
- Overall impact on Swedish life science research
- Overall impact on healthcare, industry, and society in Sweden (if applicable)

The grading and motivations shown below (with grades 9, 5 and 1, as examples) should give the evaluators an idea on how we would like the grading scale to be used.

Grade 9: Nationally unique and internationally cutting-edge unit. Excellent fit within the SciLifeLab infrastructure. Broad, nation-wide, user base. Excellent future plans including new, high-impact technologies that will facilitate ground-breaking basic and/or translational research otherwise not possible in Sweden. High importance for and impact on Swedish life science 2021–2024.

Grade 5: Nationally unique and internationally competitive unit. Good fit within the SciLifeLab infrastructure. Broad user base, but some technologies are readily available as services elsewhere including commercial providers, or might be better provided as local core facility service. Future plans are satisfactory, but some key technologies in the field are missing and/or some technologies provided are deemed out-dated as national service. Medium importance for and impact on Swedish life science 2021–2024.

Grade 1: The unit provides technologies/services that are neither nationally unique nor internationally competitive. Poor synergy and fit with other SciLifeLab platforms and facilities. User base is limited, and the unit is suited to assist mainly local users. Low importance for and impact on Swedish life science 2021–2024.

When grading, it is important to consider the size, years of operations, and type of technologies and services provided by the unit in relation to user base, deliverables and overall impact. Evaluators may comment on suggested budget and funding level for individual platform and facility units, however, we would like to keep the overall financial considerations for the panel meeting in April and the joint IEC report.

Special instructions for specific units

Swedish NMR Centre / Integrated Structural Biology. Swedish NMR Centre (SNC) is currently a facility at the Cellular and Molecular Imaging platform. However, during the platform planning process, it became evident that synergies with the other facilities within that platform, with Cryo-EM as an exception, are somewhat limited. NMR is indisputably a key technique within structural biology research, but has also applications within chemical biology, drug discovery and metabolomics. It was thus mutually decided by the SciLifeLab MG and SNC to let the facility be presented in its own context, with the mission to map synergies with other SciLifeLab platform and facilities, and also synergies with other Swedish infrastructures such as MAX IV (synchrotron radiation facility) and ESS (European Spallation Source ERIC), both located in Lund. We wish the evaluators to assess the facility in this context, and we welcome suggestions on how to best utilize the facility within the SciLifeLab infrastructure scope in the future.

Diagnostics Development. The Diagnostics Development (DD) platform bridges academia and healthcare. The role of the DD platform is to facilitate the transition of high-throughput technologies from basic science to the clinical setting. The platform will also provide link to retrospective (biobanked) and prospective patient samples and clinical data. In 2019, the platform expanded with three new facility nodes (Umeå, Linköping and Örebro) to provide a national coverage with presence in all seven university healthcare regions in Sweden. DD has recently initiated the Genomic Medicine Sweden (GMS) program that coordinates the diagnostic implementation of genomics in healthcare; in this work the DD platform provides the technical backbone and functions as a test bed for new methods. We wish the evaluators to consider the platform in this translational space, where societal impact and successful transition of technologies into clinical applications and overall interaction with the healthcare is a key mission of the platform. We also wish the evaluators to consider that three of the nodes are in the process of establishing their operational capability, but that these nodes are critical to ensure equal access to technologies in the healthcare setting.

Drug Discovery and Development. The SciLifeLab Drug Discovery and Development (DDD) Platform was established within SciLifeLab through a strategic Swedish governmental initiative in 2013. The mission of DDD is to turn academic discoveries into innovations and provide technologies and training for state-of-the-art drug discovery and development in Sweden. During the first five years of operation, DDD has become a trustworthy, efficient and professional national arena for various stakeholders in drug discovery and drug development with a proven impact on the Swedish life science research community and society. In five years, DDD has helped progress two drug discovery programs to phase 1, three to international partnerships, and three to new Swedish biotechs. Currently, the 50 persons strong organization supports 17 drug discovery programs based on small molecules, antibody therapeutics, cell therapies and new modalities. DDD is not a screening center; it is recognized globally as one of few translational academic drug discovery centers with the potential to advance targets all the way from idea to start of clinical trials. Integration of DDD within the vibrant SciLifeLab environment offers new complementary technologies and expertise that are seldom available even at large pharma companies. In the coming five years, SciLifeLab and DDD propose to increasingly venture into collaborative academia-industry collaborations.

In addition to evaluating and grading the platform with regards to the importance for and impact on Swedish life science, we ask the reviewers to comment on how DDD should *balance* the following objectives in the future:

- Being a national translational drug discovery engine that supports academic scientists in Sweden with industry-standard infrastructure and expertise that allows programs to be globally competitive for further (clinical) development.
- Being a national arena that provides education, training, and expertise in drug discovery to academic scientists, small and medium sized enterprises (SMEs), and other actors in the Swedish life science echo system.
- Through additional funding, strengthen the interaction with the Swedish innovation system, funding organizations, and international consortia, industry, and technology providers.

Feedback on the Data Centre operations and plans

In addition to the platform and facility evaluation described above, we also ask the evaluators to give feedback and comments on the Data Centre (DC). This is a central support function in SciLifeLab, not a platform. It primarily serves the infrastructure platforms, management and operations office. At the site visit April 20-22, there will be a dedicated session with the Data Centre.

The Data Centre was launched in 2016 to address issues regarding IT- and data management services at the SciLifeLab infrastructure platforms. In its first three years of operation it has developed a catalogue of services and resources, provided support for IT and data management for platforms, management and the operations office, organized outreach events, established collaborations, and represented SciLifeLab in discussions with e-infrastructures and universities regarding IT and data. Following positive feedback from the international advisory board in 2019, DC has now been given an increased base funding and is considered a permanent part of the organization.

Please use the Evaluation Portal (Anubis) to grade the Data Centre in terms of *overall importance for SciLifeLab*. Use the comment field to motivate your grade, give general feedback and address questions that need further clarification.

Pre-evaluation Report, April 2

The individual pre-evaluations from each IEC member will be compiled into a report that will be distributed to the IEC and to the SciLifeLab platforms by April 2. The platforms will only receive the part of the report concerning their corresponding units, respectively.

Panel Meeting in Stockholm, April 20–22

At the panel meeting, all platforms and facilities will briefly present their technologies, operations and future plans, followed by Q/A sessions. There will also be time for the IEC to discuss the grading and feedback to platforms and facilities, and for preparing the joint International Evaluation Committee Report. A preliminary program for the Panel Meeting is given on the next page.

Preliminary program for the International Evaluation panel meeting

Monday April 20

09:00 **Welcome and Introduction**

Coffee Break

10:45 **Bioinformatics platform**
Support, Infrastructure and Training
Compute and Storage
BioImage Informatics
AIDA Data Hub

Short Break

11:55 **Genomics platform**
National Genomics Infrastructure
Ancient DNA
Eukaryotic Single Cell Genomics
Microbial Single Cell Genomics

12:55 **Lunch including panel work**

14:45 **Chemical Biology and Genome Engineering platform**
Chemical Biology Consortium Sweden
Chemical Proteomics
High Throughput Genome Engineering
Genom Engineering Zebrafish

Short Break

15:50 **Drug Discovery and Development platform**

17–18 **Panel Work**

19-21 **Dinner**

Tuesday April 21

09:00 **Diagnostics Development platform**

Short Break

10:05 **Cellular and Molecular Imaging platform**
Advanced Light Microscopy (4 units)
Cryo-EM
Targeted Spatial Omics (3 units)
Mass Spectrometry Imaging (2 units)

11:20 **Lunch including panel work**

13:00 **Proteomics and Metabolomics**
Affinity Based Proteomics (3 units)
Mass Cytometry
Mass Spectroscopy Based Proteomics (3 units)
Swedish Metabolomics Center
Exposomics

Short Break

14:15 **Integrated Structural Biology (virtual platform)**
Swedish NMR Centre

15–17 **Panel Work**

18:30 **Dinner**

Wednesday April 22

09:00 **Data Centre**

09:45 **Joint evaluation**

11.30 **Lunch including Report Writing**

14.00 **MG Feedback**

15.00 **End of meeting**

International Evaluation Committee Report (deadline May 8)

We would like the evaluation committee to compile and submit a final evaluation report, with joint gradings and motivations, by May 8, 2020. In addition, we would like the committee to indicate how the overall infrastructure budget should be prioritized on a platform level, i.e. give a suggestion on which platforms that should be prioritized for an expanded SciLifeLab budget, and which platforms that should be able to maintain operations with a similar or decreased SciLifeLab budget as compared to current funding. More detailed instructions on the format of the IEC report will be provided in due time.

The process after the International Evaluation

Based on the IEC report, the SciLifeLab Management Group will perform an internal review of the infrastructure during the spring and summer 2020. The process will involve input from university representatives and the National SciLifeLab Committee (NSC) as well as discussions with the Platforms. A proposal on organization and funding of the infrastructure for 2021–2024 will be presented to the SciLifeLab Board in September 2020, and the final decision on the infrastructure funding will be taken by the Board in November 2020.

The outcome will be communicated to the International Evaluation Committee as soon as the decision is published.

Background Information about SciLifeLab

Introduction to SciLifeLab

The Swedish government has assigned SciLifeLab as a national infrastructure and resource, and to serve as a center for large-scale molecular biosciences. The overall goal of SciLifeLab is to facilitate cutting-edge, multi-disciplinary life science research and collaboration that otherwise would not be possible in Sweden. SciLifeLab's objective is to serve both as a research infrastructure (the sole topic of this evaluation), but also to promote research collaborations across universities and disciplines as well as to be active in recruitment, training and translational research.

SciLifeLab was launched in 2010 as a research collaboration between the four host universities in Stockholm and Uppsala: KTH Royal Institute of Technology (KTH), Karolinska Institutet (KI), Stockholm University (SU) and Uppsala University (UU), and has since 2013 been designated and funded as a national research infrastructure for molecular biosciences in Sweden. The two main sites are located in Stockholm and Uppsala, but SciLifeLab national infrastructure facilities exist at all major Swedish universities, including Lund University (LU), Umeå University (UmU), Linköping University (LiU), University of Gothenburg (GU), Chalmers University of Technology (Chalmers), the Swedish University of Agricultural Sciences (SLU) and Örebro University (ÖRU), see Figure 2.

Life science is in the midst of a technological and digital revolution that impacts basic research, biotechnology, medicine and health, environmental science and many other fields. Major developments happen in all fields, such as whole genome sequencing, proteome profiling, gene editing, single cell biology, super-resolution imaging, systems biology, "big data" and artificial intelligence. Establishing and maintaining research infrastructure within the areas described above is increasingly costly, time-consuming and requires access to considerable expertise. It is thus not economically or practically feasible for all universities in Sweden to maintain local core facilities and capabilities within all of these fields. The mission of SciLifeLab is to facilitate cutting-edge, multi-disciplinary life science research and collaboration that otherwise would not be possible in Sweden. SciLifeLab also coordinates data-driven research communities in health and environmental science, promotes recruitment and training of young scientists, fosters collaboration with industry, healthcare, public research organizations and international partners, develops translational and innovation capabilities in life science and aims to provide a sustainable framework for national coordination of life science data as stated in the SciLifeLab 10-year strategy (Appendix II, SciLifeLab Roadmap 2020–2030). The SciLifeLab strategic objectives according the Roadmap are shown on the next page.

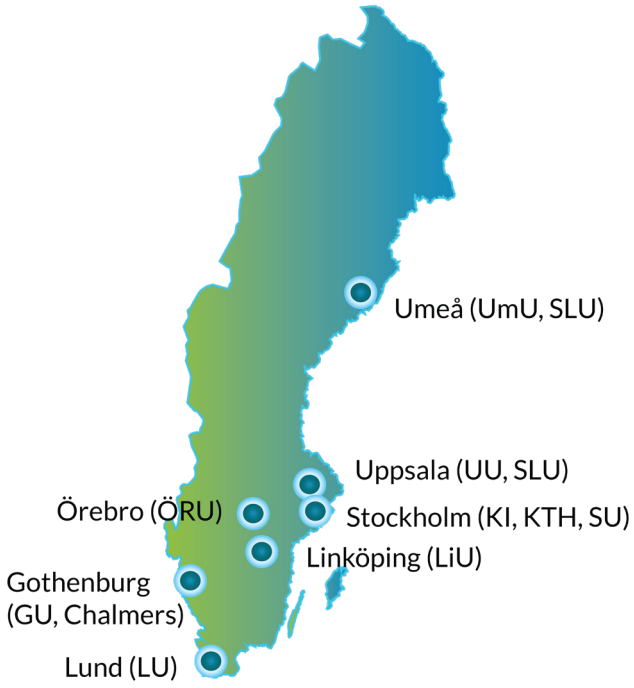


Figure 2. Distribution of SciLifeLab operations across Swedish universities

SciLifeLab's strategic objectives

- **Provide Unique and Impactful Life Science Infrastructure.** Promote continuous development and early application of cutting-edge technologies and services to deconvolute fundamental biology, address human health and biodiversity, and thereby enable research that otherwise would not be possible in Sweden.
- **Develop World Class Research Capabilities and Research Communities.** SciLifeLab will bring together national communities to enable new technology- and data-driven life science research. We will engage in multidisciplinary research programs on: i) data-driven cell biology, ii) data-driven research on individualized health, as well as iii) data-driven research on biodiversity and evolution.
- **Create A National Framework for Data-Driven Life Science.** Coordinate a national framework for life science data management, meeting the requirements of tomorrow's open, real-time data sharing and data cycles.
- **Attract Scientific Excellence and Provide Advanced Training.** Provide an attractive environment for recruitment of top international competence, and focus on advanced educational and training initiatives for a new generation of young scientists in technology- and data-driven life science.
- **Promote Collaborations Across Sectors and Borders.** Promote collaboration and knowledge exchange between different sectors of society and individual organizations, many of whom would not otherwise interact, with the intent of increasing interdisciplinary research, mobility and international visibility.
- **Build Translational and Innovation Capabilities.** Develop translational capabilities in diagnostics and drug development in collaboration with biobanks, healthcare and industry, promoting medical breakthroughs and enabling innovation in healthcare.

Leadership, Management and Operations of SciLifeLab

SciLifeLab is a collaboration effort between the four host universities, and is not a legal entity, and all SciLifeLab activities take place under one or more universities. The SciLifeLab Board carries the overall responsibility for national coordination and infrastructure funding, while each host university SciLifeLab Committee account for additional strategic research area (SFO) funding (Figure 3). The SciLifeLab International Advisory Board (IAB) advises the SciLifeLab Board on the overall development of SciLifeLab. The Management Group (MG) is the executive national leadership of SciLifeLab and prepares decisions for the SciLifeLab Board. In doing so, MG also has close links (including shared members) with the host university SciLifeLab Committees. To further strengthen the national role of SciLifeLab, the National SciLifeLab Committee (NSC) allows for a deeper engagement of non-host universities in the overall development of SciLifeLab. The role of the NSC is to advise the MG on matters relating to the national scope of SciLifeLab and is an important connection to non-host universities in Sweden.

SciLifeLab Operations Office (OO) supports MG, the infrastructure and research community in administration and execution of proposed actions. The SciLifeLab Data Centre (DC) works closely with MG, OO and infrastructure platforms with data management as a central support function.

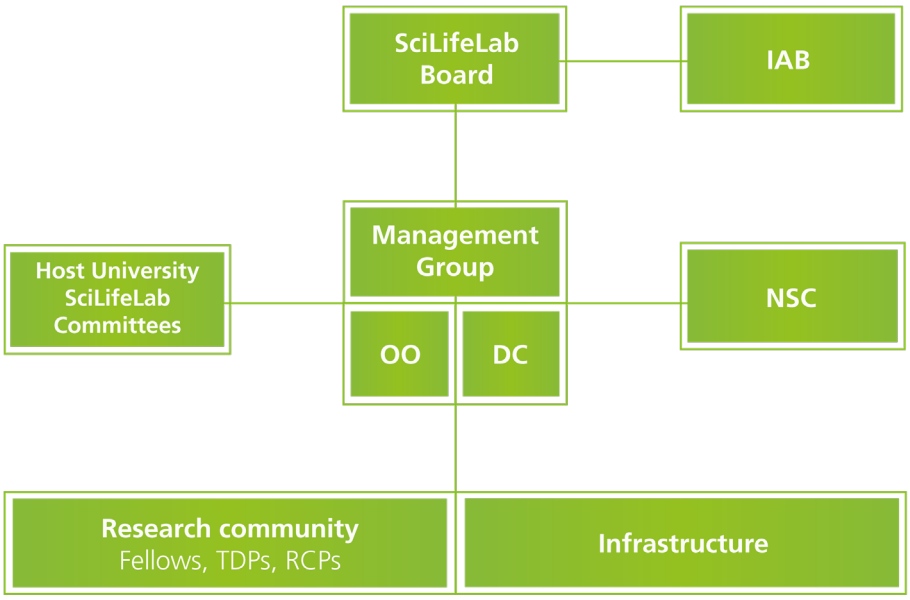


Figure 3. The SciLifeLab governance. Abbreviations: IAB, International Advisory Board; NSC, National SciLifeLab Committee; OO, Operations Office; DC, Data Centre; TDPs, Tecnology Development Projects; RCPs, Research Community Programs.

SciLifeLab Management Group (MG)

Olli Kallioniemi (KI)
Director

Siv Andersson (UU)
Co-Director

Annika Jenmalm Jensen (KI)
Infrastructure Director

Janne Lehtiö (KI)
Scientific Director

Peter Nilsson (KTH)
Scientific Director

Mats Nilsson (SU)
Scientific Director

Mia Phillipsson (UU)
Scientific Director

SciLifeLab Board

- Carl-Henrik Heldin, Government appointed Chair, Director of the Ludwig Institute in Uppsala, Professor in Molecular Cell Biology at Uppsala University and chair of the Board of the Nobel Foundation
- Lotta Ljungqvist, Government appointed Industry representative, President and CEO, GE Healthcare Nordic
- Mathias Uhlén, Professor, KTH Royal Institute of Technology
- Stellan Sandler, Vice-Chancellor, Uppsala University
- Anders Karlhede, Deputy Vice President, Stockholm University
- Anders Gustafsson, Acting Deputy Vice President, Karolinska Institutet
- Fredrik Elinder, Pro-Dean of Faculty of Medicine and Health, Linköping University
- Göran Landberg, Deputy Vice-Chancellor, Gothenburg University
- Katrine Riklund, Pro-Vice-Chancellor, Umeå University
- Gunilla Westergren-Thorsson, National SciLifeLab Committee Chair, Lund University, Co-opted member

International Advisory Board

- Jan Ellenberg, Chair (EMBL Heidelberg, Germany)
- Sören Brunak (Technical University of Denmark, Denmark)
- Jo Bury (VIB, Belgium)
- Yoshihide Hayashizaki (RIKEN Omics Science Center, Japan)
- Sirpa Jalkanen (University of Turku, Finland)
- Janet Jansson (Pacific Northwest National Laboratory, USA)
- Jonathan Knowles (FIMM, University of Helsinki, Finland)
- Svante Pääbo (Max Planck Institute for Evolutionary Anthropology, Germany)
- Aviv Regev (Broad Institute, MIT, USA)
- Sarah Teichmann (EMBL-EBI & Wellcome Sanger Institute, UK)

The SciLifeLab Infrastructure

SciLifeLab was granted funding as a national research infrastructure in 2013, with the mission to provide a cutting-edge, unique and enabling infrastructure covering a broad spectrum of molecular technologies to the life science research community across Sweden.

The infrastructure provides complementary technologies and services for assisting users in projects ranging from basic to translational research, and with the potential to support large-scale research initiatives and societal grand challenges.

The SciLifeLab infrastructure has a clear national mission, i.e. services should be offered to Swedish researchers on equal terms, regardless of academic affiliation. If demand exceeds capacity, a formal prioritization process with an external steering/advisory board is recommended. The infrastructure should also be accessible to research in sectors outside of academia, including industry and healthcare, under a full-cost fee structure.

Organization – Platforms and Facilities

The SciLifeLab infrastructure spans a broad range of service areas, and is currently organized into seven platforms. Each platform comprises a number of facilities offering specialized services, technologies, instrumentation and dedicated expert resources (Table 2 and Figure 4). Facilities are grouped into platforms based on technological synergies or, as for the Diagnostics Development and the Drug Discovery and Development platforms, providing an integrated national service capability. On the SciLifeLab web site, the infrastructure facilities are however not presented platform-wise, but based on service areas in an attempt to guide the users to relevant facilities across multiple platforms. [1] This also allows a facility to be categorized under more than one service area.

Please note that the current platform and facility structure differs slightly from the suggested infrastructure organization 2021–2024 under evaluation, shown previously in Table 1.

Governance and steering

Each platform is managed by a Platform Director (PD), who has a coordinating function to represent all facilities within the platform. The PD has currently little or no direct budget authority since SciLifeLab funding is distributed directly to the facilities. An exception is the Drug Discovery and Development platform, whose governance and organization are platform-centric. The individual facilities report directly to the SciLifeLab MG, and are managed by a Facility Director (FD) and a Head of Facility (HF). The FD is responsible for the scientific leadership and the strategic development of the facility, while the HF is responsible for the everyday operations at the facility, including project management and allocation of facility resources. The HF is usually also responsible for managing the facility staff. The platforms are encouraged to appoint a Platform Advisory Board to advise on long-term scientific development and strategic issues at the platform level. For a more detailed description of platform and facility governance, see the Terms and Conditions for Funding document (Appendix I). For the next budget period, 2021–2024, SciLifeLab plans to develop the infrastructure into a more platform-centric organization, where more mandate is given to the platform management in terms of strategic, organizational and financial decisions.

Platforms	Universities										
	Chal-mers	GU	KI	KTH	LiU	LU	SLU	SU	UmU	UU	ÖrU
Bioinformatics	●	●	●	●	●	●	●	●	●	●	
Cellular and Molecular Imaging		●	●	●				●	●	●	
Chemical Biology and Genome Engineering			●						●	●	
Diagnostics Development		●	●		●	●			●	●	●
Drug Discovery and Development			●	●		●		●		●	
Genomics			●	●				●	●	●	
Proteomics and Metabolomics	●		●	●	●		●		●	●	

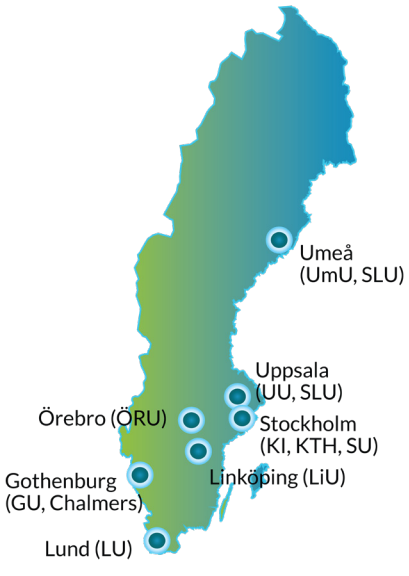


Figure 4. Distribution of infrastructure operations across Swedish universities.

[1] www.scilifelab.se/infrastructure/

Table 2. Current organization of the SciLifeLab Infrastructure (2020).

Platform	Facility
Bioinformatics	Compute and Storage
	Long-term Support
	Support and Infrastructure
	Systems Biology
Cellular and Molecular Imaging	Advanced Light Microscopy
	BioImage Informatics
	Cell Profiling
	Cryo-EM
	Protein Science Facility [1]
	Swedish NMR Centre
Chemical Biology and Genome Engineering	Chemical Biology Consortium Sweden
	Genome Engineering Zebrafish
	High Throughput Genome Engineering
Diagnostics Development	Clinical Genomics Gothenburg
	Clinical Genomics Linköping
	Clinical Genomics Lund
	Clinical Genomics Stockholm
	Clinical Genomics Umeå
	Clinical Genomics Uppsala
	Clinical Genomics Örebro
Drug Discovery and Development	Integrated services
Genomics	National Genomics Infrastructure
	Ancient DNA
	Eukaryotic Single Cell Genomics
	Microbial Single Cell Genomics
Proteomics and Metabolomics	Autoimmunity Profiling
	Chemical Proteomics and Proteogenomics
	PLA and Single Cell Proteomics
	Plasma Profiling
	Swedish Metabolomics Centre
	Mass Cytometry

[1] Under phase-out

SciLifeLab Data Centre (DC)

Research data is one of the most definitive and lasting products of SciLifeLab operations and is key to securing a high scientific impact of SciLifeLab facility services. With this in mind, the DC was established in 2016 as a central support function to the infrastructure. The primary goal of the DC is to maximize the scientific impact of SciLifeLab generated data, by providing expertise and services for facility needs on IT and research data management, and promoting Open Science, responsible data sharing, and facilitating that SciLifeLab data follows the FAIR data principles (Findable, Accessible, Interoperable, and Reusable).

SciLifeLab has a two-pronged approach to support for research data, where the Bioinformatics Platform supports and provide tools for end users in research projects, and the Data Centre supports and provides services and resources for the platforms that produce the data. The two units work in close coordination. Although the Data Centre is a central support function of SciLifeLab and not a platform, it is also the subject of evaluation. Its assignment and operation, recent developments and future plans are described in Part II of this report.

Funding

The current core funding of the SciLifeLab infrastructure, which the IEC should evaluate, consists of two governmental sources: national infrastructure funding (National) and Drug Discovery and Development funding (DDD). National and DDD funding are administered by the SciLifeLab Board. In addition, the host universities are receiving a so-called SFO funding (159 MSEK for 2019, funding from 2021 uncertain), mostly to do research within the SciLifeLab and to recruit young PIs to the SciLifeLab environment. SFO funding may also provide support for the technology development and for organizing research communities. SciLifeLab activities supported by SFO funds are however not the topic of the current IEC evaluation.

The total National and DDD funds 2019 from the government was 269 MSEK (about 25.5 MEUR) (Table 3), and how the funding was distributed, including administration and support is illustrated in Figure 5.

In addition, almost all facilities receive additional support from the host universities, from the national research council (VR), from the Knut and Alice Wallenberg Foundation (KAW) and other sources (see Figure 6). If all sources are counted together, the total annual infrastructure funding for 2019 was about 404 MSEK (about 38.5 MEUR).

The majority of National and DDD SciLifeLab funding is allocated to support the platform and facilities, including equipment and staff. The distribution of direct infrastructure funds for 2019 between the different platforms within SciLifeLab infrastructure is shown in Figure 7.

Table 3. Overview of governmental SciLifeLab infrastructure funding 2017–2019: National and DDD (Millions of SEK).

	2017	2018	2019
National	209	213	215
DDD	52	53	54
Total (MSEK)	**261**	**266**	**269**

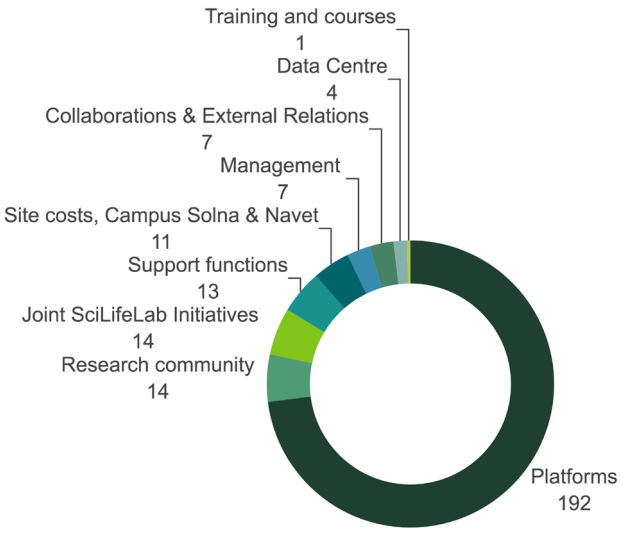


Figure 5. Distribution of SciLifeLab National and DDD funding 2019 (MSEK).

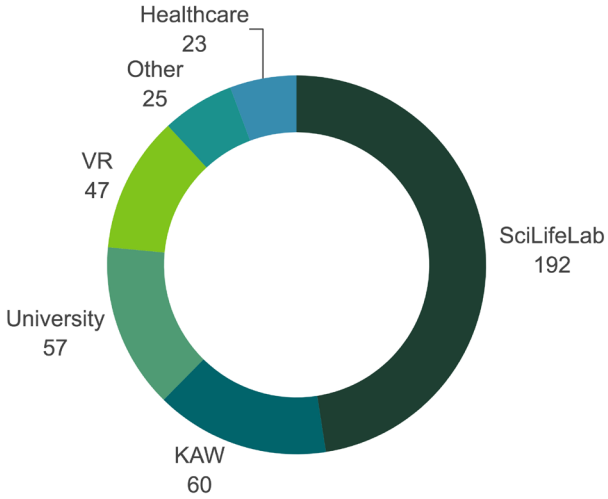


Figure 6. Total SciLifeLab and external funding of the infrastructure 2019 (MSEK). KAW: Knut and Alice Wallenberg Foundation, VR: Swedish Research Council.

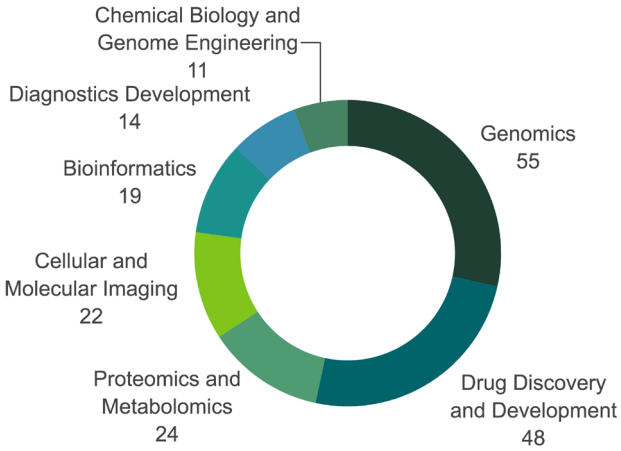


Figure 7. Distribution of SciLifeLab infrastructure funding to platforms 2019 (MSEK).

An additional important and major source of income for the facilities to cover operational expenses is the user fees, which in 2019 amounted to a total of 210 MSEK (19.5 MEUR). In general, user fees cover the facilities' costs for reagents and consumables, but may also cover part of salaries, rents, and instrument related costs. Since the type of services provided varies substantially between facilities, there is no standardized SciLifeLab user fee model. The individual user fee model for each facility is presented in more detail in the facility descriptions and plans (Part II in this report).

Annual reporting from the facilities provides important metrics, including funding sources, number of staff scientists, user statistics, and publication metrics. Comparing facilities with each other is informative, although it is not straightforward as they vary broadly in terms of the volume of their funding and resources, demonstrated in Figures 8 and 9. Ideally, we would like to see development over time so that facilities increase their sustainability by getting additional funding from universities and external sources, and that smaller facilities merge into larger units.

Currently, a total of 466 individuals (357 FTEs) work full- or part time at the infrastructure facilities, of which about 177 FTEs are financed by SciLifeLab funding. The gender distribution is well-balanced between males (54%) and females (46%). About 71% of personnel hold a PhD degree which demonstrates the high scientific level of the staff.

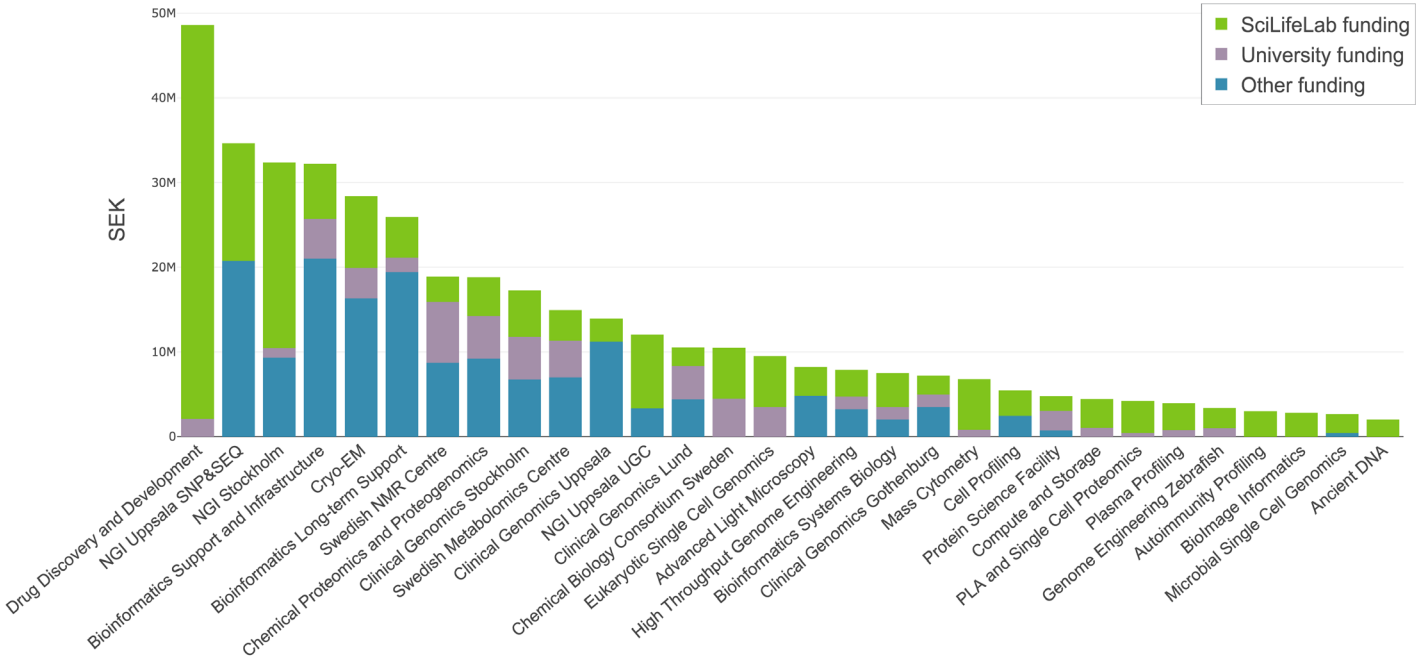


Figure 8. Distribution of total funding across SciLifeLab facilities in 2019. Funding for DDD is shown at the platform level.

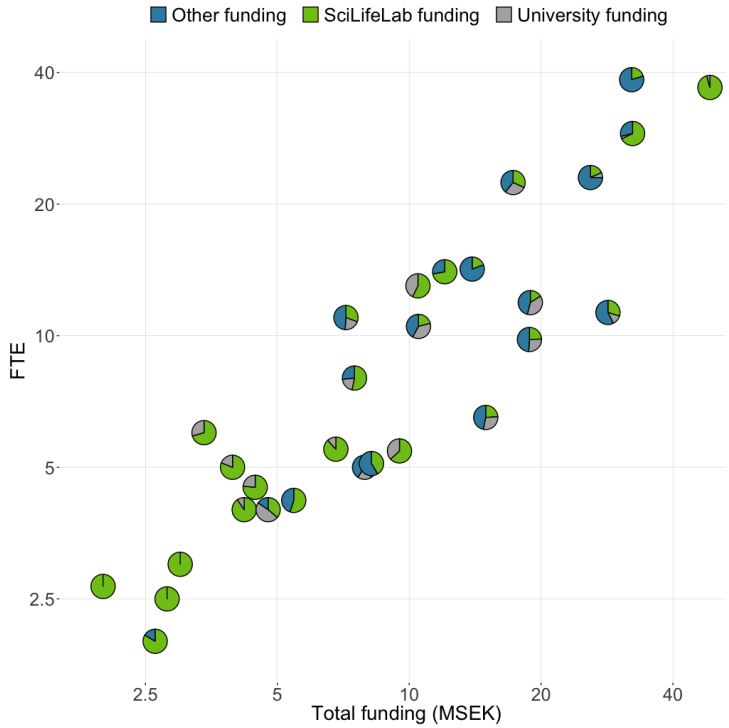


Figure 9. Total funding vs FTEs for the SciLifeLab facilities in 2019 with pies showing the distribution of total funding.

User base

The quantity and geographical distribution of infrastructure users are key parameters that SciLifeLab monitors for each facility as well as for the infrastructure as a whole. In 2019, there were nearly 1300 individual academic users of the SciLifeLab infrastructure, totaling over 3000 projects. The distribution of users based on the affiliation of the PI is shown in Figure 10. Notably, in 2019, 49% of users were from universities or institutions outside of the SciLifeLab host universities, and 6% of the users originated from international universities. In addition to the almost 1300 individual users included in Figure 10, the bioinformatics facility Compute and Storage in Uppsala reported about 1500 active user accounts spread across 900 project owners across Sweden that have utilized the data storage and computing capacities that the facility provides.

Distribution of user affiliation across facilities, illustrated in Figure 11, further demonstrates the infrastructure utility on a national level.

SciLifeLab infrastructure is also accessible for non-academic researchers, with an overall ambition that up to 15% of the infrastructure services should be devoted to non-academic users from healthcare, industry and other sectors. Based on the total infrastructure FTE resources during 2019, 10% were spent on healthcare, 2% on industry and 2% on other governmental organization projects.

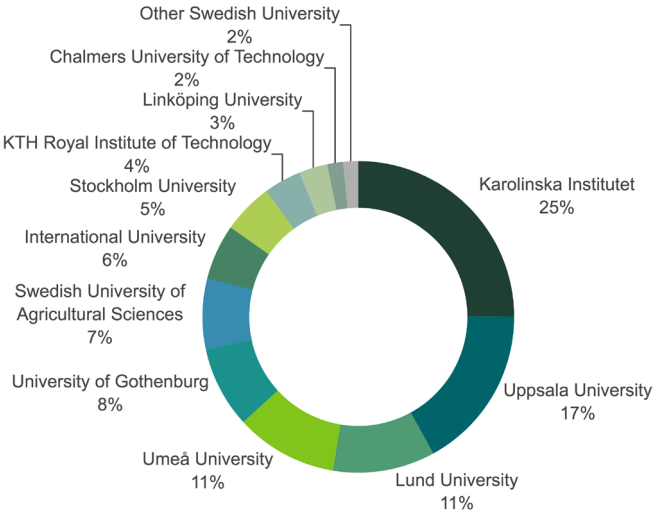


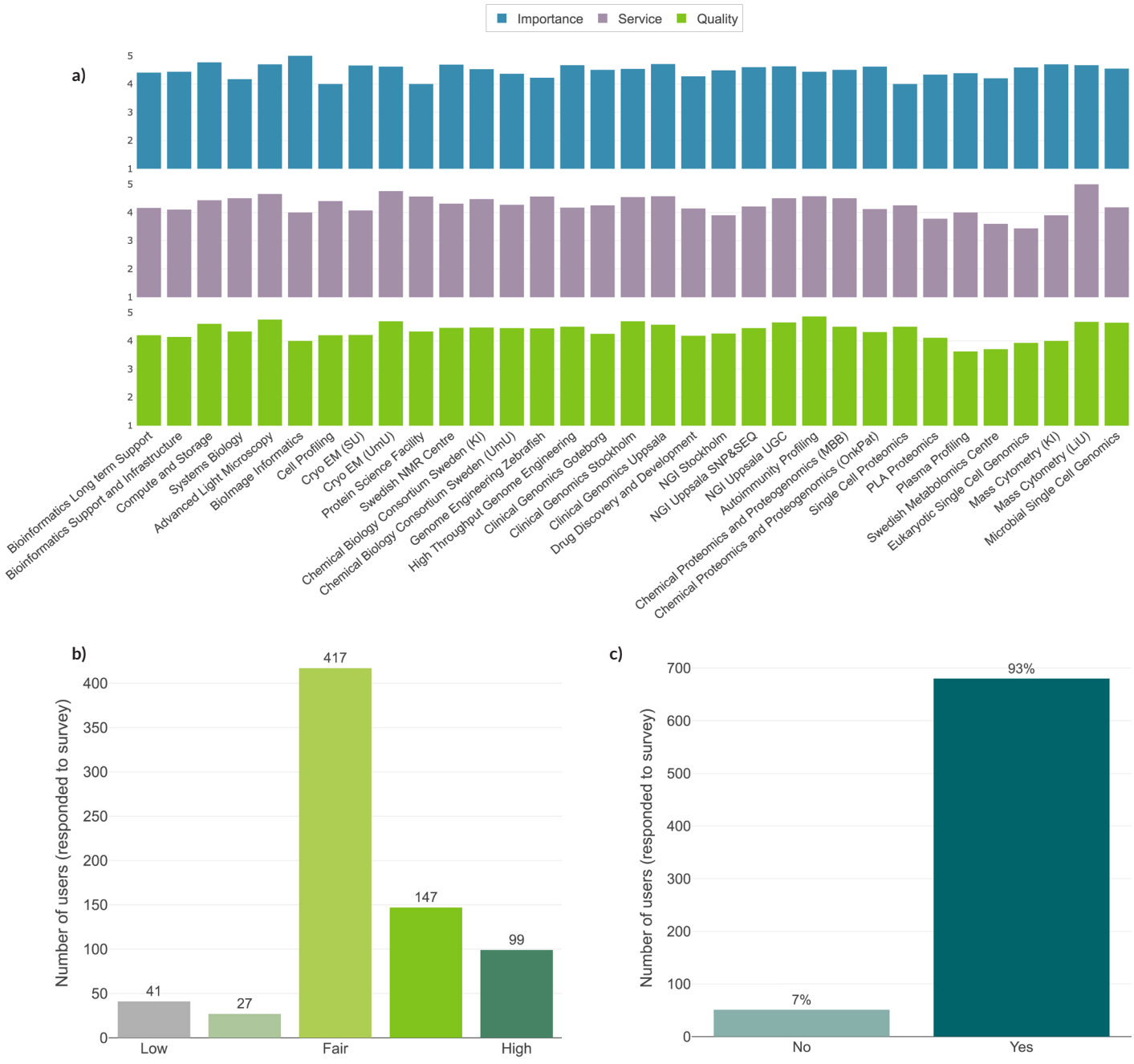
Figure 10. Academic user distribution 2019 based on individual PI affililiation. Total number of unique academic users was 1283.

Figure 11. Distribution of users 2019 from universities, healthcare and industry across all SciLifeLab facilities. The size of the circles corresponds to the number of users.

User satisfaction

In the fall of 2018, an infrastructure user satisfaction survey was conducted with 424 responses from users of SciLifeLab facilities between 2016–2018. The survey addressed overall user satisfaction and the impact facility-specific SciLifeLab services had on supported projects. Users were also asked if they would use the services again, and whether they perceived the level of user fees as appropriate.

The survey results indicated an overall high user satisfaction across all facilities with regards to importance for the scientific project, treatment and service towards the user, and quality of the work and data generated, (Figure 12a). Users considered the levels of use fees to be fair (Figure 12b), and 93% of the users declared that they would use the services again (Figure 12c). It is SciLifeLab's ambition to collect these types of statistics more systematically in the future, and provide annual, and eventually real-time, user-satisfaction data.



Figures 12 a–c. Results of the user survey conducted in 2018 including 424 users from 2016–2018 rating their use of SciLifeLab facility services. Multiple facility use resulted in 731 facility-specific responses, overall very satisfied with SciLifeLab services.

a) On a five level scale, 80% of responses express "high" or "highest" satisfaction, on a five-level scale, with the service level of SciLifeLab facilities. The quality of the service was regarded as "high" or "highest" in 88% of received responses, and the importance of the service to the user project was rated as "high" or "highest" in 89% of the cases.

b) 81% of users considered the level of user fees are fair or near fair.

c) 93% of users would use the services of the SciLifeLab facility again

Publications

The quantity and impact of scientific publications produced by both facility users or the facilities themselves are important metrics to evaluate infrastructure performance. The SciLifeLab Publication Database[1] was launched in 2017, allowing a convenient way for platforms and facilities to regularly upload publications containing data generated through the use of SciLifeLab infrastructure. In the database, publications are labelled as *service* (facility mentioned in acknowledgement), *collaborative* (facility staff in author's list) or *technology development* (facility staff as main author). From 2013 the number of publications from SciLifeLab infrastructure has more than doubled, to reach what is likely a steady-state of just over 600 publications annually (Figure 13), based on the current organizational capacity. Bibliometric analysis shows that publications whose results were generated through the use of SciLifeLab infrastructure have, in general, high scientific impact. On average, these publications are cited 40 percent more often than the world average for the same scientific field and publication year ($MNCS_{(2010-17)}$ = 1.40 ± 0,1). [2] Moreover, 16 percent of those publications belong to the top 10 percent most frequently cited publications in the same scientific field and in the same year ($PP(top10\%)_{(2010-17)}$ = 16 ± 1).[2]

An important objective of the SciLifeLab infrastructure is to promote and increase multidisciplinary research through the use of several platforms and/or facilities, utilizing multiple techniques within the SciLifeLab organization for their scientific questions. In this respect SciLifeLab is unique, even in global terms, in being able to provide complementary world-class capabilities covering a broad range of technology fields. SciLifeLab monitors cross-facility usage based on papers published by infrastructure users. For 2017, 2018 and 2019 the share of infrastructure publications resulting from cross-facility use were 10%, 13% and 13% respectively (Figure 14)

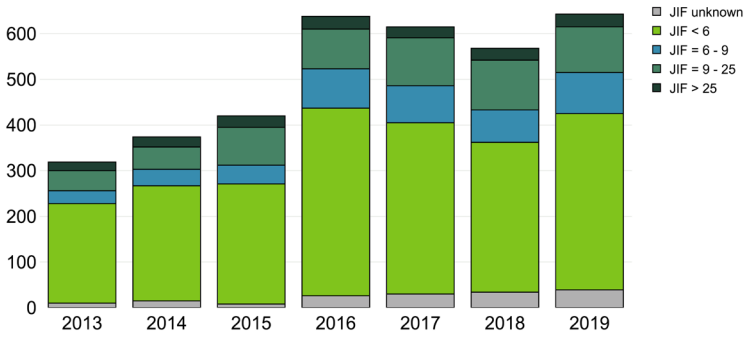


Figure 13. Infrastructure publications 2013–2019 with Journal Impact Factor (JIF) distribution.

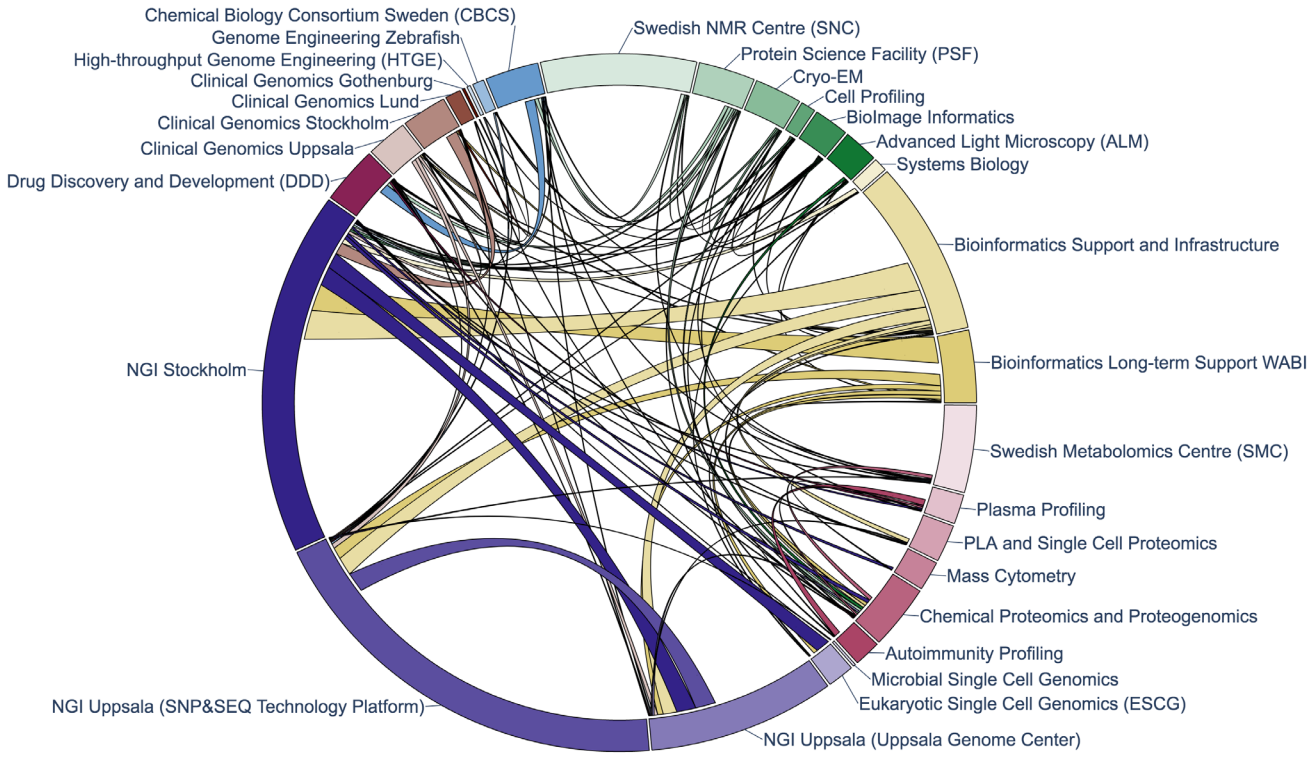


Figure 14. Circos plot illustrating cross-facility use based on infrastructure publications 2017–2019. Facilities are clustered platform-wise, and the length of the circle segments corresponds to the total number of publications for each respective facility. The ribbons represent publications where both the connected facilities contributed with service, data or analysis.

[1] https://publications.scilifelab.se
[2] The advanced bibliometric indicator mean normalized citation score (MNCS) between 2010 and 2017 showed an average value of 1,4 ± 0,1. Bibliometric analysis on publications derived from SciLifeLab facilities has been performed by CWTS at Leiden University.

Technology development

To maintain SciLifeLab infrastructure at the forefront, it is necessary to continuously update the technologies and services. This is challenging due to the wide spectrum of services, the complexity of operations across universities and the country, and the frequency of required upgrades to expensive instrumentation. To facilitate this evolution, SciLifeLab has developed four "cornerstones" for enabling infrastructure development and equipment upgrades.

1. Facilities are encouraged to use up to 20% of their National funding for internal technology development, identifying opportunities for new relevant technologies, upgrades and protocols, to complement existing capabilities.
2. As a new initiative in 2018, SciLifeLab launched a national call for Technology Development Projects (TDPs),[1] open to all researchers in Sweden. The purpose was to develop, or assimilate and optimize, novel, relevant and cutting-edge technologies for incorporation as services within existing SciLifeLab facilities. In total, 51 applications were submitted and 16 were approved for funding with up to 1.5 MSEK per year for 2019–2020. In the future SciLifeLab intends to arrange these calls biennially, and a second call is planned for in 2020.
3. A first internal call for funding of expensive instruments (in the range of 3 MSEK and above) for the infrastructure was arranged in 2018. The facilities submitted 20 applications in total, of which 11 where approved for funding. This call will be repeated annually, and will also include a platform-wide inventory of expensive instruments currently in place and needs for the future years.
4. Infrastructure technology development is also generated by the closely associated research community within SciLifeLab. Research in these groups are often conducted in collaboration with facilities and will in many cases give rise to new technology that can be implemented as service at the facilities and that provide an international edge to the services provided.

Training

In order for users and potential users to optimally utilize SciLifeLab resources, facilities actively engage in technology-focused education and training of researchers. Since 2017, SciLifeLab has increased its central support for infrastructure-related courses and training in an open call that resulted in a centrally administered course-packages covering bioinformatics, spatial proteomics, chemical proteomics, cryo-electron microscopy, drug discovery and development, and single cell genomics. During 2019, SciLifeLab coordinated, or contributed to a total of 103 national training activities at different educational levels ranging from undergraduate to post-graduate (Figure 15).

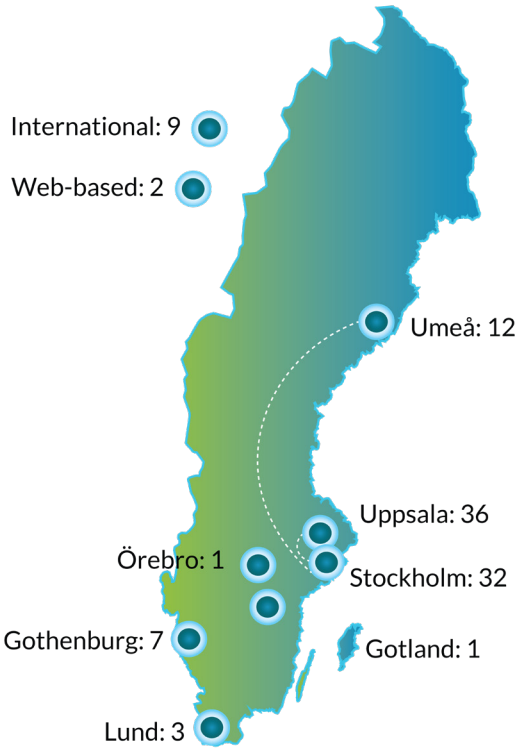


Figure 15. Number and geographical distribution of courses organized by SciLifeLab during 2019. Dotted lines show co-organized courses at different sites.

[1] https://www.scilifelab.se/call-for-tdps/

Evaluations and the SciLifeLab infrastructure life cycle

To ensure that SciLifeLab provides a dynamic and up-to-date infrastructure that meets user needs, the infrastructure is evaluated every four years by international experts (this evaluation), with an internal Midterm Checkup carried out by the SciLifeLab Management Group in between. The first Midterm Checkup was conducted in 2018, based on brief reports from the facilities about current status, future plans, and analyses of collected data on users and publications. The main purpose of the checkup is to follow-up the terms and conditions for funding, to provide feedback to the facilities on their performance, and to give recommendations for future operations. Minor adjustments in the facility budgets may also occur.

The SciLifeLab infrastructure life cycle enables upgrade and evolution of the infrastructure, incorporation of new technologies and services, as well as phasing-out or reorganizing technologies that have become obsolete or outdated as national facilities. Phased-out facilities and technologies may be returned to university-level core facilities if they fit local/regional purposes, or may be spun-out as commercial endeavors if appropriate. The components of the infrastructure life cycle, including technology development and research initiatives (TDPs, instrument calls and RCPs), are illustrated in Figure 16.

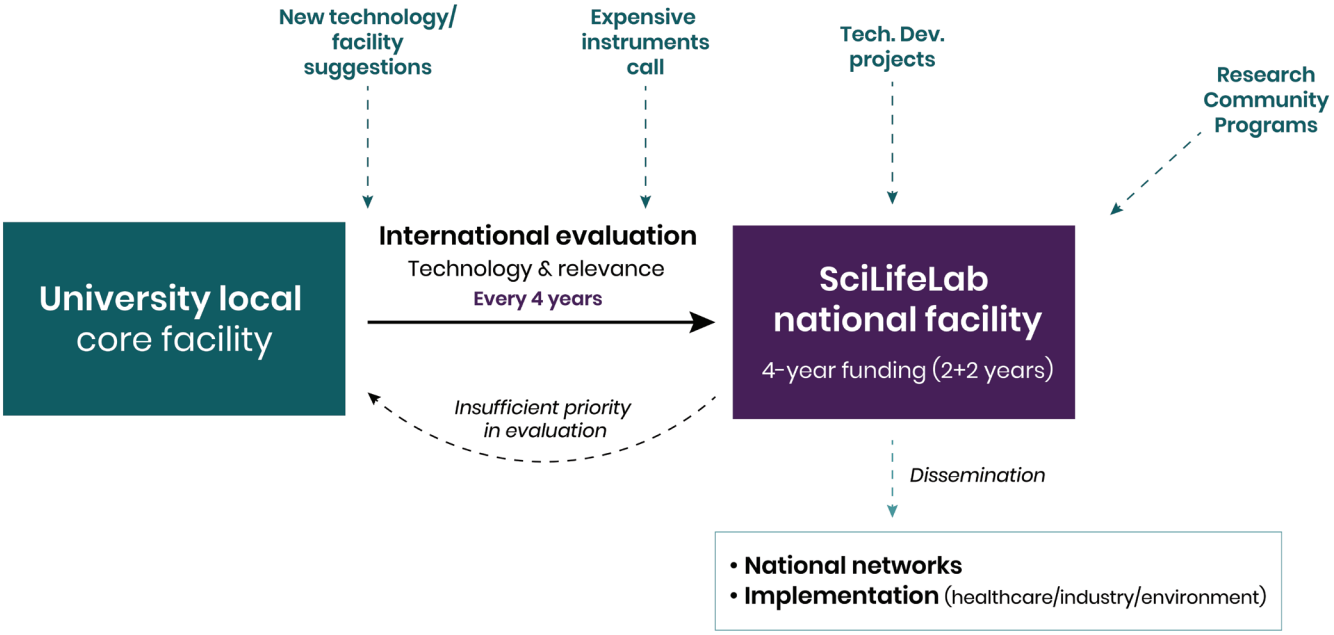


Figure 16. The SciLifeLab infrastructure life cycle.

Part II. Infrastructure Reports

Background Information
Basic information, Statistics and Metrics
Platform and Facility Plans
Data Centre Plans

Background Information

Instructions given to platforms and facilities on how to write up their reports

Below are the instructions given to the platforms and facilities on how to write up their descriptions and plans 2021–2024 for this report.

Platform plans

Background. For 2017–2020, briefly describe the development of the platform, an overview of current technologies/ services offered, and key achievements on platform level.

Plans for 2021–2024. Describe the platform development plans for 2021–2024, and specifically address the following items (if applicable and relevant):

- Overview of platform facilities including new facilities and key technologies/services planned for.
- Overall importance and impact of the platform to the Swedish life science research community and the society at large 2021–2024.
- A motivation on the importance of SciLifeLab funding of the platform as a national resource.
- Benchmarking of the platform in an international perspective.
- Future plans for governance and organisation of the platform.
- Overall platform plans to ensure that the most relevant technologies in the field are provided as services to users in Sweden.
- Synergies and capability contributions: i) within the platform, ii) with other SciLifeLab platforms and facilities/units.*
- Collaborations with healthcare, industry and other national and international external organizations.*
- Which alternative local/ national/ international facilities/ infrastructures and commercial providers are available to users? How is SciLifeLab funding justified for technologies/services available elsewhere from a Swedish user perspective?*
- How data-driven science as described in the SciLifeLab Roadmap 2021–2030 will be promoted by the platform.

*Might alternatively be described exclusively on facility/ unit level.

Budget 2021–2024. Comment on the suggested overall platform budget 2021–2024.

Facility Plans

Current Technologies and Services. List key technologies/ services in brief bullet format.

New Technologies and Services 2021–2024. List key technologies/services in brief bullet format.

Background. For 2017–2020, briefly describe the development of the facility/unit, and give an overview of current technologies/services offered. Also describe the governance of the facility/unit, competence/ background of staff, and key achievements during the period.

Plans for 2021–2024. Describe the facility/unit development plans for 2021–2024, and specifically address the following items (if applicable and relevant):

- New technologies/services planned for.
- Motivate how the technologies/services (current and new) provided are nationally unique and internationally competitive.
- Expected user base 2021–2024 in terms of national spread, number of potential users and sector (academia, healthcare, industry and other governmental agencies).
- How nation-wide user accessibility is achieved.
- How reproducibility, quality, and appropriate storage of data are ensured.
- User fee model that will be applied for 2021–2024.
- Research environment and associated research groups that are contributing to the development of the facility/unit.
- Synergies and capability contributions: i) within the platform, ii) with other SciLifeLab platforms and facilities/units.*
- Collaborations with healthcare, industry and other national and international external organizations.*
- Which alternative local/ national/ international facilities/ infrastructures and commercial providers are available to users? How is SciLifeLab funding of the facility/unit justified for technologies/services available elsewhere from a Swedish user perspective?*

*Might alternatively be described exclusively on platform level.

Budget 2021–2024. Motivate any expansion of current (2020) SciLifeLab funding.

Basic Information, Statistics and Metrics

In addition to the text and graphics material submitted by the platforms and facilities according to the instructions above, Operation Office and Data Centre have prepared background information, statistics and metrics that are presented as an introduction to each unit in the report. The content is described below.

Platforms

- Basic Information (Platform Director, Vice Platform Director and Platform Vision/Mission statement)
- Map of Sweden with geographical distribution of facilities and nodes, including Candidate Facilities.
- Table with current SciLifeLab funding (2020) and suggested annual SciLifeLab funding 2021–2024. The numbers are summed up from the facility budgets in the report, using the mean values for 2021–2024.
- Pie charts with the distribution of total current funding (2020) and distribution of total suggested annual funding 2021–2024 for the platform. The numbers are summed up from the facility budgets in the report, using the mean values for 2021–2024.

Facilities

- Basic Information (Facility Director, Head of Facility, Host University, FTEs)
- SciLifeLab funding and total funding for 2020.
- Links to the facility web page and facility publications in the SciLifeLab publication database
- Statistics on user publications 2017–2019 (by type of publications and journal impact factor, respectively).
- Total number of unique PIs and geographical user distribution 2017, 2018 and 2019.

Please note that we have included user statistics also for the new Candidate Facilities, based on user lists provided by these facilities for their current, mostly local, user base. We have also registered their user publications 2017–2019, so that these facilities can be compared with existing SciLifeLab national facilities. Finally, we have also generated statistics on the user publications for the new Candidate Facilities. However, when considering the statistics, please keep in mind that the data reflect operations without the status of a SciLifeLab national facility.

Bioinformatics platform

Basic information

Platform Director: Bengt Persson

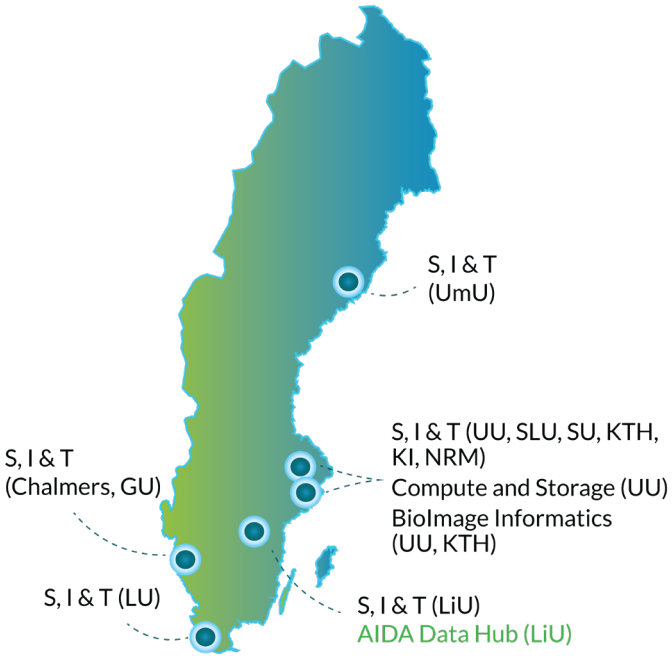
Vice Platform Director: Erik Lindahl

Platform Vision and Mission:

Enable world-class life science research and maximise scientific and societal impact of collected data by:

1. Providing expert knowledge, innovative data integration, advanced training, efficient data publication for open science, and access to high-performance data analysis methods
2. Coordinating bioinformatics support within Sweden and making bioinformatics easily accessible for life science researchers
3. Swiftly responding to changes in support needs as new techniques are developed and utilised
4. Forming the Swedish ELIXIR node and participating in relevant international projects

Geographical location of facilities



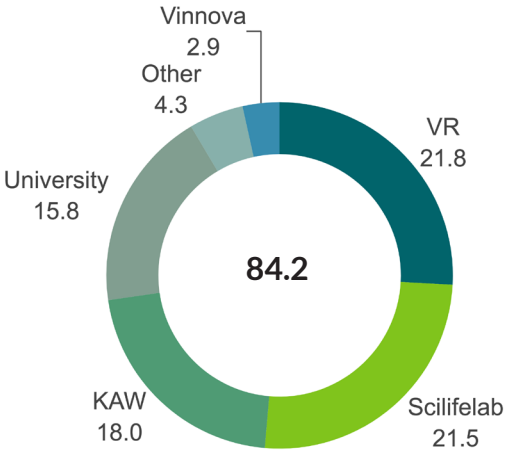
SciLifeLab funding 2020

Facility/unit	(MSEK)
Support, Infrastructure and Training (S, I & T)	15.3
Compute and Storage	3.4
BioImage Informatics	2.8
AIDA Data Hub (candidate)	0.0
Total SciLifeLab funding	**21.5**

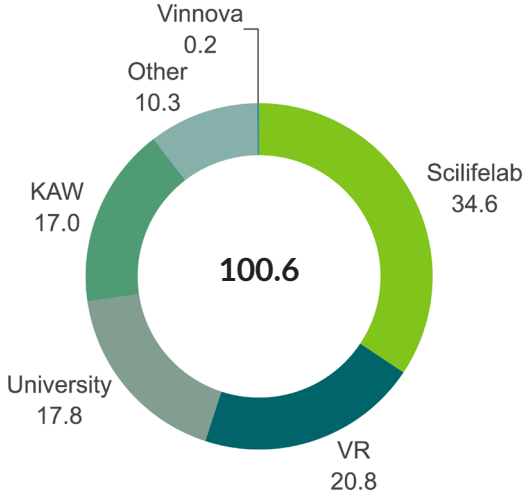
Suggested annual SciLifeLab funding 2021-2024

Facility/unit	(MSEK)
Support, Infrastructure and Training (S, I & T)	24.2
Compute and Storage	5.0
BioImage Informatics	3.4
AIDA Data Hub (candidate)	2.0
Total SciLifeLab funding	**34.6**

Total funding 2020 (MSEK)



Total suggested annual funding 2021-2024 (MSEK)



Background

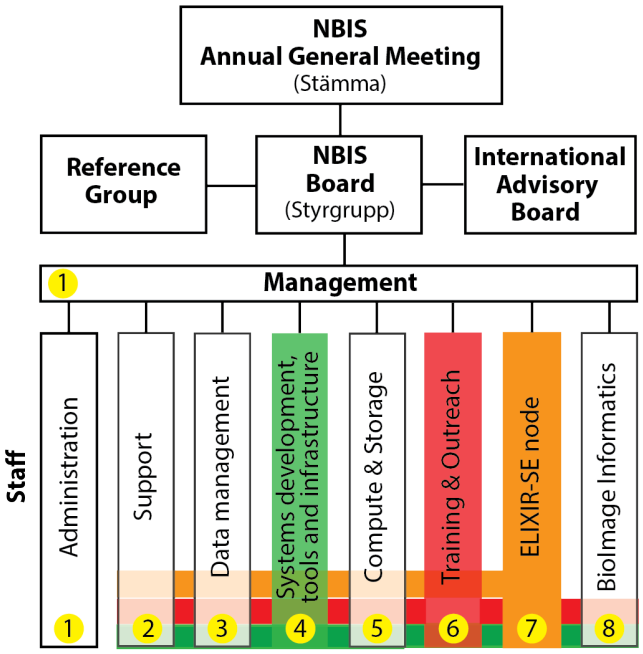
The SciLifeLab Bioinformatics platform NBIS (National Bioinformatics Infrastructure Sweden) with its extensive experience in large-scale data analysis is in a unique position to be a key driver for the SciLifeLab vision for data-driven life science. NBIS was established in 2016 after fusion of four infrastructures to form a *single point of contact* for all users needing bioinformatics support. NBIS thereby has all types of bioinformatics support within one organisation, facilitating user contacts and enabling efficient service provision. NBIS provides excellence in bioinformatics support to researchers in Sweden, *enabling world-class life science* by offering expertise, infrastructure and training. The topics covered by our experts include genome assembly, genome annotation, genetic variation, comparative genomics, phylogenomics, transcriptomics, proteomics, metabolomics, systems biology, single-cell biology, biostatistics, systems development, data management, image analysis and multi-omics integration. Furthermore, NBIS forms the Swedish node in ELIXIR (the European infrastructure for biological information). The organisational structure allows for changes in support needs over time as new techniques are developed and utilised.

NBIS is a *distributed infrastructure* with staff placed at all major universities in Sweden, creating access points to facilitate contacts with our users. Nevertheless, all projects are *nationally prioritised* and allocated to achieve best possible efficiency and competence matching. All NBIS staff are placed in excellent scientific environments in order to keep up-to-date with front-line achievements in bioinformatics and to create a critical mass at each site.

NBIS supports both research groups without bioinformatics resources and large established research groups with their own bioinformaticians needing specialised expertise. As life scientists are getting successively more educated in bioinformatics, the scope of NBIS is continuously shifting towards a focus on very advanced expertise. The advantages of an infrastructure like NBIS are: 1. *Guarantee for excellence* – NBIS can provide a multitude of expertise, which is difficult to match by a locally employed bioinformatician. 2. *Long-term stability* – NBIS is a sustainable resource, in contrast to PhD students or post-docs who need to move on when the time-limited position is ending. 3. *Effective use of resources* – The large scope of many projects puts an increased demand on the ability to analyse the data effectively, using considerable programming/scripting skills, needed to automate much of the analysis. This is outside of the competence of most biological/medical researchers. 4. *Critical mass* – It is hard to reach a critical mass of bioinformaticians in an individual research group and therefore not possible to get synergies from the collective learning. 5. *Expertise* – For research groups already having skilled bioinformaticians NBIS can, due to our breadth, provide complementary expertise.

Currently, NBIS provides support to 500+ PIs in Sweden, where our Compute & Storage module is supporting the largest number of users (cf. their report). Bioinformatics analysis support is provided to ~250 PIs annually, as detailed in the NBIS Support, Infrastructure & Training report. Over 50 PIs have received expert support in bioimage informatics, as detailed in their report.

The organisation of NBIS is shown below.



The activities are subdivided into modules as indicated by the numbers with yellow background. For the current SciLifeLab platform evaluation, we provide detailed descriptions in four sections:

- NBIS Support, Infrastructure and Training (modules 2, 3, 4 and 6)
- NBIS Compute & Storage (module 5)
- BioImage Informatics (currently a facility under the Cellular and Molecular Imaging Platform, but planned to be part of NBIS from 2021; module 8)
- AIDA Data Hub (new activity, which if evaluated positively will be part of NBIS from 2021; also module 8)

The general Bioinformatics Platform (NBIS) description (including modules 1 and 7) is provided here.

Platform plans for 2021–2024

Overview of platform activities

NBIS provides specialised competence having *experts* in multiple essential domains of large-scale analyses, but also has *generalists* able to integrate data from different omics areas. One of the strengths is our ability to assign *several experts from different domains* when required. NBIS keeps up-to-date with scientific developments, and for the period 2021–2024, we see new areas emerging, e.g. continued rapid development in single cell omics, advances in artificial intelligence (AI) techniques, and high-content imaging informatics. We see more projects

combining imaging with genomics, proteomics and other omics techniques, and it is therefore logical to formalise our collaborations with BioImage Informatics and AIDA Data Hub, which will establish important competence in the NBIS platform.

NBIS will 2021–2024 continue our activities that were favourably reviewed by the Swedish Research Council (VR) recently: "*The NBIS approach is the only way forward to enable statisticians and informaticians to use optimal methods for data access and data analysis. These aspects are well documented in the proposal. The opportunity to support emerging new fields of application is of great interest.*"

NBIS provides Sweden with the necessary means to allow for simultaneous exploitation of vast amounts of biological data coming from different research fields and derived at different scales, from the molecule to the organism, and even to the population. It also allows for integration of these data with information from other disciplines, such as chemical, medical and environmental data. A national bioinformatics infrastructure *enables advanced user support at a level that single research groups (or even single institutions) cannot reach.* We provide specialised expertise in a number of areas, and our staff can simultaneously participate in multiple projects. NBIS thereby enables our users to benefit from the data-driven life science. Furthermore, NBIS provides advanced training for PhD students, post-docs, and PIs.

Increased local interactions: In order to optimise coordination between the national infrastructure NBIS and local bioinformatics activities, e.g. core facilities, we will assign site coordinators to guide users to the right level of support, so that the future landscape of *Swedish bioinformatics support* is *optimally shaped* with respect to user satisfaction and resource usage. Bioinformatics is entering more and more research projects, and we expect local support facilities to be more involved in support needs. Already now, NBIS has regular drop-in sessions in Gothenburg together with the local core facility.

Increased interactions with other SciLifeLab platforms: NBIS is increasing the interactions with other SciLifeLab platforms as their users' needs for bioinformatics support become more pronounced. We already have *regular meetings* with NGI (National Genomics Infrastructure) and DD (Diagnostics Development). Starting 2020, we have *joint staff* with CBCS (Chemical Biology Consortium Sweden) in chemoinformatics, and *embedded NBIS staff* in other SciLifeLab platforms, as NBIS is piloting within proteomics facilities. Further details are provided below.

Overall importance and impact of the platform to the Swedish life science research community and the society at large 2021–2024

NBIS enables world-class life science research to *maximise scientific and societal impact* of publicly and privately funded research by providing expert knowledge, creative data integration, advanced training, efficient data publication and access to high-performance data analysis methods. NBIS coordinates bioinformatics support within Sweden and makes *bioinformatics easily accessible* for life science researchers.

Large-scale omics is making a major leap into translational research and diagnostics. NBIS, in close collaboration with data-producing infrastructures, e.g. DD, will provide expertise in systems development and access to ELIXIR-related databases and tools enabling improved and cost-efficient health care. We collaborate with Genomic Medicine Sweden (GMS), mainly on data and knowledge discoverability and sharing, in GA4GH Beacon and federated human genomic data technologies.

The European 1+ million genomes initiative. To fulfil this vision in the short time-span outlined, it is necessary to build on existing research infrastructures, like ELIXIR. Prime examples of technology to support this European effort are the Beacon and Federated EGA activities that NBIS is already engaged in.

A continuous technical scale-up will provide an unprecedented amount of heterogeneous omics data. Life science research is undergoing a major transformation by the rapid increase in the amounts and heterogeneity of omics data, opening opportunities to address an ever-growing palette of fundamental research questions in completely new ways. We see this as an increasing diversity in support requests from our users. NBIS gives Swedish researchers a great advantage and supports them to perform cutting edge research in many areas of life science. NBIS is also able to provide a national framework for high-performance data handling and efficient knowledge transfer.

The increased utilisation of machine learning algorithms (AI) in biomedical research. Bioinformatics has since long used machine learning for sequence pattern recognition and structure prediction. With recent advances in computational resources, these techniques have improved considerably and are summarised under terms such as Deep Learning and Artificial Intelligence (AI). NBIS will participate in national AI initiatives (e.g. "AI Innovation in Sweden") and benefit from the cross-disciplinary research on for example feature selection/extraction and pattern recognition, which are highly relevant for advancing NBIS capability on Big Data analysis. We will provide systems development support to users creating AI-based tools, and we will, together with our eInfrastructure partners, provide the computational requirements necessary for new AI-based tools. Further, NBIS has since long supported users in sharing data in a FAIR fashion, which is a prerequisite for data to be used in AI.

Importance of SciLifeLab funding to the platform

Bioinformatics is crucial in today's and future large-scale analyses of different omics data. As SciLifeLab's activities

in large-scale data generation grows, it is critical that the bioinformatics platform has sufficient capacity to provide user support in interpretation of large-scale data. This was commented upon in the SciLifeLab review 2016: "*It is a crime to generate data if these cannot be analysed*".

SciLifeLab funding guarantees sustainability and enables NBIS to help Swedish users in the data-driven life science, where bioinformatics is critical for the analysis of biological data. Sustainability of the infrastructure is also a prerequisite for scientific reproducibility. Furthermore, NBIS is actively promoting good data management practices, and is involved in the data life-cycle at several points and we have close connections with the data-generating platforms, facilitating seamless support from a user perspective, and with the international data repositories through ELIXIR.

Benchmarking of the platform in an international perspective

National bioinformatics infrastructures have proven to be both necessary and cost-effective to provide essential support for scientists. They have the ability to shift focus over time to meet the demands of the users. An independent evaluation estimated the return on EBI infrastructure investment to more than 20 times the direct operational cost. In Europe, Switzerland has pioneered this area since 20+ years with SIB, Swiss Institute of Bioinformatics, having ~800 staff, of which ~250 assigned for bioinformatics support. In Sweden, the predecessor of NBIS was piloted in 2008–2009, and established in 2010. NBIS is quite unique in its construction, as was commented upon in the evaluation by the Swedish Research Council (VR) in 2017: "*NBIS is probably the largest genuinely national and fully established bioinformatics infrastructure in Europe, although the Dutch have something approaching it. France and Germany have only established coordination structures very recently, and the UK has not attempted a national user service - effectively operating a network from a small central coordination office.*"

Future plans for governance and organisation of the platform

During the years, NBIS has successively developed an optimal organisational model (see Background). NBIS works as a unified platform, which facilitates the provision of optimal support to our users in a cost-effective way. The governance follows the rules for national infrastructures, with the *NBIS Annual General Meeting* as the highest decision body, where university representatives are taking decisions on co-funding, strategy plan, and appointment of Board and Reference group. The *NBIS Board* is the leading organ taking decisions on annual work plan, activities and budget. The NBIS Board consists of national and international experts, that are nominated by NBIS parties, elected at the NBIS Annual General Meeting, and appointed by Uppsala University as host for NBIS. There is also an International Advisory Board to provide strategic advice. For the coordination and leading the daily management of the infrastructure, an *NBIS director*, that also acts as ELIXIR-SE head of node, is appointed by the Board. The activities of NBIS are divided into *functional units* (*modules*), as depicted in the organisational scheme. The managers together with the director form the *management team* that meet monthly using video conference system to coordinate activities and discuss operational matters.

Plans to ensure that the most relevant technologies in the field are provided as services to users in Sweden

NBIS follows the fast development in bioinformatics, and our staff has up to 20% of their time available for acquiring and familiarising with new techniques. Placement in excellent scientific environments enables keeping up-to-date with state-of-the-art methods. Sharing and transfer of acquired knowledge, skills and abilities within NBIS is encouraged and takes place by internal training activities, journal clubs and seminars. As NBIS is a distributed infrastructure, we stimulate interactions among staff to maximise the benefits of the collective expertise (meetings, video conferences and retreats).

NBIS main activity is to provide user support, and we listen carefully to our users' needs, as provided in support requests and communicated at our frequent drop-in sessions. When we see emerging types of requirements, we assign staff to learn these new techniques. Our board has an important strategic role in identifying future areas of interest. In addition, we have regular open calls where the entire Swedish scientific community can propose new services, and a reference group with representatives from all NBIS universities facilitates influx of ideas from the universities.

Synergies and capability contributions

Within the NBIS platform, we have clear synergies by having multiple types of support, systems development, data management, compute, storage, and training in the same infrastructure. In addition, we foresee important synergies from including BioImage Informatics and AIDA Data Hub, since increasingly more projects are combining genomics, proteomics and other omics techniques with different types of imaging. Large-scale storage of images, of which many contain sensitive data, will benefit from the NBIS infrastructure, as exemplified with the current EU application BigPicture that NBIS has together with AIDA Data Hub. Furthermore, since image analysis to a large extent utilises AI-based methodology, the systems development team will be able to help professionalise and speed up these calculations.

With other SciLifeLab platforms, we already now have close collaborations and regular meetings with Genomics, especially regarding script developments (pipelines/workflows; one NBIS expert currently embedded at the sequencing facility NGI), new instrumentation and new data types, and training and outreach, including the high-level BiG Talks seminar

series. The regular update meetings about new techniques enable NBIS staff to explore new types of data at an early stage. Resulting feedback from NBIS staff on how new data types can be analysed is also useful for the data-generating facilities when prioritising technologies. In addition, we have, as described above regular meetings with DD (Diagnostics Development), and staff interacting with CBCS (Chemical Biology Consortium Sweden) and proteomics.

Since bioinformatics is a crucial part of all modern life science, each SciLifeLab platform needs to organise their production-related bioinformatics for initial data processing prior to data delivery to the users. With NBIS's extensive experience in bioinformatics and systems development, we are of course happy to help the platforms in this undertaking at internal cross-platform self-cost reimbursements.

We have since long a close collaboration with *SciLifeLab Data Centre*, working together on data management issues, where NBIS provides support to SciLifeLab users and Data Centre to other SciLifeLab platforms.

The Compute & Storage module enables close collaboration with providers of high-performance and cloud computing infrastructure (e.g. SNIC), assuring availability of the nationally funded digital working environment that is well suited to SciLifeLab users and platforms.

Collaborations with healthcare, industry and other national and international external organisations

ELIXIR is the European infrastructure for biological information with currently 22 countries and more to join next years. Sweden is one of the founding members, and NBIS constitutes the Swedish node. Sweden is very active, e.g. with Human Protein Atlas (HPA), now an ELIXIR Core Data Resource, reflecting its fundamental importance to the life-science community and long-term data preservation; ELIXIR-EXCELERATE 2015–2019, with NBIS efforts in data management, sensitive data (Federated EGA), genome annotation, single cell transcriptomics, data interoperability, and advanced training; ELIXIR-CONVERGE 2020–2022, where we will lead European efforts in data management; and the B1MG application for 2020–2022 to provide coordination support for the European 1+ Million Genomes Initiative.

In the *European 1+ Million Genomes initiative*, 20+ countries will provide a cross-border federated network of national genome collections associated with relevant data for advancing data-driven health. NBIS is active in building and establishing components of the technical framework, e.g. the Federated EGA for secure storage of sensitive genome data, and the GA4GH Beacon for discoverability.

NBIS services are available to private companies and healthcare "production", on a full cost-recovery basis, and we see a growing interest. We present NBIS at SME events, e.g. "Genomics and Associated Data in National Healthcare Initiatives" in March 2019. NBIS has close contacts with the recently established External Relations Office at SciLifeLab for increased industrial and healthcare utilisation.

Alternative facilities/infrastructures and commercial providers?

As described above, NBIS interacts with local core facilities to establish an optimal support landscape for our users. Regarding commercial providers, there are still only a few examples, even if this might change in the future. However, for modern life science research, bioinformatics is a central subject, and such a core activity should not be outsourced. It is cheaper and more efficient to provide bioinformatics support in close collaborations within the university sector. Furthermore, this enables knowledge transfer to the research groups, which is an important mission for NBIS.

SciLifeLab is unique in providing multiple large-scale techniques in one single organisation, facilitating access to advanced sciences for the users, enabling top-notch research. The extended NBIS expertise in multiple fields is hard to find in the private sector. Furthermore, discussions and collaborations are more easily enabled within academic organisations than with companies. Companies might be efficient in providing routine analyses, but in bioinformatics such routine work is done automatically by computer programs, which NBIS already utilises and also develops. Finally, in data-driven science, access to NBIS expertise will be central, as detailed below.

How data-driven science as described in the SciLifeLab Roadmap 2021–2030 will be promoted by the platform

NBIS activities are by nature data-driven and we warmly welcome the SciLifeLab route into data-driven science. NBIS has the capabilities, tools and structures to provide support to SciLifeLab users in data-driven science, and to meet the increased demand, we will expand our activities during 2021–2024, especially in areas of data management, provision of sensitive data, multi-omics analysis, development and applications of AI-based tools, in order to enable the data-driven science to become reality. NBIS is well prepared for this upcoming shift in science, as was described in the recent evaluation by the Swedish Research Council: "*The infrastructure will greatly enhance the quality of analyses and data management and therefore of the scientific conclusions based upon the avalanche of data available*".

Budget

NBIS has funding from multiple sources – SciLifeLab, Swedish Research Council, Knut and Alice Wallenberg Foundation, universities, user fees, and international funding (e.g. EU, ELIXIR and NordForsk) – providing long-term sustainability. However, in order to provide adequate user support also in the future with increasing number of users, expansion of the NBIS budget is necessary to be on par with the SciLifeLab data generation. The motivations for these expansions are given in the four detailed reports from our respective modules.

Support, Infrastructure and Training

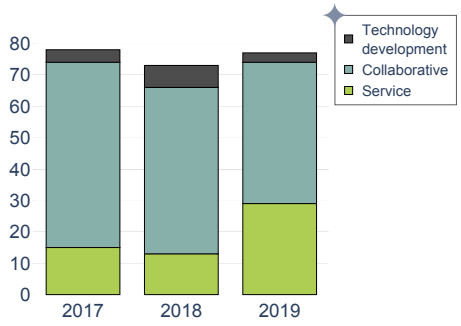
Read more: Web page, Publication Data Base

Basic Information

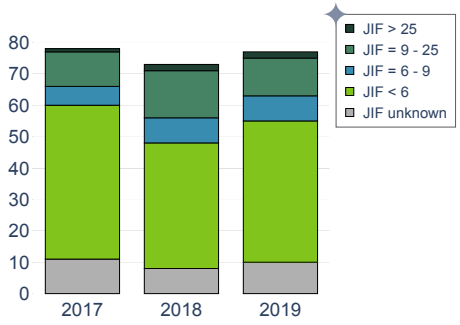
Facility director: Bengt Persson, Gunnar von Heijne
Head of facility: Pär Engström, Jonas Hagberg, Henrik Lantz, Jessica Lindvall, Björn Nystedt, Thomas Svensson
SciLifeLab facility since: 2013
Host University: Chalmers, GU, LiU, LU, KI, KTH, NRM, SLU, SU, UmU, UU
FTEs: 75
FTEs financed by SciLifeLab: 15.4

Funding 2020 (in kSEK)

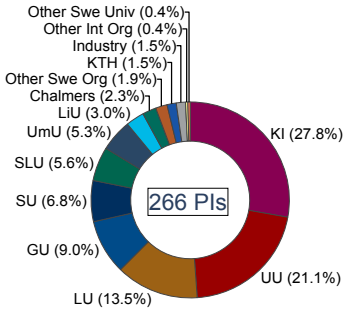
SciLifeLab: 15300
Total: 71110



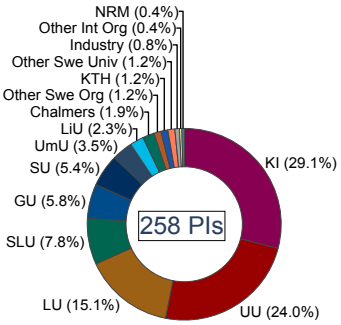
Publications by category



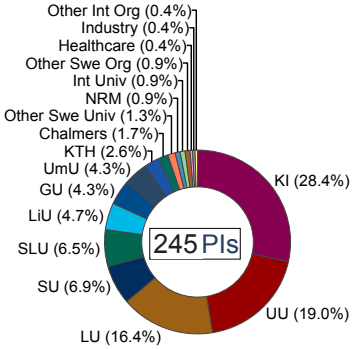
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

- Bioinformatics support in multiple areas, including genome assembly, genome annotation, genetic variation, comparative genomics, phylogenomics, transcriptomics, proteomics, metabolomics, systems biology, single-cell biology, biostatistics, and multi-omics integration
- Bioinformatics infrastructure (tools, data management, systems development)
- Bioinformatics training and outreach
- Our main asset is our experts, currently
  – 48 support experts with a total of 517 years of post-doctoral experience (average 10.8 yrs)
  – 12 skilled systems developers with a total of 132 years of experience (average 11 yrs)

New Technologies and Services 2021–2024

- Bioinformatics support in current areas as listed above with expansions within single cell transcriptomics, comparative genomics, multi-omics, biodiversity, and ancient DNA analyses.
- Bioinformatics infrastructure with expansions in provision of human data in the federated European landscape (EGA-SE and 1+ million genome project); increased data management, data publication and data stewardship; and systems development to support emerging AI techniques.
- We expect an increase in systems development support projects, in particular for web-interfaces to specific databases/tools, development of databases and development of analytical pipelines.
- Bioinformatics training and outreach, increasingly utilising remote techniques and tools and material developed within ELIXIR and GOBLET, including engagement in the SciLifeLab Advanced Training Centre and future research schools in bioinformatics and AI.
- In order to support new areas and increased number of users, we increase our staff with 11 FTEs already in 2020, additional recruitments will follow during 2021–2024, mainly in the areas of single-cell and multi-omics support, computational biology (or data driven research), image informatics, data management, and systems development.

Background

NBIS has provided support, infrastructure and training to the Swedish life science community since 2008 (pilot phase of the predecessor BILS). During 2019, NBIS worked on 171 *support* projects and provided ~100 *consultations*. In addition, we had ~250 drop-in sessions. A total of 245 PIs have utilised NBIS during 2019. On the systems development side, we have been working on several long-term projects spanning over multiple years: infrastructure for data access (Federated EGA, SweFreq, GA4GH Beacon,

Implementation of ELIXIR AAI solutions), infrastructure for training (NBIS course GitHub and virtual teaching backup cluster), and infrastructure for support. NBIS Training had over 600 *participants* in our advanced courses 2019, tailored to graduate students and post-docs.

The *utilisation* of bioinformatics infrastructure as measured by number of projects, support hours, and PIs has *increased considerably every year*, reflecting the growing demand for bioinformatics analyses. This at the same time as increasingly more research groups are recruiting and training their own bioinformatics expertise. We meet this growing demand by actions along the three lines: *a*) *increased consultancy* to help users plan their studies, *b*) *increased advanced training* activities to educate users (mainly PhD students and post-docs), and *c*) *provision of user-friendly infrastructure* (tools and databases) enabling researchers to perform more bioinformatics analyses on their own.

Plans for 2021–2024

Bioinformatics support (module 2)

Support constitutes about half of NBIS activities, and our users are from all Swedish major universities. NBIS provides bioinformatics support in the form of different services, ranging in commitment from short meetings to extensive collaborations. On the lighter end of the spectrum, we arrange *bioinformatics drop-in sessions* at all sites in Sweden, providing guidance on experimental design, choice of analysis methods, software etc. We will arrange ~250 *drop-in sessions annually*, which are much appreciated by the community. We also offer *bioinformatics consultations* for free to discuss the projects, enabling early planning of good experimental design, and which often result in a support project later.

We will continue the major activity of *bioinformatics hands-on support service*, where NBIS staff work actively in the projects for shorter or longer time, allowing research groups access to cutting-edge expertise that would otherwise be difficult to obtain. We provide three hands-on support tracks (Short- and Medium-term Support, Partner Projects, and Long-term Support), as described in the section "User fees".

Bioinformatics infrastructure (modules 3 and 4)

Data management. Proper management of research data is becoming increasingly important. NBIS shall act to guide and facilitate for Swedish life science research to make the generated data FAIR (*Findable*, *Accessible*, *Interoperable and Reusable*) to maximise impact of public investment. NBIS provides infrastructure to the Swedish life science community for data management, publishing data, and submitting data to appropriate international repositories, many within ELIXIR. NBIS, together with the SciLifeLab Data Centre, will therefore continue to support researchers to make *Data Management Plans* (DMPs). In this work, we coordinate our efforts with the Data Offices at the respective universities. To cater for the needs of publishing human genome data, NBIS is establishing the *local Swedish node* (EGA-SE) within ELIXIR to meet the large need for this service in Sweden, enabling participation in the European 1+ million genome project.

Systems development, tools and infrastructure. NBIS will continue creating *user interfaces* and providing support in *deploying tools* to be used by the entire life science community. NBIS provides assistance in programming best practices (documentation, source code management, bug tracking), and deployment. *NBIS hosts Swedish bioinformatics tools* that have entered production state and been identified as important for the global research community. We provide software packaging and distribution, hosting, and basic bug fixing. Examples are MrBayes, widely used world-wide with 53 213 citations and more than 7800 downloads in a half-year, and TOPCONS, which has completed about 12 million queries from 17000 unique users distributed in 93 countries since Feb 2015.

NBIS will continue to develop components in the HPA (Human Protein Atlas) which now is an ELIXIR core data resource. We will also make the Metabolic Atlas (genome-scale metabolic models) integrated with other ELIXIR resources and hopefully also an ELIXIR core data resource in the future. Already in 2019, curated metabolic maps were integrated in HPA.

NBIS is following the development of artificial intelligence (AI) methods and will adapt our services to match the *future demands from new technologies*. Methods and software developed within NBIS are made publicly available through Open Access publication and Open Source licensing of software. NBIS has developed and published coding guidelines to aid in developing better software, and our staff also participates in the ELIXIR task Software best practices. We maintain *public repositories* (GitHub) for codes and scripts that are developed by NBIS.

Bioinformatics training (module 6)

In the ongoing transformation of biology and medicine into large-scale data driven research, *advanced training is a key factor to ensure Sweden's scientific competitiveness*. NBIS has the mission to provide advanced bioinformatics courses. We are continuously evaluating the demand for training activities, and we are keeping our courses state-of-the-art. NBIS is encouraging our experts to professionally develop in pedagogics and cognitive science. Currently, the demand for NBIS courses is larger than our resources permit. NBIS has since 2015 run the *Bioinformatics Advisory Mentorship Programme*, a mentor programme where PhD students (typically 15–20 new per year) get a senior NBIS

expert as a personal advisor for up to two years of their PhD studies.

NBIS engages in the ELIXIR *Training Programme* for development of new software engineers, biocurators and other professionals needed to operate the bioinformatics infrastructures. NBIS will participate in ELIXIR advanced courses, e.g. single cell transcriptomics, also 2021–2024. NBIS has successfully integrated the *eLearning platform* offered by ELIXIR-Slovenia as part of our training activities. Furthermore, hackathons, train-the-trainer events, instructor training, and software carpentry workshops are regularly arranged with ELIXIR.

Nationally unique and internationally competitive services

NBIS handles all support projects at the national level and assigns the best expert for each project, regardless of geographic location. Furthermore, NBIS has the possibility to assign multiple experts, when needed for providing expertise in multiple areas or for provision of long-term redundancy. One measure of the successful outcome of NBIS support provision is that our users publish in high-impact journals. Another measure is that NBIS staff are internationally appreciated in capacity-building activities in genome assembly and annotation, and single-cell transcriptomics. NBIS staff organise and teach at international post-graduate courses, e.g. single-cell omics (with SIB, GOBLET and EMBO), molecular evolution (Evomics, Czech Republic), and advanced R programming (RaukR).

Expected user base 2021–2024

NBIS has users from *all Swedish major universities* and predominantly from the faculties of medicine, science, technology, and pharmacology. NBIS is working truly nationally as can be seen from that the support time is distributed among all major Swedish universities. As mentioned earlier, NBIS annually typically provides support to ~250 PIs, and we expect this number to increase as bioinformatics enters new fields. We also expect a continuation in the large spread between universities. The great majority (90+%) will continue to be from academia, but we expect an increase of projects from hospitals and industry in the coming years.

There are several fields that are increasingly using NBIS: Medicine, Environmental sciences, Population genomics, Ecology, Evolutionary developmental biology, and Systematics. Among emerging fields we note: Integrative multi-omics, Systems biology, Ancient DNA, Materials science, AI and deep learning, Cost-efficient long-read sequencing, and Image informatics.

Reproducibility, quality, and appropriate storage of data

NBIS has systematic procedures to ensure that *all analyses from supported projects are reproducible* and that the related data and source code becomes deposited in *public repositories* (with human sensitive data subject to controlled access). NBIS provides *courses in reproducible research* for the life science community. Reproducible research enables others to build upon previous work in a sustainable way. All support provided by NBIS strives to be FAIR and reproducible. NBIS helps our users to publish data at appropriate sites, as detailed in the Data management section above.

User fee model that will be applied for 2021–2024

From a user perspective, NBIS offers nation-wide support, data, tools and advanced training. To cater for different user needs, NBIS provides hands-on support along three well-defined tracks, either based on user fees, or based on a rigorous peer-review process with external project evaluation.

In the *Short- and Medium-term Support track*, the focus is on short and medium-sized projects (typically 40–500 h) under a user-fee based model (currently 800 SEK/h = 80 EUR/h). In the last few years, we have seen an increase in the time requested, reflecting more complex data and often of different types. Projects are accepted continuously with the aspiration of having short waiting times, with most analyses starting within a few weeks from signed contract. We make a technical evaluation of each project to assure its feasibility and that we have the specific competence within NBIS.

The *Partner Project track* is intended for projects with a large bioinformatics component, where NBIS can enter as a project partner based on cost coverage by the research project. This track is intended for projects requiring NBIS support of at least 12 person months over 2–5 years (e.g. 0.5 FTE over 2 years). During 2019, the number of partner projects has increased, and we foresee further increases during the next years.

The *Long-term Support track* provides extensive support to a limited number of scientifically outstanding projects that involve very large data sets and/or require extended, creative and customised analyses to accurately answer the scientific questions. The primary funding is from Knut and Alice Wallenberg Foundation (KAW) and no user fee is charged. Supported projects are selected in a rigorous scientific peer-review process in open national calls three times annually. Knowledge transfer is a key aspect of the support model, and dedicated researchers working hands-on alongside the support staff is required.

Research environment

To assure a continuous competence development, NBIS staff are placed in bioinformatics research environments, providing opportunities to attend lectures and seminars. In addition, the SciLifeLab vibrant community with multiple technical platforms and affiliated researchers provides

an excellent scientific environment. NBIS staff have up to 20% time for *professional development*, e.g. when involved in support tasks needing additional competence. As bioinformatics is a rapidly evolving discipline and new areas emerge, over time NBIS staff might move between different areas, depending on user needs and own interests. Additional opportunities are provided by the ELIXIR intra-European staff exchange.

Budget 2021–2024

Genomics is NBIS's largest area of custom-tailored bioinformatics support, and with a continued drop in cost-per-base, further development of long-read technologies and a dramatic improvement of single-cell sequencing, *we expect this field to remain in a high demand of advanced support*. The total number of users will increase, and even though the bioinformatics analyses will be more efficient, there will still be an increasing need for support. NBIS will through local interactions assure that the bioinformatics support is provided at the right level – national when needed due to complexity and local when possible.

We will enable staff to *spend time at other SciLifeLab platforms* in order to increase and facilitate their interactions with NBIS. For 2021 and onwards, we plan for 7 persons to be 50% embedded in other SciLifeLab platforms (3.5 FTEs).

An additional trend we see is the wish to use combined datasets to answer complex research questions. We have therefore with SciLifeLab funding established an integrated bioinformatics team, that provides support for integrative studies. NBIS already has *several multi-omics projects* running, but the scientific challenges are large, especially considering collection of appropriate data and development of adequate analytical methods. We will expand our efforts in this area in order to provide the necessary expertise for multi-omics data-driven science.

NBIS will increase our efforts in providing infrastructure and knowledge for data management and data publication (+4–7 FTE), systems development and support of bioinformatics tools (+2 FTE), and ELIXIR work (+2 FTE). In addition, we provide advanced training in all these areas mentioned above.

Costs	2020	2021	2022	2023	2024
Personnel, Support (module 2; 48 FTE)	47 550	48 250	49 210	50 189	51 188
Personnel, Data Management (module 3; 2020: 5 FTE; 2021–2024: 9–12 FTE)	5 850	9 900	11 198	12 522	13 872
Personnel, Systems Development (module 4; 2020: 12 FTE; 2021–2024: 14 FTE)	13 600	15 400	15 708	16 022	16 343
Personnel, Training (module 6)	Included in the other modules				
Personnel, ELIXIR (module 7; 2020: 3 FTE; 2021–2024: 5 FTE)	3 400	5 500	5 610	5 722	5 837
Operations (managment=module 1; 2020: 7 FTE; 2021–2024: 7.5 FTE)	6 700	7 500	7 650	7 803	7 959
Premises (only SciLifeLab; rest is included in personnel costs)	1 700	1 800	1 836	1 873	1 910
Additional costs if BigPicture is approved	-	3 750	3 750	4 000	3 500
Instrument depreciations	700	1 780	2 620	3 460	4 300
Sum costs (kSEK):	79 500	93 880	97 582	101 591	104 909

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	15 300	24 200	24 200	24 200	24 200
University funding	13 810	14 500	15 350	16 213	17 088
VR (Swedish Research Council)	21 000	20 000	20 000	20 000	20 000
KAW (Knut & Alice Wallenberg Foundation)	18 000	17 000	17 000	17 000	17 000
NordForsk	1 500	1 000	1 000	1 000	1 000
ELIXIR and EU projects	1 500	3 000	3 000	3 000	3 000
EU project BigPicture (only at application state)	-	3 750	3 750	4 000	3 500
User fees	9 000	11 000	14 000	16 000	18 000
Sum revenues (kSEK):	80 110	94 450	98 300	101 413	103 788

Table 1. Current budget (2020) and suggested budget 2021–2024

Compute and Storage

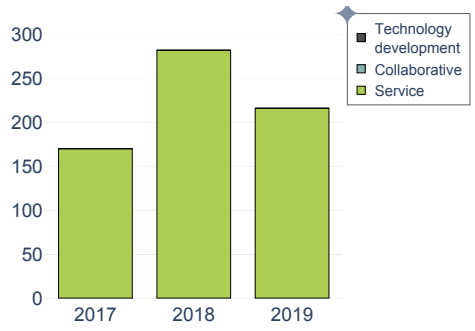
Read more: Web page, Publication Data Base

Basic Information

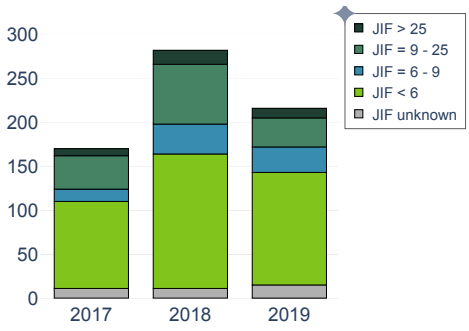
Facility director: Elisabeth Larsson
Head of facility: Marcus Lundberg
SciLifeLab facility since: 2013
Host University: UU
FTEs: 4.5
FTEs financed by SciLifeLab: 3.45

Funding 2020 (in kSEK)

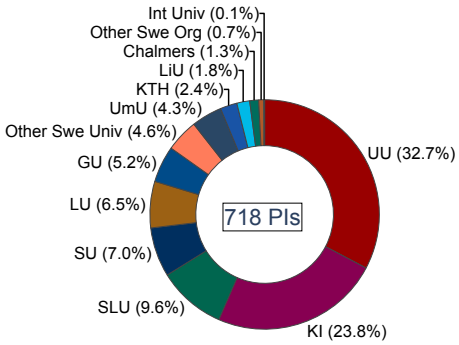
SciLifeLab: 3400
Total: 4450



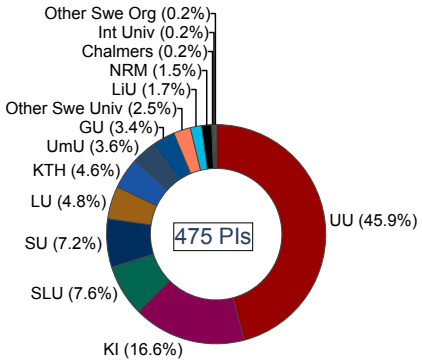
Publications by category



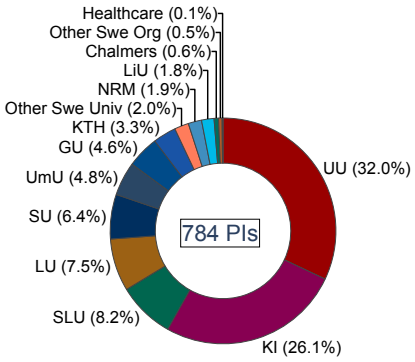
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

- User support for life science and bioinformatics projects on high-performance computing (HPC) systems provided by Swedish National Infrastructure for Computing (SNIC)
- Maintenance and development of digital research environment on SNIC HPC systems, including 800+ different tools.
- Training for life science on HPC systems
- SNIC project management support to PIs of SNIC projects
- Collect the needs of life science researchers w.r.t. compute and storage resources and communicate them to infrastructures that host resources
- Main systems where we have users:
  – Rackham: 486 nodes, 6 PB storage for general-purpose computing
  – Bianca: 200 nodes, 9 PB storage for sensitive personal data
  – Dis: a part of the SNIC Science Cloud

New Technologies and Services 2021–2024

- Support users in moving to a replacement system when the current main system reaches end-of-life.
- Support our community with artificial intelligence/machine learning (AI/ML) needs on an upcoming large-scale computer system dedicated to AI/ML methods.
- In a continually evolving data management landscape, we will continue to increase our level of support on issues related to data handling.

Background

Compute & Storage functions as a bridge between the SciLifeLab Bioinformatics Platform NBIS and the SNIC infrastructure at Uppsala University's computing center, UPPMAX. The goal is to make nationally available HPC resources more accessible to the life-science research community, which is relatively new and inexperienced at HPC (although this is rapidly improving) and has markedly different usage patterns and needs compared to more traditional HPC communities, e.g. physics and chemistry.

The needs of the community and the condition of the infrastructure both guide the activities of the group. For example, while installation and maintenance of a vast software library has been a constant activity, the methods employed have changed as technology has matured and demand has shifted – fewer users today are forced to rely on poorly maintained "one-off" codes that were common in the past and in the last few years we have been able to use technologies like Conda, Singularity, and EasyBuild to generate a more portable and robust environment. Occasionally, the retirement of a popular system requires

a migration of users, projects, data, and software to a new system, a task that requires significant effort and coordination.

Plans for 2021–2024

New technologies/services planned for

- Support for users is currently focused on the environment present at UPPMAX. By leveraging new software deployment methods, we will make this environment more portable and vastly improve our ability to support users also on other SNIC systems and elsewhere.
- Rackham reaches end-of-life during this period. We expect that at least 1500 users and their 5+ PB of data will need administrative and/or technical help moving to a replacement system.
- Increased support for automatic workflows and digital research environments. Workflows in e.g. Galaxy are growing in power and popularity, and are quickly becoming an important tool also for experts and non-experts alike.
- The Wallenberg Artificial Intelligence, Autonomous Systems and Software Program (WASP) has invested in a large-scale computer system for artificial intelligence/machine learning (AI/ML) methods, to be taken into production starting late 2020. We will support our community with AI/ML needs on that resource.
- It is expected that long-term storage systems of various kinds will continue to spring up locally and nationally to meet the need for archival and publication of research data. We will increase our level of support towards the adoption of good practices with regards to long-term data storage and publication according to FAIR principles and legal requirements.

Nationally unique and internationally competitive technologies/services

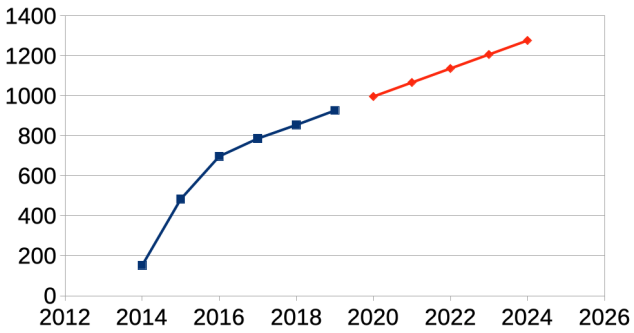
Our digital research environment provides the largest and most complete software library dedicated to bioinformatics tools, currently consisting of 800+ tools and still growing. We try to keep the barriers to entry as low as feasible by supporting potential users in writing proposals for SNIC projects. Resources and qualified support for active data analysis projects is free at the point of need.

Expected user base 2021–2024

The total number of PIs (see figure) is steadily increasing every year, lately with a linear trend of about 70–80 new PIs per year, partly as a result of bioinformatics entering more scientific disciplines. With the expanding breadth of services offered and a number of upcoming SNIC resources that could be of interest to new use cases, we expect this trend to continue. Compared to today, we can expect to have 30% more active PIs by the end of 2024.

The national spread of the users corresponds to the relative sizes of biomedical and biology research communities at the universities. Outreach activities, such as meetings with potential users and presence in relevant conferences, aim at increasing user numbers in underrepresented universities. Resources are accessed by application to the national SNIC web portal, and support is available via email to a service desk. Training is provided through SNIC and NBIS activities with a national scope.

All projects are owned by researchers with academic affiliations.



Currently, almost a quarter of PIs use the sensitive data cluster Bianca and can be assumed to have a connection to healthcare or clinical research.

How reproducibility, quality, and appropriate storage of data are ensured

Compute & Storage does not produce any data. We provide support, guides and training regarding data management plans, back-ups, and FAIR principles. Digital research environments, when used properly, can greatly increase reproducibility and transparency in research.

User fee model that will be applied for 2021–2024

No user fees.

Organisational context

Compute & Storage is hosted by and tightly integrated into UPPMAX at Uppsala University, which is partially funded by SNIC. Interactions with SNIC and other SNIC members contributes to competence transfer and coordination of efforts in the Swedish HPC community.

Compute & Storage provides support and training to NBIS staff. Most NBIS staff use UPPMAX and the environment we have created there. We have regular interactions with SciLifeLab Data Center and the Genomics platform.

A Domain Specialist funded by Swedish National Data Service, with expertise in sensitive data, is now a part of the facility at 0.5 FTE. This role is intended to foster better practices among our users, raise the awareness and skill level of our team, and to act as a contact point to Swedish National Data Service and the Uppsala University data office.

Alternative facilities/infrastructures and commercial providers

There are other SNIC centers and local compute and storage resources spread all over Sweden, but the threshold to entry can be high, and support is often lacking in relevant domain expertise. Commercial providers of cloud and cluster services exist as alternatives, but require project funding and lack a coordinated support infrastructure like that in SNIC.

Description of planned new services in 2021-2024

As stated above, the current large cluster Rackham reaches end-of-life at the end of 2022 and will sunset. At that time, there will be well over 1500 active users and more than 1000 PIs. SNIC has plans for replacing the capacity and NBIS Compute & Storage is uniquely placed to make the transition to the new system smooth and aid hundreds of ongoing research projects continue with minimal interruption.

NBIS Compute & Storage will support those parts of our community with AI/ML needs on the new WASP resource in Gothenburg by moving our software library and some other aspects of the software environment to that system, as well as by providing basic user support.

Compute & Storage will contribute together with other parts of NBIS to help users with data management tasks, as described in the NBIS Support, Infrastructure & Training section.

Budget 2021–2024

We propose a moderate increase in budget to strengthen our competence in new areas, such as AI/ML methods and related technology. We also aim to increase our team's ability to prepare for and manage the large-scale efforts that we know are coming, such as the retirement of the current main cluster. We can meet our ambitions with a small increase in funding in large part by leveraging our current efforts to make the UPPMAX digital research environment more portable.

Costs	2020	2021	2022	2023	2024
Personnel (4.5–6 FTEs)	4 400	6 000	6 000	6 000	6 000
Other	50	50	50	50	50
Sum costs (kSEK):	4 450	6 050	6 050	6 050	6 050

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	3 400	5 000	5 000	5 000	5 000
University funding (UU, SFO+TekNat)	1 050	1 050	1 050	1 050	1 050
Sum revenues (kSEK):	4 450	6 050	6 050	6 050	6 050

Table 1. Current budget (2020) and suggested budget 2021–2024

BioImage Informatics

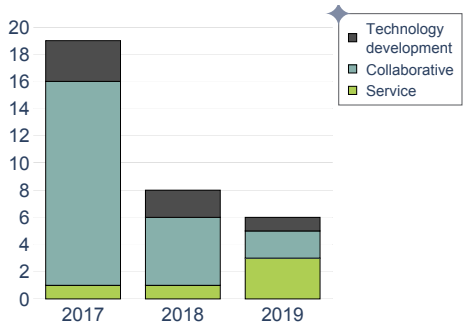
Read more: Web page, Publication Data Base

Basic Information

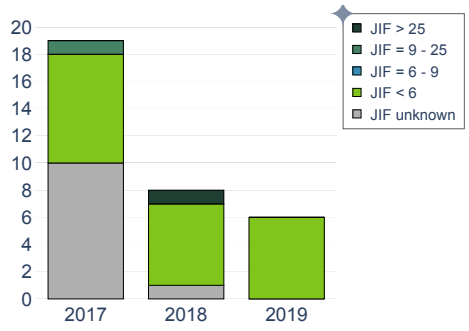
Facility director: Carolina Wählby, Kevin Smith
Head of facility: Petter Ranefall
SciLifeLab facility since: 2016
Host University: UU, KTH
FTEs: 5
FTEs financed by SciLifeLab: 2.5

Funding 2020 (in kSEK)

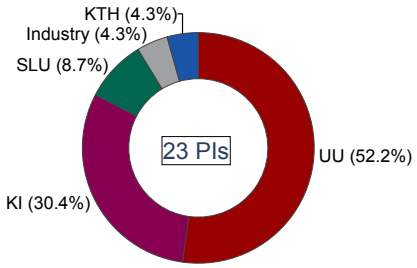
SciLifeLab: 2800
Total: 5751



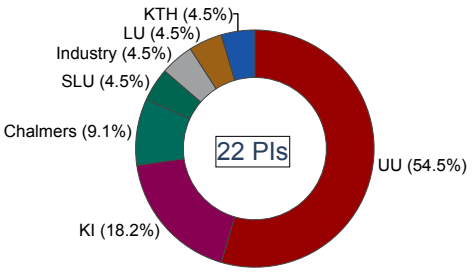
Publications by category



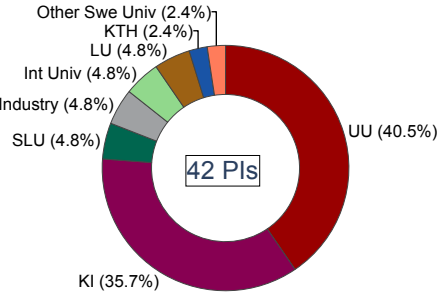
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

The value of our facility lies in the image analysis expertise of our staff. We provide:

- Image processing algorithm development and software engineering to address challenging research involving microscopy imaging aimed at quantitative evaluation.
- Overall experimental design in relation to image analysis (staining, sample preparation, image acquisition, and efficient use of computational resources).
- High throughput/large scale image processing using machine learning and deep learning, with special focus on analysis of tissue samples and spatial omics.
- Imaging and analysis tools for high-content/high-throughput research on zebrafish.
- Courses, workshops and summer schools on digital image processing and usage of image analysis software, with a strong focus on free and open source software.
- Long-term collaborative research projects, typically involving external funding.

We aim to provide facility users with a toolset and data processing pipelines that can be run by the users after proficient optimization and coaching from our staff. With this, we not only give the users full control of their analysis, but also enable reproducible science.

New Technologies and Services 2021–2024

Data-driven research, where we combine image data with other sources of information:

- Spatial omics and tissue morphology - building on SciLifeLab collaborations
- Vertebrate disease models and genomics - building on unique hardware/software
- Research on clinical data via the Analytic Imaging Diagnostics Arena Data Hub

More broadly, we will provide new services related to:

- Guidance on the design of data-driven research involving image data
- Guidance on model training and validation when using convolutional neural networks

Background

The facility has one node at the Centre for Image Analysis, Dept. of IT, Uppsala University (locally since 2011), and one node at the School of Electrical Engineering and Computer Science at KTH (added 2017, new bioinformatician started 2019). The facility currently belongs to the Cellular and Molecular Imaging Platform, motivated by the importance of being close to the imaging competence. This interaction will continue, but starting 2021 we will be part of the Bioinformatics platform for stronger synergies on the computational side.

Carolina Wählby, Professor in quantitative microscopy, is facility director, and Kevin Smith directs the node at KTH. We have five employees, all with PhDs and more than 40 years of combined postdoctoral experience from industry, academia, nationally and internationally.

Starting 2020 we are part of the VR-funded research infrastructure National Microscopy Infrastructure, supporting one FTE, creating an important bridge to this unique expertise in microscopy, facilitating exchange of competences and support.

Plans for 2021–2024

New technologies/services planned for

Data-driven research combining image data with other sources of information, such as spatially resolved omics data and/or patient records, has a great potential to lead to new discoveries and directions for hypothesis-driven research. We will expand our technological competence and service in this direction, mainly focusing on machine learning in the form of deep convolutional neural networks and its model variants. Much focus will be on tissue morphology and spatial omics, building on long-term collaborations within SciLifeLab. Here, the Analytic Imaging Diagnostics Arena (AIDA) Data Hub will become a key component (as described separately), and integration of new deep learning tools, such as those developed at the Cell Profiling Facility, will become important. We also plan to expand our services on new techniques for high-throughput/high content imaging and analysis of zebrafish embryos, enabled through technology development funding from SciLifeLab.

Nationally unique and internationally competitive technologies/services

The facility is unique by being closely integrated with image analysis research groups both at Uppsala University and KTH, allowing us to stay up to date by continuous exposure to (and involvement in) state-of-the-art research and development. Our competitiveness is exemplified by our active involvement in the training schools of NEUBIAS, a European network for BioImage Analysis, and as co-organizers of the 2020 EMBL course on Advanced Methods in Bioimage Analysis.

In March 2019 we launched a joint capability with the Genome Engineering Zebrafish facility: Zebrafish Image Informatics, building on high-throughput imaging of zebrafish larva and expertise in large scale analysis of imaging data. Zebrafish is an important model organism in drug screening and large-scale studies of e.g. cardiovascular disease, neural disorders and cancer. We provide a complete pipeline from zebrafish handling to analysis results, using cutting-edge techniques in zebrafish genome engineering, high-throughput imaging and phenotypic quantification. This is a world unique possibility for investigating the effects of genome modifications or candidate molecules on vertebrate development.

Expected user base for 2021–2024

We foresee that we will expand our user base and national spread via visibility through the National Microscopy Infrastructure and to clinical partners via the AIDA Data Hub handling patient data in a correct and safe way. There is a general increase in quantitative approaches to image-based experiments, very much due to the faster rate at which data is being collected. We also expect an increase in publications acknowledging or involving the facility; there has been a lag for larger projects.

Nation-wide user accessibility

National accessibility is comparably easy as we provide expertise and not physical instruments. This means we can visit the users or provide support online, e.g. through our regular monthly Call4Help videoconferences on image analysis and related imaging issues together with experts in microscopy. We inform about the facility and our capabilities through participation in various MSc and PhD-level courses on cell analysis, imaging, multi-dimensional data analysis etc., poster and facility presentations in connection with summits, Wallenberg Academy Fellows meetings and presence at imaging facilities. Integration with the National Microscopy Infrastructure will further increase our visibility. Recent steps have also been made for interaction with the Stockholm Medical Image Laboratory and Education facility at Karolinska Institutet, focusing on AI and toolboxes from the company NVIDIA.

Reproducibility, quality, and appropriate storage of data

We focus on free and open source software, ensuring reproducibility and spread of developed techniques. Appropriate data handling is ensured in collaboration with the AIDA Data Hub.

User fee model that will be applied for 2021–2024

Our plan is to continue with 20 h of free support per PI, and charge cost-covering fees in projects expanding this time limit.

Research environment

Our Uppsala University node is affiliated with the Wählby lab at the Centre for Image Analysis, and our KTH node of is affiliated with Smith's research group focused on computer vision and machine learning applied to biological and medical images.

Synergies and capability contributions within the platform and SciLifeLab

The main synergy within the Bioinformatics platform is access to expertise from the omics field for large scale efforts in data-driven research. We work closely with the Cellular and Molecular Imaging Platform, the Drug Discovery and Development Platform, and the Proteomics and Metabolomics Platform, both on research projects and teaching. As mentioned above, we also collaborate with the Genome Engineering Zebrafish facility.

Collaborations with healthcare, industry and other national and international external organizations

We are involved in NEUBIAS as mentioned above and collaborate with the Imaging Platform at the Broad Institute (where Wählby acted as PI 2009-2015). We also collaborate with a similar facility at ETH Zurich, where Smith worked as a postdoc from 2011-2014, and at the Biozentrum in Basel, where Smith worked in 2014. We keep our expertise up to date and disseminate developed techniques by being actively involved in national societies (Swedish Society for Automated Image Analysis and Swedish Society for Deep Learning). We have ongoing collaborations with Astra-Zeneca and Vironova, and two members have part time employment at Astrego Diagnostics AB and Q-linea AB.

Alternative facilities/infrastructures and commercial providers

There is a high demand for expertise and courses for a wide and fast developing set of bioimage analysis tools (e.g. a number of deep learning tool boxes, Fiji, CellProfiler, QuPath, Python, KNIME). Part of this expertise is offered by microscopy facilities. We aim to tackle the more challenging projects. Due to our sole focus on bioimage informatics we can integrate recent developments in our service and give support for a wide range of tools.

Budget 2021–2024

Technology development funding for zebrafish tools, currently engaging 1.5 FTE, ends 2020. We propose a budget increase of 0.5 FTE from 2021 to keep the competence in the facility.

Costs	2020	2021	2022	2023	2024
Personnel (2020:5 FTEs, 2021-2024: 4 FTEs)	5 009	4 224	4 308	4 394	4 482
Operations (UU: 0.2 FTE, KTH: 0.1 FTE, financed by university funding)	547	558	569	580	592
Premises	174	177	181	185	188
Other (travel + conf)	40	40	40	40	40
Sum costs (kSEK):	5 770	4 999	5 098	5 199	5 302

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding (increase of 0.5 FTE from 2021 for zebrafish)	2 800	3 276	3 342	3 408	3 477
University funding UU	750	750	750	750	750
Swedish Research Council, RFI National Microscopy Infrastructure	750	750	750	750	750
SciLifeLab funding TDP to UU	1 281				
University funding KTH	170	170	170	170	170
User fees (expected to increase by 50%/ year from 2021)	20	53	80	119	179
Sum revenues (kSEK):	5 771	4 999	5 091	5 198	5 325

Table 1. Current budget (2020) and suggested budget 2021–2024

AIDA Data Hub (candidate)

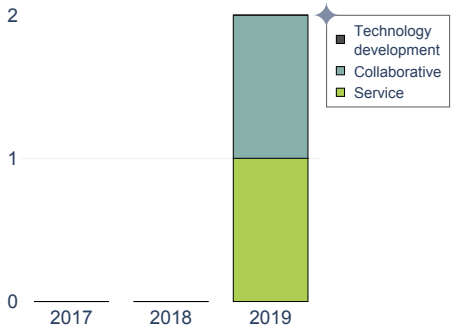
Read more: Web page, Publication Data Base

Basic Information

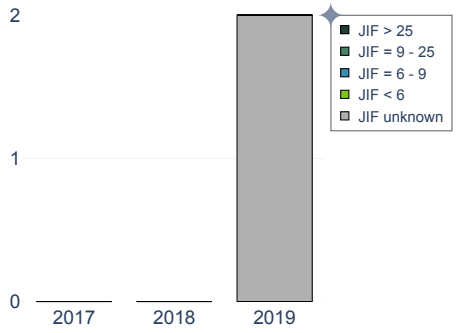
Facility director: Claes Lundström
Head of facility: Joel Hedlund
SciLifeLab facility since: N/A
Host University: LiU
FTEs: 1.5
FTEs financed by SciLifeLab: 0

Funding 2020 (in kSEK)

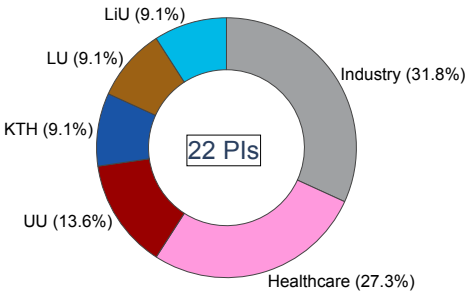
SciLifeLab: 0
Total: 2850



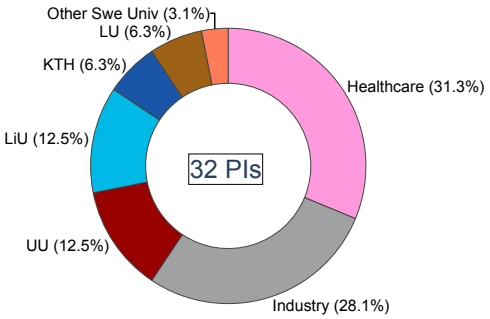
Publications by category



Publications by JIF



Users 2018



Users 2019

The AIDA Data Hub is a national facility currently operated by AIDA – the Analytic Imaging Diagnostics Arena – and proposed for incorporation into the SciLifeLab Bioimage Informatics facility and Bioinformatics platform from 2021.

Current Technologies and Services

- Open repository for DOI citable FAIR training data for medical imaging diagnostics artificial intelligence (AI) with co-located compute services.
- Priorities set by the AIDA Data Hub Clinical Council to maximize clinical and research impact, based on current data composition and identified clinical needs for new decision support tools.
- Cost coverage for work in clinics with extraction and enrichment of prioritized data.
- Tools and support for data anonymization, transfers and enrichment.
- Advanced support in medical imaging AI and ethical, legal and social issues for medical imaging research data.
- PACS (picture archive and communication system) to facilitate collaboration with clinicians and to offer realistic development target for innovation.

New Technologies and Services 2021–2024

- Extended image data repository interfaces (based on Federated EGA technologies) for improved interoperability, self-service, and support for multi-omics.
- The AIDA Data Hub currently supports processing and sharing of anonymous data only, but plans to extend this to also support pseudonymous/identifiable data.

Background

The most important factor for world-class artificial intelligence (AI) is access to massive amounts of high-quality training data, and OpenScience and FAIR data sharing are means to achieve this. The AIDA Data Hub is a common repository where 30+ partner organizations from academia, industry and healthcare collaboratively gather, enrich and share massive amounts of data for world-class AI in medical imaging diagnostics. The AIDA Data Hub is operated by 1.5 FTE staff from academia and industry with support from caregivers, engaging expertise in system management, AI development, and sensitive personal data extraction and management. We help connect the value chain and increase impact in research by facilitating large-scale data exports from clinical production systems and acquiring data proactively to support research in clinically prioritized areas.

The AIDA Data Hub has the potential to bridge proof-of-principle life science research based on microscopy imaging and bioimage informatics performed at the SciLifeLab Cellular and Molecular Imaging platform and the SciLifeLab Bioinformatics platform, and bring it all the way to clinical practice. To ensure relevance and applicability,

and marketability of the results from innovation projects in CE-marked medical devices, the AIDA Data Hub is built around a picture archive and communication system (PACS). This allows clinicians to participate throughout development from research idea into finished product using the same tools they use in their everyday work. Around this the AIDA Data Hub offers high-end GPU compute resources and AI expertise, as well as services to support data collaboration around storage, sharing and development. The AIDA Data Hub also facilitates contacts for data sharing options outside of AIDA.

The startup phase of the AIDA Data Hub was carried out within AIDA, a Swedish arena for research and innovation on AI for medical image analysis that was initiated in 2017 as an initiative within the strategic innovation program Medtech4Health, jointly supported by VINNOVA, Formas and the Swedish Energy Agency. AIDA co-funds collaboration projects where Swedish academia, healthcare and industry meet to translate technical advances in AI technology into patient benefit in the form of clinically useful tools. AIDA hosts topical AIDA days monthly where partners network and learn from national and international expertise, hosts courses and fellowships for competence development, and also facilitates clinical adoption of novel AI technology.

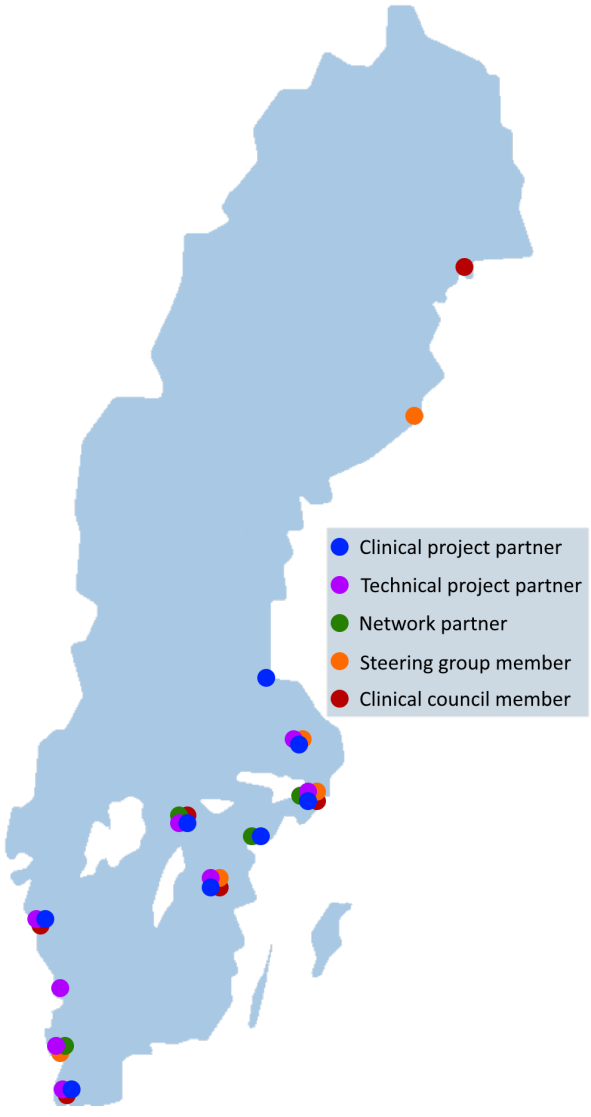
To support its co-funded projects, AIDA began developing its data hub in October 2018 in collaboration with pilot users from healthcare, industry and academia. The AIDA Data Hub went into production in June 2019, and has grown with about 500GB/month since.

Plans for 2021–2024

We plan to offer up the services of the AIDA Data Hub as a unit under the SciLifeLab BioImage Informatics facility and Bioinformatics platform, as a sustainable continuation of the startup activities that were funded by Medtech-4Health. Our current support for processing and sharing anonymous data will be extended to also support pseudonymous/identifiable data. We also plan to make the AIDA Data Hub datasets available through federated image data interfaces (based on Federated EGA technologies), for improved interoperability, self-service, and support for multi-omics.

The AIDA Data Hub is unique in that no other national activity exists with this focus on data driven clinical imaging diagnostics. The AIDA Data Hub is currently hosted by AIDA, which is operated as a nationally distributed project from the Linköping University strategic research center Center for Medical Imaging Science and Visualization (CMIV). AIDA core partners are the academic CMIV, the regional public healthcare provider Region Östergötland, and the private company Sectra which is active in medical imaging technology and high-security communications for military, diplomatic and law enforcement activities, and is the majority provider of PACS systems to clinics in many countries including the Nordics and the Netherlands. AIDA is governed by a nationally distributed steering group and has a national mission and presence, and the AIDA Data Hub was developed to support these. The AIDA Data Hub engages 30+ national partner organizations from academia, healthcare and industry, which we expect to increase to about 50 partner organizations and hundreds of users in the next period. The AIDA Data Hub priorities are set continuously by a nationally distributed Clinical Council, based on dataset composition and identified clinical needs in Sweden. The geographical distribution of AIDA activities and partners (AIDA Data Hub facility users) are shown below, with details at the AIDA organization webpage.

The international competitiveness of the AIDA Data Hub is demonstrated by its leading role in a European consortium called BigPicture, headed up by professor Jeroen van der Laak at Radboud UMC. This consortium engages world leading research groups in digital pathology as well as all fully digitized pathology clinics in Europe, to answer the



~70M€ IMI2-18 call for building a European repository for AI in digital pathology. BigPicture is now in Stage 2 of the proposal process, meaning that all competing consortia have been rejected, and work is now ongoing to formulate a detailed project plan that incorporates the contributions from the industrial partners who initiated the call and are planned to provide approximately half the funding for the effort. The AIDA Data Hub is planned to lead development of the infrastructure, to be carried out and operated by ELIXIR nodes in Sweden and Finland, mainly as extensions of ELIXIR's Federated EGA technology to provide functionality also for digital pathology data.

AIDA is collaborating with the company Nvidia in the area of medical imaging diagnostics AI research, and is in the process of installing a DGX-2 GPU compute system where research groups can build AI models on medical imaging data and receive support from AIDA and Nvidia. Nvidia also provides training courses at AIDA events.

The AIDA Data Hub services are available over the Internet. The practical mechanisms as well as best practices and legal bases are described in the AIDA data sharing policy.

The AIDA Data Hub accepts data mainly from research consortia that have active involvement from healthcare, which guarantees clinical relevance, suitability for research and quality in terms of clinical representativeness and soundness as basis for medical diagnosis. Data is stored in a PACS, which ensures that clinical experts can participate in a least-surprises way, and can provide quality assurance throughout development from research idea into finished product using the same tools they use in their everyday work. This also guarantees that standard healthcare data formats are used, and kept safe, readable and correct using the same mechanisms that protect healthcare data in clinics.

The AIDA Data Hub has elected to not charge user fees during its scaleup phase, however if incorporated as a unit under the BioImage Informatics facility and Bioinformatics platform, we plan to adopt the same user fee model as the parent facility and platform.

There exist significant synergies between the AIDA Data Hub and its proposed facility and platform in their common interest for machine learning applied to GDPR Article 9 types of sensitive personal data at scale. The AIDA Data Hub can contribute medical imaging diagnostics AI expertise, and expertise in ethical, legal and societal impacts aspects of managing large scale medical research data. The AIDA Data Hub can also facilitate large-scale exports of data for research from clinical production systems. The AIDA Data Hub PACS environment can also facilitate research collaborations with clinics, and imaging diagnostic decision support development companies.

Significant synergies also exist with the SciLifeLab Diagnostics Development platform and Data Center. The AIDA Data Hub is active in providing tools and databases to support research in medical diagnostics, just as the SciLifeLab Diagnostics Development platform, and has access to a large network of partners in healthcare, industry and academia. Its activities in service provisioning and data integration and stewardship are also similar in nature to those at the SciLifeLab Data Center. Its incorporation can be an opportunity to bring communities together and enable new venues of research where data from multiple omics can be combined.

Budget 2021–2024

Costs	2020	2021	2022	2023	2024
Personnel (1.5 FTEs)	1 500	1 550	1 600	1 600	1 600
Operations	500	550	550	550	550
Instrument depreciations	850	850	850	850	850
Additional costs if BigPicture is approved		2 245	2 291	3 233	2 386
Sum costs (kSEK):	2 850	5 195	5 291	6 233	5 386

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	-	2 000	2 000	2 000	2 000
VINNOVA Medtech4Health	2 850	850			
EU project BigPicture (only at application state)		2 245	2 291	3 233	2 386
User fees (mainly compute)		100	1 000	1 000	1 000
Sum revenues (kSEK):	2 850	5 195	5 291	6 233	5 386

Table 1. Current budget (2020) and suggested budget 2021–2024

Cellular and Molecular Imaging Platform

Basic information

Platform Director: Hjalmar Brismar

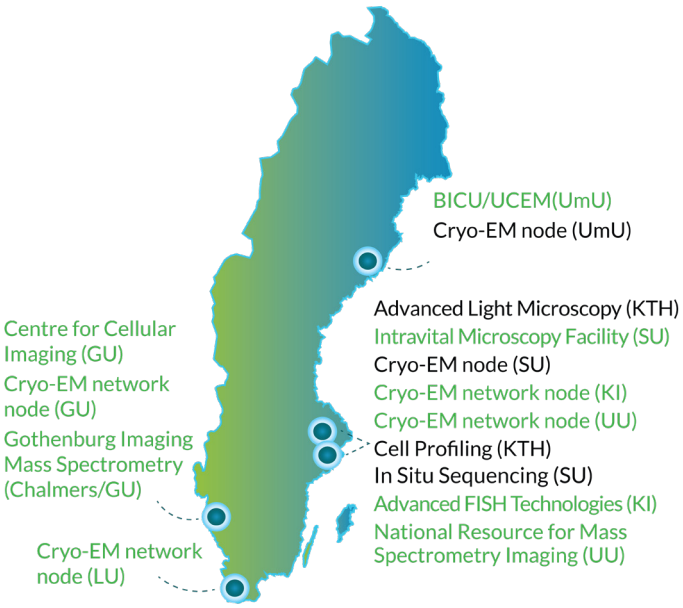
Platform Vision:

Develop a world leading platform where imaging technologies deliver high quality data for advancement of knowledge in health and environmental sciences

Platform Mission:

Provide the research community with cutting edge instruments and competence for cellular and molecular scale imaging and analysis

Geographical location of facilities



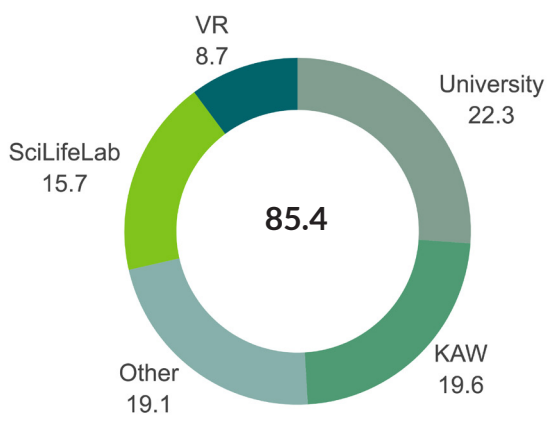
SciLifeLab funding 2020

Facility/unit	(MSEK)
Advanced Light Microscopy	3.4
Biochemical Imaging Centre Umeå/ Umeå Core facility for Electron Microscopy (candidate)	0.0
Centre for Cellular Imaging (candidate)	0.0
Intravital Microscopy (candidate)	0.0
Cryo-EM	8.5
Cell Profiling	3.0
In Situ Sequencing	0.8
Advanced FISH Technologies (candidate)	0.0
Gothenburg Imaging Mass Spectrometry (candidate)	0.0
National Resource for Mass Spectrometry Imaging (candidate)	0.0
Total SciLifeLab funding	**15.7**

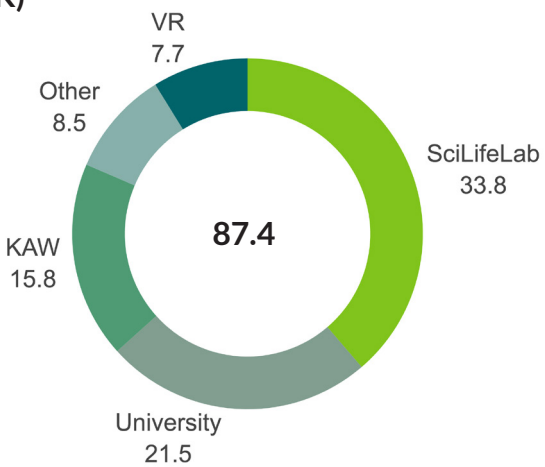
Suggested annual SciLifeLab funding 2021-2024

Facility/unit	(MSEK)
Advanced Light Microscopy	4.8
Biochemical Imaging Centre Umeå/ Umeå Core facility for Electron Microscopy (candidate)	1.5
Centre for Cellular Imaging (candidate)	1.5
Intravital Microscopy (candidate)	1.5
Cryo-EM	12.0
Cell Profiling	4.3
In Situ Sequencing	1.9
Advanced FISH Technologies (candidate)	1.8
Gothenburg Imaging Mass Spectrometry (candidate)	1.5
National Resource for Mass Spectrometry Imaging (candidate)	3.0
Total SciLifeLab funding	**33.8**

Total funding 2020 (MSEK)



Total suggested annual funding 2021-2024 (MSEK)



Background

The Cellular and Molecular Imaging platform consists of six facilities that provide service in advanced light microscopy (ALM facility), cryogenic electron microscopy (Cryo-EM Facility), high content microscopy (Cell Profiling facility), NMR analysis, protein crystal production (PSF), and image-analysis (BIIF). From 2021 we propose to develop the platform by strengthening the focus on imaging technologies. PSF will be discontinued as a SciLifeLab facility and the NMR and BIIF facilities will move to other platforms.

Plans for 2021–2024

SciLifeLab received a large number of proposals in the 2019 Technology Needs Inventory Survey. A majority of the proposals were for new techniques and increased capacity in imaging. Based on this expression of need from the scientific community and supported by developments in imaging technology, we suggest here a new organization of the platform that includes a development of new facilities and technologies.

The platform will be organized into four functional units: Advanced Light and Electron Microscopy (ALEM), Cryogenic Electron Microscopy (Cryo-EM), Targeted Spatial Omics (TSO) and Mass Spectrometry Imaging (MSI).

The ALEM unit is formed by the present ALM facility and *three new facilities* at Gothenburg, Umeå and Stockholm University providing expertise in Correlative Array Tomography (CAT), Focused Ion Beam-Scanning Electron Microscopy (FIB-SEM) and two-photon microscopy, respectively.

The Cryo-EM unit has two existing nodes (Stockholm and Umeå University) and will *expand its operations to include a cryo-EM network* for local screening of samples (Karolinska Institutet, Lund, Gothenburg, and Uppsala University). The unit will also increase the capacity to support users in refinement and modeling of 3D structures.

The TSO unit will be formed by the present Cell Profiling facility and *two new facilities*, In Situ Sequencing (ISS) (currently a service unit in the ESCG) and Advanced FISH Technologies (AFT). The TSO unit will provide full-service projects in highly multiplex imaging of fresh frozen and paraffin embedded tissue samples, for targeted profiling of genes, transcripts and proteins at single cell level.

The MSI unit is *new and* consists of two facilities (Uppsala and Gothenburg University) that offer molecular imaging technology for visualizing and quantifying the distributions of chemical species in tissue and cell sections down to the nanoscale.

An overview of the platform organization is shown below, *new facilities are marked in brown.*

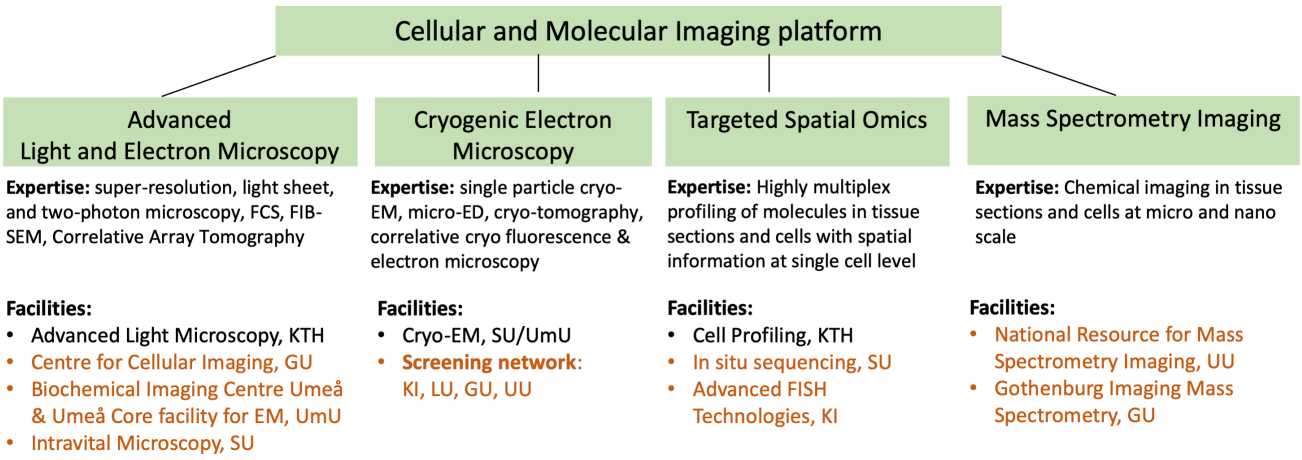
Impact on Swedish life science research community and society

The platform has a large and growing user base. Data produced in the facilities underlies an increasing stream of high-quality publications. Many of the techniques supported in our facilities were not available to Swedish researchers before they were implemented at SciLifeLab. In connection with the establishment of new technologies, we have recruited expert staff scientists internationally. These staff scientists often provide the critical expertise that enable high-impact research projects and publications. Most important, our staff scientists play a key role in training of users, both via hands-on sessions at the instruments and in regular courses.

Motivation for the importance of SciLifeLab funding of the platform as a national resource

The Imaging platform is one of the most diverse platforms in terms of technologies and expensive instrumentation. The fact that the platform has a large external funding reflects the importance of imaging as a key technology in life science, and also the ambition, expertise and performance of the facilities to apply for and successfully receive grants for their operations. However, a strong dependence on external funding is not optimal to create long-term stability and development of a research infrastructure.

Imaging platform organization



Compared to other platforms, the Cellular and Molecular Imaging platform has a relatively low funding from SciLifeLab (currently 18% of the platform operating costs are paid by SciLifeLab). Several of the facilities have been very successful in attracting external funding and also receive strong support from the research groups and university departments that host the facilities.

The interest and rapid development in imaging-based technologies is reflected in the 2019 Technology Inventory Needs survey, where this platform received the highest number of applications for new technologies and facilities. In order to answer to the expressed needs and the increased importance of imaging in life science we aim to develop the platform with new and unique technologies. Consequently, we request an increased budget from SciLifeLab.

Unique instrumentation and technologies, benchmarking of the platform in an international perspective

The strength of the platform comes from a combination of staff scientists with unique competences, state-of-the-art instruments, and access to unique resources. Several components of the platform are unique in Scandinavia, Europe and even globally.

In the ALM facility, the combination of expertise and instruments for super-resolution and advanced light microscopy is internationally competitive. Unique instruments include STED-FCS, lattice light sheet microscopy and in-house development of MFM-SIM and RESOLFT techniques. The facility hosts the national microscopy infrastructure (NMI) and coordinates Swedish participation in EuroBioImaging-ERIC. The expansion with CAT, FIB-SEM and two-photon microscopy all add unique capacities to the ALEM unit.

The Cryo-EM facility is, in collaboration with MRC-LMB (Cambridge, UK) and the National Center for Biotechnology in Madrid, world-leading in the development of image processing and user interface tools (Relion, Scipion). The facility also develops micro-electron diffraction on nanocrystals and correlative cryo fluorescence/electron microscopy as future services. The facility has excellent reputation and its staff scientists are often invited to teach at international courses.

In the TSO unit, both the proteome-wide library of antibodies from the Human Protein Atlas and the ongoing generation of a genome wide collection of FISH probes, are unique resources. The CODEX platform is one of the first instruments of its type worldwide and the only one in Sweden. The TSO unit is supported by its hosting research groups that are world-leading in spatial molecular biology which give the facility a strong potential to evolve into a world leading facility for spatial omics.

The new MSI unit will provide access to state-of-the-art molecular and elemental imaging technologies, including the only FTICR-MSI and NanoSIMS instruments in Scandinavia. The unit advances multi-modal high-resolution imaging and creates new analytical possibilities that reach beyond the traditional limits for imaging. The MSI unit has a unique combination of MALDI, SIMS and NanoSIMS instruments and is supported by internationally leading scientific expertise.

Platform synergies and capability contributions

Cellular and Molecular Imaging provide enabling technologies that inherently bring synergistic effects in all life science research. Within the platform there are significant synergistic effects between all facilities and units, e.g. development of correlative and multimodal methods, such as between super-resolution and cryo-EM. The microscopy facilities are coordinated nationally and internationally via the national microscopy infrastructure (NMI) and the European infrastructure – EuroBioImaging. Further, there is a natural link between the MSI and the TSO Facilities, which together allow for deep cellular phenotyping, metabolic states and endogenous biomolecules *in situ*, for evaluation of e.g. drug responses in individual cells. Due to the combination of *single cell spatial data*, the TSO unit has synergies with the genomics platform and components of the proteomics and metabolomics platform, as a complement to bulk and non-spatial single cell analysis.

All units have established collaborations with industry, e.g. with Astra Zeneca and Roche. The microscopy facilities are reference sites for Leica and Carl Zeiss. Furthermore, many of the platform users come from the health-care sector.

Data-driven Science of SciLifeLab´s roadmap

In data-driven science, the quality of data is of central importance. Imaging technology is well-known to generate large amounts of data and the development of new techniques, e.g. multimodal imaging, ultrafast 4D imaging and new cryo-EM detectors, dramatically increase the volume of data generated daily. The platform has established internal expertise and has platform-connected research groups with internationally recognized expertise in cloud computing, machine learning and AI. The imaging platform is thus already a key player in generating, analyzing and curating high-quality data, activities that are increasingly important for data-driven cell biology.

Budget 2021–2024

The platform requests an increased funding from SciLifeLab to integrate new technologies and make an expansion with new facilities. The proposed funding for new facilities is 1.5-1.9 MSEK, an amount that will be renegotiated based on performance after two years of operation. The MSI facility in Uppsala is proposed to be funded with 3 MSEK since it is an existing (non-SciLifeLab) facility and has already demonstrated its performance and has an established user base. For the current facilities, ALM, Cell-Pro, and Cryo-EM we ask for an increased funding in particular for new data intensive imaging technology and for data analysis support.

Advanced Light Microscopy

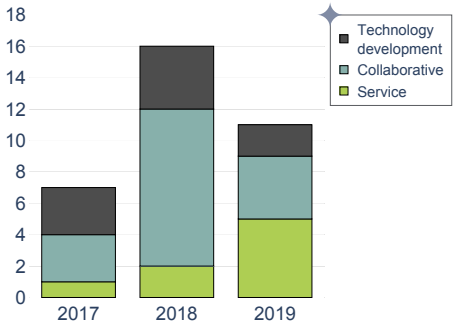
Basic Information

Facility director: Hjalmar Brismar
Head of facility: Hans Blom
SciLifeLab facility since: 2013
Host University: KTH
FTEs: 5.1
FTEs financed by SciLifeLab: 1.8

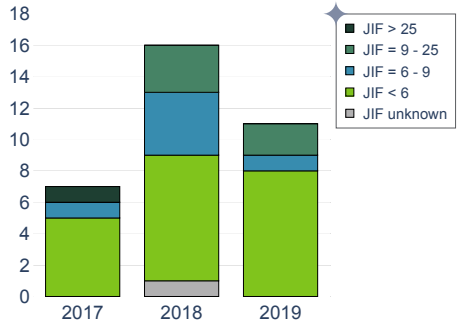
Funding 2020 (in kSEK)

SciLifeLab: 3400
Total: 9609

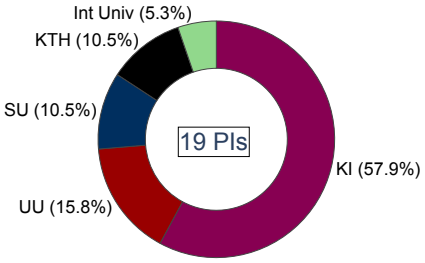
Read more: Web page, Publication Data Base



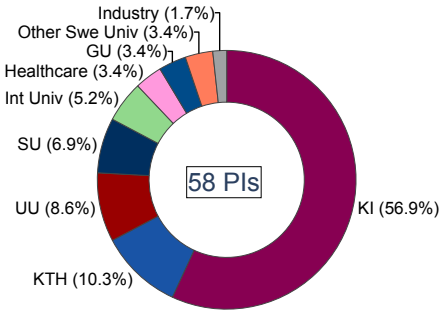
Publications by category



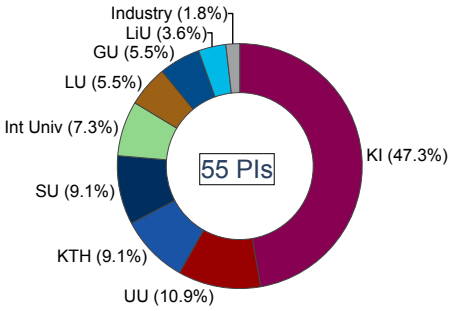
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

- 2D/3D multicolor STED microscopy
- 3D multicolor SIM microscopy
- 2D/3D multicolor STORM & PALM microscopy
- SPIM-Lightsheet microscopy, including cleared sample imaging
- FCS/FCCS/iFCS single molecule spectroscopy and microscopy
- Sample preparation for advanced light microscopy
- 3D/4D image processing and analysis

New Technologies and Services 2021–2024

- Lattice Lightsheet microscopy
- MFM-SIM microscopy
- STED-FCS

Background

The mission of the ALM facility has, since its start as a national facility in 2013, been to give access and expert support in state-of-the-art fluorescence microscopy techniques not available elsewhere. A strong focus is on super-resolution microscopy. In 2017, two new staff scientists were recruited and the repertoire of techniques was broadened by the introduction of light sheet microscopy and advanced FCS analysis in the facility.

Support in Lightsheet microscopy at ALM has attracted several new research groups with a need to image larger samples, model organisms, and also for studies of cleared tissue samples. In parallel to the introduction of new imaging techniques the facility has developed sample preparation protocols and gives now advanced support that includes clearing and expansion techniques. Single molecule dynamics studies in correlation spectroscopy have been established as a core technology in the facility and there is a continuously increased use and broadened interest for those techniques.

Staff

Facility Director: Prof. Hjalmar Brismar, PhD – 30 years of experience in fluorescence microscopy research and development.

Head of Facility: Docent Hans Blom, PhD – 17 years of experience in super-resolution microscopy research and development, initially acquired as PostDoc in Nobel Laureate Stefan Hell's lab.

Staff Scientist (super-resolution): Ana Agostinho, PhD – 10 years of experience in super-resolution microscopy for cell biological research. Postdoc training from labs in Scotland and Sweden.

Staff Scientist (FCS): Stefan Wennmalm, PhD – 23 years of experience in single molecule dynamic studies. Postdoc training from labs in Sweden, Switzerland and the United States.

Staff Scientist (SPIM): Steven Edwards, MSc – 6 years of experience in Lightsheet microscopy research and user support.

Plans for 2021–2024

New technologies/services

Lattice Light Sheet Microscopy: Lattice Light Sheet microscope (Carl Zeiss) installed in March 2020.

MFM-SIM: Multifocal structured illumination microscopy currently under development in-house in collaboration with the Abrahamsson lab at UCSC.

STED-FCS: Higher sensitivity and dynamic range of FCS by STED excitation/detection. Installed in February 2020.

Uniqueness

The focus on advanced light microscopy, in particular super-resolution, is nationally unique and highly competitive internationally. Important is the combination of state-of-the-art instruments and expert support that our staff scientist give users. ALM has been selected as one of the first sites world-wide for the Lattice Light Sheet built by Carl Zeiss (AIC Janelia Farm and Betzigs lab is the first). Our in-house development of MFM-SIM further broaden our support for live-cell super-resolution microscopy projects. The nanoscale dynamical STED-FCS platform and its connected in-house competence is nationally unique and internationally competitive.

User base

The user base has expanded when more imaging techniques and more expertise has become available. During 2013-2016, ALM supported approximately 20 projects/year, all in super-resolution techniques (SIM, STED, PALM/STORM). With the introduction of light sheet microscopy and FCS techniques, including expert staff, the number of projects has increased to approximately 50 per year.

The majority of users are from Swedish Universities and have research questions where the exploratory and experimental character of advanced microscopy, in particular super-resolution, is of great value. We foresee that the number of international users will increase with the Swedish participation in EuroBioimaging and the activities for an increased mobility among European imaging facilities.

Nation-wide accessibility and training

ALM is the hub for the National Microscopy Infrastructure (NMI) and operate a web portal that handle user projects (http://www.nmisweden.se). The NMI website is very active and function as the "goto" site for microscopy in Sweden. ALM and NMI organize courses, workshops, seminars and road-trips to educate and inform users nationwide.

Data reproducibility, quality, and storage

Quality of data is a critical component in data driven science. ALM has well-established routines for calibration and alignment of all microscopes against resolution and sensitivity standards. Staff scientists at ALM operate a weekly routine for calibration of instruments in the facility.

ALM use an OMERO data infrastructure with support from SciLifeLab data center. OMERO is used for data storage, transfer, and analysis during a user project. ALM has the responsibility for data during the project. The responsibility for long term storage is transferred to the PI (user) when the project is finished and closed in the project portal. The OMERO database is also used as a SciLifeLab IDR (image data repository). We have initiated a project with the SciLifeLab data center to make this IDR publicly available and the main repository for SciLifeLab image data.

User fee

ALM do not charge a fee for academic users. Users pay the cost for consumables in their projects. Staff, premises and instrument costs are covered by the facility budget.

Research environment

The ALM facility is associated with and supported by the Biophysics unit at the dept of Applied Physics, KTH. The Biophysics unit is located at SciLifeLab and has 57 active researchers working in development of biophysical measurement and analysis techniques, including the development of new super-resolution imaging. The research environment includes two SciLifeLab research fellows, Ilaria Testa, KTH developing super-resolution RESOLFT and related techniques, and Erdinc Sezgin, KI, developing methods in STED-FCS.

Synergies at SciLifeLab

ALM has strong synergies and share capabilities with the nodes in NMI that are proposed to become facilities in SciLifeLab - CCI at GU, BICU/UCEM at UmU, IVMSU at SU - as well as with the facilities in the TSO unit. ALM also collaborate with the BIIF facility in the Bioinformatics platform.

Collaborations with healthcare, industry and other organizations

Super-resolution imaging, nanoscale dynamical investigations, and fast imaging on tissue and organism scale are all methods of interest for healthcare and industry, however the direct use is still limited. ALM and NMI organize outreach and training sessions with open invitation to the non-academic sector to increase the transfer of knowledge and stimulate the use of all ALM microscopy modalities to new user categories.

Alternative infrastructures

Access to the combined expertise and advanced instrumentation that ALM offers is not available elsewhere in Sweden. A few similar microscopes can be found at some facilities or research labs in Swedish Universities, however generally not accessible or possible to use for external users and non-experts. Internationally, Swedish users can

apply and possibly gain access to a similar combination of support expertise and microscopes at the EMBL ALMF and at the AIC, Janelia Farm.

Budget 2021–2024

The ALM facility request an increase of budget with 1.4 MSEK to fund the operation of the new lattice light sheet microscope (1 staff scientist and running costs). The other new technologies for 2021-2024 are already funded with other means (MFM-SIM by a grant from SSF-ITM and SciLifeLab TDP, STED-FCS is funded by an SSF-RIF grant).

The introduction of conventional light sheet microscopy at ALM saw a strong increase in number of projects. Similarly, several Swedish research groups have already asked for early access (as soon as it is installed) to the new lattice light sheet microscope. We expect that there will be a strong increase in number of projects for the new technology, and thus we need to recruit a staff scientist for user support in lattice light sheet microscopy.

Costs	2020	2021	2022	2023	2024
Personnel (4.5 FTEs)	5 075	5 075	5 075	5 075	5 075
Operations	450	450	450	450	450
Premises	1 044	1 044	1 044	1 044	1 044
Instrument depreciations	2 400	2 300	1 600	1 600	1 600
Other	640	640	640	640	640
Sum costs (kSEK):	9 609	9 509	8 809	8 809	8 809

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	3 400	4 800	4 800	4 800	4 800
University funding	1 609	1 609	2 409	2 409	2 409
SSF RIF	3 000	1 500			
VR NMI	1 600	1 600	1 600	1 600	1 600
User fees					
Sum revenues (kSEK):	9 609	9 509	8 809	8 809	8 809

Table 1. Current budget (2020) and suggested budget 2021–2024

Biochemical Imaging Centre Umeå/Umeå Core facility for Electron Microscopy (candidate)

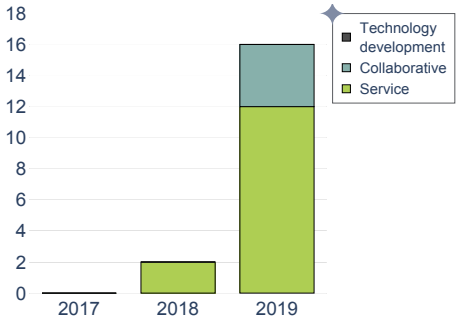
Read more: Web page, Publication Data Base

Basic Information

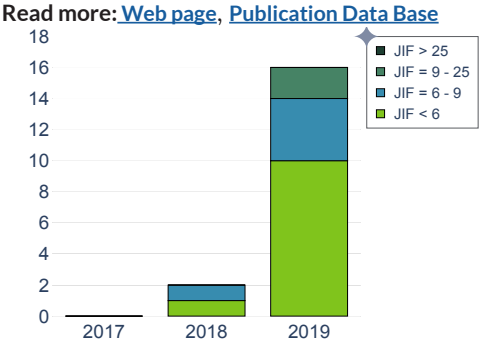
Facility director: Lina Sandblad, Richard Lundmark
Head of facility: Cheng Choo Lee, Irene Martinez Carrasco
SciLifeLab facility since: N/A
Host University: UmU
FTEs: 3.2
FTEs financed by SciLifeLab: 0

Funding 2020 (in kSEK)

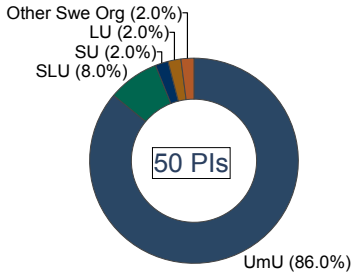
SciLifeLab: 0
Total: 3900



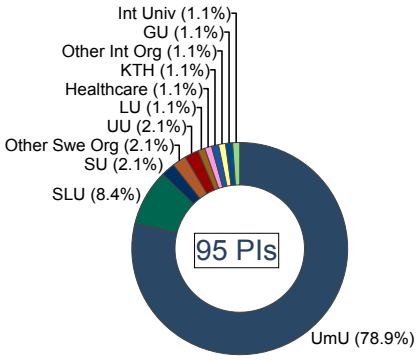
Publications by category



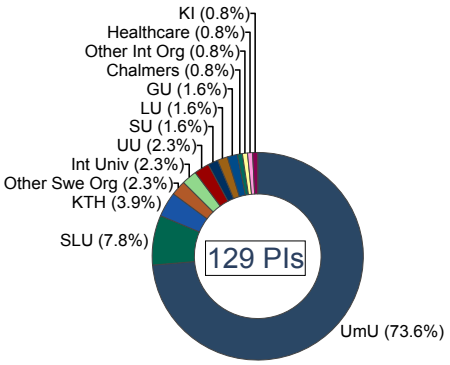
Publications by JIF



Users 2017



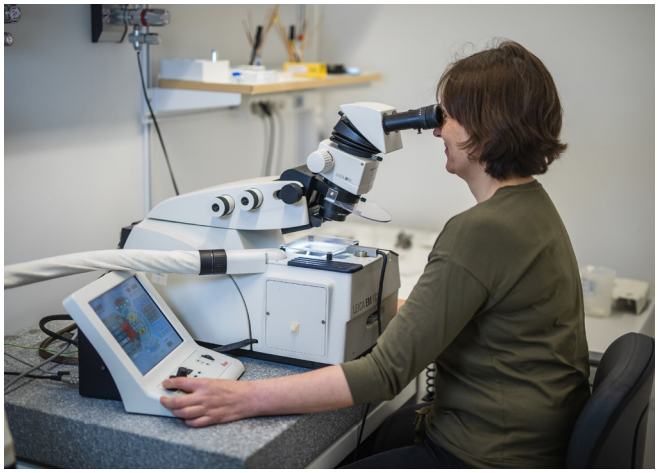
Users 2018



Users 2019

Current Technologies and Services

- Focused Ion Beam Scanning Electron Microscopy (FIB-SEM). The instrument Scios DualBeam used for cellular and tissue volume imaging.
- 3D volume image reconstruction. Graphics computer access for software packages Imaris, Amira and IMOD, seven bookable workstations.
- FIB-SEM and nanometer precision manipulation for material analyzes.
- Project-optimized correlative light and electron microscopy (CLEM) methods. Facility staff and the user group design a CLEM workflow together, based on our broad range of experiences including project support from start to end.
- Umeå Core facility for Electron Microscopy (UCEM), providing service and user training on six different EM instrument, SEM instruments Zeiss Merlin with a field emission gun for high resolution surface imaging and Zeiss Evo, both with chemical element analysis detectors and Jeol 1230 TEM, (also including SciLifeLab Cryo-EM node instruments in Umeå). EM sample preparation including high pressure freezing (HPF) and automated freeze substitution (AFS) and tissue-processing microwave for fast fixation, dehydration, polymer



infiltration and imaging contrast optimization, the ultra-microtomes in low humidity lab with user access.

- Biochemical Imaging Centre Umeå (BICU) – providing service and user training, including core facility fluorescence, light and live imaging microscopy, Atomic Force Microscopes (AFM) and affinity measurements

New Technologies and Services 2021–2024

- Improved sample preparation for FIB-SEM volume imaging, a selection of protocols for polymer embedding and contrast staining of different sample types, organisms, biopsies, tissue, plants and bacteria biofilms.
- Extended 3D image reconstruction and cell and tissue modeling support and service.
- CLEM method development, at both room and cryo temperatures, a new Leica Thunder microscope with cryo stage is already installed, and new chemical methods for gold coupled affinity tags in collaboration with CBCS nod in Umeå, are being planned.
- Large field of view 3D volume imaging of tissue, organs, organisms and other soft material. The existing Zeiss Merlin SEM will be upgraded with a Gatan 3View system, a SEM-in-chamber diamond knife ultra-microtome.
- Screening system for long time-lapse imaging under special cell culture conditions, IncuCyte, in form of a new industrial collaboration.

Background

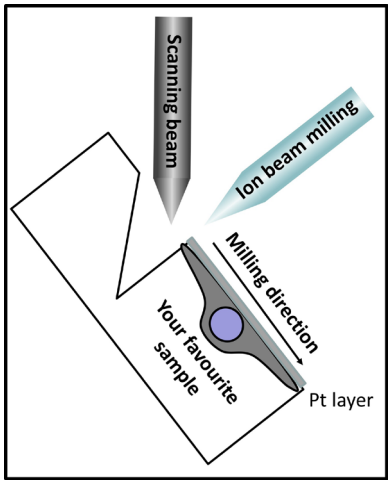
UCEM and BICU together constitute the facilities for imaging at Umeå University, established through collaborations between the strong research centra; UCMR, MIMS, KBC, UPSC and WCMM. Linda Sandblad and Richard Lundmark initiated the UCEM-BICU joint facility management, extended the staff team (today ten FTE) and established a national CLEM facility, which 2016 resulted in the Umeå NMI node. FIB-SEM and conventional room temperature EM technologies of UCEM was until now not SciLifeLab integrated. Solely our cryo-EM instruments, installed in 2016 joined the national cryo-EM facility at SciLifeLab.

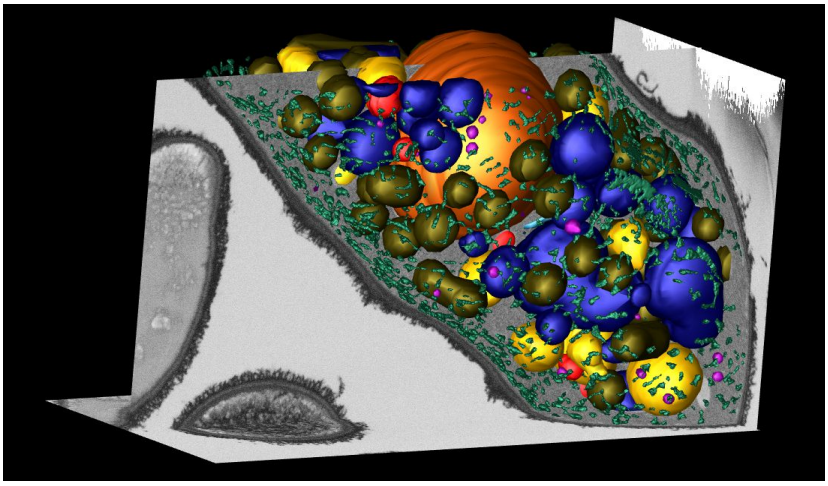
The acquisition of new microscopes and methodologies at UCEM and BICU is typically initiated by university research groups and funded by grants from e.g. the KAW and Kempe foundations, whereas the facilities maintain, service and provide the user training. We have built a user facility, where both students and experienced researcher can use and learn imaging methods and perform experiments in the facility lab. Excellent technical competence combined with user training and flexible project support makes for a unique research infrastructure environment that users from all of Sweden (and international) frequently visit and acknowledge personal support and the scientific involvement of the staff.

The facility environment with experienced staff and complementary instruments and techniques generates a roboust workflow for optimization of the sample preparation, and sample quality control (TEM and ligth microscopy) required for FIB-SEM analysis. Thus, we are able to support a wide range of research projects with specifically adapted volume imaging. We optimize sample preparation for EM, from conventional EM chemical fixation to alternative, often sample specific, methods with the ambition to enable CLEM and immunolabeling techniques for best possible image quality. For example, HPF-AFS, a cryo fixation method that avoids protein aggregation during fixation and involves dehydration at -90°C, which enables lowicryl infiltration and a non-destructive membrane preservation for in situ cell morphology imaging and both fluorescence and immunogold detection by CLEM. Recently implementation of microwave supported resin infiltration and metal staining have resulted in nice contrast imaging by SEM, which is the basis for large field of view detection of biological material in SEM and sequential FIB milling for volume data acquisition.

Plans for 2021–2024

New technologies/services: FIB-SEM volume imaging, for 3D visualization of cells and cell-cell contacts in tissue, has recently been implemented at the facility and we aim to further broaden our expertise on more diverse biological





and material samples. To fully utilize the method, we will extend the computational visualisation and modelling support, at the local facility and in collaboration with the Facility for Image Analysis in Uppsala. Further, a future installation of a Gatan 3View system (in-SEM diamond knife) in our current Merlin instrument will give volume imaging with a larger field of view. The methods are very complementary, since FIB-SEM offer higher resolution in x, y, z in a subcellular volume and 3View opens for a faster and larger field of view data collection.

Uniqueness and international competition: TFS Scios DualBeal FIB-SEM is the only instrument of its kind in Sweden today, it is especially designed for FIB nano-manipulation of biological material at both room temperature and cryo-conditions. Together with the surrounding imaging facilities of, three SEM instrument provide an unique experimental research environment, where most user needs are satisfied, including element analysis, environmental SEM and variable electron detectors at Merlin and Evo. Equal instruments and expertise are today only found abroad, e.g. at EMBL in Germany.

Expected user base: Conventional thin-section EM of cells is routinely performed locally at Swedish universities and used by a large fraction of the Swedish cell biology community. Since the same samples used for thin-section EM can be imaged by FIB-SEM volume imaging, the potential user base is very broad. At UCEM and BICU, researchers from all science disciplines, national and international users additionally will have access to to HPF-AFS, tomography, cryo ultra-microtome sectioning, cryo SEM, CLEM and the collected sample preparation expertise of UCEM and BICU. We believe that the awareness of the possibilities of FIB-SEM is still not spread according to its potential. Other organisations such as FOI, Norrlands University Hospital, RI.SE (industrial cellulose research projects) and National history museum (consultation) profit from our expertise already.

Accessibility: The facility is open and provides the same rules for access for all academic research, application through the NMI portal at SciLifeLab.

Reproducibility, quality, and data storage: Facility staff with extensive microscopy experience work together with users, all data are transferred and temporary stored on the 300 TB server at UmU, with individual user logins and remote access, including IT and image processing support.

User fee model: User fees cover all consumables and will depend on funding, eventually gradually increased to a level to sustainably cover instrument service costs.

Associated research groups that are contributing to the development: UCEM-BICU method development and new instrument investments are always in close collaboration with local research groups. Lundmark's group use CLEM in cell biology, Carlson's group develop FIB methods for infection studies. Uhlin's group has contributed with SEM and AFM systems and Sandblad's group initiated Cryo-EM.

Budget 2021–2024

Electron tomography volume imaging of cells and tissue is slowly attracting more and more national users to Umeå, frequent external visitors require support time by dedicated first research engineers. The extended SciLifeLab budget, will complement the UCEM-BICU facility environment with new facility staff to sustain FIB-SEM and the surrounding correlative work flow, and establish new autoFIB software on Scios BualBeam and new volume imaging tools (Gatan 3View) build in to our current SEMs (Zeiss Merlin FE-SEM).

Costs	2020	2021	2022	2023	2024
Personnel (4,5 FTEs), 2 for UCEM FIB-SEM, 1 for BICU, 1 for CLEM, 0,5 for IT	2 569	3 931	4 010	4 090	4 172
Operations	250	350	350	350	350
Premises	586	598	610	622	634
Instrument depreciations	2 040	2 040	-	-	-
Instrument service costs	550	550	650	650	650
Sum costs (kSEK):	5 995	7 469	5 619	5 712	5 806

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding		1 500	1 500	1 500	1 500
University funding (central for NMI, KBC, Med-infra)	2 150	2 150	1 550	1 550	1 550
National Microsciopy Infrastructure (NMI) VR-RFI	1 750	1 750	1 750	1 750	1 750
User fees	1 200	1 200	1 400	1 400	1 600
Sum revenues (kSEK):	5 100	6 600	6 200	6 200	6 400

Table 1. Current budget (2020) and suggested budget 2021–2024

Centre for Cellular Imaging (candidate)

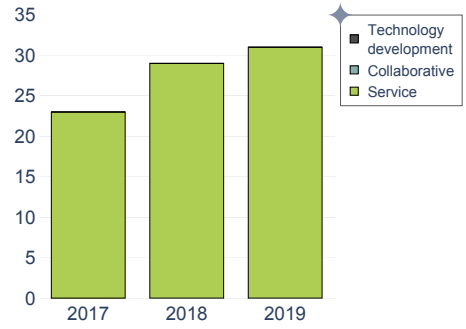
Read more: Web page, Publication Data Base

Basic Information

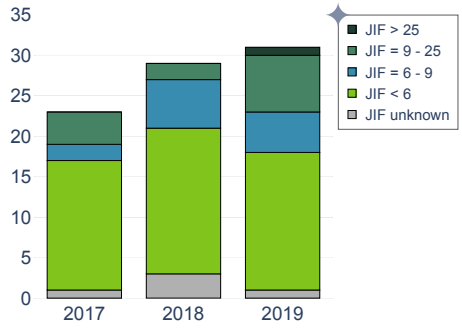
Facility director: Julia Fernandez-Rodriguez
Head of facility: Julia Fernandez-Rodriguez
SciLifeLab facility since: N/A
Host University: GU
FTEs: 7
FTEs financed by SciLifeLab: 0

Funding 2020 (in kSEK)

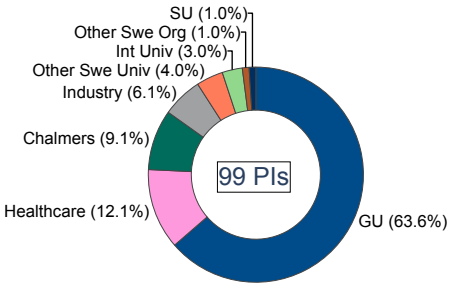
SciLifeLab: 0
Total: 9870



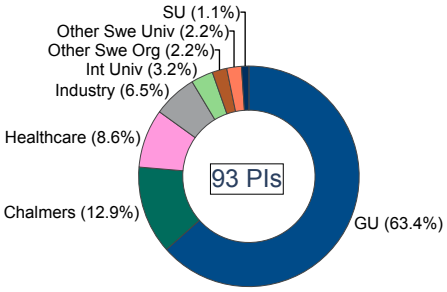
Publications by category



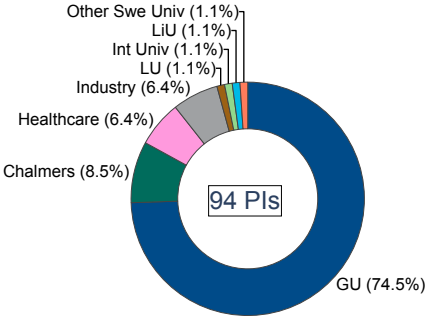
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

- 3D Super-resolution Structured illumination and Single Molecule Localization Microscopy
- Functional Microscopy: FRET, FRAP and Fluorescence Correlation Spectroscopy (FCS)
- Correlative Light Electron Microscopy (CLEM)
- Laser Scanning Confocal and Multiphoton microscopy
- Transmission Electron microscopy, Electron tomography and Scanning Electron microscopy

New Technologies and Services 2021–2024

- Cellular 3D volume – Correlative Array Tomography of large biological samples

Background

The CCI has been in operation since 2003, and is one of the advanced technology platforms at the University of Gothenburg. It is also part of the Swedish National Microscopy Infrastrucre (NMI) since 2016. This multimodal advanced microscopy facility provides technical and scientific excellence by the integration of multiple imaging technologies, which currently totals 12 microscopy-based imaging systems, together with image processing and analysis tools in a single core multi-user facility. The CCI specializes in three dimensional (3D) correlative multimodal imaging (CMI). CMI gathers information from a specimen with two or more imaging modalities that – when combined –create a highly informative, composite view of the sample. It is a holistic approach that spans the entire resolution range from nano- to millimeters, and provides complementary information about structure, function, dynamics and molecular composition of the sample. CMI is the only way to understand cells, cellular networks, organisms and diseases mechanistically by deciphering their molecular mechanisms within their native context. CMI integrates the best features of the combined imaging techniques and overcomes limitations that would be faced when applying single modalities independently. Consequently, 2 innovative technologies are today provided by the CCI: *correlative light/electron microscopy (CLEM), and functional microscopy for quantitative studies of molecular mobility in live cells by using Fluorescence Correlation Spectroscopy*: providing researchers with consultation and training on experimental design from sample preparation to image acquisition and data analysis. Our mission is to ensure that every scientist within the CCI is provided with expert imaging services and state-of-the-art equipment to answer any research question; from in vitro to in vivo, from nano- to millimeters, from morphology to mechanism. This includes not only analysis of 3D structures, but also the development of new methods for CMI to make imaging studies across scales routine, and to facilitate the use of resources by biomedical researchers. The CCI is also offering a variety of methods highly customizable to the individual projects' requirements, including conventional scanning and transmission electron microscopy and advanced light microscopy. The organization and administration of CCI is conducted

by the "Core Facilities", which is an organization within Sahlgrenska Academy at the University of Gothenburg. The success of the CCI is a result of well-maintained instruments and ancillary equipment, which facilitate both state-of-the-art and innovative research, in combination with a permanent scientific and well-trained technical staff and an open access policy: *Rafael Camacho Dejay*, PhD Chemistry, expert image analysis and advanced light microscopy; *Haijiang Zhang*, PhD Bio-nanotechnology, advanced light microscopy and microfabrication; *Maria Smedh*, PhD Physics, advanced light microscopy; *Charlotte Hamngren Blomqvist*, PhD Physics, expert in CLEM and CAT; *Anna Pielach*, PhD Biology, electron Microscopy; *Pauline Belzanne*, MSc Biomedical Engineering, image analysis. *Julia Fernandez-Rodriguez*, PhD Biochemistry, Head and expert in light/electron microscopy.

Plans for 2021–2024

The CCI *aims at extending its activities through providing a service for Cellular 3D volume – Correlative Array Tomography (CAT) that will integrate and complement the services currently offered by the SciLifeLab Advanced Light Microscopy facility*. Many biological functions depend critically upon fine details of tissue molecular architecture that have resisted exploration by existing imaging techniques. Array tomography encompasses light and electron microscopy modalities that offer unparalleled opportunities to explore 3D cellular architectures of large samples in extremely fine structural and molecular detail. Fluorescence array tomography achieves much higher resolution and molecular multiplexing than most other fluorescence microscopy methods, while electron array tomography can capture 3D ultrastructure much more easily and rapidly than traditional serial-section electron microscopy methods. The correlative mode of array tomography furthermore offers a unique capacity to merge the molecular discrimination strengths of multichannel fluorescence microscopy with the ultrastructural imaging strengths of electron microscopy. Biological processes can be studied within their overall spatio-temporal context, and pathologies and diseases can be targeted down to an individual cell and underlying molecular events. Additionally, the sequential combination and application of techniques to the same specimen and region of interest also allows validation single-modality conclusions since each technique can provide unique information based on fundamentally different contrast mechanisms. The CCI purchased in 2019 a *scanning electron microscope, Zeiss GeminiSEM 450, combined with an Automated Tape Collecting Ultramicrotome (collects hundreds to thousands of sections on a continuous tape) and the Atlas 5 Array Tomography software package*. Consequently, 2 innovative correlative technologies are being implemented at the CCI: *CAT and CLEM*: providing researchers with consultation and training on experimental design from sample preparation to image acquisition and data processing and analysis. CAT is expected to lead to significant new discoveries across the fields of biology and medicine, bridging the gap between micro and nano worlds.

Motivation – The full CAT system *is the only kind in Sweden. Hence, this new technology will cover the current state-of-the-art in volume electron microscopy imaging applied to very large and complex biological samples*, including neural circuits, organs (e.g. pancreas, kidney, heart), small model organisms and subcellular organelle networks. Based on methods for constructing and repeatedly staining and imaging ordered arrays of ultrathin resin-embedded serial sections on glass slides, silicon wafers or tapes, array tomography allows for quantitative, high-resolution, large-field volumetric imaging of large numbers of antigens, fluorescent proteins, and ultrastructure in individual tissue specimens. This will contribute further to the understanding of the complex 3D architecture of tissues in their natural context, which is crucial for gaining understanding of the structure function correlation in biological systems, and especially to resolve questions not possible to dissect with conventional scanning or transmission electron microscopy techniques. Other important advantages: i) it enables *robust registration between the light and electron microscopy*, because the same array of ultrathin sections is imaged with the two modalities; ii) CAT, as *non-destructive system* compare to en-bloc techniques (FIB-SEM and SB-SEM), permits a certain level of flexibility in experimental design. *Additional rounds of immunostaining can be added.* Subsequently, upon completion of the electron microscopic imaging, the **s***amples can be revisited again at a later time and reimaged at the SEM at a different magnification*, or in a different region. The image stacks on interest can be examined with new questions in mind; and finally, iii) when targeting *rare or specific events* within large populations or tissues, CAT is increasingly being recognized as "the method of choice".

User, accessibility, data – The CCI is an open-access facility that offers a variety of advanced microscopy-related services and training for all researcher groups in Gothenburg, scientific collaborators and also external researchers from other institutions as well as from industry. In order to create an easy and transparent user access the CCI has established a commercial core facility management system (*iLab Solutions*) to support an on-line contact sheet. This contact form is used to request access to the facility for: equipment reservation, usage tracking, billing and reporting. In addition, the national CCI users are applying for use of the facility via the NMI web project portal (http://nmisweden.se). Although, the CAT technology has been offered to the user community since November 2019, we have already 6 projects in the pipe-line. This demand shows the importance of these new technology. The potential upgrade of CCI as a Scilifelab Node will give visibility to the facility, allowing us to expand our professional technical and scientific support,

hence, we expect an important increase in the number users for this technology. Currently, the CCI works on a fee-for-service model, no co-authorship in publications is required or demanded, the intellectual property belongs to users except where other arrangements have been made, and CCI does not own scientific projects but does maintain close interactions with the research community. All investigators that pay user fees have equal access to the equipment and the technical assistance from the staff scientists regardless of their host organization. Trained users have access to the facility 24 hours/day, 7 days a week. The CCI handles and store primary image data only temporarily for quality control and analysis. Long-term storage is however the responsibility of the individual researchers utilizing CCI. For short-term data storage and transfer CCI is using a NAS server, and for remote random access of data in preparation for analysis the HIVE platform (https://www.acquifer.de/data-solutions/). At present, the CCI is sufficiently well supported by internal 10Gb networks connecting microscopes and servers.

Research environment and collaborations – In Gothenburg, expert competence is located within a very focused geographic area: Sahlgrenska University Hospital, University of Gothenburg, Chalmers University of Technology and industry of different size in the biotech and biomedical sphere. The CCI plays an increasing role in the advancement of knowledge and technology and their exploitation in and around Gothenburg, by offering high quality imaging research services, by attracting young people to science and by networking with other national and international facilities. The CCI is active at the interface between methodological developments and providing service to our community of users, and plays a key role in making advanced methods accessible to a larger number of researchers. Consequently, the CCI operates in close collaboration with research groups using advanced imaging methods: *Martin Johansson*, *Jan Borén*, *Patrik Rorsman*, *Gunnar Hansson*, *Carina Mallard*, *Åsa Tivesten*, *Max Levin*, *Jenny Nyström*, among others researcher groups, which all play key roles in advanced knowledge transfer. In addition to the national, regional and local collaboration with other imaging facilities within Sweden, the CCI has common meetings and active cooperation with the corresponding imaging national networks in Finland, Denmark and Norway. The CCI is a member of the Board of the Nordic Microscopy Society (SCANDEM) and the Bridging Nordic Microscopy Infrastructure. On the European landscape, the CCI is also well connected to several other European facilities, through the European Light Microscopy Initiative, ELMI (member of the Steering committee), and with the Euro-BioImaging ERIC consortium (member of the Nodes Board). The CCI is also a member of the Core Facilities for Life Sciences (CTLS) Association (https://www.ctls-org.eu/), (CCI Head is the Vice-president). Further, CCI represents Sweden in the Management Committee and is the Coordinator of the Short Term Scientific Missions of 2 COST Actions: NEUBIAS (CA15124) -funded network of bioimage analysts (http://eubias.org/NEUBIAS/venue/); and, COMULIS (CA17121) -funded network in Correlated Multimodal Imaging in Life Sciences (https://www.comulis.eu/). On the industrial site the CCI is a Lab@Location partners to Carl Zeiss since 2015 (https://www.zeiss.com/microscopy/int/service-support/microscopy-customer-center.html)

Budget

In order to support its increased activities in relation to SciLife lab, the CCI would need: a senior application expert in electron microscopy, and in particular in field emission scanning electron microscopy-based techniques, who will take responsibility for the full chain of activities involved from experimental planning, sample preparation, measurements, data retrieval, analysis and interpretation of the EM imaging. And some fund for basic operations of this expansion.

Costs	2020	2021	2022	2023	2024
Personnel at CCI (7 FTEs)	4 661	4 754	4 849	4 945	5 050
Operations	2 000	2 000	2 000	2 000	2 000
Premises	50	50	50	50	50
Instrument depreciations (existing equipment at CCI)	2 500	2 300	2 200	2 000	1 500
Correlative Array Tomography (1 FTE)	-	800	800	800	800
Other (OH)	1 100	1 140	850	850	850
Sum costs (kSEK):	10 311	11 044	10 749	10 645	10 250

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding		1 500	1 500	1 500	1 500
University funding	4 970	4 970	4 970	4 970	4 970
SSF	2 800	2 800	-	-	-
Swedish Research Council	1 600	1 600	1 600	1 600	1 600
Lundberg Foundation	500	500	500	-	-
User fees	2 000	2 200	2 200	2 200	2 200
Sum revenues (kSEK):	11 870	13 570	10 770	10 270	10 270

Table 1. Current budget (2020) and suggested budget 2021–2024

Intravital Microscopy (candidate)

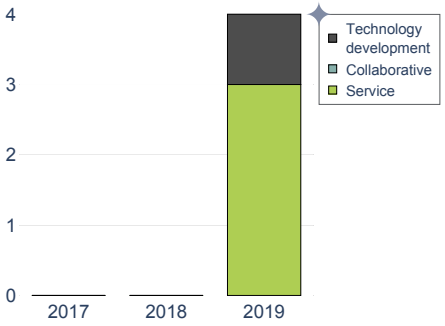
Read more: Web page, Publication Data Base

Basic Information

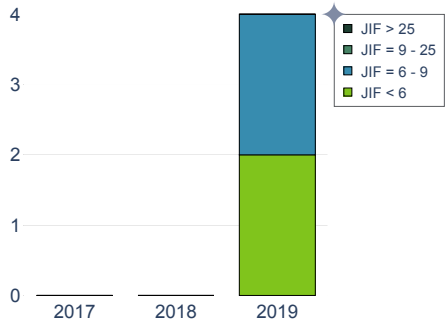
Facility director: Edouard Pesquet
Head of facility: Christiane Peuckert
SciLifeLab facility since: N/A
Host University: SU
FTEs: 1
FTEs financed by SciLifeLab: 0

Funding 2020 (in kSEK)

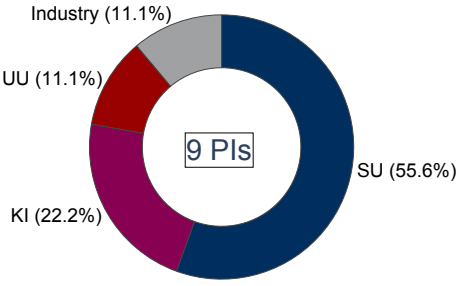
SciLifeLab: 0
Total: 4800



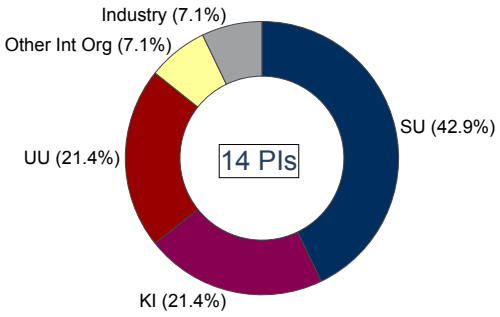
Publications by category



Publications by JIF



Users 2018



Users 2019

Current Technologies and Services

The facility for *in vivo* high-resolution multiphoton microscopy at Stockholm University (IVMSU) opened in Sept 2018 and offers unique possibilities to perform deep spectral imaging in a large range of biological samples. In contrast to other imaging facilities, IVMSU is legally authorized to image a wide spectrum of living samples ranging from single cells to whole animals. IVMSU's open-access policy makes this unique imaging possibility open to users nation-wide. IVMSU does not only provide access to on-site technical cutting edge expertise prior, during and post-imaging but also allows housing/caring of living specimen prior to and during imaging for longer time periods (days, weeks, months). IVMSU's wide range of authorized samples include cell cultures, fish, insects, plants as well as living rodents, which can be either imaged under living, non-treated conditions, or after genetic modification and/or treatment with chemical and/or biological agents. The key technologies provided by IVMSU include:

- Two-photon confocal imaging.
- Fluorescence lifetime imaging (FLIM).
- Fluorescence emission and excitation spectral imaging.
- Second and third harmonics imaging.
- High-throughput imaging screening.

The key services provided by IVMSU include:

- Open access and living sample/specimen housing.
- Training in two-photon, FLIM and spectral imaging.
- Training and expertise in sample preparation, imaging, analysis and method development.

New Technologies and Services 2021–2024

IVMSU aims to further consolidate and expand its usefulness and access to researchers nation-wide. To do so, an imaging technology expert will be recruited to increase service capacity, and new equipment/software will be acquired to offer unique cutting edge technology, such as:

- Automated on-the-flight deconvolution of two-photon deep imaging.
- Near infrared (NIR) spectral imaging.
- Advanced FLIM analysis.
- Environmental chamber/holder for simultaneous imaging and behavioral recording.
- Authorisation to image additional living biological models.

Background

Description and development of the facility: IVMSU offers academic and industrial users nation-wide access to state-of-the-art imaging to visualize biological processes at molecular, cellular and organism levels. IVMSU can image a wide range of samples, such as biomaterials, cell cultures, tissue preparation, microorganisms and insects. Moreover, IVMSU is one of Europe's unique imaging

facilities authorised to image living animals sedated or not. IVMSU's unique "open access" setup, due to its location within a state-of-the-art Experimental Core Facility (ECF) at SU, allows users nation-wide to house their living samples prior and during imaging. Direct technical support from project preparation, sample preparation to data acquisition and analysis represent an asset of IVMSU to enable both a flexible and user-focused service. In addition, on-site training ensures that researchers can become independent users. Projects using high-resolution multiphoton spectral imaging are steadily increasing since 2018. A wide range of samples have already been analyzed in the facility (stem cells and cell lines, insects, plants, fixed tissue, fossilised bones, living rodents) from multiple Swedish academic users (SU, UU, KI) and industry (Leica). IVMSU has supported 9 projects in 2018 and 11 in 2019 on different types of samples. Publications from the projects using IVMSU's unique imaging equipment are already coming out eventhough the facility opened in the end of 2018.

Overview of the current technologies/services offered: The facility is equipped with two state-of-the-art Leica SP8 systems equipped with the latest spectral detectors, resonant- and FOV-scanners, and powered by a SpectraPhysics Insight Dual X3 multiphoton laser with dual excitation lines, one fixed at 1045 nm and one tuneable 680-1300 nm, as well as a tunable pulsed White Light Laser (470-670nm), Argon and six diode lasers for one-photon excitation.

Governance of the facility: IVMSU is a node within the VR-funded National Microscopy Infrastructure (NMI). It is physically located within the ECF and is financially supported by the Faculty of Sciences of SU and the Department of Molecular Biosciences, WGI (MBW).

Competence/ background of staff:

- Edouard Pesquet, PhD, Facility head - specialist in spectral imaging and microscopy.
- Christiane Peuckert, PhD, Facility manager – specialist in imaging in living animal models.
- Stina Tucker, PhD, Director of ECF– specialist in animal ethics and translational studies.

Plans for 2021–2024

New technologies/services planned for: The service capacity will be increased by recruiting an imaging technology expert to assist the Facility manager. New technologies and software will increase image analysis capacity. IVMSU's capacity will thus be enhanced to provide an internationally unprecedented range of samples that can be deeply and differently imaged for current and future needs of the Swedish scientific community.

National uniqueness and international competitiveness: The acquisition of new technologies/services will place IVMSU at the front-line of imaging using two-photon confocal spectral imaging for functional and translational studies from single cell to whole organism. The additional staff will allow IVMSU to fulfil this mission and provide a smooth and efficient access to all national users, regardless of model system or research question.

Expected user base for 2021–2024: Expected users of IVMSU include academia, health-care but also technology imaging companies and pharmaceutical industries performing drug response and monitoring of drug delivery translational studies. We further expect users from SVA, where the specific interest lies on the breadth and variety of *in vivo* samples (from parasites, insects to mink). Users need and diversity is already observed in the projects currently running at IVMSU, increasing by 20%/year between 2018 and 2019, and is expected to further broaden with the newest technology and service acquired thanks to SciLifeLab support.

Nation-wide user accessibility: Nation-wide information of the facility has been promoted through seminar tours to various Swedish institutions by both the Facility head and manager, and by the integration of IVMSU in the National Microscopy Infrastructure (NMI). NMI web site provides nation-wide visibility for IVMSU and its services, as well as an easily accessible online portal for project applications. The NMI portal also ensures an equal nation-wide access to IVMSU imaging technology and services independently of host institutions. IVMSU has an open-access policy to house and care for living samples for user nation-wide.

Reproducibility, quality, and storage of data: Standard operating procedures of IVMSU ensure proper and safe usage of the equipment. Existing routines for user training ensure appropriate education to perform reproducible imaging. Equipment performance is garantied by a full service contract with Leica Microsystems. Imaging data is stored on a local 8TB unit, accessible by the user, during the course of the project. Once the project finished, the user has full responsibility for the storage of the data.

User fee model applied for 2021–2024: IVMSU's user fees are aligned on the NMI to ensure standard price across all imaging facility to Swedish users.

- usage of 2P confocal microscopy systems:
  Standard sample – 300SEK/h
  Living animal models – 500SEK/h
- training in 2P confocal microscopy imaging:
  Standard samples – 2000SEK
  Living animal models – 4000SEK
  Surgical implantation of imaging window on living animal models – 2000SEK
- IVMSU assistance:
  On imaging– 1000SEK/h
  On surgery– 500SEK/window

Research environment contributing to the facility/unit: IVMSU shares a unique relationship with ECF which provides unique synergy for cross-over studies using whole-animal imaging and two-photon imaging on the same animal, as well as an exchange of expertise. IVMSU is also integrated and interacts with the multiple research departments of the Arrhenius Laboratories at SU. Two external leading laboratories in animal imaging – Dr. van Rheenen (the Netherlands Cancer Institute) and Dr. Hooper (Francis Crick Institute London) as well as Dr. Anderson, head of the Advanced Light Microscopy facility (Francis Crick Institute London) – also contribute to the development of IVMSU for latest procedures, updates and advices. The Facility head and manager also attend regular workshops and visit other institutes and imaging facilities to implement latest routines and updates.

Synergies within and with other SciLifeLab facilities/units: IVMSU collaborates with the ALM at the SciLifeLab, through the NMI consortium, by providing complemenatry equipment and expertise on imaging. NMI regular meetings, discussions and collaborative projects ensure the synergy and complementarity with other imaging facilities nation-wide.

Alternative local available to users? No "open-access" high-resolution multiphoton imaging facility for a comparable wide range of samples currently exist.

Swedish user perspective? IVMSU technology is not offered elsewhere, making SciLifeLab funding of the facility justified from a Swedish user perspective.

Budget 2021–2024

Costs	2020	2021	2022	2023	2024
Personnel (2 FTEs for IVMSU + salaries for support staff)	2 269	2 306	2 338	2 370	2 403
Operations	971	971	971	971	971
Premises	116	116	116	116	116
Instrument depreciations (MP microscope, equipment associated with ECF)	2 994	2 994	2 994	2 994	2 994
Other (travel, courses)	50	50	50	50	50
Sum costs (kSEK):	6 400	6 437	6 469	6 501	6 534

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding		1 500	1 500	1 500	1 500
University funding	1 800	1 800	2 050	2 050	2 050
VR	1 600	1 600	1 600	1 600	1 600
SFO for SciLifeLab	950	950			
Foundation Wallenberglaboratoriet och Biologilaboratoriet	1 950	450	450		
User fees	100	150	250	350	500
Sum revenues (kSEK):	6 400	6 450	5 850	5 500	5 650

Table 1. Current budget (2020) and suggested budget 2021–2024 for IVMSU. SciLifeLab funding will contribute to the running, upgrading, servicing and services of IVMSU and is essential to support IVMSU's nation-wide accessibility to Swedish researchers to high-resolution multiphoton imaging.

Cryo-EM

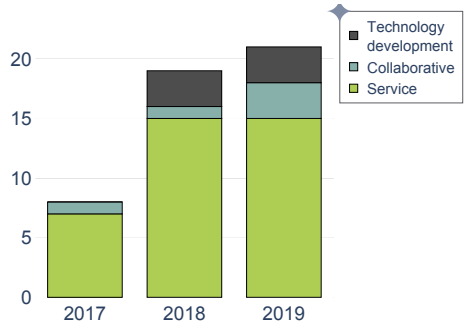
Read more: Web page, Publication Data Base

Basic Information

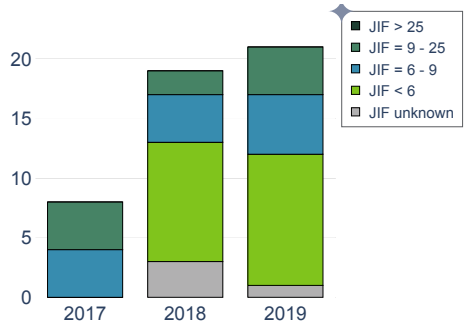
Facility director: Gunnar von Hejine, Linda Sandblad
Head of facility: Marta Carroni, Michael Hall
SciLifeLab facility since: 2016
Host University: SU, UmU
FTEs: 11.3
FTEs financed by SciLifeLab: 7.3

Funding 2020 (in kSEK)

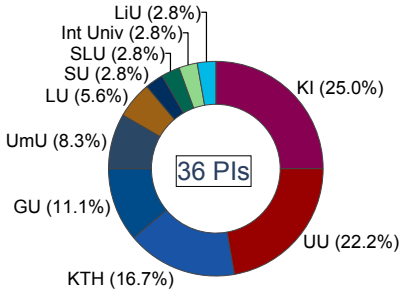
SciLifeLab: 8500
Total: 36161



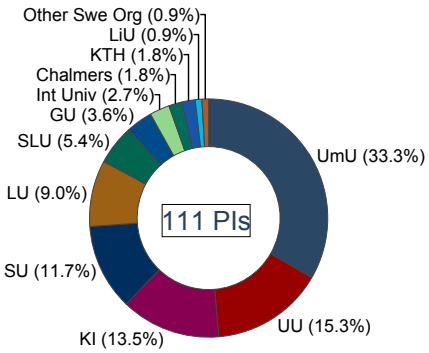
Publications by category



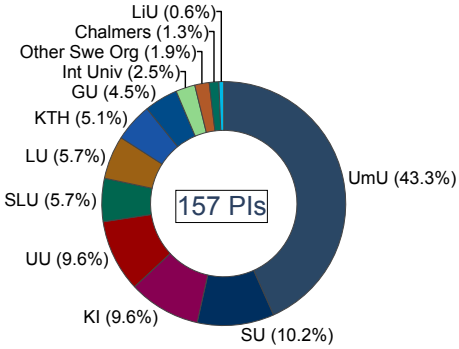
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

- Single-particle cryo-EM data acquisition on three 300 kV Titan Krios cryo-TEMs (two with Gatan K3 and one with Gatan K2 direct electron detectors, phase plates), one 200 kV Talos Arctica (Gatan K2 detector, phase plate).
- Cryo-tomography data acquisition on the above cryo-TEMs.
- Focused Ion Beam (FIB) milling for cryo-lamellae of cells with Scios DualBeam SEM.
- Screening by negative staining and conventional EM methods (Talos L120).
- Cryo-ultramicrotome sectioning.
- Cryo-EM project consultation and basic image processing.
- National training courses in sample preparation, data acquisition, and 3D image analysis.

New Technologies and Services 2021–2024

- National Grid Screening Network with personnel stationed at the universities in Lund (LU), Gothenburg (GU), Uppsala (UU), and Karolinska Institutet (KI), trained and coordinated from the Facility.
- Micro-electron diffraction on nanocrystals (micro-ED).
- Fluorescence imaging on vitreous EM grids for correlative microscopy (Leica THUNDER microscope with cryo stage compatible with cryo-EM autoloader available).
- Image processing support for specific user projects.

Background

The SciLifeLab National Cryo-EM Facility has two nodes (Solna and Umeå) that became operational in 2016-2017. Thanks to support from three major Swedish foundations (the Knut and Alice Wallenberg Foundation, the Family Erling Persson Foundation, the Kempe Foundations), and from SciLifeLab, Stockholm University (SU), and Umeå University (UmU), the Facility now has three top-of-the-line 300 kV cryo-electron microscopes and highly skilled personnel. The Facility has recently strengthened its expertise in cryo-tomography and is developing micro-ED and correlative fluorescence/electron microscopy as future services.

Together with MRC-LMB (Cambridge, UK), the Facility develops the heavily used Relion software for image processing, and is, together with the National Center for Biotechnology, Madrid, a co-developer of the Scipion cryo-EM image processing user interface. The Facility has initiated a collaboration with the MAX IV synchrotron on cryo-sample preparation for their new X-ray microscopy beamlines.

The Facility is currently led by two Directors (Linda Sandblad, UmU, and prof. Gunnar von Heijne, SU). Microscope time is allocated by a National Evaluation Committee, with representatives nominated by the main Swedish universities. The number of users has grown rapidly, and there are now ~150 registered PIs from across

Sweden using the Facility. The Facility services have been used in more than 50 publications so far. Sample screening, especially of vitreous samples on grids mounted for the cryo-EM autoloader systems, is a major bottleneck for the Facility operations. For many users, refinement and modeling of 3D structures is another major challenge. In both cases, the Facility and the National Grid Screening Network staff are/will be key to efficient and high-quality project support.

Plans for 2021–2024

New technologies/services. The most important development of the facility will be to organize and coordinate the National Grid Screening Network, together with users at LU, GU, UU, and KI. The National Grid Screening Network will also develop and coordinate image processing support. Together with UmU researchers, the Facility is developing cellular cryo-tomography by micropatterning on EM grids, which will enable better sample vitrification and beam access for both FIB and TEM. In collaboration with the EM material science group at SU (prof. Xiadong Zou), the Facility is developing a new sample-preparation technique for cryo-EM specimens and is implementing micro-ED techniques for the user community. Computational methods development (Relion, Scipion on-the-fly data processing, and shared coding libraries for the EM community) will be continued.

Uniqueness. The National Cryo-EM Facility has three of the four 300 kV Titan Krios microscopes currently available in Sweden (the fourth has just been installed at KI), and by far the best expertise in data collection and data analysis available in the country. Essentially all cryo-EM work done in Sweden today depends on the National Facility, and the planned additions to the Facility services will add to its usefulness.

User base. The user base is currently ~150 academic research groups spread across Sweden, and keeps growing. In addition, the Facility collaborates with cryo-EM facilities in Denmark, Finland, and Norway as part of the CryoNet program (funded by the Wallenberg Foundation and the Novo Nordisk Fund). A couple of projects have been done in collaboration with industry and research institutes such as FOI.

Nation-wide accessibility and training. The Cryo-EM Facility invests heavily in user training, both in the form of national courses in sample preparation and image processing, and in on-site training when users visit the Facility for data acquisition sessions. Time on the microscopes is allocated through an annual application for Block Allocation Grants (BAGs) where each university is awarded a certain number of 24 h data acquisition slots. A limited amount of microscope time is reserved for Rapid Access projects, mainly for new users not yet part of a BAG. The allocation decisions are taken by a National Evaluation Committee, with representatives for the main Swedish universities. Each BAG decides internally on how their allotted microscope time is divided between the participating research groups. This model is similar to the one used at, e.g., the Diamond facility in the UK.

Data quality and storage. Sample quality is evaluated by the Facility staff before grids are allowed to go to data acquisition, and initial image processing is also performed during data collection at the Facility before the data is shipped to the user. The Facility provides short-term data storage (currently 1 month, with servers accessible for users during active image processing and for remote data transfer), but does not have the capacity to permanently store all user data (the Facility currently produces 4-5 TB of data per day; this is expected to increase to 7-8 TB per day during 2020). New data compression algorithms are currently being implemented. Once a project is complete, users are required to upload images and processed data to the EBI databases EMPIAR and EMDB.

User fee model. The current fee (5,000 SEK/24 h) will need to be increased during the coming years to cover increased costs for service contracts.

Research environment. The Facility has close interactions with local cryo-EM research groups at SciLifeLab Solna (Amunts, Lindahl), SU (Zou, Drew, Högbom, Ott, Stenmark, Brzezinski, Ädelroth), and UmU WCMM groups (Carlson, Berntsson, Mir-Sanchis) and SciLifeLab Cryo-EM/MIMS (Barandun, Sandblad). These groups both use and help develop the Facility services. Facility staff further interacts closely with the staff at the cryo-EM facilities in Copenhagen and Aarhus through the CryoNet program.

Collaborations with healthcare, industry and organizations. See Platform Report.

Alternative infrastructures (academic or commercial). None in Sweden. A small number of users have obtained time at the Diamond facility in the UK or ESRF in France. Other, in principle open, facilities in Europe are NeCEN in Holland and EMBL in Germany.

Synergies and Collaborations. See Platform Report.

Budget 2021–2024

The Facility proposes an expansion of 3.5 MSEK/year to fund a National Grid Screening Network, set up to make it possible for researchers at the main Swedish universities (LU, GU, UU, KI) to screen and optimize grids locally, before sending them for data collection at the Facility. This will ensure a more efficient use of the Facility's high-end microscopes, will create a national network of skilled cryo-EM personnel, and will serve to bolster the cryo-EM expertise available locally at each university. The same personnel will also be

the first contact person for new users and for post-data collection questions, and will set up local user groups for image processing. 0.5 FTE will be funded at each of the four satellite universities; the Facility will organize and train the network personnel. Screening microscopes will be provided by the individual universities, including a possible new autoloader cryo-TEM system at UmU.

Costs	2020	2021	2022	2023	2024
Personnel (13 FTEs from 2021)	10 481	11 567	12 768	13 023	13 284
Operations	4 195	4 420	4 670	4 670	4 670
Premises	1 837	1 929	1 955	1 981	2 007
Instrument depreciations	18 763	17 082	13 055	12 157	10 795
Instrument service fees	3 649	6 944	8 390	8 526	8 666
National Screening Network (4x0.5 FTE)	-	2 000	2 000	2 000	2 000
Sum costs (kSEK):	38 925	43 943	42 838	42 357	41 421

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	8 500	12 000	12 000	12 000	12 000
University funding (SU+UmU)	5 150	5 150	5 150	5 000	5 000
Knut and Alice Wallenberg Foundation	18 137	17 487	17 037	15 410	12 622
Erling Persson Foundation	2 874	2 874	2 874	2 874	2 874
Kempe Foundations	700	-	-	-	-
Swedish Research Council	800	800	800	-	-
User fees	3 950	4 750	5 750	6 950	7 950
Sum revenue (kSEK):	40 111	43 061	43 611	42 234	40 446

Table 1. Current budget (2020) and suggested budget 2021–2024

Cell Profiling

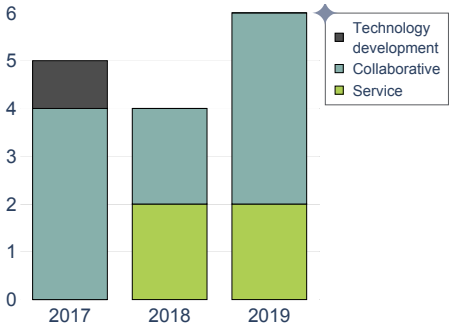
Read more: Web page, Publication Data Base

Basic Information

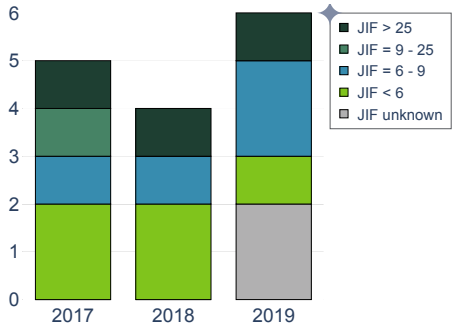
Facility director: Emma Lundberg
Head of facility: Charlotte Stadler
SciLifeLab facility since: 2013
Host University: KTH
FTEs: 4
FTEs financed by SciLifeLab: 2

Funding 2020 (in kSEK)

SciLifeLab: 3000
Total: 5150



Publications by category



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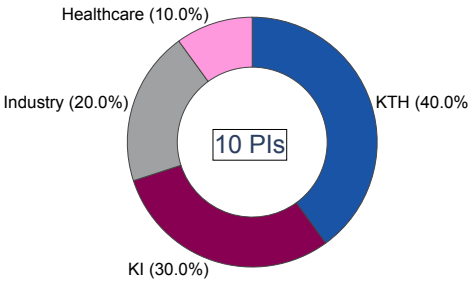
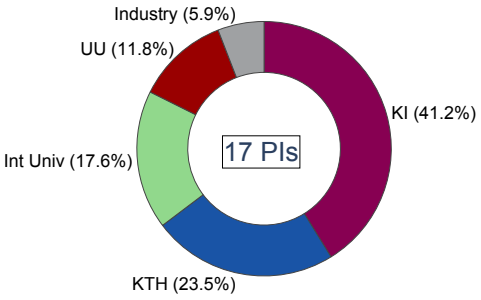
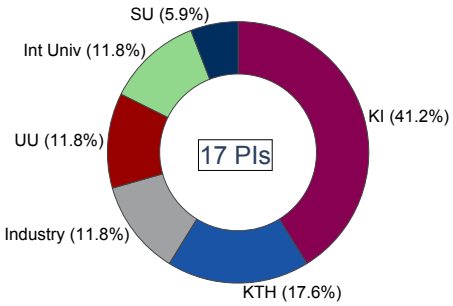


Users 2017



Users 2018



Users 2019

Current Technologies and Services

- Cell cultivation as part of immunofluorescence projects
- Automated high-throughput immunofluorescence of cells using HPA antibodies*
- Immunohistochemistry and immunofluorescence of tissue sections (FF and FFPE)
- Confocal and screening microscopy
- Highly multiplex imaging of proteins (20-30 plex) of FF and FFPE sections using the CODEX platform (from 2020).

**The facility has access to the unique proteome wide library of antibodies for human and rodent targets generated within the Human Protein Atlas project.*

New Technologies and Services 2021–2024

- All of the reported current services above
- Tissue sectioning of fresh frozen and paraffin embedded tissues
- In-house conjugation of antibodies for CODEX
- Advanced analysis support of highly multiplex imaging data from CODEX
- Delivery of user-friendly cytometric data from the CODEX platform
- In situ sequencing (ISS) and services described in the ISS Facility report*
- Multiplex RNA and DNA FISH and services described in the Advanced FISH technologies Facility report*
- RNA and DNA in-house probe design*

**If successful evaluation and funding for each of Cell Profiling, ISS and AFT facilities these technologies and services will expand the current Cell profiling Facility to form a new facility named Targeted Spatial Omics.*

Background

The Cell Profiling has been a SciLifeLab National Facility since 2013 and stem from the globally recognized Human protein Atlas Project, HPA (Uhlén et al, Science 2015, Thul et al Science 2017). Being involved in the Cell Atlas as part of HPA for more than a decade, the facility staff holds great experience of large-scale immunofluorescence experiments, antibody validation, confocal microscopy and image analysis. Further, the facility has access to the *world unique proteome wide library of polyclonal antibodies* (>50,000 antibodies representing 18,884 human genes) generated within HPA. These reagents are offered to facility users for exploring spatial biology in human and rodent tissues and cells. The facility user is charged only for the amount of antibody being used for the experiment, enabling hundreds of protein targets to be analyzed with confocal microscopy at a very limited cost. This gives unique and valuable opportunities to explore cellular responses at a much deeper level than ordinary phenotypic screens, as demonstrated in a study of amylotrophic laterhal sclerosis (Corman et al, *Cell Chemical Biology* 2018). The concept of the facility has been to offer full-service project support, from cell cultivation to image analysis, but also the flexibility to perform the sample preparation and staining only.

The facility shares labs, infrastructure and resources with the research group of Dr Emma Lundberg, who is also the Facility Director. In total, 4 employees are dedicated to facility activities, led by Dr Charlotte Stadler, Head of Facility. The governance and close integration with the research group enables more efficient and cost-effective activities and an overall higher capacity due to associated personnel from the research group. From the research of the Lundberg group, the facility benefit from expertise in advanced image analysis, programming, bioinformatics and AI, highly relevant in the era of data driven cell biology.

Recognized for the unique resource of antibodies and expertise in high throughput immunofluorescence for subcellular protein profiling, the facility is part of the National Microscopy Infrastructure (NMI) and is also a member of the European Proteomics Network EPIC-XS, since 2019. The NMI membership and funding for additional four years has recently been granted. The Lundberg Lab, including the facility, is an official reference site for Leica Microsystems and work closely together with their developer team to improve solutions for automated microscopy.

Driven by the growing need for deeper tissue profiling at single cell resolution, *the facility and the associated research group of Prof Lundberg, were selected as one out of ten labs worldwide to be part of an early access program in 2018 for a technology enabling highly multiplex imaging of up to 50 protein* markers at single cell resolution. The technology called CODEX, (co-Detection by inDEXing) is currently being integrated as a facility service to offer deep phenotypic profiling of single cells in tissue sections. Together with the Lundberg lab, the facility received several grants for continued development of this technology. Although not yet advertised, the facility has a line of projects to get started during spring 2020 from both national and international users.

Protein profiling of tissue sections using the CODEX platform

The data obtained from the CODEX platform, enables deep interrogation of tissues and a key application is to generate *multi parametric cellular maps at single cell resolution to uncover new phenotypes, insights to disease pathology, and find novel correlations of biomarkers and cell interactions.* Compared to other technologies developed for single cell profiling such as single cell RNA sequencing (scRNA seq) and flow-based methods like mass cytometry, the imaging approach retain the tissue architecture, and the spatial component is an important parameter for understanding tissue heterogeneity. The CODEX platform generates images of subcellular resolution and quantitative data of all markers for every cell in the tissue. Cytometric analysis is then used to identify distribution of cell phenotypes, proliferating cells, signaling events and any group of cells that can be distinguished from the panel of markers used. Because of this, highly multiplex imaging is currently being used in 4 clinical trials, for obtaining additional layers of information to be used in discovery and translational research.

The CODEX platform is the foundation of future plans to expand the Cell profiling facility with additional methods for highly multiplex spatial biology.

Plans for 2021–2024

Cell profiling expand to "Targeted Spatial Omics"

The overall future plan for Cell profiling is to extend on highly multiplex imaging methods and create a "*Targeted Spatial Omics*" (TSO) *facility* by merging with the In situ sequencing (ISS) facility, currently part of the Eukaryotic Single Cell Genomics (ESCG) and by integration of a new facility – Advanced FISH Technologies (AFT). The TSO will offer *emerging cutting edge technologies for highly multiplex profiling of targeted genes, transcripts and proteins at single cell level in fresh frozen and paraffin embedded tissue sections or cell cultures.* In this evaluation Cell Profiling, ISS and AFT will be evaluated separately, but our ambition is to combine these into one functional unit (TSO) to benefit from synergies both at operational and financial level. The ISS and AFT will be described in detail following the Cell Profiling Facility report.

Synergies and added value of combined Spatial Omics methods

Over the last years, advancement in single cell technologies such as single cell RNA sequencing (sc-RNA seq) and mass cytometry (CyTOF) has led to numerous new discoveries and revealed a complex plethora of cell phenotypes and single cell heterogeneity.

To fully understand human biology, individual cells should be studied in situ to explore their spatial relationships and cellular neighborhoods in a tissue context, which can only be obtained from imaging based methods. Further, combining multiple omics layers of single cell information provides deeper understanding by giving a complete map of components from genes, transcripts and proteins.

While the CODEX, ISS and advanced FISH technologies generate information from different omics, the output data share common structure with spatial components and quantitative measurements for each parameter/marker at single cell level. The complex and massive amount of data generated with spatial omics technologies provide synergies and mutual benefits also with the BioImage Informatics Facility (BIIF) and connected research to explore and develop analysis tools and AI models in the era of data driven cell biology.

The samples for each technology undergo similar preparation steps and require instrumentation common for tissue handling. This allows for shared resources not only from instrumentation but also from human resources. Expertise in tissue handling, microscope maintenance, image acquisition, and advanced analysis of spatial single cell data can be shared. Combining these technologies

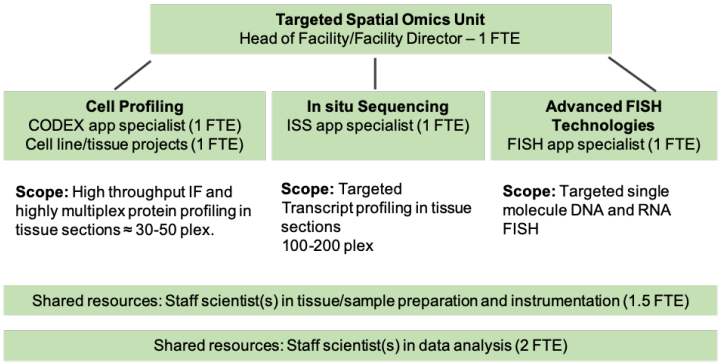


Figure 1. Organization and resources of the proposed TSO facility.

into one TSO facility as proposed, thus creates synergies, benefits and research opportunities beyond each technology on its own, illustrated in Figure 1 and further described in the Budget section of the report.

Unique services and cutting edge research

A key advantage of the current Cell Profiling and ISS facility respectively, is the close link to the SciLifeLab research groups of Prof Lundberg and Prof Nilsson, respectively. Via the integration of AFT, the research groups of Dr. Bienko and Dr. Crosetto will add additional links from research to the proposed TSO facility. The expertise and cutting edge research performed in the associated groups, provide additional opportunities for new discoveries and continued technology development of the facility service portfolio, and put the facility in a strong position to maintain emerging services both nationally and globally. The Lundberg and Nilsson research groups are already engaged in a joint flagship research project – The Human Developmental Cell Atlas (HDCA) – where ISS and CODEX are being used to profile fetal lung, heart and brain tissue, together with Prof. Linnarsson and Prof. Lundeberg, pioneering the respective field of sc-RNA seq and spatial transcriptomics. The spatial transcriptomics (ST/Visium) is provided as a service by the genomics platform and is an additional component of spatial biology technologies offered at SciLifeLab, by offering transcriptomics profiles at a *global untargeted level.* This transcriptional profiling can directly be connected with the targeted spatial omics technologies to explore global findings at deeper level and at higher spatial resolution.

Sweden has a world leading role in spatial molecular research thanks to strong research groups and funders like KAW. By embedding the facility into this environment, it has the potential to become the world leading facility for spatial biology. The ability to perform and generate data for several omics layers of information as in the suggested Targeted Spatial Omics facility is unique. However, this field is emerging rapidly and to leverage its full potential and make it accessible to other users of the Swedish research community it is crucial to invest in generating user friendly data at a high capacity as *we anticipate this field to become the next boom after sequencing.*

Facility user accessibility, external synergies and outreach

For a facility to be an asset to the research community at national scale, the technologies offered should not only be unique, but also preferentially allow for samples to easily be sent to the facility without loss of quality. For tissue sections, this is easily achieved and the facility therefore has the prerequisites for providing service independent on user location.

An overview of synergies and connections between the TSO unit and additional SciLifeLab facilities/platforms and external partners are illustrated in Figure 2.

From a SciLifeLab perspective, the synergies between the Mass spectrometry Imaging (MSI), BIIF Facility and the ST service as part of the genomics platform has already been mentioned. Further, the addition of *spatial components at single cell level* from the proposed TSO facility is a strong complement to other single cell technologies and thereby add natural links to the Eukaryotic single cell Genomics (ESCG) and Mass Cytometry facility. As an example, ST, scRNAseq smFISH. and ISS data were integrated to provide a first spatial map of molecularly defined cell types in human fetal hearts of different stages (Asp et al. *Cell*, 2019). Last, single cell spatial data from TSO is complementary to mass spectrometry derived data from the Proteogenomics Facility, to deeper explore findings from bulk populations, such as translocations upon various conditions. An example of such a project was recently published, confirming translocating proteins upon T-cell activation (Joshi et al, *Frontiers in Immunology*, 2019).

At a national level, the combined TSO facility benefit from being a member of the National Microscopy Infrastructure (NMI) and part of three SciLifeLab funded Research Community Programs - HPA, HDCA and the Swedish Tumor Microenvironment Network. The AFT is a partner of the global 4D Nucleome Consortia. Further, the proposed facility has an excellent channel of outreach via the associated research groups and via the connection to the Human Protein Atlas. In addition, the AFT Unit has budgeted 200 000 SEK for outsourcing the production of a professional video and brochure, which can be disseminated across researchers in Sweden and internationally.

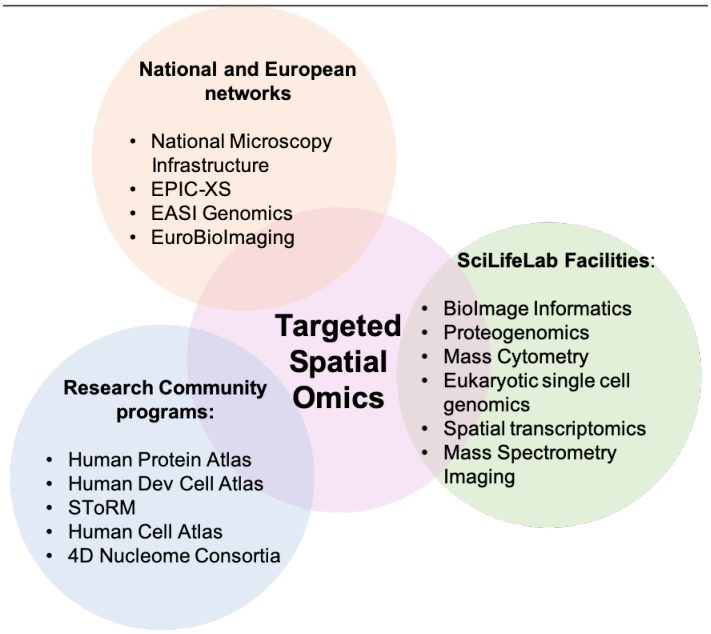


Figure 2. Connections of Targeted Spatial Omics with internal SciLifeLab infrastructure, national and global communities.

With start in 2019 and for the coming 3 years, the Cell profiling facility is a European access site for proteomics infrastructure as part of EPIC-XS consortia funded by the Horizon 2020 program. Similarly, the ISS facility is part of the EU network EASI Genomics infrastructure program. Being a partner in these European networks, as well as the EuroBioImaging, will allow the facility to extend its service and thus related research to the European arena.

Budget 2021–2024

The current Cell profiling Facility requests additional 1.3 MSEK from SciLifeLab to fund 1 FTE dedicated to analysis of high parametric data and increased operational costs (instruments). Currently the facility holds several additional grants, that will expire during the budget period. We intend to apply for additional grants to retain a stable total income of 6 MSEK/year. For the complete Targeted Spatial Omics Facility, additional funding of 1.9 + 1.8 MSEK is requested for integrating ISS and AFT service packages respectively, to contribute mainly to salary of an additional 3.5 FTE and increased total operational costs from these activities. In total the Targeted Spatial omics Facility would employ 8.5 FTE where 1 FTE act as Head/Director, 4 FTE are application specialists for CODEX, ISS and AFT respectively and 3,5 FTE are shared resources dedicated for tissue handling, sample preparation and data analysis of generated high parametric data. By the combined operations of Cell Profiling, ISS and AFT, the reduced total cost is estimated to be around 5 MSEK compared to operations as "stand alone" facilities. The cost model followed by current facilities and the proposed TSO facility will follow a non-profit model for Swedish academics (i.e., they will be charged only the costs of reagents, equipment maintenance and a smaller contribution to personnel work-hours for the service) and a full-cost-model for international academics and private companies.

Costs	2020	2021	2022	2023	2024
5 FTE from 2021 for Cell Profiling (4 during 2020)	3 814	4 675	4 792	4 912	5 034
2.05 FTE from 2021 for ISS		1 748	1 792	1 836	1 882
1.5 FTE from 2021 for AFT.		1 171	1 200	1 230	1 261
Operations Cell Profiling	667	900	900	900	900
Operations ISS		1 215	1 215	800	800
Operations AFT		1 000	1 000	750	750
Premises Cell Profiling	893	995	900	900	900
Premises ISS		280	200	200	200
Premises AFT		339	200	200	200
Instrument depreciations Cell Profiling (CODEX)	241	60	660	600	600
Instrument depreciations ISS	-	251	251	251	-
Instrument depreciations AFT (StellarVision)		560	560	560	560
Other Cell Profiling	100	150	120	120	120
Other ISS		337	337	337	337
Other AFT		242	242	242	242
Sum costs (kSEK):	5 715	13 923	14 369	13 838	13 787

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding (Cell profiling)	3 000	4 300	4 300	4 300	4 300
SciLifeLab funding (ISS)		1 900	1 900	1 900	1 900
SciLifeLab funding (AFT)		1 800	1 800	1 800	1 800
University funding (SU)	-	64	64	64	64
VR NMI (Cell profiling)	600	600	600	600	600
VR Infra Cell profiling)	750	750	-	-	-
EU EPIC XS (Cell profiling)	800	800	800	-	-
KAW (ISS)	-	251	251	251	-
EU EASI-Genomics (ISS)	-	1 330	1 330	-	-
User fees Cell profiling	500	500	650	700	750
User fees ISS		500	620	620	650
User fees AFT		200	300	400	500
ERC-Proof-of-Concept funding (AFT)		750	750	-	-
Other funding for instruments (Cell Profiling)			600	600	600
Other funding for instruments (AFT)		560	560	560	560
Funding agency X (Cell profiling predicted)	-	-	-	500	500
Funding agency X (ISS predicted)				1 000	1 000
Sum revenues (kSEK):	5 650	14 305	14 525	13 295	13 224

Table 1. Current budget (2020) and suggested budget 2021–2024

In Situ Sequencing

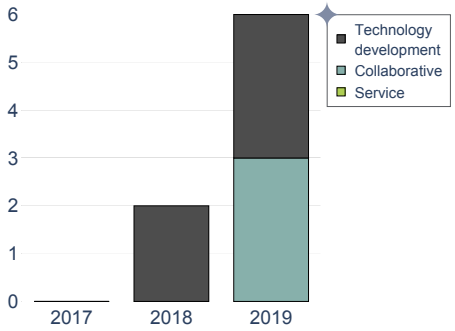
Read more: Web page, Publication Data Base

Basic Information

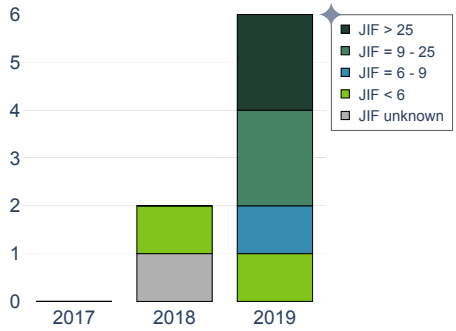
Facility director: Mats Nilsson
Head of facility: Chika Yokota
SciLifeLab facility since: 2019
Host University: SU
FTEs: 2.05
FTEs financed by SciLifeLab: 1

Funding 2020 (in kSEK)

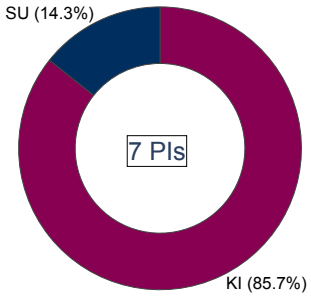
SciLifeLab: 800
Total: 3102



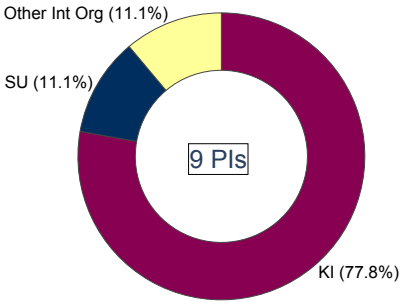
Publications by category



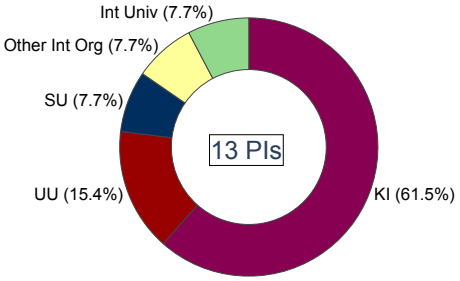
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

- Probe and assay design
- Multiplex mRNA profiling in situ
- Sample preparation training
- In situ Sequencing by ligation and by hybridization
- Primary image analysis (transcript and cell coordinates in tissues).

New Technologies and Services 2021–2024

- Launching Cartana kits for ISS library preparation and in situ sequencing.
- Micro RNA, Mutation and Protein profiling in situ
- Implementation of fully automated ISS analysis

Background

The in situ sequencing (ISS) facility unit offers targeted in situ gene expression profiling as a service. The unit is currently organized under the ESCG facility in SciLifeLab. The technique was incorporated to the ESCG from January 2019 after being developed as a pilot facility project 2017-2018. ISS enables localization and quantification of few hundred transcripts simultaneously with single cell resolution in a single tissue section in a single experiment. The technique has been developed by Mats Nilsson's group, who has pioneered in the field of generating gene expression (Ke, R., et al. 2013 Nature Methods 10, 857-860) and mutation profiling (Grundberg, I., et al. 2013 Oncotarget 4, 2407-2418) information *in situ*, and it has been successfully demonstrated for a variety of applications such as mapping of molecularly defined cell types (Qian, X., et al. 2020 Nature Methods 17, 101-106) RNA editing (Lundin, E., et al. 2020 BMC Biol 18, 6), intra-tumoral heterogeneity (Svedlund, J., et al. 2019 EBioMedicine 48, 212-223) and immune-cell profiling (Carow, B., et al. 2019 Nature Commun. 10, 1823) across sections of various tissue types. It is a technology with some unique features comprising 1) targeting method using padlock probes, 2) highly specific amplification providing robust detection also in "dirty" tissues such as human brain and tumors with high autofluorescence, 3) multiplexing, up to few hundred transcripts per sample, 4) sensitivity is tunable, 5) high throughput due to wide-field imaging, 6) compatibility with formalin fixed paraffin embedded (FFPE) tissue.

During the pilot facility phase, the facility implemented a semi-automated instrument which improved sample throughput and consistency in the sample preparation. 18 projects representing different kinds of potential user cases has been run by the facility and resulted in 9 publications in journals, e.g. Nature communications and Science. The experimental procedure consists of two parts: 1) ISS library preparation in tissue sections on slides. This is conducted by the user in the user's lab. 2) ISS decoding of the prepared slides. This is done by the facility and involves a series of

alternating sequencing chemistry and imaging rounds. The facility unit helps planning experiments, designing assays, ordering reagents, training users in ISS library preparation. It also performs primary image analysis which results in a file containing the spatial coordinates of all detected transcripts, as well as nuclei. Finally, the users get help from the facility unit with finding computational solutions for interpretation of the data. The ISS facility unit includes a unit director (Dr. Mats Nilsson) and two employees. Dr. Chika Yokota, who was recruited as a facility head in 2017 to engage 100% in establishing the facility unit. Thanks to KAW funding in the Human Development Cell Atlas (HDCA) project (https://hdca-sweden.scilifelab.se/) to establish a Spatial Omics facility at SciLifeLab, the facility unit could purchase a microscope dedicated for service projects, and to recruit the lab engineer Amitha Raman. The facility unit is a part of the EASI-Genomics (https://www.easi-genomics.eu/) transnational access program, which provides access to European genomics core-facilities.

Key achievements during the period:

1) We have proven the usefulness of ISS for providing spatial cellular atlases for the Human Cell Atlas (HCA). HCA is a global mega project, aiming to describe all human cell types at a molecular level, to provide a systems level understanding of how human organs works, and why they fail to work in disease. 2) Establishing ISS as a service at SciLifeLab. During the period, we have worked on SOP:s, routines, workflows, customer communication, protocols and procurement of instruments. During 2019 most of the projects has been run as collaborative projects to learn how to establish a working service. 3) In collaboration with Nilsson lab, we have started implementing the pciSeq method (Qian et al Nature methods 2020) to generate spatial atlases of scRNAseq defined cell types. This is of high relevance for Human Cell Atlas projects.

Plans for 2021–2024

New technologies/services. We suggest that the ISS service will be organized within the TSO facility from 2021 in order to achieve synergies outlined in the TSO report. ISS complements smFISH since ISS generates much brighter detection signals but with a lower detection efficiency compared to smFISH. ISS therefore enables much wider field of imaging using lower magnification objectives, and thus a much larger throughput in terms of imaged cells. The signals also overcome high auto fluorescence background encountered in manys human tissue specimens. During 2020, we will gradually go over from home-brewed assays to commercially available ISS library preparation and ISS decoding kits. These are currently only available from Cartana AB (www.cartana.se), a spin-out company from the Nilsson group. The new kits are based on a new direct RNA padlock probe targeting, and sequencing by hybridization (SBH) based chemistries respectively. The direct RNA approach is more sensitive than the current cDNA based method, and the SBH chemistry provides better contrast and versatility in the ISS decoding scheme, allowing even higher multiplexing and better dynamic range. We will also implement antibody based in situ profiling of proteins, using oligonucleotide tagged antibodies, which is another reason to work closely with the Cell Profiling facility, due to their expertise in antibody based imaging and conjugation of DNA barcodes to antibodies for the CODEX platform. Ultimately, we will combine these methods to offer in situ multi-omic profiling. We envision that during the coming few years, there will be fully automated systems for ISS available. The facility unit aims to acquire such a system to increase through-put in a more cost-effective way than hiring more personnel and microscopes. We also envision that other suppliers of ISS reagents will emerge, and then these will be incorporated too.

Uniqueness and competitiveness of the technologies/services. The ISS facility unit is the only service unit in Sweden which provides spatially resolved gene expression data for panels of few hundred genes at single cell resolution in a single tissue section in a single experiment. In order to meet the requirements of single cell genomics community, the ISS method is currently being set up at many different places in the world. But the ISS facility unit in Stockholm still provides absolute technology forefront in a global perspective. Cartana AB is currently also offering ISS service, but is also actively promoting other labs to set the method at core facilities.

Expected user base for 2021–2024. Despite the unit has just been launched in 2019 as a national facility unit, fifteen projects were processed in 2019, and there are many more in queue. The service has not yet been actively promoted, pending acquisition of a dedicated microscope to enable scale up. The system was delivered November 2019, and will be in production from February 2020. Therefore, we expect to be able to process more projects in coming four years. In addition, we will improve our productivity by 1) sharing personnel within the proposed Targeted Spatial Omics facility, 2) making instruments automated, 3) using commercial kits. Typical users have generated scRNA seq data and want to know how they are spatially organized. In principle, neuroscientists, developmental- and tumor biologists, could be potential users of the service.

Accessibility of nation-wide user. Current Swedish users of the ISS facility unit are located in Stockholm and Uppsala. However, we have established a workflow for nation-wide and international users, who prepare samples at their lab and ship samples to us for ISS. We expect to have more users from outside of Stockholm area coming years when we start promoting the service nationwide.

Reproducibility, quality, and data storage. By gradually transitioning to commercial grade kits, we expect increase in the reproducibility and comparability with other published

ISS data. The ISS facility unit is currently storing data during the data generation phase of a project, and then transfer the responsibility of data to the users after finalizing primary analysis. We are currently storing our data on a local server.

Research environment and associated research groups. The ISS facility unit is collaborating closely with the Nilsson group to implement applications and methods, both experimental and computational. The facility unit also generates data for the HDCA project. ISS is a beta test site for Cartana kits. Through the collaboration with the Nilsson group, the ISS facility unit also has access to Jens Hjerling-Leffler's group at KI, who is implementing novel ISS applications in neuroscience; Berit Carow at KI, who is developing immunoprofiling applications of ISS; Kenneth Harris at UCL and Carolina Wählby at UU, who are developing computational methods for ISS data; and, Omer Bayraktar at Sanger, who is setting up an automated ISS facility there.

Budget 2021–2024

The ISS facility requests 2.7 MSEK/year from SciLifeLab, to balance the reduced funds from KAW from 2021 and to recruit one FTE for ISS data analysis and to contribute for increased operational costs.

Costs	2020	2021	2022	2023	2024
Personnel (2.05 FTEs for 2020, and 3.05 FTEs after 2021)	1 748	2 832	2 878	2 934	2 991
Operations	1 215	1 215	1 215	800	800
Premises	280	280	280	280	280
Instrument depreciations	251	251	251	251	-
Other	108	337	337	337	337
Sum costs (kSEK):	3 602	4 915	4 961	4 602	4 408

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	800	2 700	2 700	2 700	2 700
University funding	64	64	64	64	64
KAW	908	251	251	251	-
EASI-Genomics	1 330	1 330	1 330	-	-
Additional funding X				1 000	1 000
User fees	500	570	620	620	650
Sum revenues (kSEK):	3 602	4 915	4 965	4 635	4 414

Table 1. Current budget (2020) and suggested budget 2021–2024

Advanced FISH Technologies (candidate)

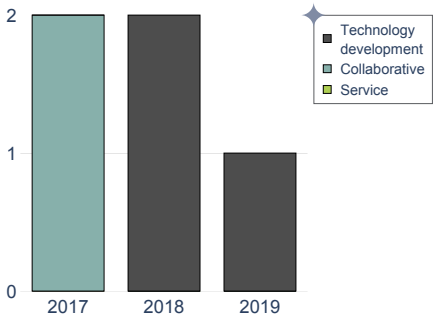
Read more: Publication Data Base

Basic Information

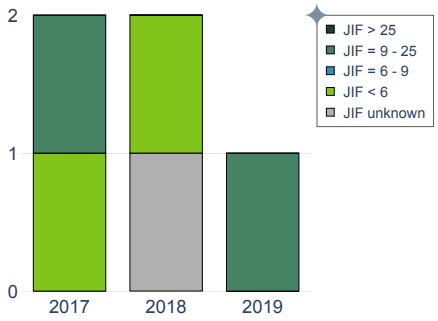
Facility director: Magda Bienko, Nicola Crosetto
Head of facility: N/A
SciLifeLab facility since: N/A
Host University: KI
FTEs: N/A
FTEs financed by SciLifeLab: N/A

Funding 2020 (in kSEK)

SciLifeLab: 0
Total: 0



Publications by category



Publications by JIF

Current Technologies and Services

No service is offered now as this is a candidate facility. The technology expertise is described below.

New Technologies and Services 2021–2024

- Single-molecule RNA FISH (**smFISH**)
- Multiplexed error-robust fluorescence in situ hybridization (**MERFISH**)
- High-resolution DNA FISH (**iFISH**)

The connected research group and proposed facility is currently building a large FISH Probe Repository to offer these service at competitive cost. *This repository will be a unique resource, similar to the proteome wide antibody library generated by the Human Protein Atlas.*

Background

Fluorescence *In Situ* Hybridization (FISH) techniques are widely used for genetic testing. The recent availability of high-throughput oligonucleotide (oligo) synthesis technologies has spurred the development of oligo-based Advanced FISH Technologies (AFTs), such as single-molecule RNA FISH (smFISH) (PMID: 18806792) and MERFISH (PMID: 25858977), which offer improved performance and throughput compared to classical FISH techniques. Despite the large number of potential AFTs users (Fig. 1), even big research infrastructures such as SciLifeLab do not offer AFTs on a regular basis. This is because AFTs remain technically challenging and because there is a lack of 'user-friendly' tools such as open-access probe repositories and image analysis software.

The proposed facility Director/Head, Dr Bienko and Dr Crosetto, have >10 yrs experience in FISH technologies and were previously together in the van Oudenaarden lab at MIT, where smFISH was originally developed. They have developed various FISH methods such as HD-FISH (Bienko et al, *Nat Meth* 2012), FuseFISH (Semrau et al, *Cell Rep* 2014), RollFISH (Wu et al, *Commun Biol* 2018) and more recently iFISH (Gelali et al, *Nat Commun* 2019). The Bienko-Crosetto lab at SciLifeLab (www.bienkocrosettolab.se) has already supported numerous groups locally and internationally on smFISH and high-resolution DNA FISH, which has resulted in several co-authorships in high-profile journals (e.g., Kind et al, Cell 2015; Dey et al, Nat Biotechnol 2015; Asim et al, Nat Commun 2017; Asp et al, Cell 2019). One epifluorescence microscope (Ti-E, Nikon) specifically designed for smFISH/iFISH in BiCroLab is currently heavily underused, and thus will be made available to the facility free-of-charge. The lab has developed a pipeline (*iOligo*) enabling high-throughput cost-effective production of hundreds of oligo probes for iFISH, smFISH and MERFISH (Gelali et al, Nat Commun 2019). Using iOligo, the lab recently started building a large *FISH Probe Repository*, aiming at generating smFISH probes for all human and mouse protein-coding genes, and iFISH probes targeting every 1 Mb of human and mouse genome. The lab is also building oligo databases covering the genome/transcriptome of many species, including human, mouse, drosophila and yeast, and has developed a user-friendly web interface for designing smFISH/iFISH probes (www.ifish4u.org). *All these tools will be integrated in the facility and used to provide the services described in the Table 1 below.*

Plans for 2021–2024

If funded, this would be a new facility that is suggested to be part of the proposed Targeted Spatial Omics (TSO) unit together with Cell Profiling (CellPro) and in situ sequencing (ISS). AFT and ISS technologies are highly complementary, i.e. depending on the sample type, desired resolution, multiplexing and biological question. For example, iFISH can visualize DNA loci/chromosomes, while ISS can detect mutations in situ. *Thus the AST and ISS facility will work in tight cooperation and offer complementary services.*

Organization. 0.1 FTE as Facility Head (Magda Bienko); 0.1 FTE as Facility Director (Nicola Crosetto); 1 FTE as FISH specialist; 1 FTE as Data analyst.

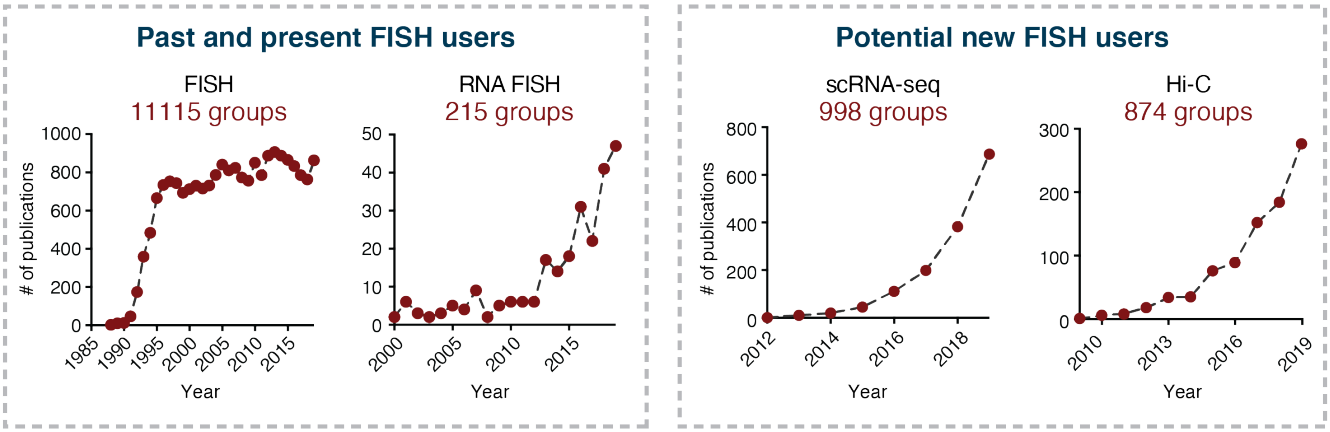


Figure 1. There is a growing number of potential AFT users. Estimates are based on the number of unique last authors (as proxy of research groups) on PubMed publications reporting the use of DNA/RNA FISH (left) or single-cell (sc) RNA-seq and Hi-C (right).

Uniqueness and expected user base. *There is currently no facility/infrastructure in Sweden or the EU that can provide any of the services described in Table 1.* The FISH probe repository that will be established is also unique in the world and will provide an invaluable resource for the life science community. Based on the number of collaboration requests that BiCroLab receives and estimated number of potential AFT users (Fig. 1), the number of services is expected to be 20–30 in 2021 and up to 50–60 per year by 2024.

Quality assurance. The facility will develop Standard Operation Procedures (SOPs) and best practices. *Dr. Bienko has recently applied for an ERC Proof-of-Concept grant to establish an International Committee on AFT Standards (ICAS).* The facility will cooperate with ICAS to develop and implement SOPs for probe design, probe production, assay conditions, image acquisition, and image analysis.

Data security. The facility will work with the KI Legal Office to establish a user contract covering data security and apply for ethical permits for handling users' samples. Users will be asked permission for storing their data, helping the facility develop reliable AI-based algorithms to analyze AFT images.

Technology	Service	Description	User	Fee [1]	From
smFISH	Standard smFISH in human or mouse cells (max 6 genes/sample) [2]	Probe design and production, hybridization, imaging	Researchers	200SEK/gene/sample	2021
	smFISH sample preparation (optional) [3]	Add-on for S1.1 or S1.2	Researchers	1,000SEK/sample	
	smFISH image analysis (optional) [4]			500SEK/sample	
	Optimization of smFISH in human or mouse tissues (frozen or FFPE, max 3 genes/sample)	All steps from probe design to image analysis	Researchers, pathology labs	Depending on project	
	Optimization of smFISH in other species (max 6 genes/sample)	All steps from probe design to image analysis	Researchers		
	IVD test development	Diagnostic assay development	Pharma industry		
MERFISH [5]	Low-throughput MERFISH in human or mouse cells/tissues (frozen, max 100 genes)	All steps from probe design to image analysis	Researchers, pathology labs	5,000SEK/sample	2022
	High-throughput MERFISH in human or mouse cells (frozen, max 1,000 genes)	All steps from probe design to image analysis	Researchers	10,000SEK/sample	2023
iFISH	Single-locus detection in human or mouse cells (max 4 loci/sample)	All steps from probe design to image analysis	Researchers, cytogenetics labs	400SEK/locus/sample	2021
	Chromosome spotting in human or mouse cells (max 4 chromosomes/sample)				
	Optimization of iFISH in human or mouse tissues (frozen or FFPE, max 3 loci or chr/sample)			Depending on project	
	IVD test development	Diagnostic assay development	Pharma industry		
iOligo	Production of smFISH/MERFISH/iFISH probes	Probe design, production and testing	Researchers, facilities, consortia	Depending on probe	2021
	Production of NGS capture probes [5]	Probe design, production and testing			

Table 1. Services that will be offered by the AFT facility.
[1] Tentative fees based on the estimated number of users in 2021 and current reagent costs
[2] In the standard service, users send ready-to-use samples (either fixed cells or tissue sections) and receive back images ready for analysis.
[3] Preparation of samples will be performed by an Application Specialist shared between all the Units of the Targeted Spatial Omics Facility.
[4] The service will be performed by E. Wernersson and will be initially based on DOTTER, a sub-pixel resolution image-analysis suite which he originally developed for FISH images. Dr. Wernersson is now developing an AI-based version of DOTTER, which builds on an enormous database of manually annotated FISH images generated in BiCroLab over the past five years. We expect that starting from 2022 the Unit users will be able to analyse their FISH images using a cloud version of iDOT (free-of-charge for academia).
[5] This service will be developed in synergy with the NGI and Clinical Genomics Platforms at SciLifeLab.

Synergies and collaborations. *Advanced FISH Technologies as part of TSO.* The facility will work closely with the CellPro and ISS facilities within the TSO unit, sharing space, equipment, knowledge, and personnel. The facility will work closely with the CellPro and ISS facilities within the TSO unit, sharing space, equipment, knowledge, and personnel. The TSO facilities will work with Prof Nilsson and Prof Lundberg's research groups at SciLifeLab to develop tools for integrating AFT, ISS and CODEX data and develop plug-ins for the cloud based ImJOY AI platform developed by members of Lundberg´s group (Ouyang et al, *Nature Methods* 2019).

External collaborations. The facility will partner with large research consortia such as the Human Cell Atlas and 4D Nucleome (https://www.4dnucleome.org/), aiming to become their trusted provider of FISH probes and services. The 4D Nucleome is a large NIH-funded program with the overarching goal of studying the three-dimensional organization of the nucleus in space and time.

Budget 2021–2024

We apply for SciLifeLab support of 2 MSEK/yr to focus on expanding the FISH probe repository in 2021 and offer services with the instrumentation currently available in the Bienko-Crosetto lab. From 2021 on, the funding will be used for increased support in data analysis as we expect the number of projects and users to increase. To be able to offer MERFISH as a service starting in 2022, we will apply for large equipment funding at SciLifeLab and, if possible, the Swedish Research Council to purchase the StellarVision system (www.opticalbiosystems.com) that is specifically tailored for high-throughput smFISH/MERFISH. *The aim is to have StellarVision fully operational by the end of 2021.* Dr. Bienko has recently applied for the ERC Proof-of-Concept Grant to build the FISH Probe Repository (results expected in Apr 2020).

Costs	2020	2021	2022	2023	2024
Personnel (2.2 FTEs)		1 717	1 760	1 804	1 849
Operations		968	968	968	968
Premises		339	339	339	339
Instrument depreciations		560	560	560	560
Other		242	242	242	242
Sum costs (kSEK):	-	3 826	3 869	3 913	3 958

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding (AFT)		2 200	2 000	2 000	2 000
KI funding			100	100	100
User fees		400	500	500	500
ERC-Proof-of-Concept funding (AFT)		750	750	-	-
Other funding for instruments (AFT)		560	560	560	560
Funding agency X (predicted)				1 000	1 000
Sum revenues (kSEK):	-	3 910	3 910	4 160	4 160

Table 1. Current budget (2020) and suggested budget 2021–2024

Gothenburg Imaging Mass Spectrometry Imaging (candidate)

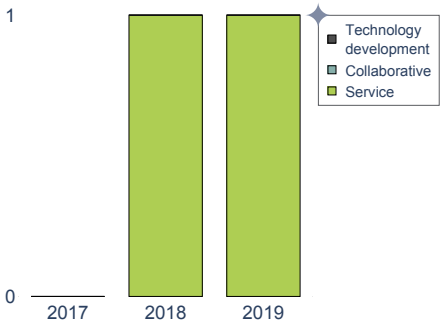
Read more: Web page, Publication Data Base

Basic Information

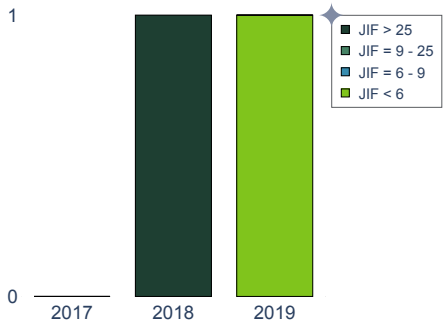
Facility director: Andrew Ewing
Head of facility: Thomen Aurélien
SciLifeLab facility since: N/A
Host University: Chalmers, GU
FTEs: 1.25
FTEs financed by SciLifeLab: 0

Funding 2020 (in kSEK)

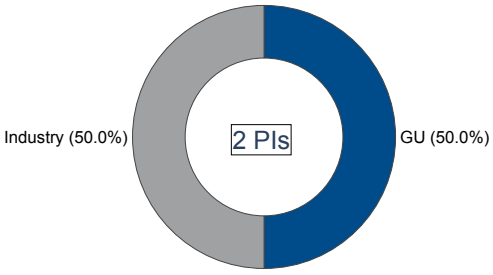
SciLifeLab: 0
Total: 1800



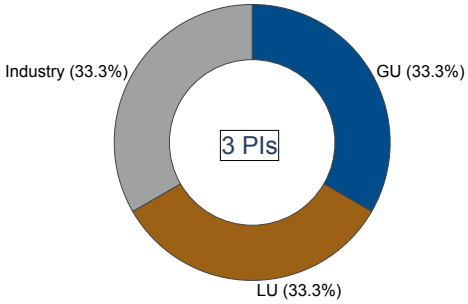
Publications by category



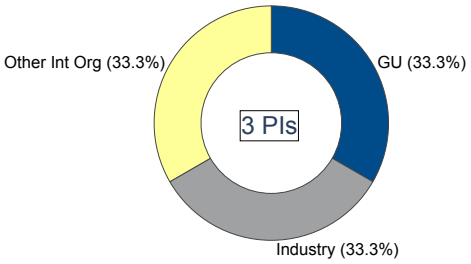
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

- CAMECA NanoSIMS secondary ion microprobe (29 MSEK, 2015) to analyse cells, subcellular organelles for metal ions, metabolites, lipids, peptides with spatial resolution down to 50 nm.
- IonTof V SIMS (10 MSEK, 2009) instrument for mass spectrometry imaging of lipids and metabolites in tissues and cells with spatial resolution typically 200 nm to 3 µm.
- Bruker UltraFlexTreme MALDI instrument (4 MSEK, 2012). Complementary analysis of metabolites, lipids, peptides at spatial resolution to 10 µm.
- The Cii offers consulting and experimental design, data acquisition and processing support.

New Technologies and Services 2021–2024

- A radio frequency (RF) source (applied for funding) to analyse metals, alkalines and lanthanides/actinides with a smaller spatial resolution (x3) or better sensitivity (x5).
- Embedding/ultramicrotome and gold coater to ensure stability of image acquisition.

Background

The Chemical Imaging Infrastructure (Cii) is unique in having access to NanoSIMS (the only one in Scandinavia) and static SIMS as well as MALDI mass spectrometry for multimodal SIMS/MALDI imaging at the micro/nanoscale, all in the same facility. The NanoSIMS facility at the BioVentureHub, AstraZeneca offers consulting, experiment design, imaging and data mining services in various field from life science to material characterization. The NanoSIMS instrument can be used to perform isotopic and elemental mapping of virtually all elements of the periodic table with down to 50 nm spatial resolution. The Chalmers node of the Cii has ToF SIMS and MALDI instruments that are used to image molecular ions and larger fragments with spatial resolution from 200 nm to about 10 µm, respectively. This site also has the affiliated Ionoptika J105 3D SIMS chemical imaginer with MSMS capability for structural identification and cluster ion sources to allow examining somewhat larger molecules like the molecular ions of lipids and sulfatides. The associated scientists are widely recognized for development of imaging lipids and metabolites in tissues, cells, and subcellular organelles (for example, Prof. Ewing has a second ERC Advanced Grant and is a two-time Wallenberg Scholar). The overall Cii is rather young, but it has already produced approximately 60 papers since 2015, including papers in Nature, ACS Nano, Nature Communications, etc. The NanoSIMS node is led by Dr. Aurélien Thomen, a highly experienced NanoSIMS research engineer from GU. The TOF-SIMS/MALDI infrastructure is led by Prof. Per Malmberg, a docent from Chalmers.

Plans for 2021–2024

New technologies/services

New instrumentation. A new high-spatial resolution radio frequency oxygen source is planned for the NanoSIMS. This radio frequency source will allow us to analyse metals, alkalines and lanthanides/actinides as labels for biomolecules with a smaller spatial resolution (x3) or better sensitivity (x 5) and will expand our customer base considerably. A new MALDI instrument is planned for complementary studies.

Development of an in-house sample preparation laboratory. We plan to establish a sample preparation laboratory in-house to help us to be reactive to customer needs.

Improved data mining and development of NanoSIMS standards. New efforts into development of reproducible data mining methods are planned with our novel data mining software based on an open source R language. We are at the forefront of developing standards for quantitative analysis of element/isotopes to label biomolecules are being developed (I and ^{13}C) and we will extend this to other biological elements of interest, especially for drug analysis, such as F and Br, Pt, Au.

Uniqueness. The NanoSIMS facility is unique in Sweden and Scandinavia, and only a few sites in the world have the combination of NanoSIMS, SIMS, and MALDI. About half of the 43 NanoSIMS in the World are dedicated to material sciences and geology. We have unparalleled expertise in high-resolution mass spectrometry imaging, absolute quantification of concentrations - recently developed by us, and multimodal imaging, as well as development of new standards for NanoSIMS and SIMS.

User base. At the NanoSIMS, we currently plan for approximately 20 users per year with 3-15 days per year use, from academia, industry (especially AstraZeneca), and other governmental agencies. The capacity is to have double that user base and this is growing. At the static SIMS and MALDI facility, we have a similar but more fluctuating user base. We have a strong connection with AstraZeneca, which has purchased 10% time on the NanoSIMS with a multiyear contract.

Nation-wide accessibility and training. Access to the facility is via our website at https://www.chalmers.se/en/researchinfrastructure/chemicalimaging/Pages/default.aspx. The advisory board for the Cii gathers several top-leading life scientists in Sweden achieving international visibility though their network. Regular "SIMS days" are held as a local event with users (local or national) from our facility to demonstrate how the Cii can answers various scientific questions and export the concept to other universities (Stockholm, Uppsala, Lund, Umeå). Academic and industrial potential customers as well as investors are invited to the talks and a tour of the facility. Lectures for master students are planned and specific training days for PhD students are scheduled regularly. These are available for users throughout Sweden.

Data quality and storage. The data obtained from all instruments in the Cii, image measurements and their metadata, are backed up in a control computer for each instrument as well as at a remote server located at the GU IT service. Commercial (CAMECA) and free software (ImageJ) image analysis packages are available on site. Support in data mining is offered and data are processed either by the local committee or by the user. In both cases the data are validated by the local committee. Quality of the data is ensured both by a continuous maintenance of the instruments to keep the specifications valid and by oversight of data mining.

User fee model. All projects are based on short proposals submitted via the Cii website and evaluated by the local committee with science the first consideration and feasibility the second. After scientific feedback from the local committee, the user is asked to further develop or finalize the project plan. The project time is estimated and starting date established. NanoSIMS time is 940 SEK/hr for Chalmers/GU local users, 1375 SEK/hr for other academic users, 1875 SEK/hr for industrial users. Data mining and report writing time are billed at 750 SEK/hr for academic and 1000 SEK/hr for industrial users. SIMS/MALDI time is 350 and 700 SEK/hr, respectively.

Research environment. Most of our customers have biological projects. Andrew Ewing and his chemistry and neurochemistry group at GU, Rachel FOSTER and her environment microbiology group at SU, Per Malmberg at Chalmers with medical collaborations at Sahlgrenska Academy, Michael KURCZY at AstraZeneca examining pharmaceutical locations in cells at AstraZeneca are currently our largest customers helping to develop the Cii and its presence in Sweden. John Fletcher is a world expert in SIMS imaging is affiliated with his Ionoptika J105 3D imager. The Ewing group has a STED super-resolution microscope used for correlative STED-MSI imaging. The Cii has close interactions with a number of other mass spectrometry imaging research groups, particularly the Uppsala-Imaging MS facility with Prof Andren.

Collaborations with healthcare, industry and organizations. Major collaborations currently take place with AstraZeneca and Sahlgrenska Hospital among others. Members of the team have collaborations with researchers at the University of Göttingen, Germany, EPFL in Switzerland, and University of Aarhus in Denmark. The Cryo-EM facility will be an excellent partner in cell and sample preparations as well as in Transmission Electron Microscopy imaging, crucial in identifying subcellular structure of interest before chemical imaging.

Alternative infrastructures (academic or commercial). There is nothing equivalent to the Cii or the NanoSIMS in

Sweden. For NanoSIMS, the closest would be in Göttingen or Bremen, Germany. Only a newly developed facility at the National Physical Laboratory in the UK provides the NanoSIMS and the ToF SIMS synergy.

Synergies and Collaborations. See platform report.

Budget 2021–2024

The facility proposes to acquire a high-spatial resolution radio frequency oxygen source for the NanoSIMS. This radio frequency source will allow us to analyse metals, alkalines and lanthanides/actinides as labels for biomolecules with a smaller spatial resolution (x3) or better sensitivity (x 5). Although the overall budget includes funds for 25% of a director of the complementary SIMS/MALDI MSI node, SciLifeLab funding is requested only for the NanoSIMS Director salary, service contract, and depreciation for the RF source.

Costs	2020	2021	2022	2023	2024
Personnel (1.25 FTEs, Aurélien THOMEN, Per Malmberg)	1 300	1 326	1 353	1 380	1 407
Operations	320	330	339	350	360
Premises (rent of the local to the Biohub)	113	115	118	120	123
Instrument depreciations (oxygen source)	-	800	800	800	800
Other (Service contracts)	500	500	500	500	500
Sum costs (kSEK):	2 233	3 071	3 110	3 149	3 190

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	-	1 500	1 500	1 500	1 500
Industrial cillaboration with AstraZeneca	100	100	100	100	100
University funding (GU, Chalmers)	1 000	1 000	1 000	1 000	1 000
KAW Funding (ends 2020)	600				
Ewing co funding	100	-	-		
User fees	433	471	510	549	590
Sum revenues (kSEK):	2 233	3 071	3 110	3 149	3 190

Table 1. Current budget (2020) and suggested budget 2021–2024

National Resource for Mass Spectrometry Imaging (candidate)

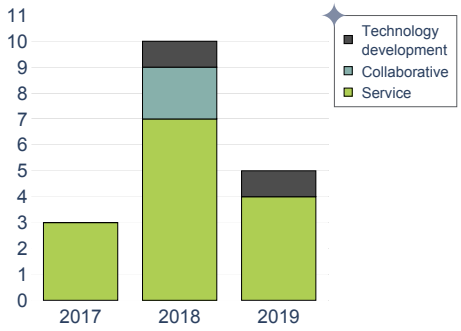
Read more: Web page, Publication Data Base

Basic Information

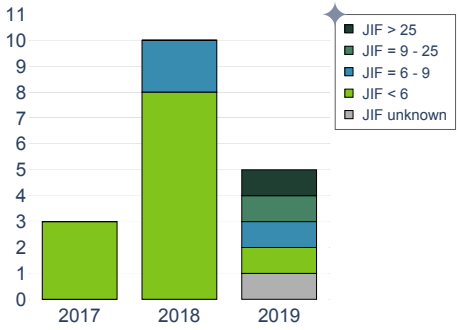
Facility director: Per Andrén
Head of facility: Anna Nilsson, Reza Shariatgorji
SciLifeLab facility since: N/A
Host University: UU
FTEs: 4
FTEs financed by SciLifeLab: 0

Funding 2020 (in kSEK)

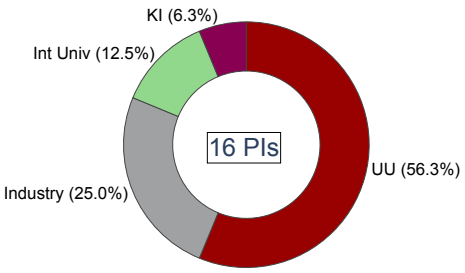
SciLifeLab: 0
Total: 11097



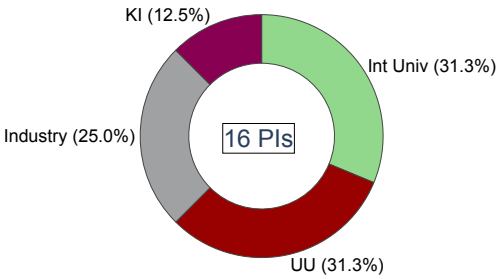
Publications by category



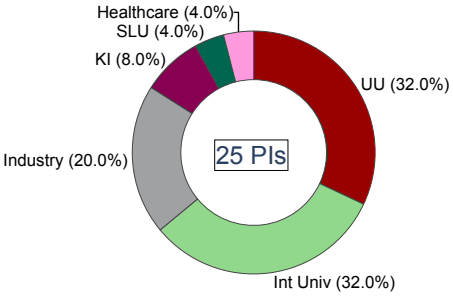
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

- Molecular-specific mass spectrometry imaging (MSI) directly in biological tissue sections (brain, lung, kidney, liver, muscle, tumors, etc.) of metabolites, nucleotides, neurotransmitters, pharmaceuticals, lipids, peptides, and small proteins.
- Matrix-assisted laser desorption ionization (MALDI) and desorption electrospray ionization (DESI) MSI, lateral resolution 15 µm and 25 µm, respectively (cell layer resolution).
- Ultrahigh mass resolution MALDI MSI using Fourier transform ion cyclotron resonance (FTICR) enabling mass accuracy <1 ppm and resolving power >10M (isotopic resolution).
- Quantitative MALDI and DESI MSI, i.e., absolute quantitation of endogenous metabolites, neurotransmitters as well as drugs and drug metabolites directly in tissue sections.

New Technologies and Services 2021–2024

- MALDI MSI high-lateral resolution imaging (<5 µm, cellular resolution).
- Artificial intelligence morphology-guided deep learning for super-resolution enhancement of single MS images enabling lateral resolution <1 µm (sub-cellular resolution).
- Quantitative MALDI and DESI MSI of comprehensive neurotransmitter systems.
- High resolution ion mobility combined with ultrahigh mass selectivity quadrupole time-of-flight (QTOF) enabling MALDI MSI of isobaric compounds.

Background

The National Resource for MSI (NR-MSI) at Uppsala University is a leading laboratory in the field and is one of the largest and most modern MSI laboratories in the world. In 2017, two new MSI instruments (12.6 MSEK) were purchased, one ultrahigh mass resolution instrument MALDI-FTICR (solariX 7T-2ω) and one ultrahigh lateral resolution TOF-TOF mass spectrometer (rapifleX Tissue Typer). A 2nd MALDI-FTICR instrument is being installed in March 2020 (9.25 MSEK). The facility also has another MALDI-TOF-TOF mass spectrometer (Ultraflextreme, installed 2014), and a MALDI-Q-TOF instrument with a dual MALDI/DESI ion source (Synapt G2-Si HDMS, ion mobility separation, installed 2015).

Many significant MSI developments during the last decade were pioneered in Andrén's laboratory, such as absolute quantification and visualization of drugs, metabolites, and neurotransmitter as well as development of associated software and protocols. The resulting technologies have been applied in a wide range of biological and clinical

studies. Andrén received a Research Infrastructure Fellow grant (15 MSEK, 2016-2020) from the Swedish Foundation for Strategic Research to upgrade and improve the NR-MSI facility. The laboratory possesses the collective expertise required to both develop new MSI technologies and to interact effectively with collaborating scientists working on biological studies, clinical and preclinical projects, and other investigations. The Facility services have generated >80 publications so far (since 2010). The NR-MSI infrastructure has one director (prof. Per Andrén) and two Facility Managers (Dr. Anna Nilsson and Dr. Reza Shariatgorji).

Plans for 2021–2024

New technologies/services. The NR-MSI will provide novel molecular-specific technologies such as, a) simultaneous, direct and quantitative imaging of comprehensive neurotransmitter systems in brain tissue sections (method recently published in *Nature Methods*, 2019, 16:1021), b) super-resolution enhancement of MS images enabling lateral resolution <1 µm (e.g., visualization of individual neurons) by artificial intelligence morphology-guided deep learning, c) imaging of isobaric compound by ion mobility high mass resolution MS and high throughput imaging (50 pixels/s). The mission of the NR-MSI is to accelerate the adoption of MSI technology to the biological and medical research community by providing access to advanced technologies and promoting interactions between scientists.

Uniqueness. The NR-MSI at UU has the only ultrahigh mass resolution MALDI-FTICR MSI instruments in Scandinavia. It has by far the best expertise and experience in MSI regarding quantitation, method and software development, and imaging of multimodal molecular species. It is one of the most modern MSI laboratory in the world.

User base. The user base is currently >20 academic research groups in Sweden (and Europe), as well as Pharma industry and government agencies (e.g., FDA, US). The user base is steadily increasing. The capacity of accepting projects will increase after the installation of the 2nd MALDI-FTICR MSI instrument (March 2020). In addition, the Facility collaborates with a number of MSI facilities in Europe through the MSI Society (emerged 2012 under the auspices of the EU network COST Action BM1104). The facility has participated in numerous projects with Pharma industry (imaged over >100 different drugs and metabolites in different organs, as well as 50 potential drug candidates).

Nation-wide accessibility and training. The NR-MSI platform can be contacted via the internet (www.farmbio.uu.se/plattformar/ncmsi). The training mission of the infrastructure is accomplished through a variety of educational programs whereby the platform's scientists and collaborators share their knowledge and experience with those interested in learning more about the technology. A goal for the NC-MSI-platform will be to organize various master and PhD courses, workshops and seminars on MSI-based analysis. These activities should be available to researchers at all Swedish universities to ensure that the facility serves as a national resource.

Data quality and storage. Sample tissue quality is always evaluated by the Facility staff before a project is started. Different MALDI matrices are tested for optimization of signal-to-noise value. Image processing is performed using the in-house built software msIQuant or commercially available MSI software (e.g., SCiLS Lab, Bruker Daltonics). The Facility provides data storage through our own servers (~300 TB). Data compression algorithms have been implemented in the msIQuant software.

User fee model. First, the time required for each project is estimated (i.e., number of tissue sections, size of tissue, desired lateral resolution, sample preparation protocol, type of imaging instrument, amount of data generated, and type of data processing). Each project is usually unique and therefore a pilot test is performed on the substance(s) to be imaged. Such test including method optimization takes about one week (1 FTE). After tests, a 'stop/go' decision is made. Final pricing is determined depending on the above-mentioned parameters. The cost for academic customers is about 25% of the budget for commercial customers (who pays full cost coverage).

Research environment. The Facility has close interactions with a number of other MSI research groups, particularly the Gothenburg-Imaging MS facility and European research groups. It also collaborates directly with several national MSI platforms in other countries and continents. The Mass Spectrometry Research Center, Vanderbilt University, Nashville TN has arguably the world's leading MSI laboratory. It is headed by prof. Richard Caprioli, with whom prof. Andrén has a long-term collaboration (>30 yrs.). Another MSI collaborator is the Australia's National Collaborative Research Infrastructure (headed by Prof. Peter Hoffmann).

Collaborations with healthcare, industry and organizations. Collaborations are established with several Pharma companies, including AstraZeneca (Sweden and UK), Medivir, SOBI (Stockholm), Novartis (Basel), Bayer AG (Germany), Chiesi Farmaceutici (Italy) and GSK (UK). For example, during 2017-2019 the NR-MSI platform delivered imaging data in 11 different AstraZeneca projects, where the MSI results were instrumental in project progression or termination because of the unparalleled molecular-specific information provided at cellular level. The facility has also a collaboration agreement with FDA, USA, and MS companies such Waters, UK and Bruker Daltonics, Germany.

Alternative infrastructures (academic or commercial). None in Sweden. There are only a few MSI infrastructures in Europe. The Gothenburg Imaging Mass Spectrometry

facility focus on secondary ion mass spectrometry (SIMS) imaging and is therefore an excellent complement to the NR-MSI at UU (and vice versa), not a competitor. The National Center of Excellence in Mass Spectrometry Imaging, NPL, UK, offers commercial service, research partnerships, and collaborative research. There is only one commercial company (ImaBiotech) in Europe/USA that performs MSI services. The Vanderbilt University mass spectrometry laboratory (mentioned above) also serves also as USA's national MSI infrastructure.

Synergies and Collaborations. See platform report.

Budget 2021–2024

The Facility proposes to acquire another mass spectrometer a MALDI Q-TOF MSI instrument (with ion mobility, 6 MSEK) to maximize lateral resolution (<5 µm), throughput, sensitivity, and molecular specificity by new funding from UU-Rådet för Infrastruktur (2 MSEK/year, starting 2020). This will ensure a more efficient use of the Facility's high-end instrumentation and will increase the capacity significantly due to its high throughput (laser speed (50 pixels/s). Together with the two ultrahigh mass resolution FTICR instruments it will provide the highest quality possible of MS imaging. It should be noted that the metrics method used for users' statistics in the present application poorly reflect the activities of our facility. For example, several users (PI's) have utilized the facility several times per year but this is not shown in the report (reported as one user). Furthermore, the projects also span from weeks to several months of work, i.e., the user statistics do not reflect the extent of the projects.

Costs	2020	2021	2022	2023	2024
Personnel (4 FTEs)	4 199	4 283	4 369	4 456	4 545
Operations	380	400	400	450	450
Premises	862	862	900	900	900
Instrument depreciations	3 296	3 000	2 500	2 500	2 500
Other	1 070	900	900	800	800
Sum costs (kSEK):	9 807	9 445	9 069	9 106	9 195

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	-	3 000	3 000	3 000	3 000
University funding (UU), Rådet för infrastruktur, Fakultetsmedel	4 597	4 500	4 500	4 500	4 500
Stiftelsen för Strategisk Forskning (SSF)	5 200	2 000	1 500		
TDP funding SciLifeLab	1 300				
User fees	836	900	1 100	1 300	1 400
Sum revenues (kSEK):	11 933	10 400	10 100	8 800	8 900

Table 1. Current budget (2020) and suggested budget 2021–2024

Chemical Biology and Genome Engineering Platform

Basic information

Platform Director: Anna-Lena Gustavsson

Vice Platform Director: Bernhard Schmierer

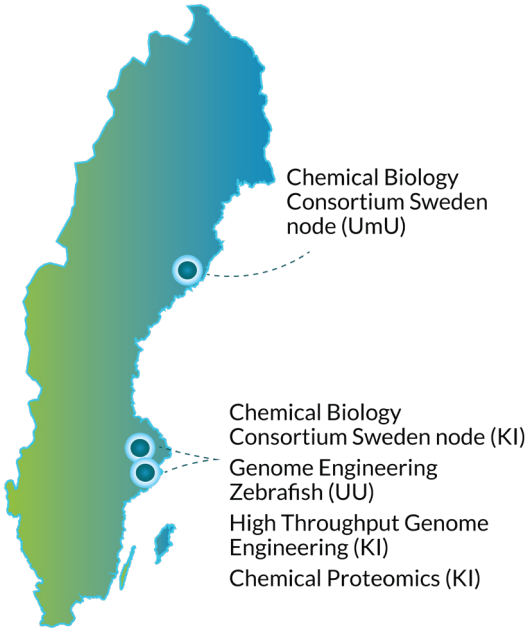
Platform Vision:

Turning phenotypic observation into mechanistic insight

Platform Mission:

- To perform chemical and genetic screens as well as chemical proteomics profiling for data-driven hypothesis generation
- To offer multidisciplinary pipelines for target deconvolution and mechanism-of-action determination
- To validate and characterize small molecule-target interactions

Geographical location of facilities



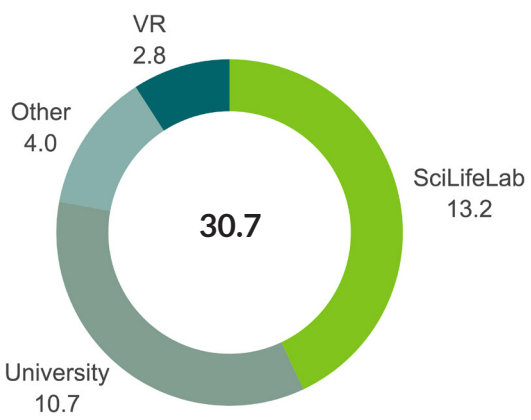
SciLifeLab funding 2020

Facility/unit	(MSEK)
Chemical Biology Consortium Sweden	6.0
Chemical Proteomics	1.6
High Throughput Genome Engineering	3.2
Genome Engineering Zebrafish	2.4
Total SciLifeLab funding	**13.2**

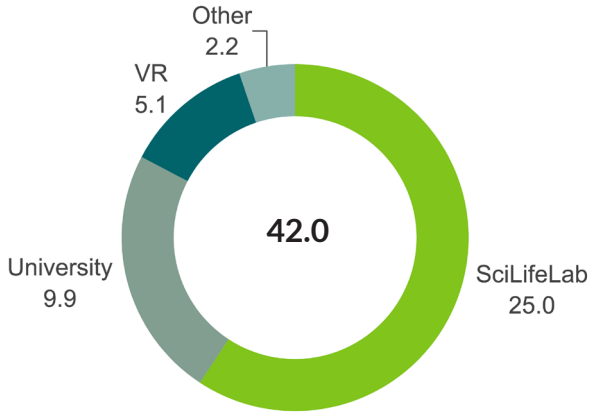
Suggested annual SciLifeLab funding 2021-2024

Facility/unit	(MSEK)
Chemical Biology Consortium Sweden	11.5
Chemical Proteomics	3.3
High Throughput Genome Engineering	5.3
Genome Engineering Zebrafish	4.9
Total SciLifeLab funding	**25.0**

Total funding 2020 (MSEK)



Total suggested annual funding 2021-2024 (MSEK)



Background

The SciLifeLab platform *Chemical Biology and Genome Engineering* was created in 2017 and consists of three national research facilities: The established Chemical Biology Consortium Sweden (CBCS), and two new facilities, High Throughput Genome Engineering (HTGE), and Genome Engineering Zebrafish (GEZ). For a detailed description of the wide range of services and technologies offered by these facilities, please refer to the individual facility reports. This document is dedicated to the platform's joint capabilities, which have been developed by combining some of the complementary technologies hosted at the individual facilities and will be fully implemented and promoted to users during the funding period 2021-24. The common platform focus area is target deconvolution, mechanism of action elucidation, and small molecule (SM)-target interaction studies. By supporting users all the way from large-scale screening through to validated SM-target pairs, platform services will close a gap in SciLifeLab's service portfolio and lower the barriers for users to advance their projects into the Swedish innovation system, such as the DDD platform. To achieve this goal, the platform will incorporate a fourth facility, Chemical Proteomics (ChemProt), currently part of the *Proteomics and Metabolomics platform*. ChemProt's focus on advanced chemical proteomic techniques will contribute critical capabilities to the platform's workflows. Increased national funding is requested to build up and sustain these cross-disciplinary pipelines, and to guarantee affordable access for the Swedish research community.

Platform plans for 2021-2024

Chemical, proteomic and genetic tools have been hugely successful in the discovery of novel biology and the development of therapies. Chemical Biology and Genome Engineering will combine existing and newly developed chemical, proteomic and genetic tools into cross-disciplinary pipelines for target deconvolution, mechanism of action elucidation and SM-target interaction studies. These pipelines are not commonly accessible outside the pharmaceutical industry and will take user projects all the way from large-scale chemical or genetic screens to detailed mechanistic insight and high-confidence targets (Figure 1).

The envisaged platform pipelines, which consist of four modules, are shown in Figure 2 and described in detail in the text. The pipelines are flexible, and user projects can enter and exit at any stage depending on need.

1. **Creation of relevant model systems for chemical and genetic screens (Figure 2.1).** The platform will create model systems for high-throughput (HT) chemical and genetic screening by precision gene-editing in cells and zebrafish. These can be cell or zebrafish reporter lines with knock-in of fluorescent proteins, luciferase, or other tags into endogenous loci; or cell and zebrafish lines recapitulating pathogenic mutations (disease models, isogenic models).

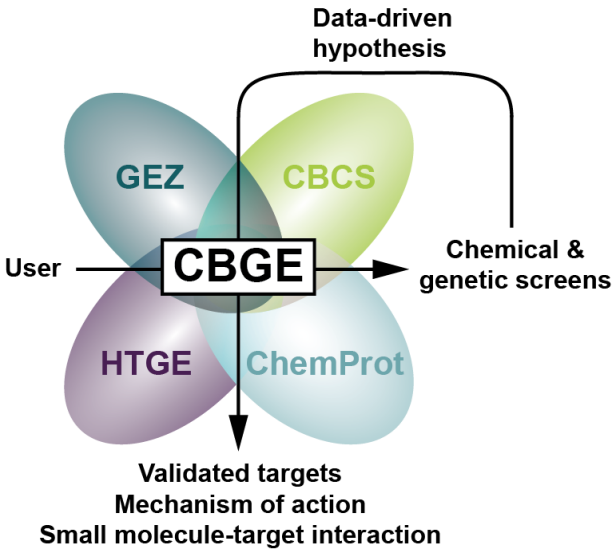
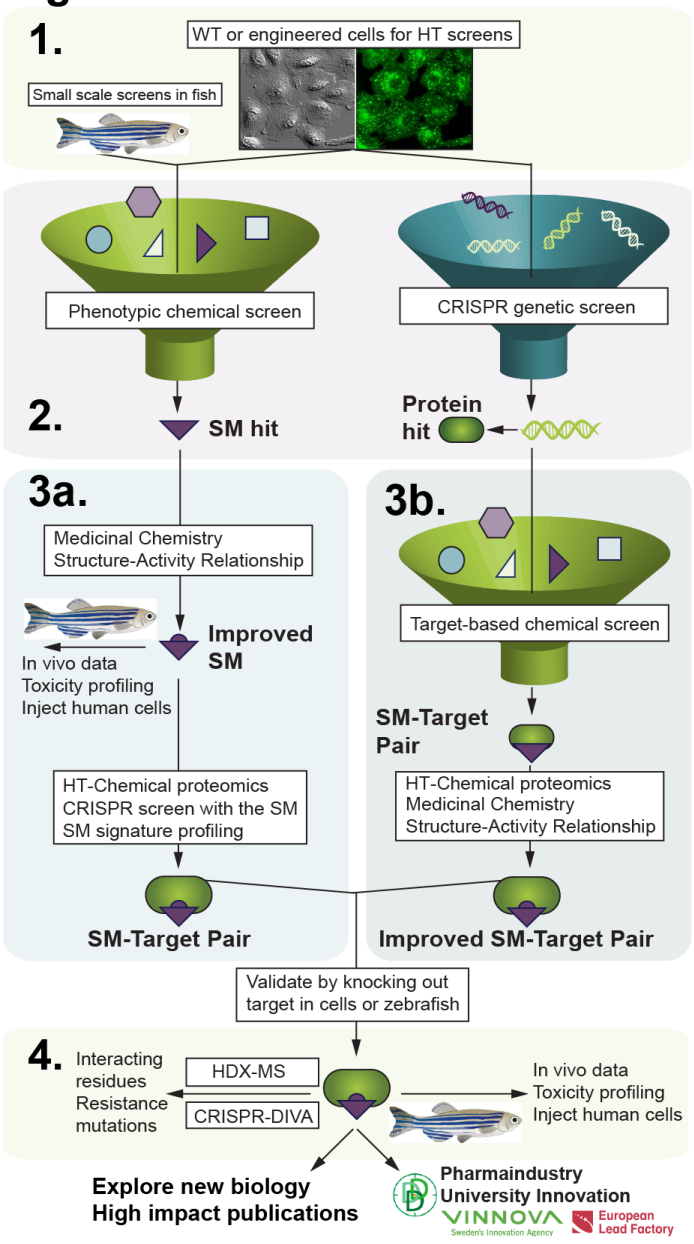


Figure 1. Chemical Biology and Genome Engineering (CBGE) generates chemical, genetic and proteomic high-throughput data, supports the user in creating data-driven hypotheses and helps validate initial results in cells and in whole organisms. CBGE enables users to explore new biology, or to further develop small molecules with the help of DDD at SciLifeLab and other available infrastructure. CBCS, Chemical Biology Consortium Sweden. ChemProt, Chemical Proteomics. HTGE, High Throughput Genome Engineering. GEZ, Genome Engineering Zebrafish.

2. **Chemical and genetic screens (Figure 2.2).** Comparison of SM hits from phenotypic chemical screens with gene hits from CRISPR screens can pinpoint target pathways and proteins. Depending on the application, smaller screens of up to several hundred SMs (e.g. approved drugs) can also be performed directly in zebrafish.

3. **Complementary approaches to target identification and mechanism of action (MoA) determination downstream of phenotypic SM screens (Figure 2.3a)** Medicinal/synthetic chemistry downstream of phenotypic SM screens will im-prove activity and/or specificity of hit molecules and establish a structure-activity relationship. CRISPR-based genetic screens for sensitivity- and resistance genes are a logical follow-up to SM screens to identify SM targets and pathways. *In vivo* testing of SMs in zebrafish will give an initial toxicity profile, and injection of human reporter cell lines into zebrafish will allow studying SM effects on reporter cells in an intact organism. Genetic target deconvolution and MoA determination will be complemented by chemical proteomic high-throughput techniques to assess SM-induced signatures in protein solubility/stability, protein levels, as well as proteome redox balance. Combining chemical, proteomic and genetic methods will allow unprecedented precision in target deconvolution, MoA studies and the exploration of

Figure 2.



off-target space. Ninety-seven percent of cancer drugs never make it to the clinic, often because the proposed MoA is incorrect and observed drug effects are in fact due to off-target toxicity. Thus, once a bonafide target has been identified, it will be knocked out in cells and/or zebrafish to validate the proposed target and to assess any off-target toxicity. Target-based SM screens downstream of genetic screens (Figure 2.3b). Protein candidates obtained by loss- and gain-of-function CRISPR screens will be assessed for ligandibility and followed up by biochemical and biophysical target-based SM screens. Medicinal/synthetic chemistry will improve SM hits and establish their structure-activity relationships. Off target signatures of SM variants will be mapped by chemical proteomics.

4. **High-resolution characterization of SM-target interactions by chemical and genetic means (Figure 2.4).** In medicinal chemistry as applied at CBCS, systematic variation of SM structure is used to obtain structure-activity relationships. A complementary approach is to use CRISPR-Cas9 to obtain structure-activity relationships by systematically varying target protein structure. HTGE is developing a modified CRISPR-X approach (CRISPR-DIVA or Diversification and Interrogation of VAriants), which will be used to hypermutate protein domains of interest in a massively parallel fashion to identify residues or structural motifs that mediate SM/target interactions. ChemProt in turn will characterize SM-target interaction by methods such as Hydrogen-Deuterium Exchange Mass Spectrometry (HDX-MS), to directly verify binding, provide structural information and pin-point conformational changes upon SM binding. High-throughput chemical proteomics will characterize differences among different SM variants. To study the systemic effects of SMs, zebrafish represent a cost- and time-effective model. Whole-organism studies will provide vital insight into in vivo effects of SMs, and allow timely decisions on whether a SM should be developed further.

Pilot pipeline project: A bioactivatable inhibitor of the ubiquitin-proteasome system (with Nico Dantuma, Karolinska Institutet). A SM screen in a melanoma cell line expressing fluorescent reporter substrate identified a small molecule inhibiting the ubiquitin-proteasome system. A structure-activity relationship was established, and affinity probe-based mass spectrometry yielded several potential interactors. Mass spectrometry results were complemented by a genome-wide CRISPR knock-out screen. By combining these methods, the list of candidates could be narrowed down to the redox enzyme NQO-1, which proved to be absolutely required for SM action. Further study indicated that the SM is bioactivated by NQO-1, and irreversibly inhibits the ubiquitin-proteasome system, making the SM a potential anti-cancer drug. Injection of the reporter cell line into zebrafish will establish the drug's effect on tumor growth *in vivo*.

National importance and impact.

The platform pipelines are modeled after cutting-edge workflows in industry and top academic research clusters (AstraZeneca, Broad Institute, Milner Institute, Sanger, etc.). To the best of our knowledge, the platform is unique in Europe in offering these workflows as facility services, enabling Swedish researchers to pursue complex projects commonly only possible in big pharma. CBCS has strong ties with industry including access to AstraZeneca's phenotypic compound collection, a large set of annotated bioactive small molecules. The platform's cross-disciplinary pipelines will help build confidence in a target and shift MoA-studies forward to an early stage in the drug discovery process, thus preventing waste of time and resources on less promising starting points. Our

common user base is already distributed over the entire nation and includes international users, which testifies to the uniqueness of platform services.

Plans for Governance and Organization.

The platform is governed by a platform steering group consisting of the four Facility Directors and chaired by the Platform Director. This group identifies user projects that might benefit from joint platform pipelines. The facilities will remain economically separate, but will strategically align their service portfolio according to platform needs. To ensure that facility- and platform services remain internationally competitive, we have recruited five international experts as platform advisors (John Doench, Broad/MIT; James Inglese, NCATS, NIH; Thomas Lundbäck, AstraZeneca; Bernhard Küster, TU Munich; and Shawn Burgess, NHGRI, NIH). All four facilities will run regular outreach activities and information events to educate potential users on facility services and platform capabilities. All four facilities have a multitude of interactions, and the entire platform is part of PhenoTarget, a SciLifeLab funded network of more than 30 research groups and facilities from all over Sweden who share an interest in phenotypic screening and target identification.

Promotion of data-driven science.

Chemical Biology and Genome Engineering not only generates big data (next generation sequencing data, imaging data, multivariate data from phenotypic screens), but is instrumental in data-driven hypothesis generation and validation of initial results. Each platform unit will actively support users in making their data publicly available (Findable and Accessible), while striving to deliver standardized data in an Interoperable and Reusable format (FAIR criteria).

Budget 2021–2024

The proposed budget increase will contribute to platform integration and expansion into the described new service areas and will create a platform offering unique and truly enabling capabilities. A motivation of the requested increase is given in the individual facility reports.

Chemical Biology Consortium Sweden

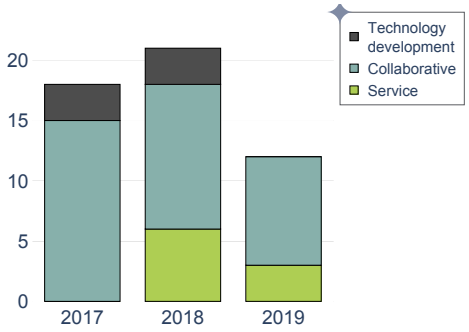
Read more: Web page, Publication Data Base

Basic Information

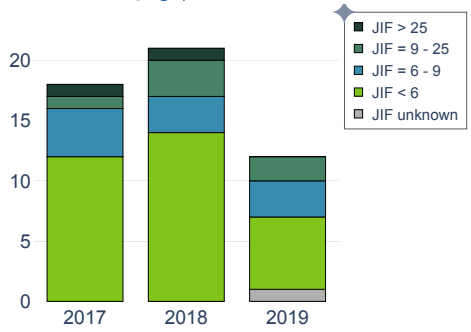
Facility director: Anna-Lena Gustavsson
Co-Facility director: Erik Chorell
Head of facility: Anna-Lena Gustavsson, Stina Berglund Fick
SciLifeLab facility since: 2013
Host University: KI, UmU
FTEs: 13
FTEs financed by SciLifeLab: 6

Funding 2020 (in kSEK)

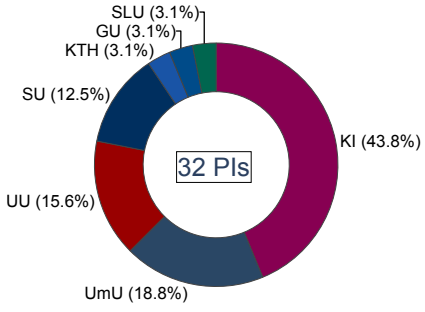
SciLifeLab: 6000
Total: 13410



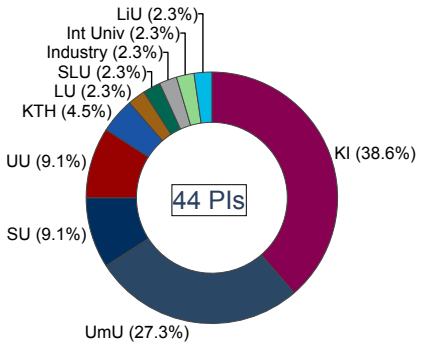
Publications by category



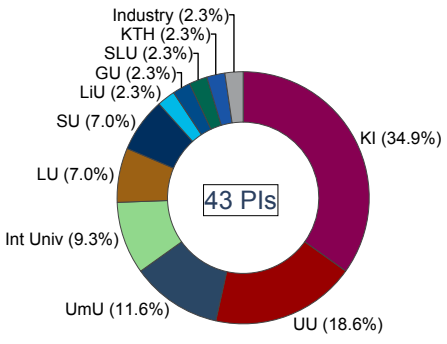
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

- Assay design and development for screening
- Screening of small-molecule (SM) libraries in assays ranging from purified proteins to complex cellular systems, such as organoids
- Compound Center access to customized and proprietary SM libraries, (~200,000 compounds)
- Medicinal/synthetic chemistry to establish and optimize structure activity relationships of hit SMs and synthesis of custom SMs for chemical biology studies, such as photo affinity-based probes, fluorescent probes, and biorthogonal chemical reporter probes
- Target identification (Target ID) and mode of action (MoA) elucidation: affinity based approaches

New Technologies and Services 2021–2024

- Update and chemical space expansion of SM libraries, including improved SM distribution with enhanced data handling and data analysis tools for external users.
- Multidisciplinary approaches for target ID and MoA downstream of phenotypic SM screens by integration of platform capabilities and other emerging phenotypic profiling methods
- Functional precision medicine support
- Chemical biology support of plant and environmental research

Background

Chemical Biology Consortium Sweden (CBCS) is located at Karolinska Institutet (KI) and at Umeå University (UmU). The facility was launched in 2010 with the aim to assist researchers in Sweden to identify, develop and use bioactive small molecules (SMs) as tools to study complex biology. CBCS provides expertise and cutting-edge instrumentation for assay development, SM screening, computational chemistry, cheminformatics, medicinal/synthetic chemistry, and target ID efforts. The experienced staff at CBCS have expertise ranging from synthetic organic/medicinal chemistry to biochemistry and molecular/cell biology. The Compound Center provides access to SciLifeLab´s collection of over 200,000 SMs for biological screening purposes, readily available through acoustic nano-liter scale liquid dispensing, a unique asset for the Swedish academic community. The collection includes both chemically diverse and more focused sets such as chemogenomics libraries (bioactive SMs with known MoA and approved drugs). CBCS resources are provided to users through an objective and transparent selection process by an external Project Review Committee (PRC). CBCS currently has six FTEs in biology and four FTEs in chemistry, a number absolutely critical to maintaining expertise in a multidisciplinary field such as chemical biology (covering all areas of biochemistry, biophysical profiling, cell biology and high content screening, synthetic/medicinal and computational chemistry). Between 2010-2019, CBCS has engaged in over 400 projects,

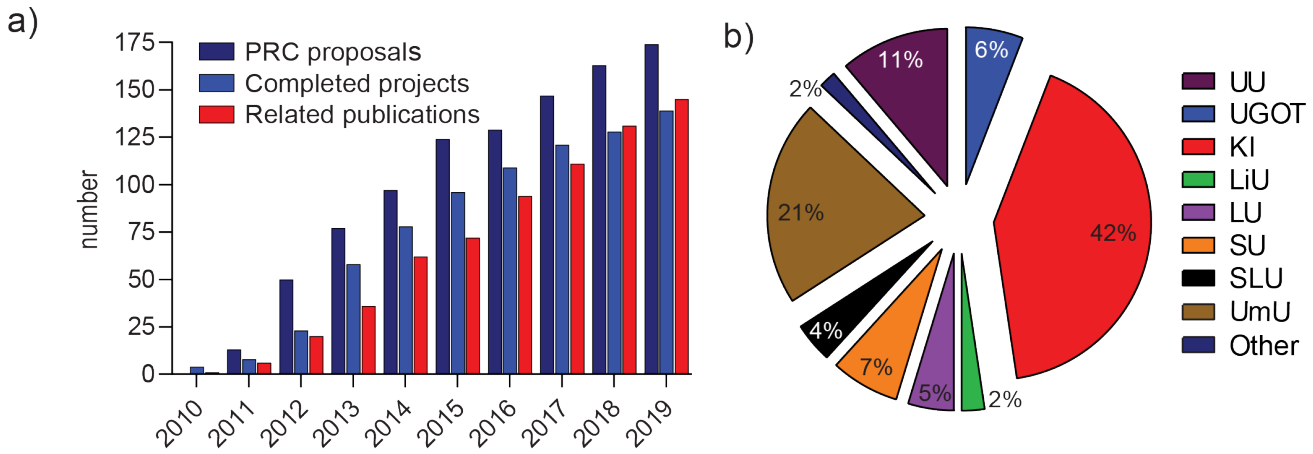


Figure 1. Interest in CBCS services and user distribution. a) A project prioritization system was introduced in 2011. The graph shows the cumulative number of applications, the number of completed larger projects and resulting publications involving CBCS. b) Distribution of user affiliations for approved full-scale projects 2010-2019.

both full-scale projects (Figure 1) and smaller service projects. Over ten patents, six start-up companies, and 140 publications testify to the value of CBCS collaborations for research and innovation with a broad distribution across Swedish universities.

Plans for 2021–2024

New technologies and services. For the coming funding period we need to continue to build on the existing CBCS's expertise, performance and deliveries with developments and improvements in two major areas, and a natural expansion of our services in two directions.

1) Increased capabilities for compound distribution (Compound Center) and data handling. CBCSs SM libraries are the cornerstone of our services. It is of key importance to update, extend and maintain these collections to meet the increased demand for special screening libraries. The rich data-sets from previous projects contain key information on unwanted compound liabilities, and potential insight into biological mechanisms. To ensure further implementation of the FAIR (Findable, Accessible, Interoperable and Reusable) principles, databases need to be aligned between the nodes and CBCS screening data has to be connected to public databases (e.g. PubChem) with a grace period to ensure intellectual property if necessary. To address this, CBCS will update the cheminformatic system and strengthen capabilities and routines for making data publicly available.

2) Development of orthogonal technologies for phenotypic profiling and MoA elucidation: CBCS is involved in a technology development project of *in situ* RNASeq after SM treatment together with Mats Nilsson's research group at SU and SciLifeLab. By leaving the cells intact, the method can combine transcriptomic analysis with image-based phenotypic profiling (e.g. cell painting techniques). CBCS has pioneered high throughput adaptations of Cellular Thermal Shift Assay (CETSA), including the recent publication of the first high-content imaging assay (CETSA in situ) with single-cell resolution. Together with a research group at SciLifeLab (Brinton Seashore-Ludlow, KI) CBCS is continuing the development of high-content imaging-based methods that enable information-rich, multiplexed, time-resolved assays to link SM target engagement to a phenotypic response.

3) Functional precision medicine support. Translational research requires the capability to assess the pharmacological benefits of research tool SMs in patient-derived cells, with the aim of drug repurposing and patient-tailored treatment. CBCS will support assay miniaturization, standard formating and quality control for the application of primary and patient-derived cells. The expansion of our SM collection and creation of disease area-relevant sub libraries will allow researchers to perform flexible drug combination screens.

4) Improved support for plant and environmental chemical biology. In recent years, chemical biology has expanded into areas such as crop protection, accelerating plant growth, CO2 fixation, fuel production, and the supply of vegetarian alternatives to a growing world population. CBCS has already made contributions to this emerging research field, and aims to strengthen its support in this area in close collaboration with the Swedish University of Agricultural Sciences.

CBCS is processing an application to the Swedish Research Councils (VR) support to infrastructures. The aim is to expand to Lund, Gothenburg and Linköping Universities to broaden the user base and in turn benefit from local expertise.

Uniqueness and Competitiveness. CBCS is a unique asset to the Swedish research community. Even at an international level, there are few chemical biology infrastructures that integrate all required elements for efficient discovery and characterization of bioactive SMs in a comparably comprehensive way. CBCS has complementary and synergistic capabilities within the Chemical Biology and Genetic Engineering platform, and a strong alliance with shared resources with the Drug Discovery & Development

Platform (DDD). Almost 50% of SM projects within DDD originate from CBCS projects. CBCS interacts with the National Bioinformatics Infrastructure for pathway analysis and joint cheminformatics capabilities needed for e.g. precision medicine data analysis.

Expected user base and national access. We see a continuous and even increase of interest in CBCS capabilities from researchers at most Swedish universities (Figure 1). CBCS's plan to establish smaller new geographical nodes (part of VR application) will further improve the national spread.

User Fees. CBCS has established a user fee model that is partly subsidized to ensure access for a broad user base, including young researchers. A user fee including salaries, premises, depreciation costs and overhead is applied, and consumable costs and compound access fees are added. Industrial users can access the infrastructure at full cost.

Reproducibility, quality and robustness of the generated data are of the utmost importance for a successful project, satisfied user, and scientific impact. User experience spreads quickly, and CBCS's good reputation after ten years of operation proves CBCS's high quality output. Staff has extensive experience in quality assurance gained by working with a wide variety of projects and from prior experience in industry.

Research environment and collaborations. CBCS is strategically situated at KI and UmU with strong positions in Swedish chemical biology, and the nodes are surrounded by relevant research groups - both users and contributors to the development of new services and capabilities, e.g. O. Kallionemi, O. Fernandez-Capetillo, T. Helleday (all KI), F. Almqvist, M. Elofsson, A. Linusson (all UmU), S. Robert (Swedish University of Agricultural Sciences), J. Carlsson (Uppsala University). The Chemical Biology and Genetic Engineering platform provides unique opportunities to build joint capabilities within target ID and MoA exploration. For alternative screening strategies such as fragment based approaches, CBCS collaborates with facilities offering access to this type of screening methods (e.g. Swedish NMR Center and FragMax at MAXIV laboratory).

Industrial and international collaborations. To stay at the forefront of chemical biology being part of both international and industrial collaborations is crucial. CBCS is an active partner in the Nordic Chemical Biology Network and the Nordic High content screening community. Further, Sweden is, through CBCS, an observing candidate country with the potential to become a full member of EU-OPENSCREEN. CBCS interacts with the pharmaceutical industry (e.g. AstraZeneca Open Innovation, Merck Darmstadt, Sprint Biosciences) and Swedish biotech companies such as Pelago Biosciences. To date, two CBCS projects have benefited from additional large-scale screening at the Innovative Medicines Initiative (IMI) funded European Lead Factory (ELF). CBCS is an associated partner to the newly funded IMI program EUbOPEN. In line with CBCS's development plans, the overall goals of EUbOPEN are to generate a high quality chemogenomics compound set hitting a substantial fraction of the druggable genome; and the establishment of translational and predictive patient-derived cell assays.

Budget 2021–2024

The budget from 2021 includes maintaining the critical mass of FTEs to provide services in chemical biology and the suggested improvements and expansion areas as described above.

Costs	2020	2021	2022	2023	2024
Personnel (11 FTEs) Chem Biol (7 KI - 4 UmU)	10000	10250	10 506	10 769	11 038
Comp Center & informatics (2=> 3FTE)	1600	2400	2 460	2 522	2 585
New service - Functional Precision Medicine (1 FTE)		800	820	841	862
New Service - Plant screening (1 FTE)		800	820	841	862
New geographical nodes (LU, GU,LiU) application to VR (3 FTEs)			2 400	2 460	2 522
Operations includes	2500	3000	3 600	3 690	3 782
Premises	1900	1900	1 948	1 996	2 046
Instrument depreciations - echon och IX	1240	1240	1 240	500	500
Other	250	350	359	368	377
Sum costs (kSEK):	17490	20740	24 153	23 985	24 572

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	6000	11500	11500	11500	11500
Bridge funding from KI	1800				
University funding (KI & UmU)	4470	4470	4470	4470	4470
VR funding for new geographical nodes (LU, GU, LiU)			3000	3000	3000
Scilifelab expensive instrument	740	740	740		
Instrument funding Kempe foundation and UmU Science&tech. fac	400	400	400	400	400
User fees	4260	4400	4700	4900	5200
Sum revenues (kSEK):	17670	21510	24 810	24 270	24 570

Table 1. Current budget (2020) and suggested budget 2021–2024

Chemical Proteomics

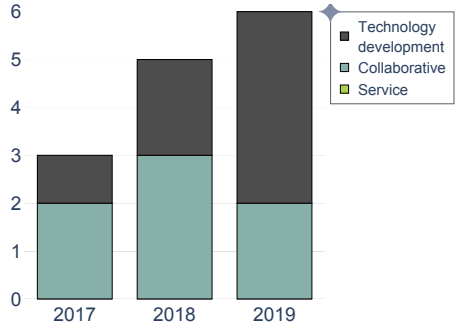
Read more: Web page, Publication Data Base

Basic Information

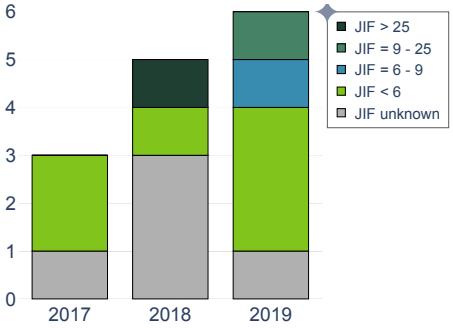
Facility director: Roman Zubarev
Head of facility: Massimiliano Gaetani
SciLifeLab facility since: 2017
Host University: KI
FTEs: 3
FTEs financed by SciLifeLab: 1.5

Funding 2020 (in kSEK)

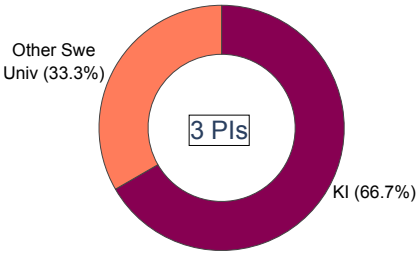
SciLifeLab: 1600
Total: 6900



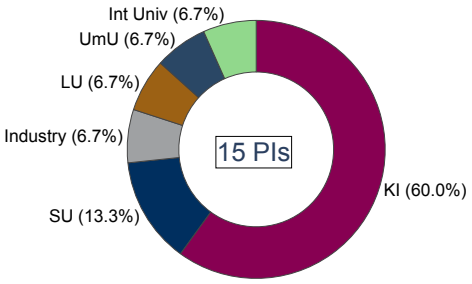
Publications by category



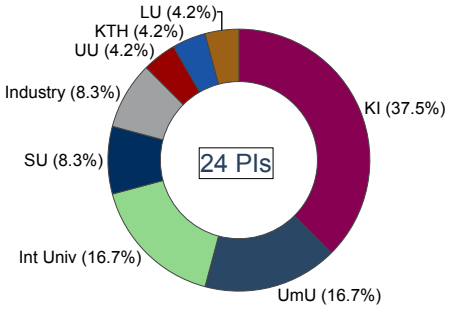
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

Major categories listed below; please visit the ChemProt webpage for more details.

A) Deconvolution of small molecule (SM) targets, mechanism of action (MoA) and off-target landscape through mass spectrometry (MS)-based deep quantitative proteomics:

A1. Proteome Integral Solubility Alteration (PISA) Assay *

A2. Functional Identification of Target by Expression Proteomics (FITExP)

A3. ProTargetMiner *

A4. Identification of interacting proteins by affinity-based approaches

A5. Thermal Proteome Profiling (TPP)

A6. RedOx Proteomics.

B) Analysis of protein structure by Hydrogen-deuterium exchange MS (HDX-MS)

C) Identification of enzyme substrates

* High-throughput (HT) methods, where HT is ≥ tenfold increase in throughput compared to former methods

New Technologies and Services 2021–2024

- PISA in low number of cells, enabling HT chemical proteomics at low sample amount, suitable for primary cells and precision medicine
- PISA with latest multiplexing technologies using Tandem Mass Tag pro 16-plex, allowing parallel study of multiple cell types or multiple SM
- PISA optimisation for membrane protein targets
- Orthogonal combination of PISA and ProTargetMiner for anticancer SM
- Multiplexed high throughput HDX-MS (in development).

Background

Overview. Our main goal is to decipher SM-induced proteome signatures for MoA elucidation. We have adopted the latest technologies and developed new high-throughput (HT) methods. Using multidisciplinary laboratory resources, ChemProt represents an innovative facility model with complete pipelines for target deconvolution and MoA determination of SM, by directly treating cell cultures, performing MS-based proteomics and data analysis, including data bioinformatics processing, publication figures and data representation.

Development, governance and people. ChemProt opened its doors to users in mid 2017 and is part of the Department of Medical Biochemistry and Biophysics (MBB) at Karolinska Institute (KI), in the Division of Chemistry I, headed by Prof. R. Zubarev. Apart from the director and the head of facility, ChemProt employs a senior proteomics expert, and a senior HDX-MS expert, as well as a research

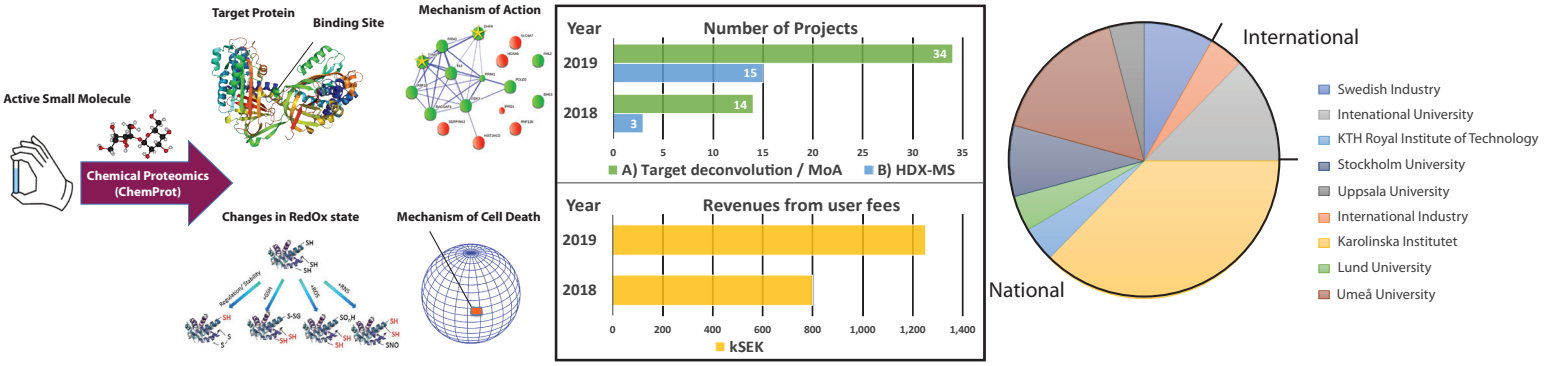


Figure 1. ChemProt outputs (left); Projects and user fees in 2018 and 2019 (center); Distribution of ChemProt users (right).

engineer and a LC-MS engineer. Nearly all staff members hold a PhD and have several years of postdoc experience, combining a range of competences such as cell culture, SM treatment studies, protein biochemistry, biophysics, thermodynamics, proteomics, MS and bioinformatics. Prof. B. Küster (TUM, Technische Universität München) is the international facility advisor.

Equipment. Our MS instrument park has been significantly upgraded. Today we have seven UPLC systems, each connected to a high resolution orbitrap MS system. In 2020, the oldest LC-MS instrument will be replaced by two new, more advanced instruments. In the last years, reproducibility and precision of HDX-MS analysis has been increased by full automation with a robot for sample preparation, connected on-line with chromatography and MS analysis.

Current services and key achievements. The HDX-MS technology for protein structure analyses uses MS on purified proteins. HDX-MS contributes to the mission of ChemProt and the Chemical Biology and Genome Engineering (CBGE) platform by determining the site of interaction of the SM and conformational changes in response to SM binding. HDX-MS was pioneered by scientists of our division and further developed at ChemProt. In the last years, our constant method optimization and infrastructural upgrades have successfully supported high impact research (examples: Visnes et al., Science 2018; a project on plastic degrading enzymes with Per-Olof Syrén at KTH, currently ongoing). For target deconvolution and determination of MoA through chemical proteomics, we can combine three orthogonal strategies: 1) SM-induced proteome signatures due to alteration of protein solubility/stability in thermal profiling; 2) SM-induced specific proteome regulation signatures; 3) SM-induced RedOx proteome signatures. We have obtained and published key methodological achievements, our new HT methods, namely: ProTargetMiner and PISA. PISA is a game changer in our field, which overcomes several limits of thermal proteome profiling, boosts reproducibility and the number of tested samples.

Plans for 2021–2024

New technologies and services, uniqueness and competitiveness. From early adoption of latest methods, ChemProt successfully challenged methodological flaws turning bottlenecks into new solutions. Thanks to PISA, today ChemProt is the only facility in the world providing target deconvolution by MS-based proteomics with such HT per biological replicate and at such high statistical relevance, due to the much higher number of replicates tested in PISA than in TPP. Furthermore, minimization of sample amount in PISA enables analysis of primary cells, moving towards personalized medicine. Latest advances of the Tandem Mass Tag technology further increased its potential. After having developed HDX-MS into a successful service at the international level, competitivness will be increased by method development aiming at tenfold increase in throughput. HDX-MS projects have been rapidly increasing in the last years for academic users, industry and DDD platform (15 projects in 2019, a fivefold increase compared to 2018). For these reasons, we urgently need more funds to support more full time equivalents (FTEs) dedicated to HDX-MS.

Reproducibility and quality. Data reproducibility, quality and robustness are keys to deliver success and scientific impact and our methods boost quality, reproducibility and confidence in SM-targets candidate interactions and MoA. PISA allows to include ten times higher number of samples at the same cost and time of previous methods, and is therefore suitable to study more biological systems or larger numbers of SM. Orthogonal approaches at the facility level and at the CBGE platform can provide relevant crossvalidation. Process automation in HDX-MS has increased not only throughput, but also reproducibility and quality of service. Data is safely stored on a KI server and data delivery options will be implemented at SciLifeLab.

Expected Userbase. Userbase has strongly grown in Sweden and internationally. Most users are from universities, however two Swedish industries and one multinational pharma were supported in 2019. ChemProt supports the DDD platform´s projects, particularly through HDX-MS; they are expected to grow in number. The number of projects almost tripled between 2018 and 2019 a userbase

increase with 60%. Today ChemProt supports more than 20 research groups. Based on the recent growth and on other factors, it appears fair to assume that the ChemProt´s userbase will continue to increase during the next years. Should the current trend be continued, the growth would be mostly due to projects in Swedish academia, but also with international and industrial contribution.

National uniqueness and access. As a node of the Swedish infrastructure for biological mass spectrometry (BioMS, www.bioms.se), ChemProt is responsible for chemical proteomics and one of two nodes providing HDX-MS. Requests for chemical protemics projects and HDX-MS are placed through the BioMS portal and channeled to ChemProt. Furthermore, ChemProt is strongly connected with the Swedish and international MS communities. By entering into the CBGE platform, ChemProt´s technologies for MS-based proteomics and HDX-MS protein structure analysis will produce strong benefits for the whole scientific community.

User fees and costs. User fees are based on KI´s cost model with hourly rates including salaries, premises and depreciation, plus costs of consumables. No overheads or indirect costs are charged to academic users who also benefit of an equal and high level of subsidy. Industry is charged full cost.

Research environment and collaborations. Thanks to its location in Biomedicum, ChemProt has increased *local interactions* at KI, for example with the groups of Galina Selivanova, Thomas Helleday, Nils-Göran Larsson, Jussi Taipale and Birgitta Henriques Normark. *On the national level* ChemProt collaborates with PIs from KTH Royal Institute of Technology, Lund University (LU), Stockholm University, Umeå University and Uppsala University, including Per-Olof Syren, Jonas Larsson, Leopold Ilag, Sun Nyunt Wai, and Susanne Lindquist. BioMS and its nodes (LU, KI and Gothenburg University) also provide an additional strategic network. For protein structure analysis, ChemProt provides HDX-MS, which fits well into CBGE platform pipelines and supports cooperation with DDD. In addition, ChemProt connects to the Lund node of BioMS for cross-linking MS, as well as to X-Ray and NMR facilities, either directly or through the CBGE platform. Our scientific *international network* includes top proteomics experts: M. Savitski (EMBL Heidelberg), B. Küster (TUM, Munich), P. Picotti (ETH Zurich), M.R. Larsen (University of Southern Denmark) and K. Mechtler (IMP, Vienna). ChemProt has collaborated with three major Chinese universities, and has recently entered into a new consortium, future candidate as a new EU infrastructure. Exploiting *synergies within SciLifeLab* is key for the creation of new capabilities, within and beyond the CGBE platform. The collaboration with DDD will be improved, due to ChemProt's HDX-MS expertise on epitope mapping, which is most suitable for the type of DDD's needs. ChemProt and its division are an active part of the PhenoTarget Research Community Program at SciLifeLab, coordinated by O. Fernández-Capetillo. ChemProt has discussed with NBIS initial plans to start building together new bioinformatics capabilities specific for chemical proteomics.

Budget 2021–2024

Total FTEs were 3 in 2019 and will be 3.5 in 2020. We need to increase FTEs to 4.5 from 2021 onwards to support developments along with acquisition of new MS-instruments (at least two) and associated to our service expansions, particularly on HDX-MS. The last is currently carried out with personnel associated to (and not hired by) ChemProt and its division at MBB department of KI.

Costs	2020	2021	2022	2023	2024
Personnel for Chemical proteomics (3 FTEs)	3 000	3 000	3 000	3 000	3 000
Personnel for HDX-MS (0.5 => 1.5 FTEs for HDX-MS)	500	1 500	1 500	1 500	1 500
Operations	1 300	1 350	1 350	1 400	1 400
Premises	722	722	722	830	830
Instrument depreciations	2 270	3 720	3 550	3 370	3 000
Other (including platform pipeline projects)	300	300	300	300	300
Sum costs (kSEK):	8 092	10 592	10 422	10 400	10 030

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	1 600	3 300	3 300	3 300	3 300
VR (for BioMS)	2 800	2 800	2 800	2 800	2 800
KI (for BioMS)	1 900	1 900	1 900	1 900	1 900
Approved SciLifeLab Espensive Instrument application 2019	600	600	600	600	450
Incoming Balance (residual from extra user fees from previous years)	1 006	914	222	-100	-200
User fees	1 100	1 300	1 500	1 700	1 800
Sum revenues (kSEK):	9 006	10 814	10 322	10 200	10 050

Table 1. Current budget (2020) and suggested budget 2021–2024

High Throughput Genome Engineering

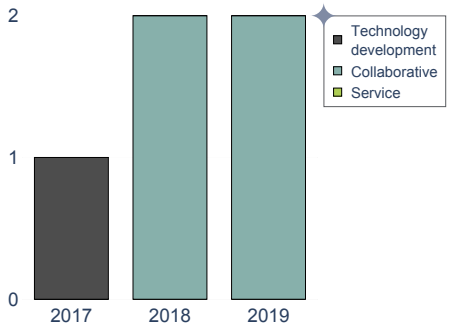
Read more: Web page, Publication Data Base

Basic Information

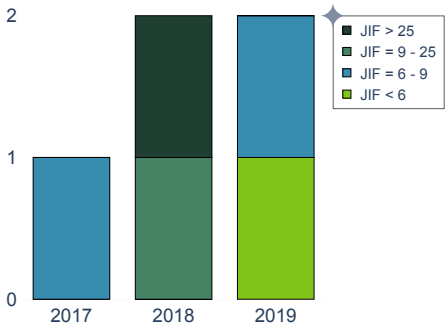
Facility director: Bernhard Schmierer
Head of facility: Bernhard Schmierer
SciLifeLab facility since: 2017
Host University: KI
FTEs: 5
FTEs financed by SciLifeLab: 3.2

Funding 2020 (in kSEK)

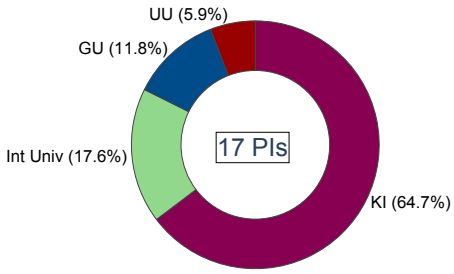
SciLifeLab: 3200
Total: 6395



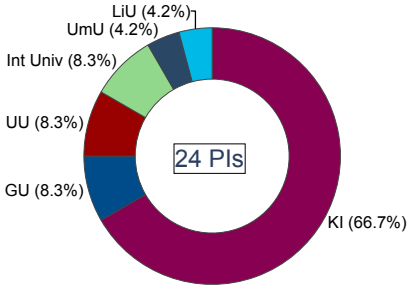
Publications by category



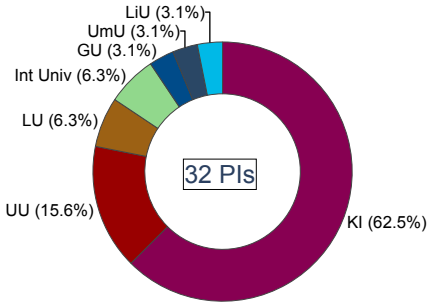
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

- Custom-made barcoded CRISPR guide libraries from design to lentivirus
- Genome-wide or custom pooled loss-of-function screens by CRISPR-knock-out or CRISPR-inhibition
- Genome-wide or custom pooled gain-of-function screens by CRISPR-activation
- CRISPR-based perturbation of non-coding RNAs and functional genomic elements
- Highly multiplexed CRISPR-Cas9 perturbations with single-cell RNASeq readout (CRISPR-scRNASeq)

New Technologies and Services 2021–2024

- CRISPR-DIVA (Sequence Diversification and Interrogation of protein VAriants). Massively parallel, targeted mutagenesis to characterize small molecule-protein or protein-protein interactions at single amino acid resolution
- Highly multiplexed CRISPR-Cas9 perturbations with imaging of phenotypes and in situ sequencing of guides
- Precision gene editing in cell lines to create disease models or reporter lines for chemical and genetic screens

Background

HTGE was established as a CRISPR-screening facility in January 2017. The facility began with two staff members, and expanded to three in August 2018. In 2019, additional funding was obtained from Karolinska Institutet to establish Karolinska Genome Engineering (KGE). KGE is HTGE's local core facility branch performing knock-outs and precision edits in mammalian cells, as well as designing CRISPR reagents for mouse transgenesis. HTGE/KGE has five current staff members, three of which are funded by SciLifeLab.

Services and technologies. HTGE's core services are pooled CRISPR-Cas9 genetic screening by either gene knock-out (*CRISPR-KO*), gene repression (*CRISPR-inhibition*) or gene activation (*CRISPR-activation*) in cell lines and primary cells. HTGE provides human and mouse genome-wide guide libraries, and designs and creates any custom library tailored to user specifications. For details, see https://www.scilifelab.se/facilities/htge/. In 2019, HTGE and Eukaryotic Single Cell Genomics (ESCG) have together launched *Highly multiplexed CRISPR-Cas9 perturbations with single-cell RNASeq readout* (CRISPR-scRNASeq, Figure 1), a workflow in which single-cell RNASeq is used to read out both the transcriptome and the guide RNA from single cells. This service is particularly amenable to studies requiring an *in vivo* transplantation readout, and is also being used to study murine neural development through introduction of the guide library directly into the developing embryo.

Organisation and governance. HTGE is part of the *Chemical Biology and Genome Engineering* platform and interacts closely with the other platform units. All staff at HTGE/KGE have several years of postdoctoral experience. Maintaining these experts is critical for the facility, which is driven primarily by expertise and know-how rather than expensive instrumentation. Facility staff discuss and prioritize projects. HTGE has recruited an outstanding CRISPR

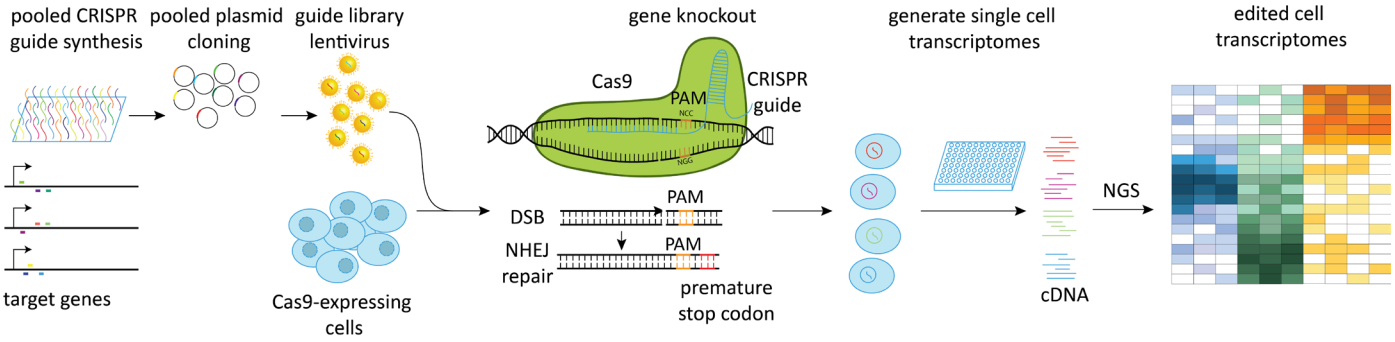


Figure 1. Highly multiplexed CRISPR-Cas9 perturbations with single-cell RNASeq readout (CRISPR-scRNASeq). Hundreds of guides are synthesized as oligos, cloned in pool into a lentiviral plasmid, packaged and transduced into Cas9 expressing cells in pool. Single cells are then isolated and their transcriptomes, including the identity of the guide RNA present in each cell, are recorded. Example shown is for WT Cas9 and gene knock-out, an identical workflow is being set up for gene activation.

screening expert, John Doench (Associate Director of R&D, Genetic Perturbation Platform at the Broad Institute), as facility advisor. His input is invaluable to keep the service internationally competitive and to decide on which new technologies to implement. The HTGE and KGE branches are economically separate, but scientifically fully integrated.

Key achievements 2017-2019. Since its inception in 2017, HTGE has greatly expanded its service portfolio and experienced ever increasing local, national, and international user demand. Projects cover a wide range of topics such as cell differentiation, cancer, diabetes, neurodegenerative diseases, autoimmune disorders, bacterial or viral infection, drug resistance, drug sensitivity, epigenetics, and others. In a 2019 anonymous user feedback survey, 23 out of 24 respondents rated HTGE's services as "critically important" (12) or "important" (11) for their research projects. Cost recovery has more than doubled since 2017 and currently accounts for one third of HTGE's available funds. In collaboration with Jussi Taipale's lab, HTGE has published two key papers: "*CRISPR/Cas9 screening using unique molecular identifiers*" in Molecular Systems Biology described an improvement in CRISPR screening using barcode technology, which is routinely applied in all HTGE screens. Our 2018 Nature Medicine paper "*CRISPR–Cas9 genome editing induces a p53-mediated DNA damage response*" was picked up by 149 news outlets around the world, and, in the past 18 months, has been accessed 14,000 times and cited 188 times. Establishing KGE in 2019 with funds from Karolinska Institutet was an important milestone. KGE delivered 30 edited cell lines (knock-outs and knock-ins) to users in its first 12 months of operation.

Plans for 2021–2024

New technologies and services.

CRISPR-DIVA for mechanism-of-action and drug-target interaction studies. HTGE often applies CRISPR screens to identify sensitivity and resistance mechanisms downstream of phenotypic small molecule (SM) screens. A more detailed mechanism-of-action determination requires zooming in on defined protein domains, and high-resolution tools are required. HTGE is establishing such a genetic tool, the novel base-editing method CRISPR *Diversification and Interrogation of VAriants* (CRISPR-DIVA, Figure 2). In contrast to other screening methods, which modulate entire genes, CRISPR-DIVA allows modulation of specific amino acid residues. CRISPR-DIVA can generate high resolution information on SM binding, and can predict potential resistance mechanisms. Throughput can be tailored according to needs, from interrogating one single known target to several hundred potential targets. As a genetic method, CRISPR-DIVA is orthogonal to chemoproteomic approaches, and its inclusion will greatly improve overall success rates of target identification in the pipelines proposed at the platform level. CRISPR-DIVA is also applicable to mapping of regulatory domains, enhancer elements, and other non-coding regions of interest.

Pooled CRISPR screens with image-based phenotyping and in situ guide sequencing. This 2019 method combines pooled screening with microscopy-based phenotypic profiling of cells, sections or organoids. A two-step microscopy procedure is used, where high-content phenotypic characterization is followed by a fluorescence-based in situ sequencing protocol to determine the guide RNA in each phenotyped cell. This method greatly expands the phenotypic variability that can be interrogated in a pooled screen and is of special interest to researchers investigating cell differentiation and cell-cell interactions *in vivo* and has the potential to reduce the number of animals needed. HTGE is planning to adopt the technology with the help of Mats Nilsson, a leading expert in *in situ* sequencing, the *In situ Sequencing* pilot facility, and Oscar Fernández Capetillo's lab at SciLifeLab.

Creating relevant model systems for chemical and genetic screening. We will include the generation of tailor-made screening systems (disease models, reporter lines) by precision gene editing into HTGE's national service portfolio. This would be strictly limited to models used for downstream chemical or genetic screens. This service is vital for establishing cross-disciplinary pipelines at the platform level.

Uniqueness and Competitiveness. HTGE is at the forefront in Europe in implementing technical innovations in the CRISPR screening field, which have tended to originate in the U.S. HTGE's services are unique in Sweden, and to the best of our knowledge, also in Europe.

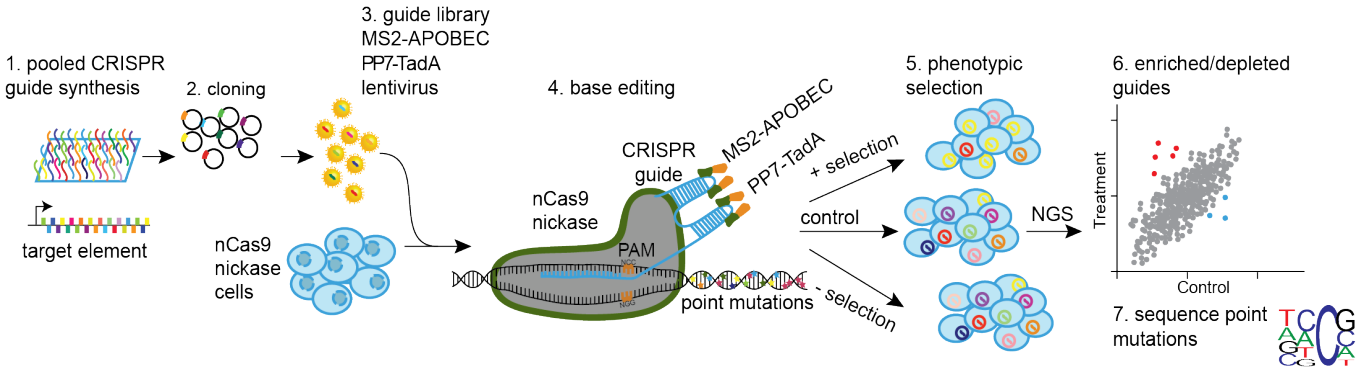


Figure 2. CRISPR-DIVA. Guide libraries densely tiling genomic loci of interest are introduced lentivirally into a cell popula-tion together with CRISPR-guided base-editing enzymes. Each cell obtains a single guide, and base-editing in close proximity to the guide position creates a cell population where each cell contains a random mutation at the small locus defined by the guide present in the cell. Mutations that disrupt SM-target binding will revert the cellular phenotype elicited by the SM. Revertants are isolated, and NGS then catalogues the responsible mutations and, by extension, small protein motifs and single amino acids that mediate the SM-target interaction.

Expected user base, national access and user fees. We expect stable or increasing demand for our highly demanded core services, and rolling out additional state-of-the-art pipelines will increase user demand further. HTGE currently has a user base of roughly 50 academic research groups, many running several projects. Attracting the private sector is a priority for 2021-2024, and discussions with both regional enterprises and international companies are ongoing. Thanks to intensive outreach activities, users distribution across the entire nation has been achieved, and HTGE will continue its efforts to actively engage users from all Swedish universities. User fees are based on Karolinska's full cost model. An hourly rate including salaries, premises, depreciation costs and overheads is applied, consumable costs are added. Industry is charged at full cost; all academic users enjoy the same subsidy.

Reproducibility and Quality. In our user feedback survey, 80% (19 out of 24) respondents found working with HTGE "excellent" or "very good", and 100% had either already recommended HTGE or thought it likely they would. HTGE's services mostly create initial screening data, and after less than three years in full operation, most user projects are still in the pre-publication stage. The first paper using HTGE screening data was published in January 2020 (*Shahin Varnoosfaderani et al., A regulatory role for CHD2 in myelopoiesis. Epigenetics. 2020 Jan 10:1-13*). At least two more papers are under review, and a further five are in preparation.

Research environment and collaborations. Research environment and collaborations. HTGE is a local ambassador for SciLifeLab in Karolinska's new Biomedicum, and collaborates locally with the labs of Jussi Taipale, Molly Stevens, Goncalo Castelo Branco, Ernest Arenas, as well as the the iPSC, VirusTech, FACS and mouse transgenics core facilities. Cross-platform pipelines are in place with NGI and Eukaryotic Single Cell Genomics, and HTGE is in close contact with DDD. HTGE collaborates with the company Moligo Technologies (ssDNA templates in gene editing), and Pfizer regarding contract research. HTGE has regular exchanges with other relevant core facilities in Europe (Johan Jakobsson, Lund; Michael Howell, London; Antony Adamson, Manchester; Philip Hublitz, Oxford; Floris Foijer, Groningen; Vasco Barreto, Lisbon).

Budget Justification. SciLifeLab funding is currently covering three FTEs for HTGE's pooled CRISPR-screening service. If the increasing demand for this service is to be met also in the future, this needs to be raised to four FTEs. In addition, one more FTE is required for developing the new technologies described and rolling them out as national services.

Costs	2020	2021	2022	2023	2024
Personnel (5 FTEs)	4 584	4 699	4 816	4 936	5 060
Operations	1 800	2 000	2 050	2 101	2 154
Premises	850	900	923	946	969
Instrument depreciations	1 000	1 000	1 200	1 200	1 200
Other	250	256	263	269	276
Sum costs (kSEK):	8 484	8 855	9 251	9 453	9 659

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	3 200	5 300	5 300	5 300	5 300
University funding	1 495	1 495	1 495	1 495	1 495
SciLifeLab TDP	1 300				
SciLifeLab expensive instrument grant	400	400	400	400	400
User fees	1 700	1 900	2 100	2 153	2 206
Sum revenues (kSEK):	8 095	9 095	9 295	9 348	9 401

Table 1. Current budget (2020) and suggested budget 2021–2024

Genome Engineering Zebrafish

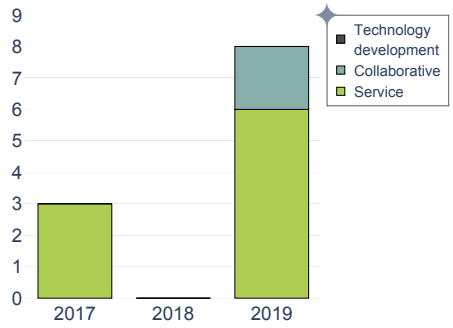
Read more: Web page, Publication Data Base

Basic Information

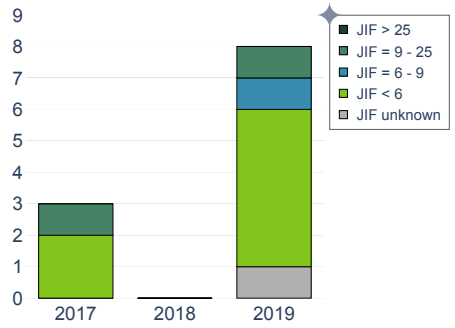
Facility director: Johan Ledin
Head of facility: Tiffany Klingström, Beata Filipek
SciLifeLab facility since: 2016
Host University: UU
FTEs: 6
FTEs financed by SciLifeLab: 2.4

Funding 2020 (in kSEK)

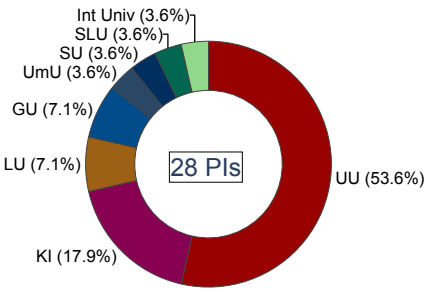
SciLifeLab: 2400
Total: 3960



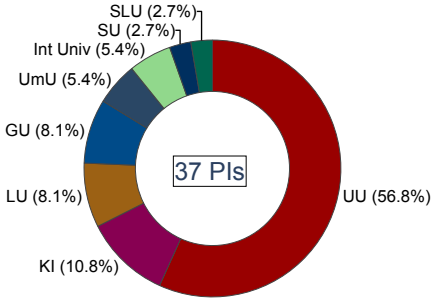
Publications by category



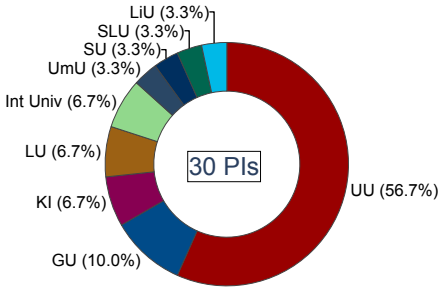
Publications by JIF



Users 2017



Users 2018



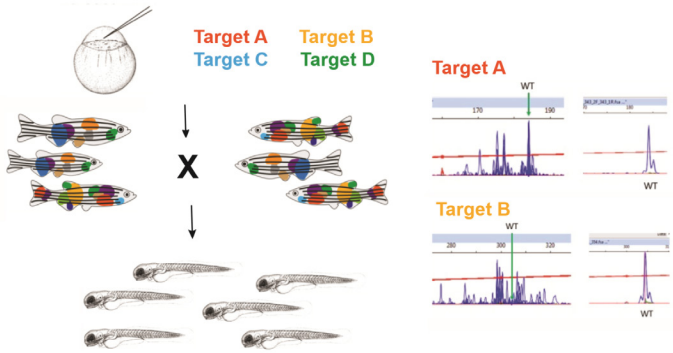
Users 2019

Current Technologies and Services

- CRISPR/Cas9 genome modification in wildtype or reporter lines
- Support in Tol2 transgenesis and site-specific DNA insertion projects
- Genotyping by fluorescent PCR (fin clip and embryos)
- Chemical screening on zebrafish larvae
- Vertebrate Automated Screening Technology (VAST) services
- Stereo microscopy and light sheet microscopy services

New Technologies and Services 2021–2024

- Zebrafish image informatics (Zii) capability together with the SciLifeLab BioImage Informatics (BIIF) facility.
- Multiplex CRISPR-mediated gene inactivation for directed, combinatorial screening of alleles that induce distinct phenotypes
- Customized deletions in the zebrafish genome such as removal of exons or promoter regions
- Targeted DNA insertion and base editing in the zebrafish genome



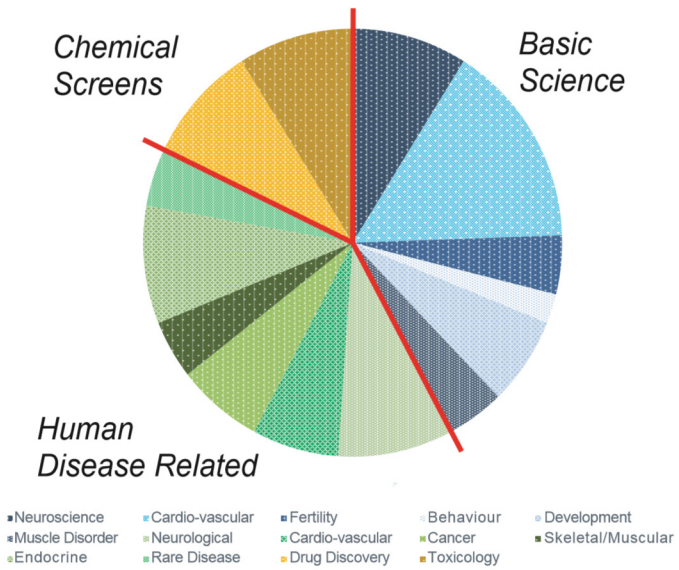
Background

Genome Engineering Zebrafish (GEZ) offer low cost, high-throughput phenotypic testing of large sets of candidate genes or molecules in a living organism. GEZ offers researchers without the possibility of experimentation in a vertebrate model the resources required to investigate the effects of genome engineering and substance exposure in vivo. GEZ provides an efficient, “high-speed” link between genomic data and the investigation of phenotypes in the context of a whole animal. GEZ is both an open facility accessible to the Swedish research community, and a conduit for the exchange of methods and techniques between labs.

GEZ has been operating as a national SciLifeLab facility since January 2017. As of today, we have provided CRISPR/Cas9 mediated genome editing, services, expertise, and access to instrumentation to researchers from Uppsala University, SLU, the Karolinska Institute, the University of Gothenburg, Lund University, Umeå University and the University of Copenhagen.

The current core service of GEZ is allowing researchers to investigate candidate gene function in the zebrafish model at low cost. Zebrafish transgenic lines may be generated directly in our selection of validated "readout" lines imported from other labs and stock centers. The embryo is small enough to be handled in 96-well format, uniquely enabling large scale chemical screens in a vertebrate organism. Its transparency allows for rapid visual readouts and stunning, high resolution imaging of individual cells. To make GEZ truly useful to users, GEZ established a VAST BioImager™ service during 2019. The VAST service is designed for automated handling and high-resolution fluorescence imaging of large numbers of 2-7 day old zebrafish larvae. The 96 well format enables high throughput chemical screens and genotyping. GEZ is a part of the department of Organismal Biology at Uppsala University with six full time equivalents, including two researchers, two research engineers, two research assistants and several part time animal care staff.

The facility has experienced a steady increase in user demand and enabled research projects for more than 30 researchers at seven universities during 2018. GEZ also promotes national collaboration and cross disciplinary research projects by consulting and arranging national workshops and meetings. Many of GEZ services are requested in the initial phase of research projects, e.g. development of a new zebrafish disease model, which manifests as a long delay between delivered GEZ service and publication. Consequentely, the publication record is stronger towards the end of the 2017-2019 period. We predict that publication rate will increase in coming years,



as GEZ has contributed to additional studies either already published 2020 (in Nat Communication and Chemosphere), or studies currently in revision, submission, or preparation stage. During 2019, GEZ delivered around 25 genetically modified zebrafish lines and the new Zii capability (see below) has already contributed to several publications since service initiation in spring 2019.

Plans for 2021–2024

1) Enhanced Zii capability. GEZ and the BioImage Informatics Facility (BIIF) have launched Zebrafish image informatics (Zii), a joint capability for zebrafish experiments. The Zii capability utilises GEZ's capacity for high-throughput imaging of zebrafish larva, and BIIF expertise in large scale analysis of imaging data. The large collection of zebrafish readout lines at the Zebrafish Core Facility at Karolinska institute (ZCF) is an integrated resource, enabling the Zii capability to quickly adapt to user-specific needs. Gathering high quality images of zebrafish phenotypes was before a slow task, which restricted the capacity of the facility. Ongoing technology development in the Zebrafish image informatics (Zii) capability aims to develop integrated services, ranging from the generation of genome engineered zebrafish to state-of-the-art, high-throughput quantification of distinct phenotypes. Further development of the Zii capability will produce more automatized systems for analysis of image data, involving machine learning and artificial intelligence. GEZ will work together with researchers at Uppsala with complementary expertise (Kaska Koltowska, Amin Allalou, Marcel den Hoed) to develop methods for high throughput phenotype analysis in cardiovascular research, inherited rare diseases, and drug screening.

2) Multiplex CRISPR-mediated gene inactivation. Multiplex CRISPR-mediated gene inactivation is a service where 2-8 genes are targeted simultaneously in such way that a large number of individuals are generated with different combinations of loss-of-function alleles. This cohort of individuals with complex genotypes is then subjected to phenotypic screening, typically in the Zii capability, followed by genotyping. This service offers unique possibilities to investigate the genetic basis of complex phenotypes involving multiple loci in a vertebrate model system.

3) Customized deletions in the zebrafish genome. Recent studies suggest that mRNA decay-triggered upregulation of compensating genes can occur in response to non-sense mutations. Many CRISPR/Cas9 knock-outs (including in zebrafish) are based on this type of mutation. GEZ will offer customized deletions of promoter regions, which does not trigger genetic compensation in the same way, as a complement to out-of-frame deletions in exons.

4) Targeted DNA insertion and base editing in the zebrafish genome. Methods for site specific DNA insertion and

base editing are rapidly developing and GEZ offers support in such projects, with the aim to develop cost effective standardized genome editing services. Genome editing can be applied to recapitulate human disease mutations or to create transgenic reporter zebrafish, where a specific gene product is labeled with a fluorescent protein, which is compatible with the Zii capability.

Uniqueness and Competitiveness. The GEZ facility is unique in Sweden in offering users development and evaluation of transgenic zebrafish lines and in its national focus, accepting researchers from all Swedish universities. As far as we know, no facility in the world offers similar integrated services in the zebrafish model system, from editing of a gene to a customized, detailed, large-scale analysis of phenotypic effects – ready for publication. GEZ thus enables experimental biology in a vertebrate model system for the many researchers in Sweden who lack easy access to animal models.

Expected user base and National access. We expect that GEZ's user base will be dominated by Swedish universities in the 2021-2024 period, but we also experience an increased interest in the zebrafish model system from the biothech industry. For example, the Uppsala University PI Marcel den Hoed has recently initiated a large collaboration with a pharmaceutical company, for which GEZ will provide complementary services, illustrating how GEZ can facilitate academia / industrial collaborations.

Expected user base and National access. All GEZ services are equally accessible on a national level without restrictions. GEZ actively reaches out to researchers nationwide by organizing meetings and workshops (the last workshop in October 2019 had 80+ participants from all Swedish universities), and GEZ staff regularly travel to Swedish universities to discuss potential projects. GEZ has a subsidized user fee model to ensure access for a broad user base, including young researchers. A user fee including salaries, premises, depreciation costs and overhead is applied, and consumable costs are added. Industrial users can access the infrastructure at full cost.

Research environment and collaborations. The GEZ facility has attracted young PIs such as Kaska Koltowska, Marcel den Hoed, Henrik Boije, Amin Allalou, Tatjana Haitina (with prestigious grants from the Swedish research council, Ragnar Söderbers stiftelse, Hjärt-Lung foundation, SciLifeLab, Wallenberg Academy Fellows and the NIH), who depend on GEZ for important parts their research. The combination of 1) advanced users requesting GEZ to offer newly developed methods, 2) GEZ expert staff and infrastructure and 3) close interactions with national and international research communities together create a vibrant research environment at Uppsala University which contributes to the attractiveness of GEZ for new users and interdiciplinary initiatives. GEZ further collaborate with the following national resources and specialists:

- CBGE (*Chemical Biology and Genome Engineering*) platform. GEZ, and our national partners (listed below) will make services in the zebrafish model system available for CBGE users to screen and investigate the effect of small molecules on organism development and homeostasis. GEZ role in the CBGE platform is further described in the CBGE platform report.

- BIIF (*National SciLifeLab Bioimage Informatics Facility, Uppsala universitet*). BIIF and GEZ develop services together on advanced image analysis, and have several ongoing projects to establish services for high throughput screening in live or fixed animals.

- ZCF (*Zebrafish Core Facility, Karolinska institutet*). The Uppsala GEZ facility and the Karolinska ZCF collaborate closely on a number of issues, aiming to offer joint open zebrafish resources for Swedish researchers.

- CBT (*Chemical Biology and Therapeutics at Lund University*). CBT has the capacity to perform advanced behavioral analysis on zebrafish exposed to compounds or genomic engineering. Since CBT already has this competence, GEZ will not invest in capacity for behavioral analysis and instead develop integrated services with the CBT.

Budget justification. The increased funding 2021-2024 will be used to develop and integrate services with GEZ national parters.

Costs	2020	2021	2022	2023	2024
Personnel (6+2 FTEs)	4 133	6 043	6 164	6 287	6 413
Operations	691	900	918	936	955
Premises	850	867	884	902	920
Instrument depreciations	1 360	1 387	1 415	1 443	912
Other	306	312	318	325	331
Sum costs (kSEK):	7 340	9 509	9 700	9 893	9 531

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	2 400	4 850	4 850	4 850	4 850
University funding (VR?)	1 000	2 000	2 000	2 000	2 000
Expensive instrument grant SciLifeLab	560	560	560	560	
User fees	2 131	2 238	2 349	2 467	2 590
Sum revenues (kSEK):	6 091	9 648	9 759	9 877	9 440

Table 1. Current budget (2020) and suggested budget 2021–2024

Genomics Platform

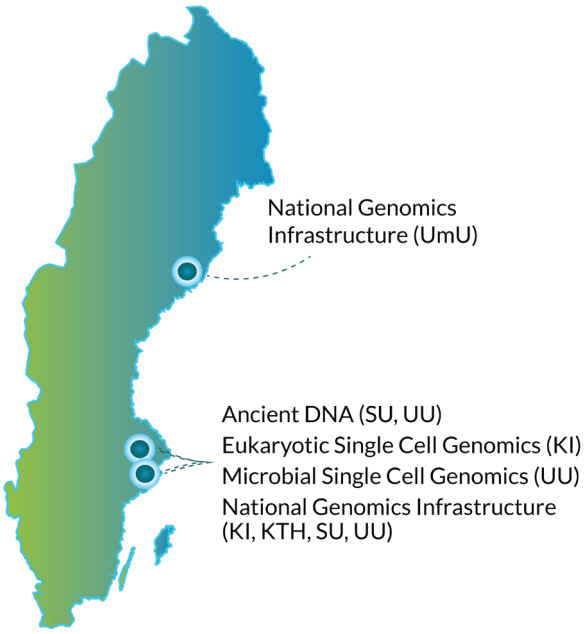
Basic information

Platform Director: Ulf Gyllensten

Platform Vision and Mission:

- Enable world-class research and industrial development in genomics.
- Provide access to both established and cutting-edge genomics technology.
- Assist users in project design, generation, analysis and management of data.
- Support genomics research in all subject areas.
- Support scientists, core facilities and industry in all parts of Sweden.
- Support data-driven science according to FAIR principles.
- Attract and retain highly skilled staff.

Geographical location of facilities



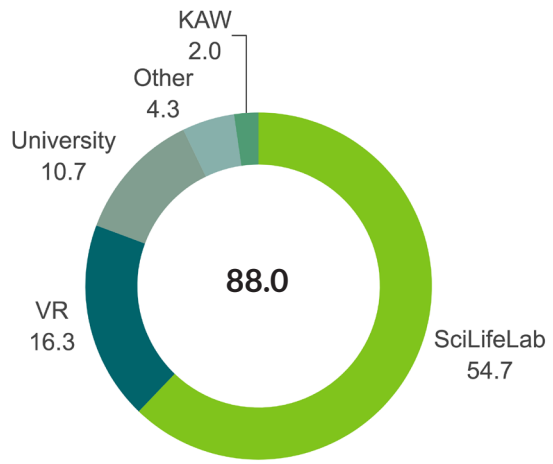
SciLifeLab funding 2020

Facility/unit	(MSEK)
National Genomics Infrastructure	44.5
Ancient DNA	2.0
Eukaryotic Single Cell Genomics	6.0
Microbial Single Cell Genomics	2.2
Total SciLifeLab funding	**54.7**

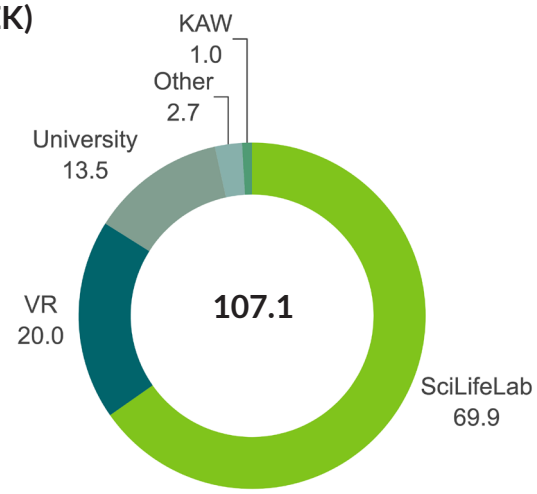
Suggested annual SciLifeLab funding 2021-2024

Facility/unit	(MSEK)
National Genomics Infrastructure	54.9
Ancient DNA	3.0
Eukaryotic Single Cell Genomics	9.0
Microbial Single Cell Genomics	3.0
Total SciLifeLab funding	**69.9**

Total funding 2020 (MSEK)



Total suggested annual funding 2021-2024 (MSEK)



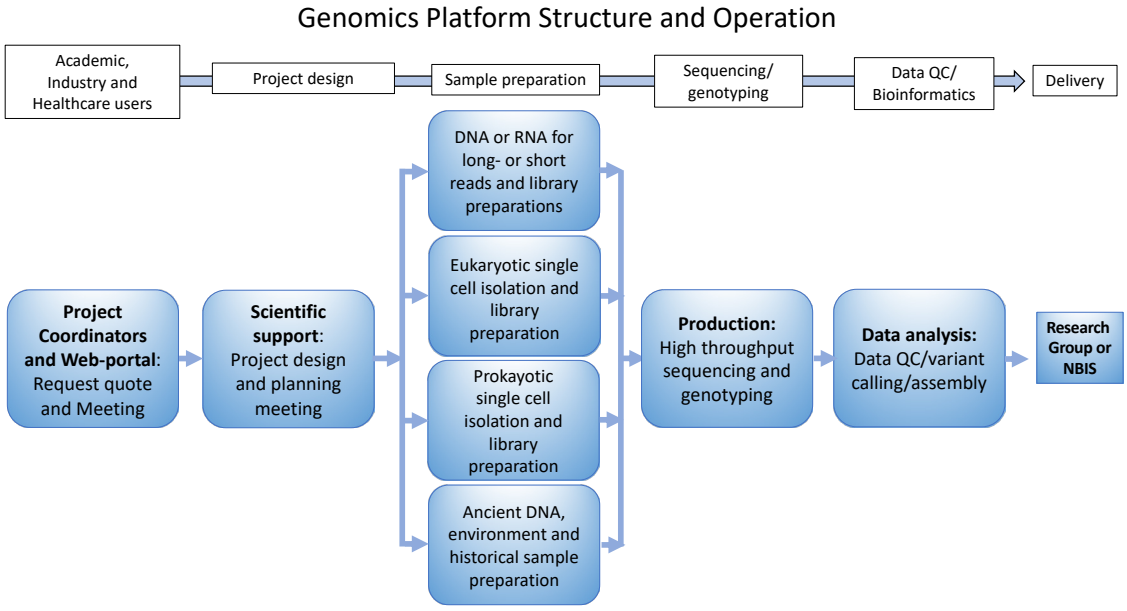


Figure 1. Structure and services provided by the Genomics Platform.

Background

The SciLifeLab Genomics Platform consists of four facilities, the National Genomics Infrastructure (NGI), Eukaryotic Single-Cell Genomics (ESCG), Microbial Single-Cell Genomics (MSCG) and Ancient DNA (AD). In addition, the SciLifeLab pilot facilities Spatial Transcriptomics (ST) and In Situ Sequencing are integrated into NGI and ESGC, respectively. The Uppsala Multidisciplinary Center for Advanced Computational Science (UPPMAX) hosts the compute resources used for processing the large amount of data produced by the Genomics Platform.

The Genomics Platform provides services to a large number of users at Swedish universities, state institutes, hospitals and industry, as well as other SciLifeLab facilities and some international institutes. The platform integrates a series of unique competences, spanning from project design, sample handling and library preparation for long and short read sequencing, eukaryotic and prokaryotic single-cell isolation and library preparation, preparation of ancient and degraded DNA, with use of a wide range of sequencing and genotyping technologies (Figure 1). In addition, the Genomics Platform hosts ultra-specialized capabilities such as a Biosafety Level 3 laboratory, ultra clean rooms for ancient DNA extraction, and for high molecular weight DNA extraction from non-standard sample types. The different facilities in the Genomics Platform complement each other, resulting in a platform which has an exceedingly unique capability to support PIs in their use of different genomics technologies.

Platform plans for 2021-2024

The Genomics Platform offers a range of cutting-edge genomic applications. The field of genomics is rapidly changing and the Platform will devote additional resources to the following areas:

- **Technological breakthroughs in single-cell technologies, including multi-omics,** have made transcriptomic, genomic, epigenomic, and proteomic measurements in individual cells a possibility. Single-cell, low-input, library preparation is the most rapidly growing application at the Genomics Platform and these capabilities will be expanded with nation-wide project coordination and educational efforts, as well as implementation of new technologies and methods.
- **Spatial-omics:** Technological advances have enabled multiple measurement of RNA, DNA and chromatin, protein while maintaining the cellular context in tissues. Dedicated resources will be allocated to expand the spatial transcriptomics capabilities from 2020.
- **Biodiversity and environmental genomics, including the Earth Biogenome Project (EBP).** The Genomics Platform is one of the few genome centers in Europe that has the technical capability to produce and analyze high quality de novo whole genome assemblies that meet EBP standards.
- **Microbial pathogen and host-pathogen interaction,** including expanding capabilities for handling and analyzing biosafety classed organisms.
- **Single-molecule long-read DNA sequencing.** Long-read sequencing is becoming important in combination with single cell genomic, transcriptomic and epigenetic analysis, as well de novo assembly of complex genomes within the EBP.
- **Clinical research using** fast-track sequencing and novel long-read technologies for clinical diagnostics in genetics and microbiology.
- **Ancient DNA analysis** is a rapidly expanding field where a series of new applications are under development to improve analysis of fragmented, chemically modified, and contaminated DNA.

Importance of the platform to the Swedish life science research

Genomics is a rapidly growing field, in terms of the number of new scientists, research areas and technologies. SciLifeLab Genomics has the ability to offer state-of-the-art services and represent a competence center for local core facilities across Sweden. At present there is no other core facility in Sweden with a similar broad range of expertise in genomics and track record to serve the scientific community, and the Genomics Platform expects to continue to represent an invaluable asset to the Swedish research community.

Importance of SciLifeLab funding of the platform as a national resource

The Genomics Platform is an enabler of genome science with a nation-wide user base and an ability to guide first-time users, and SciLifeLab funding has been pivotal in the development of the Genomics Platform. Nearly 50% of all publications reported by SciLifeLab are based on data generated by the Genomics Platform, and half of the PIs of Genomics Platform projects are from universities or institutes located outside of Uppsala or Stockholm.

The Genomics Platform has an ambitious mission to:

- *Provide comprehensive scientific support* not available from any commercial supplier. This includes the entire process with project design, dedicated sample preparation, high quality sequencing and genotyping, data QC and primary data analysis.
- *Enable access to state-of-the-art technologies*, in particular methods not commercially available.
- *A solution to perform human genome research* in Sweden that complies with GDPR.
- *Close interaction* with other SciLifeLab facilities that use genomics data as a read-out such as Bioinformatics (NBIS), Diagnostics Development (DD), Biobanking (BIS), Proteomics and Drug Discovery (DDD).

Benchmarking of the platform in an international perspective

The Genomics Platform is one of the three largest European genome centers, and a offer a very wide range of technologies (genomics, genotyping, single-cell genomics, spatial transcriptomics, ancient DNA). Of note, the Genomics Platform include facilities that are led by world-leading researchers in areas such as single-cell genomics, ancient DNA and human genomics. The Genomics Platform is open to researchers across the entire country, in contrast to institute-level closed centers, e.g. Broad Institute and Wellcome Sanger Institute. We recently compared ourselves to Mount Sinai Genome Center (MSGC) and New York Genome Center (NYGC). These two centers are large recipients of external research grants, a direction the Genomics Platform would also like to pursue.

Future plans for governance and organization of the platform

The Genomics Platform was reorganized in 2019 to improve collaboration, technology development and management of the Platform. Today, the Platform takes advantage of NGI's Steering Group, which has a wide representation of Swedish universities, has a Management group with all facilities and strategic groups for overarching functions such as a) Communication and project coordination, b) Outreach, c) Research and development, d) Quality assurance, e) Laboratory Information Management Systems (LIMS) and e) E-infrastructure.

Synergies and capability contributions

The Genomics Platform works closely together with the DD and NBIS platforms to ensure that collaboration thrives. Interaction with NBIS is vital to support projects, promote handover of projects for analysis, for collaboration around development, and for joint outreach activities. We co-organize the "BiG seminar series" and hold joint information meetings before major grant deadlines to support researchers. With DD we work closely in development and evaluation of new technologies and methods, as well as joint investments and outreach. We see synergies within spatial transcriptomics with the planned 'Targeted Spatial Omics' facility as well as with the Single-Cell Proteomics in particular. There are already close collaborations within the Human Developmental Cell Atlas, including capabilities from both platforms.

Promoting data-driven science

Genomics is the largest producer of data among the SciLifeLab Platforms, and in 2019 we generated >700 terabases of sequence data for over 1200 projects. In order to enable its users to promote and maintain data that meets FAIR (Findable, Accessible, Interoperable, Reusable) principles, the Genomics Platform works closely with the SciLifeLab Data Centre. The Genomics Platform promotes systematic annotation of samples and data using standardized vocabulary together with its users at an early stage of project planning. Data delivered from primary bioinformatics analysis are in standardized, best-practice formats, with version control in order to make data easily comparable across studies or projects.

Budget

See facility budget for comments.

National Genomics Infrastructure

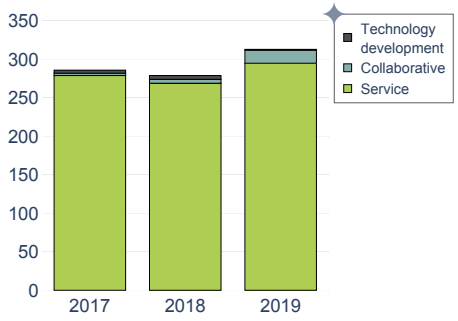
Read more: Web page, Publication Data Base

Basic Information

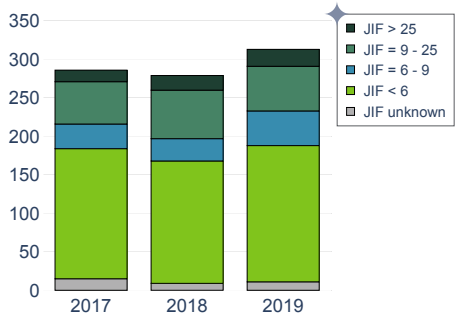
Facility director: Carsten Daub, Lars Feuk, Jessica Nordlund, Ellen Sherwood
Head of facility: Tomas Axelsson, Susanne Hellstedt Kerje, Ulrika Liljedahl, Carl-Johan Rubin, Ellen Sherwood
SciLifeLab facility since: 2013
Host University: KI, KTH, SU, UU
FTEs: 81
FTEs financed by SciLifeLab: 51.5

Funding 2020 (in kSEK)

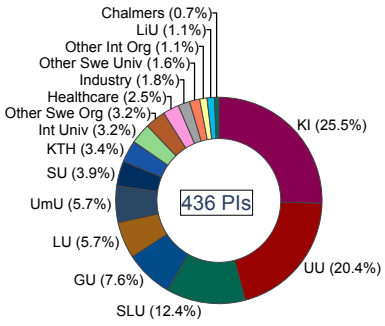
SciLifeLab: 44500
Total: 73850



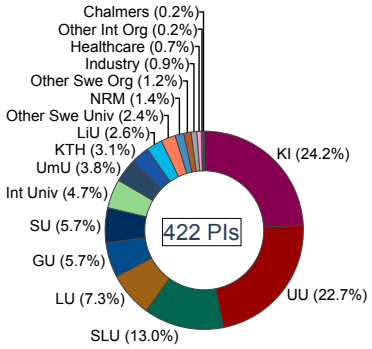
Publications by category



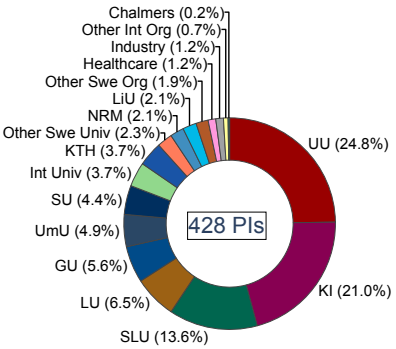
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

Sequencing technologies:

- Illumina NovaSeq 6000
- PacBio Sequel I and II
- Oxford Nanopore Promethion
- Illumina NextSeq/MiSeq/iSeq
- Thermo Fisher Ion Torrent S5

Supporting technologies:

- 10x Genomics, single-cell library preparation
- Dolomite Bio Nadia
- MetaSystems Microscope

Key services:

- SNP genotyping
- Transcriptomics
- Spatial Transcriptomics
- Single-cell sequencing
- DNA resequencing
- Targeted sequencing
- de Novo sequencing
- Epigenetics
- Environmental sequencing
- High Molecular Weight DNA extraction

New Technologies and Services 2021–2024

New technologies considered:

- MGI-Tech
- BioNano Genomics
- Mission Bio Tapestri

New services considered:

- Microbiome profiling
- Quantitative ChIPSeq and epigenomics
- Platinum de Novo Assembly

Background

Development of the facility

The National Genomics Infrastructure (NGI) has been the key provider of high throughput NGS and genotyping in Sweden for more than 20 years. In 2013, the SNP&SEQ Technology Platform (established 2001), the Uppsala Genome Center (established 1998), and the SciLifeLab Genomics Platform in Stockholm (former KTH Genome Center, established 1998) merged to become the largest technical platform at SciLifeLab. Since 2020 NGI operates as one SciLifeLab facility with two nodes, one in Stockholm and one in Uppsala. NGI is funded by SciLifeLab, the Swedish Research Council (VR), and the Knut and Alice Wallenberg Foundation (KAW), as well as several EU and local grants. These large grants have ensured access to the latest generation of high throughput sequencing technologies and computing resources (HPC) to analyze the large amount of data generated by NGI. Importantly, these grants have enabled NGI to perform internationally competitive projects in Sweden.

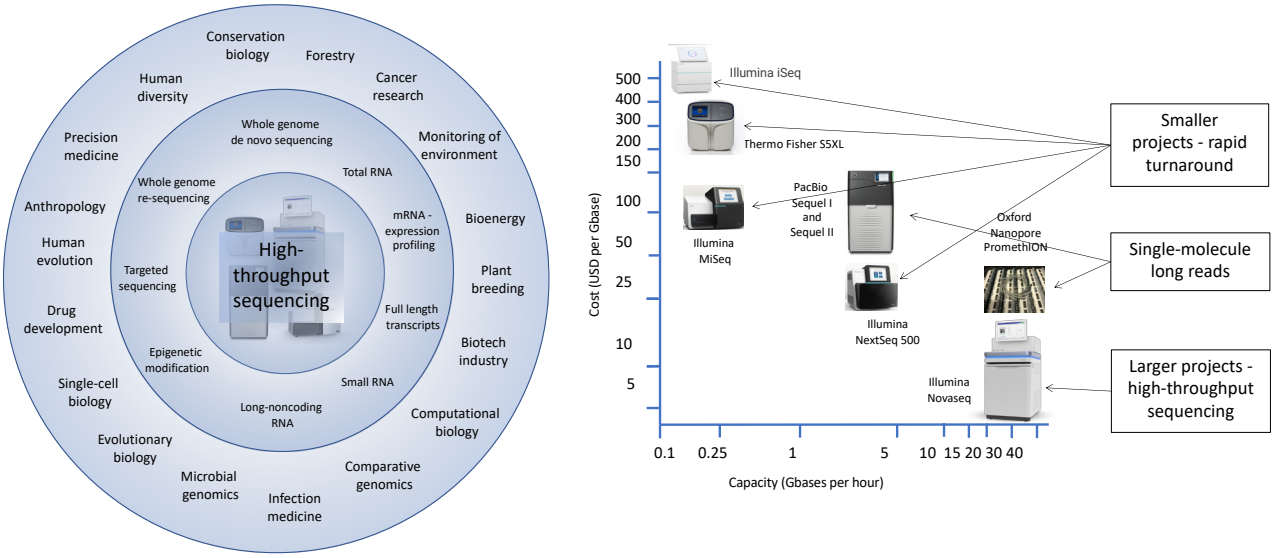


Figure 1. Research fields and applications depending on high throughput DNA sequencing (left) and the range of sequence technology platforms operated by NGI (right).

Reproducibility, quality, and storage of data

The genotyping and sequencing applications at NGI are accredited by SWEDAC according to the European quality standard ISO/IEC 17025 as a guarantee for high quality standards. All data generated by NGI are handled in accordance with the GDPR. This rigorous focus on quality is essential to the scale of the NGI operations, and meets the demands of all MTA and ethics requirements the users might have. NGI is actively involved in international projects regarding reproducibility, such as consortia for proficiency testing, and is driving the development of high-quality bioinformatics workflows (nf-core).

Technologies and services offered

NGI provides its users access to a comprehensive range of technologies, instruments and services for a wide range of applications in genomics, transcriptomics and epigenomics (Figure 1, left). NGI operates most of the available NGS platforms and by leveraging their various capabilities, can accommodate a broad range of project types and applications (Figure 1, right). In addition to standard bioinformatics (alignment, variant calling, quality control), advanced computational support is offered for specific applications, e.g. when necessary for QC of the data or for the research group to be able to proceed with their analysis, such genome assembly of long-read data. Method development, testing novel or emerging technologies and protocols, and establishing reproducible bioinformatics pipelines for different applications, are core operations in order to maintain a state-of-the-art genomics infrastructure.

Governance

NGI is a national research infrastructure hosted by the KTH Royal Institute of Technology and Uppsala University (UU), Karolinska Institute (KI) and Stockholm University (SU) are member universities. NGI's steering group, led by Marju-Ohro Melander from Lund University (LU), includes representatives from all over Sweden, including UU, KI, SU, Gothenburg University (GU), Umeå University (UmU) and the Swedish University of Agricultural Sciences (SLU). The present NGI director, Joakim Lundeberg (KTH), will be replaced by a new professor in Genomics at KTH during 2020. A second professor will be recruited in Molecular Medicine (UU), with the possibility to become Director/co-Director of the SciLifeLab Genomics Platform. In 2019, NGI employed 78 full time equivalents (FTE), including heads of facilities, project coordinators, personnel for laboratory, informatics and IT duties. These staff resources are divided into:

- 12% for *user support* (user meetings, project portal management, outreach activities),
- 30% for *production sequencing and genotyping*,
- 27% for *development* of technology platforms, laboratory and bioinformatics methods,
- 31% for *internal management*, such as meetings, documentation, purchasing and internal education.

Key achievements (2017-2020)

- NGI contributed to 878 publications, representing 45% of all publications from SciLifeLab between 2017-2020.
- In 2019:
  – NGI received the highest rating by the Swedish Research Council and funding as a national research infrastructure for 2021-2025.
  – 57,501 samples were sequenced, generating 711 tera base pairs of data, and 50,123 samples were genotyped, generating 3.5 billion genotypes.
  – 1,145 projects were performed, and 217 of these had PIs that were first time users of NGI.
  – NGI underwent a reorganization to form one SciLifeLab facility.
- Partner in a number of EU grants including EAT-RIS-plus, EASI-Genomics, PRECODE.

- Partner in national research projects (KAW forest genomics) and member of the Earth Biogenome Project.
- NGI is a major contributor to the nf-core project, which has established use of bioinformatics pipelines with excellent reporting and validated releases to ensure reproducibility (Ewels et al, Nat Biotech 2020).

Plans for 2021–2024

New technologies and services planned

NGI will offer the most modern, cost effective and state-of-the-art genomics methods that are demanded by the research community. Maintaining a top tier genome center requires updating of the large-scale sequencing technologies with the most recent sequencers, as well as perpetual efforts in development, testing, and implementing new methods. NGI foresees rapid growth in a number of areas:

- **Single-cell technologies, including multi-omics.** Technological advances have made transcriptomic, genomic, epigenomic, and proteomic measurements in individual cells a possibility. Since 2017, NGI has offered single-cell RNA sequencing (scRNA-seq) as a service and single-cell applications are the fastest growing request. An increasing number of methods is available for multimodal and integrative single-cell measurements and NGI will address these needs and work on applications not met by commercial vendors, such as single-cell whole genome methylome sequencing. NGI together with the Single Cell Proteomics facility can assist in combining single-cell proteomic and genomic readout and custom antibody conjugation. NGI will devote additional resources to accommodate the growing need for single-cell applications and work together with the ESGC and MSCG facilities to ensure national availability of a broad range of methods, project scales and expertise in single cell genomics on a national scale. This includes a national coordinator to support single cell applications.
- **Spatial-omics.** Recent technological advances have enabled measurement of RNA, DNA, chromatin, and/or protein while maintaining the spatial relationship to cellular context in tissues, thereby enabling three-dimensional analysis approaching single-cell resolution. In 2018, the SciLifeLab Spatial Transcriptomics Pilot Facility was incorporated into NGI. During 2019, NGI initiated its first pilot projects. NGI aims to become the world-leading provider of spatial transcriptomics services.
- **Biodiversity and environmental genomics, including the Earth Biogenome Project** (EBP) and environmental monitoring. In 2019, NGI partnered with the EBP for "sequencing life for the future of life." NGI will provide access to a sample-to-assembly approach for high quality *de novo* whole genome sequencing. NGI is one of the few genome centers in Europe which has the know-how and technical capability to perform all of the required steps to generate complete genome assemblies that meet EBP standards. In addition, NGI will continue to offer rapid and cost-efficient methods such as RAD-seq in order to fully meet user demands in this important area of research.
- **Single-molecule long-read DNA sequencing.** The lower cost of long-read sequencing is making it an attractive alternative for a range of applications. Sequencing of full-length transcripts and the possibility to decode base modifications from native DNA and RNA sequencing data are unique applications possible with PacBio and Oxford Nanopore platforms. Long-read sequencing is needed for the high quality *de novo* assemblies required by EBP. NGI also foresees an important role for single-molecule long-read technologies in single cell genomic, transcriptomic and epigenetic applications.
- **Clinical research applications** such as fast-track sequencing in precision medicine and the use of long-read technologies for clinical diagnosis in genetics and microbiology. The long-read technologies provide novel opportunities to resolve complex rearrangements, but require clinical validation. Clinical research trials require fast turnaround time to be clinical useful. Dedicated resources are needed to develop and support such applications in order to achieve their goals.
- **Use of sequencing as a read-out for functional genomics applications** such as CRISPR/Cas9 approaches for large-scale pooled perturbation screening and use of oligonucleotide tags for proteins and other metabolites to study cellular signaling pathways. In this area, NGI may also work with other SciLifeLab facilities, including Single Cell proteomics, Genome engineering and the DDD platform.
- **Expanded project support.** A strength of NGI is its ability to guide research groups from the project planning stage to data delivery, even for projects that require complex sample preparation, combinations of sequencing platforms or custom data handling. This capability will be further developed to assure that the projects initiated are optimally productive.

Expected user base 2021–2024

To date, the majority of NGI users are academic research groups located in Sweden whose projects are funded by national and international agencies, the vast majority of which are peer reviewed grants. Thus, the projects utilizing NGI's services have been scientifically reviewed. In 2019, 46% of the PIs were from universities other than the four NGI member universities, a number which has remained

stable throughout the years. In 2019, 43% of the PI's using NGI were first time users, and we still see new research fields emerging among our users, such as for ancient DNA applications.

Nation-wide user accessibility

NGI is able to accommodate users from all over Sweden. The key contact point for users is the group of knowledgeable NGI project coordinators, who are physically located in Uppsala, Stockholm, and since 2020 also in Umeå. Users can easily contact NGI through the "NGI Sweden Order Portal" (https://ngisweden.scilifelab.se/), a tool used for submitting orders. NGI offers over 700 project planning meetings per year either physically or via video link to accommodate users from all over Sweden. NGI has well-established routines that enable users to easily ship samples (DNA, RNA, libraries, cells) to Uppsala or Stockholm for sequencing or genotyping.

User support and outreach are the key activities that set NGI apart from commercial NGS suppliers. NGI frequently visits other universities for informational seminars and project planning meetings, often in collaboration with other SciLifeLab platforms, such as NBIS. Since 2015, NGI has hosted an annual "Long Read Sequencing Symposium". The meeting was attended by over 300 researchers in 2019 and the meeting in 2020 is expected to attract 500 attendees.

From 2021 outreach and user support will be expanded with the following activities:

- Increased support for cross-technology and platform projects.
- Yearly genomics symposia, following the success of the long-read meetings.
- Expanded use of NGI Web and Social media: Twitter, website, YouTube.
- Coordination of lectures in undergraduate and masters' program courses, and courses for PhD students.
- Evaluation of a distributed method for project coordination and support at other Swedish universities.

User fee model to be applied in 2021–2024

NGI offers favorable prices on all of its services to academic researchers in Sweden, who typically only pay for reagents and other consumables. From 2021, NGI will introduce a three-tiered cost model:

- *Subsidized cost model* for research projects with methods under testing and development, or stages of scaling up. This includes projects with manual steps that are not amenable to automation. The users pay for reagents and other items used in the project.
- *Cost-neutral model* for established high-throughput methods, such as large-scale genotyping, RNA sequencing, standard WGS and sequencing-only (user prepared libraries). This model includes all costs directly related to the project, such as reagents and other items used and salaries for the personnel performing the work.
- *Full cost model* applies to non-academic research projects and are according to guidelines of the Swedish National Financial Management Authority, including flat rates for instrument usage and service fees and costs for the methods development.

This cost model will enable NGI to allocate its SciLifeLab funding towards project support, outreach and development of novel methods, as well as other costs inherent to operating a large infrastructure.

Research environment and associated research groups

Staying at the forefront of the genomics field requires a strong research and development program. NGI allocate almost 30% of its personnel resources to development (see above). There is a long history of technology development in the surrounding research groups, starting from the development of pyrosequencing at KTH to the Spatial Transcriptomics technology we use today. NGI has a dedicated process to identify new technologies and development projects in dialogue with researchers and commercial vendors. This process is based on:

- Actively collaborating with research groups that develop novel technologies or laboratory protocols.
- A program for PhD-students and postdocs to be associated with NGI on a project-basis and perform their projects partly within the facility.
- Engaging with other SciLifeLab facilities/platform in development projects, such as with NBIS and DD.
- Active in Technology Development Projects (SciLifeLab or external funding).
- Partnering with research groups such as the KAW Forest Tree Genomics and EASI-Genomics projects).

Collaborations with healthcare, industry and other external organizations

- *Biotechnology industry*: Beta-testing and joint development of methods with genomics companies.
- *Health-care*: Validation of methods in collaboration with the DD Platform or directly with clinics.
- *EU-projects*: Continued participation in Horizon 2020 projects such as EASI-Genomics, PRECODE and EATRIS-plus.
- *Other Genomics Core Facilities*: Meetings with Nordic Genome Centers are planned for 2021.
- *Bioinformatics Community*: Driving force in the nf-core community.
- *Research community building*: SciLifeLab Research Community Programs Large-scale clinical genomics,

Human Developmental Cell Atlas and Aquatic Microbiome Research Initiative.

- *International initiatives*: Membership in EBP, collaboration with GA4H.

Alternative facilities/ infrastructures and commercial providers

NGI is the largest genomics service supplier in Sweden, and a competence center supporting research groups and sequencing providers in the academic domain. There is no commercial supplier of genomics services in Sweden with a similar breadth of technologies as NGI. Compared to international commercial alternatives, NGI offers more comprehensive project support, and a wider range of non-standardized protocols.

Budget explanation 2021–2024

- SciLifeLab funding (44.5 MSEK) to NGI increased by 3% yearly for inflation-
- Investing in New sequencing platforms (e.g. MGI and BioNano), 10 MSEK divided on 2.5 M per year.
- Support to the EBP. Personnel for HMW DNA extraction and *de-novo* assembly (1.5 M/year).
- National representation by part-time project coordinators outside the Stockholm/Uppsala region.
- National coordination of single-cell reported in the ESCG budget.
- Additional personnel to support high throughput analysis of single cell sequencing (1.5 M/year) and equipment for automation of high throughput single-cell applications (1 M total, 0.25 /year).

Costs	2020	2021	2022	2023	2024
Personnel (81 FTEs 2020, 85 FTEs 2021-2024, 3% increase per year)	62 094	68 077	70 119	72 223	74 389
Operations	97 756	101 500	103 650	106 760	109 962
Premises (3% increase per year)	9 425	9 770	9 998	10 298	10 607
Instrument depreciations	14 035	14 000	14 000	14 000	14 000
Other (including e-infrastructure)	2 766	9 900	9 000	9 000	9 000
Sum costs (kSEK):	186 076	203 247	206 767	212 281	217 958

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding (see specification in facility text)	44 500	52 500	54 075	55 697	57 368
University co-funding (e-infrastructure+instrument) predicted	7 200	10 900	9 890	9 980	10 050
Swedish Research Council (granted)	16 300	20 000	20 000	20 000	20 000
EU (prediction)	3 350	1 000	1 000	1 000	1 000
KAW (predicted)	2 000	1 000	1 000	1 000	1 000
Other external funding	500	500	500	500	500
User fees (predicted) (Reagents and surcharge such as instrument costs)	110 000	113 000	116 000	119 225	121 175
Sum revenues (kSEK):	183 850	198 900	202 465	207 402	211 093

Table 1. Current budget (2020) and suggested budget 2021–2024

Ancient DNA

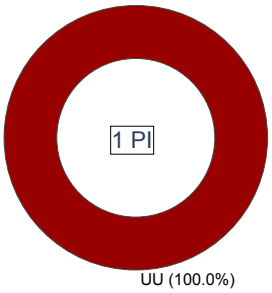
Read more: Web page, Publication Data Base

Basic Information

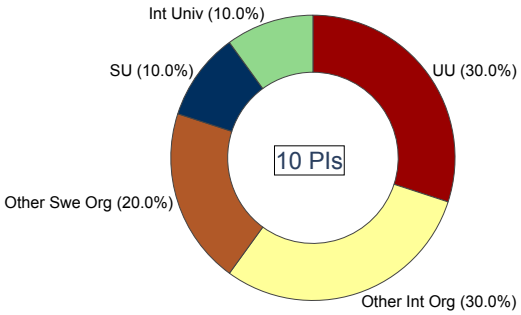
Facility director: Mattias Jakobsson, Anders Götherström
Head of facility: Magnus Lundgren
SciLifeLab facility since: 2017
Host University: UU, SU
FTEs: 2.67
FTEs financed by SciLifeLab: 2.67

Funding 2020 (in kSEK)

SciLifeLab: 2000
Total: 2403



Users 2018



Users 2019

Current Technologies and Services

- Sampling and extraction of DNA in clean-room laboratory
- Ancient DNA-specific library preparation in clean-room laboratory
- DNA sequencing in collaboration with SciLifeLab National Genomics Infrastructure
- Bioinformatic quality controls: endogenous content, ancient origin, contamination
- Analysis of species, sex, kinship, and mitochondrial and Y-chromosome haplotype
- Custom bioinformatic analysis

New Technologies and Services 2021–2024

- Analysis of ancestry and demography based on ancient DNA and population genetics
- Analysis of ancient DNA from microorganisms, including pathogens
- Analysis of traits from ancient DNA, including heritable medical conditions
- Analysis of ancient DNA in sediments
- Analysis of ancient DNA in plant material
- Metabarcoding of ancient DNA
- Capture of ancient DNA from specific organisms or genomic regions

Background

DNA can be preserved long after the death of the individual, in exceptional cases for hundreds of thousands of years. Such DNA is a time capsule that provide direct information of the individual, the population it belonged to, and the environment at the time. However, ancient DNA is highly fragmented and chemically modified, and the source material is typically colonized by microorganisms and fungi, requiring dedicated analysis procedures. Further, contamination with modern DNA during processing must be minimized. To enable reliable analysis, the Ancient DNA facility uses stringent ancient DNA-specific procedures and clean-room laboratories. Regular services have been provided as of August 2019.

Services: The facility performs complete analysis, from assisting with project design to cleaning and decontamination of material, DNA extraction, library preparation and quality controls. We routinely analyze osteological material, but also offer investigation of other materials. DNA sequence data is processed using specialized workflows, where quality controls, mapping to reference genome, and analysis of endogenous content (fraction of DNA originating from the individual) is performed. If the endogenous content allows, we sequence DNA to a desired level of genome coverage. Data quality controls includes analysis of DNA depurination, indicative of age of material. We offer several standardized analyses, and if several samples are analyzed we offer analysis of close kinship between them. The facility also offers custom data analysis.

Governance: The facility is located at the Dept. of Organismal Biology, Uppsala University, and the Dept. of Archaeology and Classic Studies, Stockholm University, in order to benefit from both scientific environments, but operates as a single unit. The directors are distinguished researchers in the field who initiated the facility and provide scientific leadership. Head of Facility and manage projects, outreach, staff and economy. Thijessen Naidoo and E-Jean Tan is the facility's bioinformatician and research engineer, respectively. All staff have a PhD and additional research experience.

Key achievements: The Ancient DNA facility has established a state-of-the-art ancient DNA laboratory and routines for project management, laboratory procedures and data analysis. The interest for the facility's services is large, both nationally and internationally. After the facility's first five months, eleven projects are ongoing or completed, including two bioinformatics-only, and 58 samples have been analyzed. As the analyses are recent, they have not yet been included in any publications. The facility has been

selected as prioritized infrastructure by Uppsala University for the Swedish Research Council infrastructure support. Several grants have been acquired for development of services and other activities. The facility has arranged a range of outreach and educational events, including a large international symposium with more than one hundred participants discussing the applications of ancient DNA analysis in archaeology and biology.

Plans for 2021–2024

New services: As ancient DNA analysis is a young field, there is rapid development. The facility follows the development to implement new services. Examples of planned additional services include analysis of sediment cores, for investigation of flora, fauna and microbial ecology, and their change over time. Sediment analysis will be performed both through whole genome sequencing and directed analysis for specific groups of organisms (metabarcoding). Methods will be implemented for extracting DNA from e.g. hair, soft tissue and plant material. Laboratory methods will be developed for capture of selected DNA, and improved DNA extraction, library construction, and repair of chemically modified DNA. Procedures will be automated in order to increase reproducibility and throughput, and to reduce costs. There are also plans for additional computational methods, including analysis of environmental and pathogenic microorganisms, metagenomes, traits, and heritable medical conditions. Analysis of ancestry and demography will also be implemented.

Competitiveness and alternative infrastructure: Reliable ancient DNA analysis requires specialized technology, procedures and laboratories. The SciLifeLab Ancient DNA facility is the only core facility in Sweden that provides analysis of ancient DNA, and one of a very small number world-wide. Ancient DNA analysis is unique in being a life science technique with importance to humanities research, such as in archaeology, history and anthropology. The methodology is also valuable in medical and biological research. Ancient DNA allows access to the genetic state of past organisms, which enable investigation of speciation, evolution and population genetics, as well as the development of pathogens and heritable diseases.

User base and nation-wide access: As a recently initiated facility, the user base is expected to increase substantially in 2021-2024. We perform outreach to inform researchers across Sweden how ancient DNA analysis can benefit their projects, but also to discuss unmet needs and what services may address such needs. We also inform about our services through university courses, presentations at national and international conferences, and by arranging seminars, workshops and symposiums. Samples for analysis can readily be sent by mail, facilitating nation-wide and international access. Academic users can come from any university or college that perform research in

e.g. archaeology, biology or medicine. In addition, we expect an increase in users from both Swedish and international museums, research institutes, and governmental organizations. Contract archaeologists are a large group of potential users for which we expect an increase in projects.

Data management: As the material we work with is irreplaceable, qualitative analysis and secure data storage is important to us. We inform users about data storage options, and our goal is to assist users with data management according to the FAIR principles (Findable, Accessible, Interoperable, and Reusable). Internally, we work with SciLifeLab Data Centre to establish data management routines.

User fees: User fees are based on the materials, working hours and indirect costs of a project. For academic and government research, we support project costs using SciLifeLab funding. For e.g. contract archaeology projects, private companies, healthcare, non-governmental organizations, we apply a full-cost model.

Links to research environment: The Ancient DNA facility is directly linked to the strong ancient DNA research environments at the Human Evolution program (Uppsala University) and the Centre for Palaeogenetics (Stockholm University and Swedish Museum of Natural History),

providing access to knowledge and recent developments in the field.

SciLifeLab synergies: The Ancient DNA facility directly collaborate with the National Genomics Infrastructure for DNA sequencing. We are currently reorganizing the Genomics platform, which will provide shared organizational support and improved use of resources. We interact closely with the SciLifeLab Bioinformatics Platform, where we have shared projects and provide support for each other. We are also discussing future collaboration with the SciLifeLab Diagnostics Development platform with regard to medical DNA analysis of prehistoric individuals.

Collaborations: We are involved in collaboration and discussion with external organizations to develop new services and identify community needs. We have an ongoing joint project with The Archaeologist, part of the Swedish Historical Museums. We are also part of the Heritage Science Sweden network, organized by the Swedish National Heritage Board. On European Union level, we are part of the Iperion HS program, which will provide heritage science services and is funded by the European Commission.

Budget 2021–2024

Costs: For 2020, the staff consists of 2.75 FTEs. In 2021 and forward an additional FTE is added to the facility to allow analysis of sediments and a range of other samples, including different types of museum specimens. For 2021 there is also a specific cost of 1 MSEK for establishment of a laboratory for storing, handling and sampling sediment cores. Instrument depreciation costs are for laboratory equipment, automated liquid handling system, and computers. The increase in operational costs 2021 and forward is due to the expected increase in projects with the additional FTE.

Revenues: For 2020 SciLifeLab will provide 2 MSEK maintaining current level of operation. For 2021 and forward an increase in funding to 3 MSEK is proposed in order to support the additional FTE and associated costs. Stockholm University and Uppsala University are proposed to provide co-funding of the facility as of 2021. In addition, the facility will apply for funding to support basic facility operations, development of additional services and specific projects. Potential sources include the Swedish Research Council, research foundations, the European Union and SciLifeLab Technology Development Projects. Approved research grants are listed.

Costs	2020	2021	2022	2023	2024
Personnel (2.75 FTEs 2020, 4 FTEs 2021-2024)	2 603	3 800	3 848	3 896	3 944
Operations	548	1 612	2 119	2 119	2 119
Premises	250	417	427	437	447
Instrument depreciations	20	119	110	110	102
Other	-	1 000	-	-	-
Sum costs (kSEK):	3 421	6 948	6 504	6 562	6 612

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	2 000	3 000	3 000	3 000	3 000
University funding		1 000	500	500	500
Planned applications	200	1 000	500	500	500
EU Iperion HS	163				
Gunvor and Josef Anér's Foundation	40				
User fees	1 018	1 948	2 504	2 562	2 612
Sum revenues (kSEK):	3 421	6 948	6 504	6 562	6 612

Table 1. Current budget (2020) and suggested budget 2021–2024

Eukaryotic Single Cell Genomics

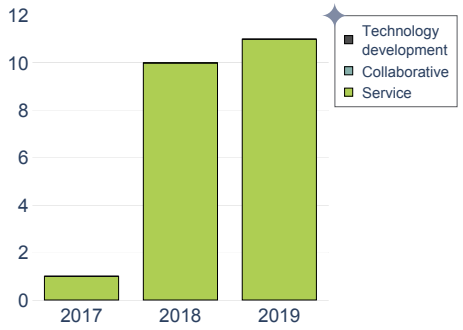
Read more: Web page, Publication Data Base

Basic Information

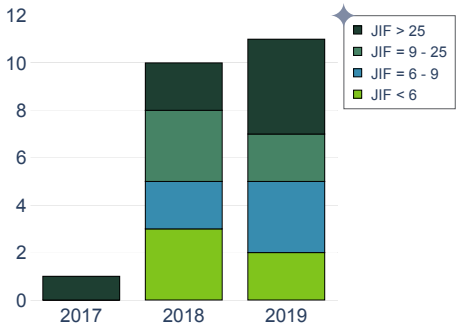
Facility director: Rickard Sandberg
Head of facility: Karolina Wallenborg
SciLifeLab facility since: 2015
Host University: KI
FTEs: 5.45
FTEs financed by SciLifeLab: 5.4

Funding 2020 (in kSEK)

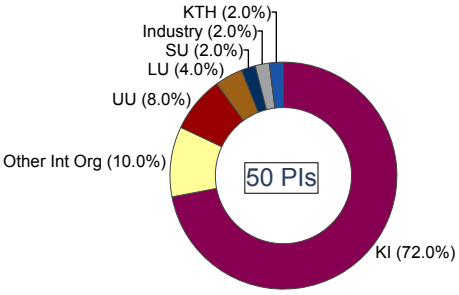
SciLifeLab: 6000
Total: 9500



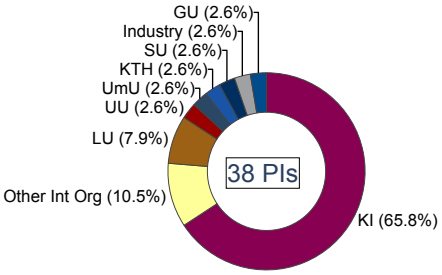
Publications by category



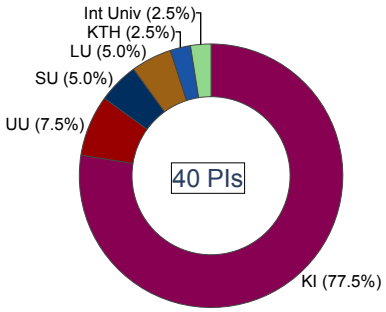
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

We provide support at all stages of planning and executing single-cell genomics projects. For detailed information, visit https://www.scilifelab.se/facilities/eukaryotic-single-cell-genomics/

- *Single-cell transcriptomics*
  – 384-well plate based Smart-seq2 (2015-2019), Smart-seq3 (2019-)
  – Droplet based 10x Genomics (3' GE, 5' GE)
  – Microwell-based Potential for Smart-seq2 5000 well plates (iCELL8,Takara Bio)
- *Single-cell epigenomics*
  – Single-cell ATAC-seq (10x Genomics)
- *Single-cell immune receptor profiling*
  – T- and B-cells (10x Genomics)
- *Single-cell transcriptomics based CRISPR screens (with the HTGE facility)*
- *Multi-omics single-cell profiling*
  – Transcriptomics + protein
  – (10x Genomics + Cite-seq)
- *Single-cell sample multiplexing*
  – Cell hashing (10x Genomics + Biolegend)

New Technologies and Services 2021–2024

We constantly survey emerging technologies for scale and performance. We currently anticipate or consider the following important new technologies for ESCG:

- *Single-cell epigenomics*
  – Histone modifications (cut&tag, adapted for 10x Genomics)
  – Protein-DNA interactions (single-cell cut&run)
- *Multimodal sc-genomics.*
  – RNA combined with ATAC-seq and/or DNA methylation
  – RNA combined with internal protein quantification
- *Single-cell genomics.* Shallow, cost-effective DNA-seq (e.g. DLP+) and/or Shallow methylation sequencing (eg. Ecker lab, 384-well plates)
- *Long-read scRNA-seq.* PacBio or nanopore sequencing (if read-throughput improves further)
- *Spatial single-cell trancriptomics (and multi-omics).* Depends on further development, we hope to establish 1-2 spatial methods.

Background

The Eukaryotic Single Cell Genomics facility (ESCG) was founded in 2015 by Professors Rickard Sandberg and Sten Linnarsson (both Karolinska Institutet) to provide state-of-the-art single-cell genomics technologies to researchers in Sweden. The governance is founded on iterating facility directorships (Sten L: 2015-2017; Rickard S: 2018-2021), a head of facility (Karolina Wallenborg, PhD) and additionally five employees (3 PhDs working in the lab and administration; 1 MSc with full-time lab work and

1 MSc bioinformatician). The work-force is slim and we have always prioritized to deliver as good data as possible to our users. Despite the small work force, we have a 18M SEK annual turnover (roughly 10M in user fees, 8M in funds). We currently offer a range of single-cell genomics methods (see list on page above) that have sufficiently matured to have scale and cost that permits its nation-wide service. We have produced single-cell data to over 23 papers in 2017-2019 (including several in Nature and Cell), significantly advancing single-cell genomics in Sweden.

Plans for 2021–2024

We envision ourselves taking a larger role (in 2021-2024) in the coordination of single-cell genomics activities in Sweden, to improve local quality and facilitate knowledge transfer. We will also organize local workshops and training opportunities for users (PhD students and postdocs) around Sweden, ideally arranged with NBIS. Finally, we will organize a national workshop to introduce new technologies and obtain valuable feedback from our user base.

Technology: On the horizon for the next four years are strategies for obtaining multiple measurements from the same cell and preserving spatial context of cells.

Single-cell RNA-seq: Will continue to be important, we strive for cost-effective profiling with high quality. High cell numbers can be achieved by pooling strategies combined with 10x Genomics (e.g. scifi-seq) and high-quality can be achived with Smart-seq3 in denser well plates and further minituarized volumes.

Multi-modal techniques: Multiple cost-effective strategies for simultaneous profiling of RNA, accessible chromatin (ATAC-seq) and/or DNA methylation are becoming available. Even 10x Genomics is anticipated to launch RNA+ATAC-seq in 2020. Additionally, we are surveying any possibilities in extending RNA+ quantifications of internal proteins.

Spatial technologies: We are eager to expand RNA profiling with a spatial dimension, although this area is currently the hardest to predict as it is evolving rapidly. The 10x Genomics offered spatial transcriptomics has not yet reached single-cell resolutiom, whereas existing single-cell methods don't scale for national use. Interesting also to follow the progress in using Smart-seq3 with microfluidics directly on tissue slides.

Long-read sequencing of RNA in single cells: Despite tremendous recent progress (e.g. PacBio Sequel II), the read throughput is not applicable to large-scale single-cell RNA-seq. We see a unique opportunity in offering PacBio sequencing of rare important cells profiled with Smart-seq3, indeed proof-of-principle PacBio sequencing of Smart-seq3 cDNA is done.

Cost-reducing strategies: Cell hashing, early barcoding or pooling of genetically distinct individuals can all improve cell throughputs e.g. in 10x Genomics droplets.

General information

Competitive edge: The ESCG facility has been world-leading, i.e. having produced the most single-cell genomics data to research groups. ESCG is uniquely guided by Professors Sandberg and Linnarsson who are well-established international pioneers in single-cell genomics. Moreover, ESCG has initiated additional collaborations with research groups to establish important new methods. For example, in collaboration with Goncalo Castelo-Branco's lab, we adapted cut&tag for 10x Genomics and this will likely be offered in 2020. Moreover, the ESCG personnel participate annually in the single-cell genomics meeting (iterating in Europe between Weizmann, KI, Utrecht and Cambridge) to keep up to date in the field.

Expected user base: We foresee a continued increase in single cell genomics projects. During 2019, 50% of ESCG users (Principal Investigators) where new users to ESCG. The majority of ESCG users are from the medical sciences field, however as the single cell genomics field is moving in to all areas of biology we expect to see an increased number of samples from the natural sciences area (plants, diverse species).

Nation-wide user accessibility: We have since the start in 2015 had users nation-wide by providing methods that can survey whole Sweden (mostly, 384-well based Smart-seq2, although arriving at ESCG with cell suspensions is also possible). As outlined above, we will become more visible throughout Sweden as we coordinate and improve quality in local single-cell genomics nodes and arrange local workshops. Thus, we forsee having an even increased national presence.

Reproducibility and quality: We have always prioritized reproducibility, and established the methods on automated instruments with dedicated SOPs. Quality is verified by analysis scripts that control all generated data before sending it back to users. We currently store data on more than one server, and is investigating storage solutions by KI.

User fee model: We are aiming for overall balanced costs and expenses and our user fee model is designed accordingly. Academia and clinical researchers pay reduced cost, whereas industry pay according to full-cost model. The cost model includes reagents, consumables, depreciation and service costs of used equipment (estimated in proportion to total samples analysed per machine), and personnel time devoted to each project. This model is updated biannually, and we strive to comply with EU level regulations in terms of user fee transparency.

Synergies and capabilities: We naturally coordinate and synergise with other Genomic platform facilities, with dedicated microbial single-cell sequencing and BSL3-certified Smart-seq2 on human samples in Uppsala. ESCG currently performs all sequencing through NGI Stockholm

and we interact with NBIS for single-cell data analysis. We strive to increase synergies with NBIS through coordinating workshops and outreach events nationally. We are actively working with the high-throughput genome engineering facility for CRISPR screens with scRNA-seq readouts. Potential new synergies are being explored with the Diagnostic Development platform, to identify opportunities with single-cell genomics technologies for improved diagnostics, patient group stratification and disease understanding.

Collaborations and networks: We are part of a Nordic network of single-cell genomics facilities, through a Nordforsk application (sent 2019), and we are participating in a national scilifelab network (STorM).

Alternatives: Although single-cell genomics capabilities are prolific around Sweden, most new facilities operate local 10x Genomics instruments for the the local researchers, without nation-wide services. International facilities are becoming very common, although none have the history, breath or visibility as our facility. Again, multiple facilities focus on 10x Genomics based offerings (e.g. Columbia Genome Center, VIB-KU Leuven, CGR Barcelona) that are limited to the local environment. Several centers have copied our Smart-seq2 setup (e.g. ICMC, KI, Sanger Institutet) although these have been closed to the department or institute.

Justification: Thanks to our competitiveness and close connection to pioneering labs in single-cell genomics, we are constantly the first facility to introduce important new methods developed, and we have their strategic input on all major decisions on methods to acquire and establish. Moreover, the ESCG personnel have aquired unique experience in single-cell isolation and can quickly adapt to new methodologies in the field (5 years experience). We envision ourselves taking a larger role (in 2021-2024) in coordination of national single-cell genomics activities (quality control of local facilities, knowledge transfer and user training).

Budget 2021–2024

SciLifeLab funding for 2020 is 6000 kSEK. Budgeted funding from SciLifeLab 2021-2024 is 9000 kSEK. The increase of 3000 kSEK will fund (a) 1 FTE for coordinating national activities within single-cell genomics, including competences transfer, regional and national workshops, webbinars, user meetings and (b) 1 FTE and 1000 kSEK for pilot experiments within single-cell genomics applications suggested in the SciLifeLab Technology Needs Inventory 2019 and prioritized by the Genomics Platform Technology Development group.

Costs	2020	2021	2022	2023	2024
Personnel (5.45 FTEs 2020, 8 FTEs 2021-2024, 2.5% increase/year)	5 600	7 000	7 175	7 354	7 538
Operations (2.5% increase/year)	8 500	8 713	8 930	9 154	9 382
Premises (2.5% increase/year)	856	877	899	922	945
Instrument depreciations	1 050	1 050	1 000	1 000	1 000
Other					
Sum costs (kSEK):	16 006	17 640	18 005	18 430	18 866

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	6 000	9 000	9 000	9 000	9 000
University funding (predicted 2022-2024)	2 500	2 500	2 500	2 500	2 500
SFO Stratregen	1 000				
User fees	6 500	6 500	6 500	6 500	6 500
Sum revenues (kSEK):	16 000	18 000	18 000	18 000	18 000

Table 1. Current budget (2020) and suggested budget 2021–2024

Microbial Single Cell Genomics

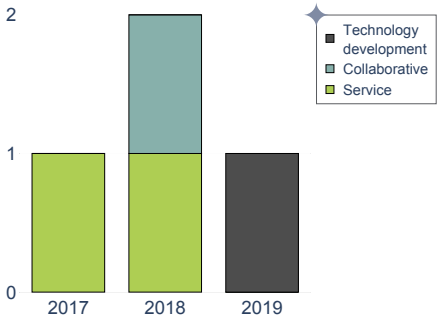
Read more: Web page, Publication Data Base

Basic Information

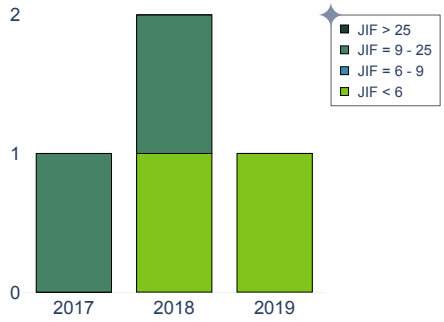
Facility director: Stefan Bertilsson
Head of facility: Johan Ankarklev
SciLifeLab facility since: 2017
Host University: UU
FTEs: 2
FTEs financed by SciLifeLab: 2

Funding 2020 (in kSEK)

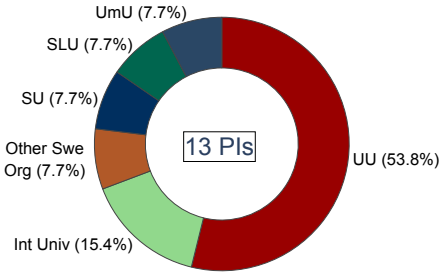
SciLifeLab: 2200
Total: 2200



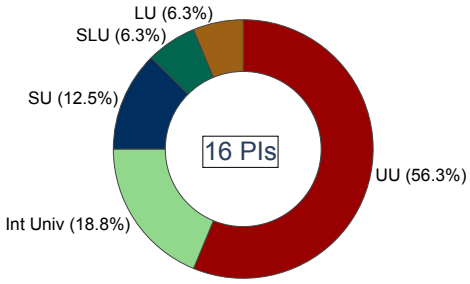
Publications by category



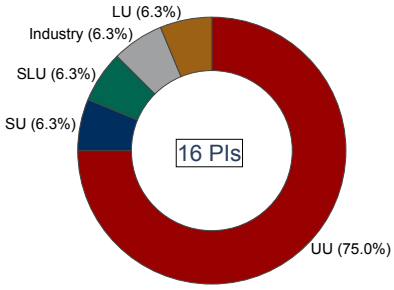
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

- Cell preparation and isolation of microbial pathogens in Bio Safety Level (BSL) 3 laboratories
- Project consultation of work relating to BSL classified pathogens
- FACS-based single cell sorting of pro- and eukaryotic cells
- Micromanipulation-based sorting of eukaryotic microbes
- Single-cell genome amplification and sequencing of pro- and eukaryotic microbes
- Single-cell RNA-seq of eukaryotic microbes and host-microbe complexes
- Automated bioinformatic analyses of single cell genome data (basic assembly, quality control)

New Technologies and Services 2021–2024

- Laser Microdissection Microscopy: for cell capture from infected tissues and microbial aggregates/biofilms
- Celsee: for size-based cell enrichment followed by cell separation in high density micro-well format
- Particle-Templated Emulsification (PTE) for single-cell droplet encapsulation
- Total RNA-seq of pro- and eukaryotic microbes and host-microbe complexes in small populations down to the single-cell level
- ATAC-seq of single or small populations of eukaryotic microbes

Background

Microbiology is a broad and diverse research area in rapid development. Thus the potential user base of Microbial Single Cell Genomics (MSCG) is large and includes the majority of the larger Swedish universities, medical and veterinary institutes. The central concept of the facility is to provide a varity of adaptable single-cell technologies to enable global genomic studies of both pro- and eukaryotic microbes. MSCG was initially established in 2014 by Profs Stefan Bertilsson and Thijs Ettema to mainly provide service for researchers studying microbial diversity and molecular evolution. With the addition of Dr Johan Ankarklev in 2019, the facility expanded its scope to also enable services and technologies aimed at infection biology of human, veterinary and agricultural importance, also including vector biology (microbial pathogens transmitted through insects). Specifically, the facility capacitates work with live microbial pathogens and aims to provide methods to study the interactions between a variety of microbes and their hosts. MSCG is part of the SciLifeLab Genomics platform and directly collaborates with NGI Uppsala for sequencing and single-cell transcriptome technologies. MSCG further collaborates with several other SciLifeLab facilities with regards to method and service implementation, including Single-Cell Proteomics, Spatial Transcriptomics and ESCG. Ongoing discussions regarding collaborations with NBIS and Ancient DNA.

Services: The aim of MSCG is to provide an infrastructure where users in the field of microbiology, including infection biology, have the possibility to experimentally work together with the facility staff to optimize sorting/cell isolation, extraction and amplification schemes. Further, MSCG provides expertise in handling the highly diverse samples that are prepared within the facility, both at the cellular and molecular level. Thus, MSCG's mission includes the possibility to provide users with the infrastructure and technology for the entire workflow of their respective experimental set up.

Governance: MSCG is a national infrastructure, hosted by the Department of Cell and Molecular Biology (ICM), Uppsala University. The aim is to ensure a leadership structure that includes expertise in the topics of microbial diversity and infection biology. Prof Bertilsson and Dr Burki study microbial diversity of both pro and eukarytic microbes and Dr Ankarklev research covers topics on infection biology including host-pathogen interactions both in mammalian hosts and insect vectors. MSCG presently employs 2 FTEs but aims to expand to 3 FTEs during 2020. These positions include laboratory personell/project coordinators.

Key achievements: MSCG has established a state-of-the-art microbiology-adapted cleanroom laboratory, where the key infrastructure for cell sorting has been classified to include pathogenic organisms up to biosafety level 3 (BSL3) non-airborne. The BSL3 permit can be expanded to include additional organisms on a per project basis as the facility staff sees fit. Since MSCG recently started catering to the infection biology field, there are an additional eight collaborations and several more are anticipated once the facililty has fully implemented the new technologies listed above. The facility has been part of arranging several symposia and congresses relating to environmental microbiology and has held multiple courses on the topic Microbial Single Cell Genomics. Several outreach and educational events relating to infection biology are part of the future plan.

Plans for 2021–2024

New technologies and services: We aim to implement novel technologies that cover i) cell isolation for a variety of complex samples, such as pathogen-host complexes in suspension or tissues, environmental samples, including cells in suspension or aggregates of microbes, such as biofilm. The anticipated approaches include Laser Capture Microdissection (LCM), droplet-based single-cell encapsulation and Celsee, which will all be coupled to library preparation and sequencing. Second ii) we aim to provide our users with a variety of library preparation protocols for single cells, including both pro and eukaryotic microbes and host-microbe complexes (HMC). The new technologies include; mRNA-seq (Smart-seq3) eukaryotic microbes and HMCs; totalRNA-seq (choice of protocol currently under debate, e.g. RamDA-seq) for bacterial HMCs. We also aim to provide a modified version of ATAC-seq to complement our users' needs. Key infrastructure within the facility has been BSL3 certified (see above). MSCG will further expand this permit to include infrastructure that enables droplet encapsulation of microbial pathogens and live cell microscopy for time lapse imaging of microbial pathogen development and/or host-pathogen interactions during 2021-2024.

Uniqueness/Competitive Edge: MSCG currently provides the only infrastructure within the entire SciLifeLab that enables work with biosafety classed organisms, i.e. microbial pathogens. The possibility of providing users with infrastructure to work with pathoges in combination with state-of-the-art cell isolation and sequencing platforms are highly unique in Sweden and internationally. To our knowledge there are no other single-cell genomics facilities that focus exclusively on microbes and microbial pathogens. Furthermore, the combination of cell isolation methods, which are necessary to encompass the projects run at the facility and the possibility for users to work with the MSCG staff in optimizing these methods are unique within SciLifeLab. Finally, due to the broad userbase at MSCG our mission is to provide a large variety of cell isolation and molecular preparation protocols including single-cell preparation of eukaryotic but also prokaryotic microbes and single-cell microbe-host complexes. The combination of strategies described above are unique within the field of microbiology and infection biology and taken together provide an internationally highly competitive resource.

User base: MSCG currently has multiple users that study polymicrobial population genomics from the larger Universities across Sweden, but also in other parts of Europe, including the Czech Republic, France and England. There are also multiple recently established collaborations related to infection biology with academic groups in Sweden, including UmU, UU, KI and SU; in Europe including Oxford University, the Francis Crick Institute; Latin America including UNIFESP and Fiocruz (Brazil); and in the U.S., including NIAID-NIH, Johns Hopkins University, Iowa State University and the University of Washington. We expect to significantly expand our academic user base from 2021 and onward in light of our anticipated expansion of services and technologies, including BSL work. Interest for this has been communicated from academic research groups from several of the larger Life Science Universities in Sweden, including; LU, SU, GU, UU, SLU, SVA, UmU, LiU, and KI. We have discussed the potential of collaboration with ECDC and other government agencies in Sweden relating to our capacity of handling BSL classed samples, this would however require an expansion of the personell and infrastructure within the facility. Furthermore, there are ongoing discussions with stakeholders in the health care sector who are interested in collaborating with MSCG

for the purpose of developing diagnostic methods for the detection of microbial pathogens of medical and veterinary importance.

User accessibility: MSCG accommodates users from all over Sweden, also including international users, services can easily be requested online through the "MSCG project request" form. We inform about our services through outreach programs, including participation in university courses, presenting at national and international conferences, and by arranging seminars, workshops and symposia. Outreach days are also planned for 2020 at Universities with few current users. We further aim to expand our outreach through social media, including the website, Twitter and Instagram. Users may ship samples with clear instructions of how they want their samples sorted and prepared..

Reproducibility: MSCG has established standardized protocols, which are routinely reproduced within the facility starting from sample preparation, cell isolation and through to final sequencing libraries. MSCG is a facility with a high degree of flexibility, enabling users to perform sample preparation and cell isolation together with the technical staff, a highly important aspect for our users.

Quality: Can be ensured through the combination of well-defined cell sorting and molecular protocols, with sample preparations, real time monitoring of single genome amplification and by the use of liquid-handling robots to minimize human exposure and sample variability. Notably MSCG handles a multitude of different samples, ranging from environmental microbes, to *ex vivo* or *in vitro* cultured microbes and host cells, presenting a challenge from a standardization perspective.

Storage: MSCG only takes on the role as consultant regarding data storage beyond sequence delivery to Uppmax. This task needs to be taken care of by the user but where MSCG staff can provide contacts and initial communications with service providers and the Data Office.

User fees: Since there is naturally an extensive variability among projects at MSCG, the facility has until 2020 applied a "case-by-case" user fee depending on resource demand and reagent requirement. During 2020, MSCG aims to implement a more standardized user fee model for predefined projects, where user fees will be directly based on the materials, working hours and indirect costs of a project.

Links to research environment: Located at ICM, Uppsala University, MSCG is embedded in an environment featuring multiple strong micro- and infection biology research groups. MSCG has an ongoing dialog and collaboration with microbiologists and infection biologists at IMBIM, UU, and KI; methods development EBC, UU and MIMS, UmU as well as collaborations and exchange with international research groups, EU and U.S. The facility is actively approaching institutes and research groups both nationally and internationally to bring in new technologies and discuss recent developments in the fields relating to MSCG.

Collaborations:

- MIMS, Umeå University: library preparation protocols for pro- and eukaryotic microbes
- Zoonosis Center, IMBIM, UU, sample preparation protocols for studies of insect vectors
- Health-care: validation of novel molecular diagnostics methods, Karolinska Hospital
- SciLifeLab Research Community Program AMRI (Aquatic Microbiome Research Initiative)
- Meeting with Bigelow – microbial single-cell genomics center (U.S.) planned for 2021
- Ongoing plans of initiating network (2021) based at MSCG, targeting vector-borne diseases with academic research groups in Europe, Latin America, U.S., including industry stakeholders

Alternative facilities and commercial providers:
For general alternatives for single-cell genomics see ESCG and examples ESCG facility report. Note however, that several of the protocols are not overlapping and the general approaches differ significantly. There are to the best of our knowledge no facilities or commercial providers focusing on microbial single cell genomics in Europe. Bigelow in the U.S. is a single cell genomics center focusing on microbes and provides commercial services (https://scgc.bigelow.org). For single-cell genomic approaches of microbial pathogens there are no facilities nationally or internationally providing the set of services that MSCG provide. Additionally, MSCG offers comprehensive project support and a wide range of implementation of non-standardized protocols essential to meet our user's needs.

Budget 2021–2024

*The budget for 2020 covers current operations

- For 2021-24 MSCG requires an additional FTE (research technician) to meet the labor needs of the strategic vision. This is estimated at 0.8 MSEK per annum.
- For 2021, there is an anticipated one-time instrument cost of 2 MSEK for a Laser Microdissection Microscope, which the facility aims to procure through an "expensive equipment grant"
- Furthermore, MSCG plans to apply for external funding through VR and SSF for technology development linked to single-cell technologies to study host-microbe interactions.

Costs	2020	2021	2022	2023	2024
Personnel (2 FTEs 2020, 3 FTEs 2021-2024)	1 850	2 650	2 680	2 710	2 740
Operations	650	1 000	1 200	1 300	1 400
Premises	250	250	250	250	250
Instrument depreciations	0	500	500	500	500
Other	50	50	50	50	50
Sum costs (kSEK):	2 800	4 450	4 680	4 810	4 940

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	2 200	3 000	3 000	3 000	3 000
University funding		150	150	150	150
Funding agency A		400	400	400	400
Funding agency B		150	150	150	150
User fees	600	800	1 000	1 100	1 250
Sum revenues (kSEK):	2 800	4 500	4 700	4 800	4 950

Table 1. Current budget (2020) and suggested budget 2021–2024

Proteomics and Metabolomics Platform

Basic information

Platform Director: Jochen Schwenk

Vice Platform Director: Masood Kamali-Moghaddam

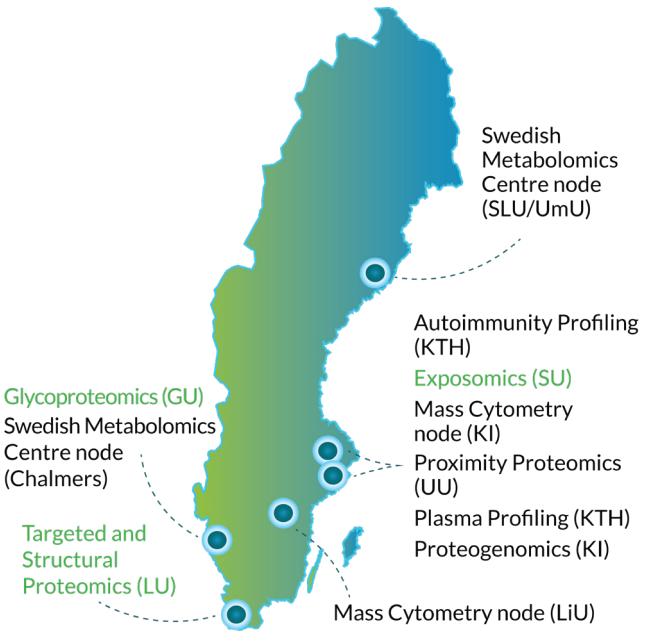
Platform Vision:

To enhance the understanding of biological systems, advance the analyses of molecular phenotypes, and translate our capabilities into clinical utility

Platform Mission:

To generate the best possible data, make the data actionable and thereby increase its value and utility for the Swedish research and clinical community

Geographical location of facilities



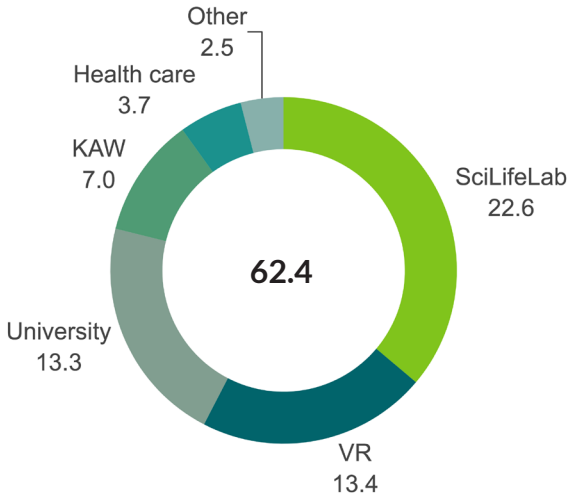
SciLifeLab funding 2020

Facility/unit	(MSEK)
Autoimmunity Profiling	3.0
Plasma Profiling	3.2
Proximity Proteomics	3.8
Mass Cytometry	6.0
Proteogenomics	3.0
Glycoproteomics (candidate)	0.0
Targeted and Structural Proteomics (candidate)	0.0
Swedish Metabolomics Centre	3.6
Exposomics (candidate)	0.0
Bioinformatics Hub	0.0
Total SciLifeLab funding	**22.6**

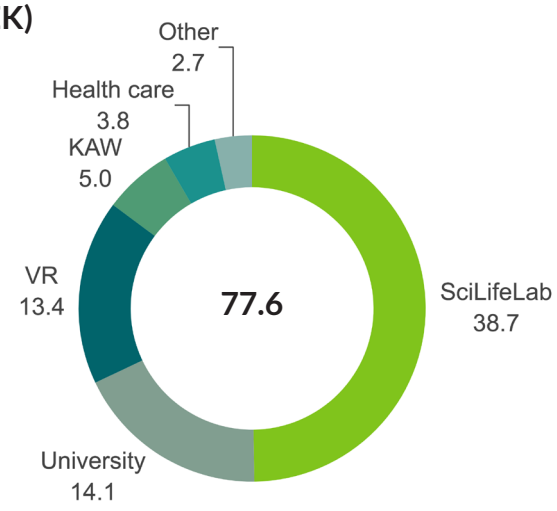
Suggested annual SciLifeLab funding 2021-2024

Facility/unit	(MSEK)
Autoimmunity Profiling	4.0
Plasma Profiling	4.4
Proximity Proteomics	7.2
Mass Cytometry	7.0
Proteogenomics	5.5
Glycoproteomics (candidate)	2.0
Targeted and Structural Proteomics (candidate)	2.0
Swedish Metabolomics Centre	3.0
Exposomics (candidate)	2.6
Bioinformatics Hub	1.0
Total SciLifeLab funding	**38.7**

Total funding 2020 (MSEK)



Total suggested annual funding 2021-2024 (MSEK)



Background

The Proteomics and Metabolomics Platform (PaMP) hosts seven national facilities offering services based on mass spectrometry (MS) and affinity-based assays. These are the MS-proteomics facilities at KI, the KTH-associated facilities linked to the Human Protein Atlas, PLA and Single Cell Proteomics facility associated with Molecular Tools at UU, Mass Cytometry facilities from KI and Linköping and the Swedish Metabolomics Center in Umeå. PaMP comprehensive and world-unique portfolio covers cutting-edge technologies for a wide rage of applications from screening of population biobanks to single cell analyses. All of PaMP's facilities are associcated to nationally and internationally leading groups. This ensures the seemless transfer and implementation of innovative assays, advanced technologies, resources and reagents into the facilities services.

Platform plans for 2021-2024

Our vision is to enhance the understanding of biological systems, make our capabilities translatable into clinical utility, and drive precision medicine forward. We therefore aim to strengthen our platform to support the clinical and basic research community by an exquisite infrastructure with excellence, nationwide, unique and complementary services. PaMP already offers services to users from academia, health care and industry, and we are now further expanding our capability portfolio with three additional, national, complementary and research-excellence-driven facilities. Two additional MS-proteomics facilities with focus on structural proteomics (Lund Univ.) and the proteomics of post-translational modifications (Gothenburg Univ.) will be added to complement well the current MS-proteomics capabilities (Proteogenomics Facility). A third candidate facility will offer national service in MS-based exposomics (Stockholm Univ.), with characterization of environmental chemicals in biofluids. This globally unique service will be aligned with those offered by the Metabolomics Facility, hence expand the capabilities of PaMP to also environmental researchers. The facilities using affinity-based technologies strive to continuously expand their application toolbox to new sample types (e.g. exosomes), new technologies (e.g. IsoPlexis, Quanterix, Navinicy). Each of the now 10 facilities has high bioinformatics expertise in their respective area, which lays the foundation to connect us with the data-driven schemes of SciLifeLab.

Impact on Swedish life science research community and society

Technology-enhanced science is moving forward with an ever-growing pace. This puts a demand on continuously updating the expensive infrastructure and also maintaining a high level of expertise of the staff scientists. Adding to this are the trends towards more multi-omics integrative and data-driven analyses in all areas of life science, and it is where protein and small molecule level data are crucial components. Fortunately, PaMP already offers a broad spectrum of capabilities and we collaborate and interact with the international stakeholders, for example number of HUPO, International Cancer Moonshot at NCI, or EATRIS of the EU. PaMP is actively involved in cross-facility research tracks, collaborations with local clinicians, and initiatives such as Genome Medicine Sweden. To make PaMPs toolbox clinically useful we strive to obtain certification for the different assays, workflows and types of analyses.

The importance of SciLifeLab funding

Biotechnology is in a phase of rapid development and it's expected that the genomics wave is followed by proteome and metabolome analyses as these technologies mature. Connecting expertise in data generation with evolving data analyses, including AI, is important because each data type has its own characteristics. Continued and longer-term funding is essential for PaMP to maintain the world unique infrastructure and capabilities and thereby drive the omics data integration forward by delivering complementary services and highest data quality. PaMP will be an important element for keeping the Swedish research community competitive.

Benchmarking of the platform from an international perspective

While some of the services offered by the platform are commercially available or provided elsewhere, several molecular tools and reagents remain unique for PaMP. On an international level, currently there are, to our knowledge, nearly no nationwide infrastructures that can be compared to PaMP. There are, however, centers of excellence in that each drive the communities forward. One example is the Novo Nordisk Foundation Center for Protein Research in Denmark, where clinical proteomics and bioinformatics is being combined. Stanford or Harvard in the US, Cambridge in the UK, or the Helmholtz Centers in Germany host similar technologies but offer access to their infrastructure on a local and less community-focused manner. Meaning, there is no such coordinated platform as PaMP that can provide the wide range of capabilities and expertise. Commercial service providers also exist, but these often lack the ability to adjust their services and develop research in even smaller projects.

Future plans for governance and relevant technologies

PaMP is governed by a chair and co-chair with support of a platform coordinator. PaMP has an external advisory board with representatives from industry (Dr. Maria Lagerström-Fermér, AstraZeneca), biobanking (Docent Åsa Torinsson Naluai, Sahlgrenska Academy, Gothenburg) and university (Prof. Maréne Landström, Umeå Univ.). The platfom management group consists of the all facility directors

and heads. The communication within the platform groups works very well, the facility teams participate actively in discussions about the platform's activities and future. We gather at quarterly calls and annual face-to-face meetings, to review scientific and administrative matters related to PaMP and SciLifeLab. Hence, we have built a strong platfrom community that shares insights from user experience, infrastructure updates, data management and analysis routines, or ideas about the development of a common user and community portal. We have planed to start a rotation program in which laboratory staff can spend a few days at another PaMP facility to allow futher exchange of ideas, improvement of workflows, development of new skill, but also to provide staff a perspective about their value and contribution. Annual meetings are planned for entire facility staff to build an even stronger cross-facility connections. To make also the services more aligned and more attractive for clinical routines, the facilities will jointly work towards obtaining accreditation for their analyses. The future plans include a rotation for chair positions among the different host universities. Recruitment of an external chair is possible but there is currently a lacking mandate for the PaMP leadership to impose budget and strategic decisions on all facilities.

Our mission is generate the best possible data, make the data actionable and thereby increase its value and utility for Swedish research community. Hence, the close collaboration with associate research groups will be key for the co-development and implementation of advanced approaches. To enable transitions into the facilities, it is essential to keep the knowledgeable and excellent staff scientists, by offering them career paths and opportunities for personal development. It also requires funding our infrastructure either by support from SciLifeLab, the host universities and the affiliated research groups. Because no single technology will be most suited for all applications, a broad spectrum of technologies and capabilities must be maintained. Collaboration between facilities to co-develop or benchmark technologies is always highly encouraged. Lastly, we need to increase the awareness and visibility of our services by coordinated outreach activities at universities, hospitals and international conferences to attract new users.

Synergies and capability contributions

Each facility hosts a unique set of capabilities and offers dedicated and complementary expertise. Despite some overlap, a particular technology or assay are more suitable for the different types of analytes or samples. Cross-facility collaborations to benchmark the systems or optimize workflows are already ongoing. Establishing these projects, such a tracks for immuno-monitoring in blood, will allow us to further interconnect our capabilities. The exchange of common routines within bioinformatics approaches will strengthen the current synergies. We indeed requested funding to establish a "Bioinformatics Hub" to coordinate a forum focusing on computational, biostatical and bioinformatics analysis of data. This will make our data ready for integration and cross-omics analyses also elsewhere. Examples of these are GWAS analysis with circulating analytes to identify quantitative trait locis (QTLs) for proteins, protein modifications or metabolites, or exposome-wide association studies (EWAS). All projects do need bioinformatic support and external resources usually don't have the dedicated knowledge to deal with the facility-specific types of data and follow the latest trends in the field. Hence, long-term bioinformatic expertise is a cornerstone of each facility.

A great potential of SciLifeLab is to connect different platforms and facilities in so called "tracks". We envision these tracks as cross-technology capabilities to provide unique insights into, for example, approaches of precision medicine. Here, an aligned project management would be needed to enable transfer of samples, the generation, storage and analyses of the data across different centers of expertise in order to deliver completely new insights into phenotypes of health and disease, develop and test new drugs to more precisely treat each individual. Coordination of such multi-omics efforts with different data types can only be achieved if these efforts are aligned with the SciLifeLab's governance and visions.

Collaborations with healthcare, industry and other organizations

Services beyond academia offer a great potential for growth to the PaMP, via integrating these into tracks, clinical trials or certification of assays. PaMP facilities have already established relationships with instrument and kit providers to beta-test, participate in national infrastructures (eg BioMS), or international EU projects (eg Cancer Core Europe, H2020 or IMI). However, there are comparably few bilateral projects with industry, which can be due to more time-consuming legal negotiations that handles by the host universities.

Alternative service providers

There are some alternative service providers, for example Nightingale, Metabolon, Biocratis (all metabolomics); Biognosys or MRM Proteomics (MS-proteomics), Olink Proteomics, Somalogic, RayBiotech, Myriad RBM (Plasma Profiling and PLA Proteomics), as well as Protagen, CDI Laboratories (Autoantibody Profiling). Nonetheless, as mentioned above PaMP is in a great position to cover a very wide range and unique sets of technologies and services.

Justification of SciLifeLab funding

The capabilities offered by PaMP go beyond the services available elsewhere. Technology-drive research and excellent staff is our core. PaMP is fueled by our associated,

long-standing and world-leading research teams, who enable PaMP's project flexibility and have the interest in further advancing the field by co-developing novel applications for a next project generation. Moreover, the seemless access and low costs for support to Swedish academic users also offers them an advantage to actually utilize state-of-the-art infrastructures and expertise.

Data-driven science of SciLifeLab's Roadmap

PaMP is extremely well positioned within all three areas of data-driven life science. We are already working towards a more synergistically coordinated data infrastructure to combine our data pipelines, reproducibility and accessibility efforts, hence brings data-driven Life Science of SciLifeLab to a next level. This is exemplified for (i) Data-driven Cell Biology, where single cell analysis, subcellular profiling, analyses of protein structure and modifications will be made possible.; (ii) Data-Driven Molecular Precision Medicine, where deeper molecular phenotyping via the proteins on human blood cells, of vesicles and those circulating in body fluids will be made possible; (iii) Data-driven Biodiversity and Molecular Environmental Profiling, where the analysis of small molecules will deliver novel insights about the impact and interactions of the environment on human health.

Budget

The details about the future budget is being discussed in the facility reports, respectivly. The continued success and value of PaMP does depend on the continued support from SciLifeLab. Competition is fierce for the latest technologies but also for the best staff. For the latter, longer term contracts and development opportunities will make working at PaMP facilities even more attractive. We also request specific support for a PaMP-dedicated "Bioinformatics Hub", which will coordinate a forum of computational workflows and pipelines for PaMP-derived the data.

Autoimmunity Profiling

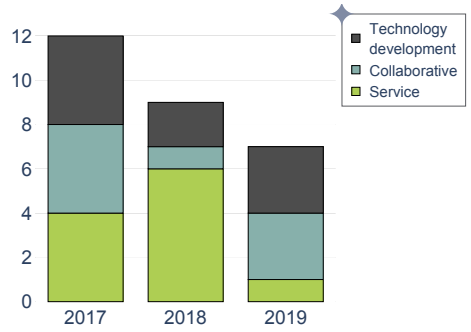
Read more: Web page, Publication Data Base

Basic Information

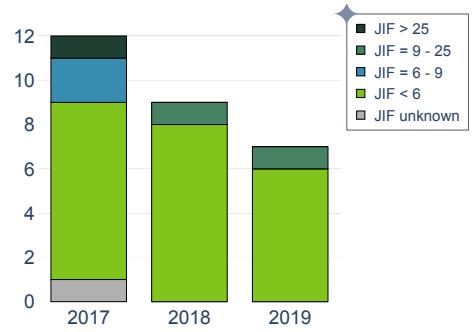
Facility director: Peter Nilsson
Head of facility: Ronald Sjöberg
SciLifeLab facility since: 2013
Host University: KTH
FTEs: 3
FTEs financed by SciLifeLab: 3

Funding 2020 (in kSEK)

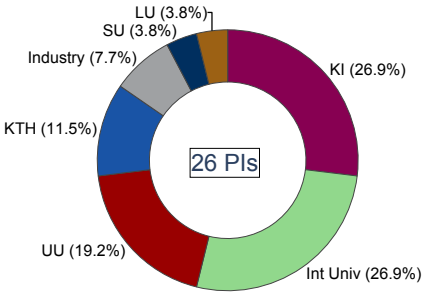
SciLifeLab: 3000
Total: 3700



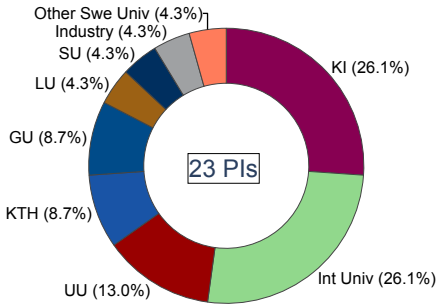
Publications by category



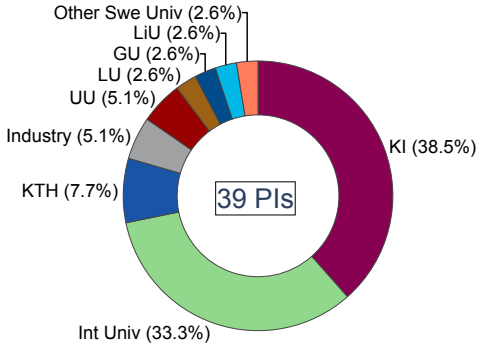
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

- Analysis of autoantibody repertoires in body fluids
- Antibody validation on protein arrays
- Production of custom designed protein and peptide arrays
- Proteome wide screening on large arrays
- Epitope mapping on peptide arrays
- Infrastructure for all types of commercial protein arrays
- Access to affinity reagents and extensive experimental and analytical array experience and expertise

New Technologies and Services 2021–2024

- Development of next generation proteome wide arrays
- New three-colour ultra-high resolution fluorescence imager for increased multiplexing and data collection
- Development of a secretome array with 2000 full-length proteins
- Development of a data base on global autoantibody repertoires

Background

The Autoimmunity profiling facility originates from the protein array group that performed antibody validation of more than 50 000 antibodies for the Human Protein Atlas and is currently comprised of two researchers (0.8 and 0.2 FTE) and three research engineers (2x 0.8 and 0.2 FTE), in total 2,8 FTE, with extensive experience and knowledge in the production and utilization of protein arrays. It provides infrastructure and technologies for analysis of the autoantibody repertoire in body fluids and antibody validation, using custom designed protein and peptide arrays, to both Swedish and international academia, as well as to industry.

Supported by the resource of more than 42 000 unique human protein fragments generated within the Human Protein Atlas, representing more than 18 000 human protein coding genes, the facility offer proteome-wide screening for autoantibody reactivity with one of the world's largest protein coverages on planar arrays. It additionally offer downstream solutions with higher multiplexing capabilities for directed investigation of autoantibody repertoires in hundreds of patient samples in parallel using high-throughput bead-arrays. Instrumentation and know-how is available for generating customized protein arrays as well as utilisation of commercially available protein arrays.

These arrays, and the related infrastructure and knowledge, have proven to be an important tool not only for large-scale screening of sample cohorts relating to various fields such as autoimmunity, allergy, neuroproteomics and cancer, but also for affinity binder validation and epitope mapping.

The Autoimmunity Profiling facility have so far contributed to nearly 50 publications during the past six years,

showcasing its success. It provides not only access to equipment necessary for array production and analysis but also invaluable expertise, to both Swedish and international academia as well as industrial partners.

During the period 2017-2020 the facility have taken part in the wellness profiling project, generating continuous autoantibody profiles for approximately 200 normal individuals. This analysis resulted in autoantibody barcodes for each individual that have been shown to be maintained over a whole year. These reactivity signatures were shown to be person specific in the number of reactivities and targeted antigens. The ability to generate information such as this is becoming increasingly important as modern medicine moves further towards an individualised medicine, maybe even more so in the complex field of autoimmune disorders. Additionally new arrays comprising of full-length proteins representing approximately 2000 secreted proteins are being designed and will soon become available to facility users. This can be seen as a first step towards building a comprehensive library of full-length proteins that would nicely complement the current library of protein fragments.

Plans for 2021–2024

A three-colour ultra-high resolution fluorescence imager is being purchased, which offer increased multiplexing by the addition of an additional colour channel and enable increased data collection capabilities through ultra-high resolution. Additionally this imager will enable a dynamic range of 106, as compared to the current instrumentation which offer a dynamic range of 104, which is expected to simplify the image acquiring as the internal relationship between high-intensity signals that previously could not be resolved in one scan now to a higher degree will be separated already in the initial imaging..

A new generation of the in-house produced proteome wide planar antigen arrays are being designed and will offer increased reliability, reproducibility, and robustness for antibody and affinity binder repertoire profiling.

Additional competency in bioinformatics is being added to the facility with the expressed goal of performing meta-analysis of the vast amount of data that is being aggregated by the facility. This is expected to bring new insight in the autoantibody reactivity in human biofluids over a number of disease groups.

There is currently no other research group or facility that offer the same capabilities in neither infrastructure nor know-how for protein arrays within Sweden, and barely neither in the entirety of Europe. During the year 2019 a new arrayer was installed, which offer the very latest in technology for array production, and this in combination with the new fluorescence imager will ensure that the facility continues to offer the very latest in infrastructure and technology within the protein array field.

The facility is currently operating at its maximum capacity where the number of personnel FTE is the limiting factor, and is expected to continue to do so during the coming four years with approximately 60 projects, spread over approximately 40 users, finished or ongoing each year. These users could be expected to be mainly Swedish and international academia, as well as be comprised of a some industry collaborations.

The facility aims to increase its outreach program to ensure that the awareness of the existence of the facility and its capabilities and possibilities is raised even further among the Swedish research community in order to ensure that those researchers and clinicians who are in need, or will become in need, of the facilities services are aware of its existence and understand how to initiate a project together with the facility. Previous experience have shown that many Swedish researchers and clinicians become aware of the existence of the facility through international engagement, few clear venues for outreach within Sweden exists and international exposure is therefore critical for reaching national potential users. The facility have therefore joined the European Infrastructure for Translational Medicine, EATRIS, in order to gain increased exposure to the European research community. Additionally, the facility will participate in, and co-organise, a webinar series centred on the use of protein arrays, which is planned to be a reoccurring event.

There is also an ambition to reach further out in to the more clinical setting by closer collaborations with clinicians in designing specialised customised arrays with the end goal of constructing a set of disease-specific arrays that can be used not only for basic research but also for aiding in diagnosis of autoimmune disorders.

Furthermore, the facility have during 2019 appointed a coordinator for the bioinformatics needs of the facility to ensure that the data is being evaluated and stored in an optimal setting. A new model for calculating project costs have been developed and is currently being evaluated with the goal of simplifying the process of determining user fees for non-standard projects. This should cover costs of reagents as well as instrument maintenance, as well as personnel costs for non-academic and non-Swedish users.

The facility will continue working in close collaboration with the associated research group Nilsson Lab as well as with the closely related Plasma Profiling facility, and its associated research group Schwenk Lab. This close association between facilities and research groups have previously proven to generate positive synergistic effects in instrument, laboratory, and office space usages, as well as transfer of knowledge, and will continue to do so during the coming years.

A close relationship between the facility and the two most important suppliers of reagents and instrumentation, Luminex and Arrayjet, is expected to continue as well, with exchange of ideas and information regarding the implementation of the related technologies.

In conclusion, the Autoimmunity Profiling facility is unique in Sweden, as no other research groups or commercial entities offer a comparable service. This holds true even in a European perspective as none of the academic or commercial alternatives can offer both the capabilities in producing customized protein arrays and easy access to such a large library of antigens.

Budget 2021–2024

Costs	2020	2021	2022	2023	2024
Personnel (2.8 -->4.0 FTEs)	2 470	3 400	3 450	3 450	3 500
Operations	350	450	450	450	450
Premises	200	250	250	250	250
Instrument depreciations	800	700	700	700	700
Other	380	400	400	400	400
Sum costs (kSEK):	4 200	5 200	5 250	5 250	5 300

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	3 000	4 000	4 000	4 000	4 000
University funding					
KTH SFO, Array Scanner, 900 kSEK/5 year	180	180	180	180	180
SciLifeLab, Arrayer, 2600 kSEK/5 year	520	520	520	520	520
User fees	500	500	550	550	600
Sum revenues (kSEK):	4 200	5 200	5 250	5 250	5 300

Table 1. Current budget (2020) and suggested budget 2021–2024

Plasma Profiling

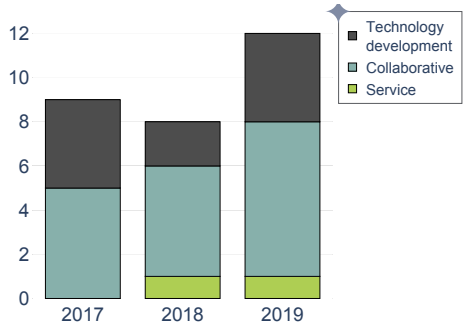
Read more: Web page, Publication Data Base

Basic Information

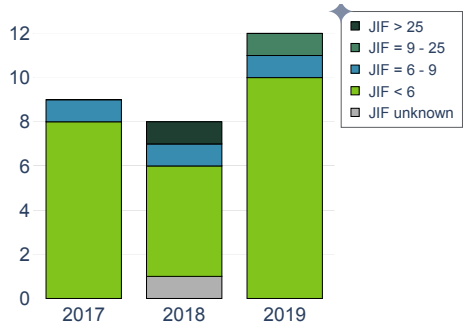
Facility director: Jochen Schwenk
Head of facility: Claudia Fredolini
SciLifeLab facility since: 2013
Host University: KTH
FTEs: 3.5
FTEs financed by SciLifeLab: 2.5

Funding 2020 (in kSEK)

SciLifeLab: 3200
Total: 3350



Publications by category



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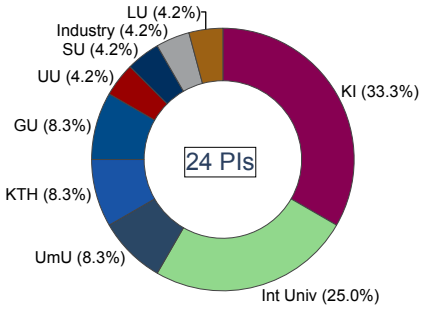
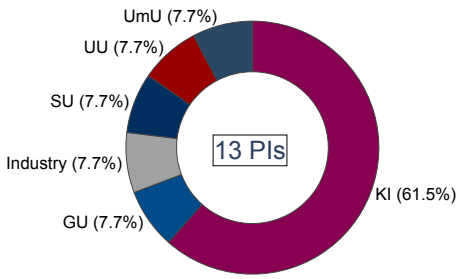
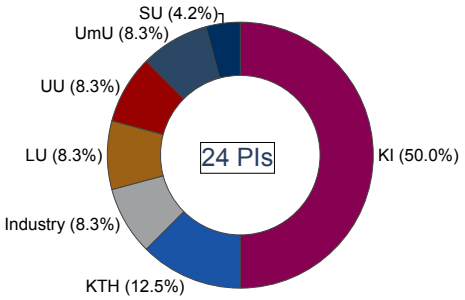


Users 2017



Users 2018



Users 2019

Current Technologies and Services

- Consultation for antibody-based proteomics analyses.
- Quantification of protein biomarkers in human body fluids.
- Automated and high throughput sample analyses.
- Luminex-based assays for versatile multiplexed protein quantification.
- Development of novel multiplexed immunoassays using HPA antibodies.
- Olink's PEA assays for highly multiplexed proteomic profiling (up to 92 targets).
- Quanterix-based assays for ultra-sensitive protein quantification (sub 1 pg/mL).
- ProteinSimple-based assays for automated protein quantification (low hands-on time).
- Biostatistic data analyses and integration of affinity proteomics data.

New Technologies and Services 2021–2024

- Upgrading Luminex-based systems to expand sensitivity, versatility and throughput.
- Pipeline for the development of highly sensitive immunoassays for novel clinical biomakers that currently lack validated immunoassays.
- GLP and ISO certifications for established laboratory routines
- Additional multi-analyte assays for protein-protein interactions, protein enrichment analysis, post-translational modifications (eg. glycosylations).
- PCR-free detection of DNA (PMID: 23331316) and miRNA (PMID: 28637221) in body fluids.
- Support for designing and analysing large scale epidemiological studies.
- Data analysis pipelines from univariate models to advanced machine learning tools and data integration (eg GWAS)
- Evaluate novel technologies (eg non-MS protein sequencing and new emerging immunoassay techniques)

Background

The Plasma Profiling National Facility (PPNF) was founded in 2013 on long-standing experience and research using multiplexed immunoassays. During the last decade, the facility and the associated Schwenk Lab focussed on the development and application of advanced immunoassay methods for the primary purpose of exploring the plasma proteome. The facility has therefore continuously expanded the portfolio of complementary technologies and competences. It now offers a unique combination of platfroms and systems for protein quantification in biological fluids for advanced molecular diagnostics. We have experianced staff and know-how to perform today's most innovative and sensitive immunoassay technologies

including: Highly multiplexed Olink's Proximity Extension Assay, versatile Luminex-based immunoassays, automated microfluidic assays (ProteinSimple), and ultra-sensitive assay (detect fg/ml) by Quanterix' Single Molecule Arrays (SiMoA) technology.

The facility team includes a Director, Head, two Research Engineers and a bioinformatician, each with > 5 years expertise about immunoassays and the biomarker research pipelines. Since 2013, we decisively supported research in Sweden (processing > 5000 samples annually). We strive for use and offer the best technologies and assays to generate the highest quality data, and to support users from study design into data analyses and interpretation.

Biomarkers in biofluids have always played a crucial role in diagnostic and treatment decisions, but new technologies have more recently enabled us to take an even deeper and more precise look into states of human health and disease. To make this a reality also for the patients, however, robust assays, reproducible data and a validation scheme that can enter the clinic setting are needed. We therefore invested into the validation of antibodies and expanded our competence into other multiplexed quantitative protein detection technologies, aligning with SciLifeLab's vision towards excellence, integrity and reproducibility of data. There are three recent and important publications that exemplify the development introduced above: in a study lead by Fredolini et al (PMID:31171813) a new assessment of antibody selectivity in plasma was described; Häussler et al demonstrated our capabilities of developing, validating and applying novel quantitative sandwich immunoassays for hundreds of proteins in parallel (PMID: 31278833); a third study by Lorenzen et al (PMID:31555726) showed how new capabilities and applications of multiplexed assays can arise, by which we expanded our capabilities into protein-protein interaction of the challenging membrane proteins.

Plans for 2021–2024

Our vision is to make the PPNF a cornerstone of SciLifeLab and further develeop our services in four main areas: (i) development and certification of high-quality assays to support translational research; (ii) multi-analyte analysis for users in collaboration with other SciLifeLab facilities, (iii) versatile assays for protein characterization such as PTMs or protein complexes, and (iv) enhance and streamline the pipeline for in depth analyses of affinity proteomics data. This entails to build on our current strengths in terms of a multi-technology portfolio, exquisite affinity reagents and expertise about lab work and data analyses.

(i) Over the past years, we have introduced the most innovative immunoassay technologies into our lab, and we will continue to upgrade our assay portfolio. All these complementary technologies will give us the unique capability to provide a high-quality service of protein quantification for a large and growing number of proteins targets across the concentrations scale. Eventually, implementing new sample preparation strategies can further increase the sensitivity and versatility of existing assays. In particular, potentially clinically relevant targets, discovered by mass spectrometry or other methods, may lack suitable immunoassays, hence we will use our expertise and resources to develop novel, robust and validated assays for our users. Technology integration is indeed considered pivotal in the path to biomarker validation and translation. A close collaboration between PPNF and the mass spectrometry facilities at SciLifeLab will advance the knowledge of plasma proteome and of the circulating biomarkers. To facilitate translational research nationally, we aim to strength our collaborations with colleagues at Karolinska hospital and the clinical chemistry in Stockholm as well as with hospitals across Sweden, or biobanks such as form the U-CAN (PMID: 28631533) or the KARMA project (PMID: 29444691). To expand our efforts and experience at an international level, the facility recently became a member of EATRIS, the European Infrastructure for Translational Medicine. The latter will help us attract international users, bring SOPs and routines forwards to later obtain Good Laboratory Practice (GLP) and ISO certification.

(ii) We will also become involved in multi-omics precision medicine efforts that require many different facilities and platforms. There is a huge potential in using and connecting the different types of data and molecular analyses to advance biology as well as for personalizing the diagnosis and treatment possibilities. Plasma proteomics data will be excellent for monitoring patient health over time. Our capabilities will therefore play an important part in data-driven precision medicine, where each data has its own characteristics and contribute differently to the utility of multi-omics strategies. Moreover, a coordinate activity with the National Bioinformatics Infrastructure (NBIS) will guarantee the most suitable quality utility of data analysis. It will here also be valuable to explore the potential to develop multi-analyte assays.

(iii) Advanced immunoassay can do more than measure protein abundance. We see a huge potential in utilizing ultra-sensitive methods to study post translational modifications and protein complexes in cell extracts and body fluids. This will be synergistic to efforts lead by PLA and mass spectrometry facilities, and adds further opportunities for researchers in Sweden. Our assay protocols will offer the flexibility and versatility to analyse proteins complexes, miRNA and possibly other molecular traits.

(iv) Our facility already generates and handles large volumes of proteomics data, which is managed locally by us as part of our SciLifeLab infrastructure. Together with other facilities from our platform, other SciLifeLab units

(e.g. NBIS, data office, NGI), we want to further streamline the pipeline for data processing, management, integration and analyses. We see a great value in giving users access to browse their data even without prior expertise about biostatistical rules or advanced bioinformatic algorithms. Our team should therefore have one data analyst that can directly support each project and develop interfaces for scanning the data.

Budget 2021–2024

Our infrastructure currently allows us to perform more than ~2 projects per month, with 70% coming from the Swedish Academia. We planned to increase this to ~ 3-4 per month and expand our interactions for clinical and non-academic users. The facility aims to charge users for experimental analysis a user fee that is 15-20% of the reagent costs. Since consumption of reagents and time on task/instrument are propotional, the cost model is meant to simplify the description of pricing. A cost model for any additional project work such as sample aliquotation or bioinformatics support is currently set to 500 SEK per hour. Both user fees and additional project work can be adjusted based on the currently discussed national directives.

The facility operates a wide range of equipment and technologies. There is an increase in the size and number of the projects, hence more staff is needed to manage these in paralell. Even though staff can be invovled in work on several projects in parallel, flexibility and more ahnds are needed to coordiante and manage smaller projects while conducting larger projects. In discussions with the platform and NBIS, bioinformatics support will also increase over time with expertise on the type of data needed. The PPNF will optimally have its own bioinformatician to support users directly and to connect data with other units at SciLifeLab.

Costs	2020	2021	2022	2023	2024
Personnel (3.5->4.5 FTEs)	3 000	4 000	4 050	4 100	4 100
Operations (kits, consumables, maintainance, services)	3 550	4 800	5 000	5 200	5 500
Premises	300	300	300	300	300
Instrument depreciations	50	100	150	200	200
Other (staff training, events, conference travels)	100	200	200	200	200
Sum costs (kSEK):	7 000	9 400	9 700	10 000	10 300

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	3 200	4 400	4 400	4 400	4 400
University Funding					
SFO funding 750 kSEK (5 years)	150	150	150	150	150
Project Invoices Operation (is ~80% of Project Cost)	3 000	4 050	4 300	4 550	4 800
User fees (is ~ 20% of Operations Cost)	650	800	850	900	950
Sum revenues (kSEK):	7 000	9 400	9 700	10 000	10 300

Table 1. Current budget (2020) and suggested budget 2021–2024

Proximity Proteomics

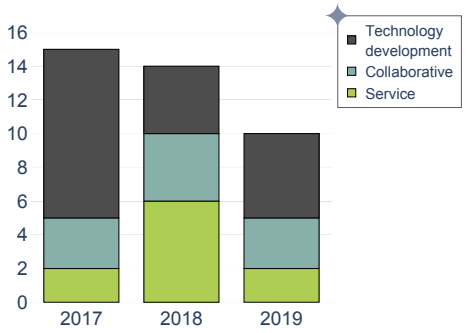
Read more: Web page, Publication Data Base

Basic Information

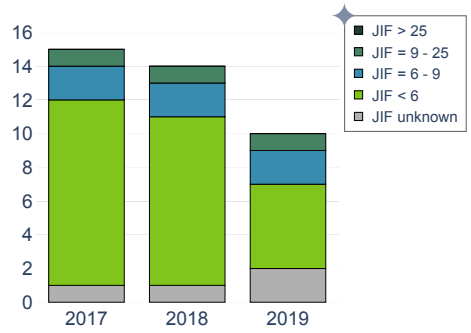
Facility director: Masood Kamali-Moghaddam
Head of facility: Maria Hammond
SciLifeLab facility since: 2013
Host University: UU
FTEs: 4
FTEs financed by SciLifeLab: 3.6

Funding 2020 (in kSEK)

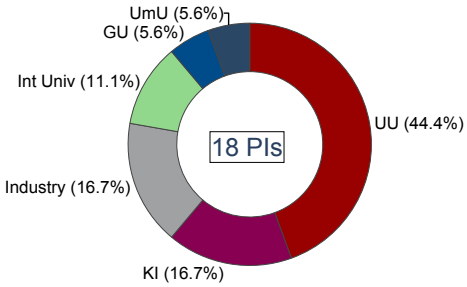
SciLifeLab: 3800
Total: 4200



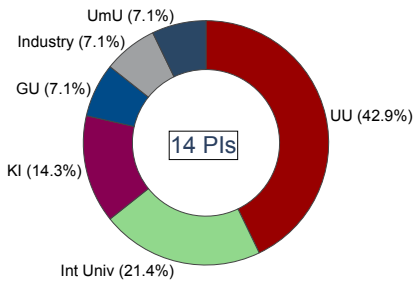
Publications by category



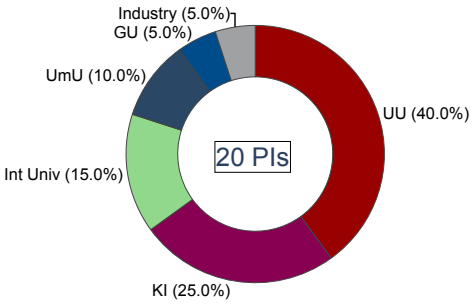
Publications by JIF



Users 2017



Users 2018



Users 2019

NB! Publication and user statistics shown for the current SciLifeLab facility PLA and Single Cell Proteomics.

Current Technologies and Services

- *In situ* proximity ligation assays (isPLA) in fixed cells or tissue sections for high-specificity detection of proteins, protein interactions and post-translational modifications with microscopy or flow cytometry readout.
- Customized protein analysis by single- or multiplex PLA or proximity extension assays (PEA) for highly sensitive and specific protein detection in solutions such as plasma and cell/tissue lysates, using down to 1 µl sample volumes.
- PLA-based western blot (PLA-WB) for highly specific and sensitive protein detection.
- Conjugation of DNA oligonucleotides to antibodies for custom DNA-assisted protein assays.
- Single cell analyses of proteins or combinations of proteins and transcripts.

New Technologies and Services 2021–2024

- Detection and proteomic characterization of exosomes and other extracellular vesicles
- Multiplex isPLA
- Full service of Olink 96x96 PEA panels with the option of absolute quantification
- Full service of Olink 384x24 cutomized PEA panels with the option of absolute quantification
- Full service of Meso Scale Diagnostics analysis kits
- Multiplex protein analysis of dried blood spot (DBS) including sample handling

Background

The PLA and Single Cell Proteomics facility offers customized assays for detection of proteins, protein interactions and protein modifications in fixed cells or tissue sections, or in liquid samples such as blood fractions or cell lysates. For *in situ* detection we offer image-based read out with microscopy for digital enumeration of detected events via image analysis, or flow cytometry readout in collaboration with the local core facility, Biovis, UU. For detection of proteins in solutions we can assist researchers who are interested in targets for which no sufficiently sensitive assays are available or who need a focused panel of proteins targeting proteins of interest for validation in larger sample cohorts.

During 2017-2020 several new technologies have been implemented. We prepare custom DNA-conjugated antibodies to offer combined detection of proteins and transcripts using CITE-seq for sets of thousands of single cells in a collaboration with NGI Uppsala SNP&SEQ. A new approach for detecting products of gene fusions at the protein level, initially applied for detection of BCR-ABL fusion proteins in patients with chronic myeloid leukemia, is now offered as a service to the research community. The

technique has also been transferred to a clinical research group for possible application in clinical routine. Supported by a local technology development grant from SciLifeLab Uppsala we are developing these assays to include more proteins and fusion proteins to address a wider range of leukemias.

Innovative new tools for protein analysis have been developed as a result of the close collaboration between the facility and the Molecular Tools unit (IGP, UU). Many of these tools, such as the proximity barcoding assay (PBA) for characterization of surface proteins on exosomes and other extracellular vesicles (Wu, *Nat. Commun.*10:3854, 2019), and single-cell protein and RNA co-profiling (SPARC) (Reimegård, *bioRxiv* doi: 10.1101/749473, 2019) are now ready for implementation within the facility.

The Clinical Biomarkers Facility (CBF) offers nation-wide service with high-throughput multiplex analysis of protein biomarkers in cardiovascular disease, inflammation, cancer and neurobiology using Olink's PEA and more recently also MesoScale's electrochemiluminescence assays, giving Swedish researchers a head start with these technologies. Since 2013, around 180,000 samples in small and large studies have been analyzed and the number of individual PI's has averaged around 30 for the last three years (please see *Metrics* below). By January 2020, 119 confirmed publications had resulted from the works performed at CBF. Since CBF has analyzed samples from many large cohorts e.g. Malmö Diet Cancer, SCAPIS, COSM, SMCC, and ULSAM the clinical findings and the number of published papers are expected to continue to rise. CBF was discontinued and phased out as a national facility 2017 but has remained a local Uppsala SciLifeLab facility.

Clinical Biomarkers Facility Metrics 2019 (2018; 2017): FTEs 3.3 (3.1; 3.1); Publications 30 (23, 30); Individual PIs 34 (25, 27); User fees 25.1 Mkr (17.8 Mkr; 8.9 Mkr). Funding 2019 (mainly from UU) 1.7 Mkr.

Both facilities continuously take part in outreach activities. We have arranged seminars and symposia, participated in advanced and research level teaching in Sweden and in Kenya, and invited individual researchers to our lab for hands-on training.

Plans for 2021–2024

New technologies

We propose a merger between the PLA and Single Cell Proteomics and the Clinical Biomarkers facilities to collect a broad repertoire of both standard and customized assays for protein detection in biofluids, single cells and *in situ* in one facility. The facility will remain in close collaboration with the unit for Molecular Tools to ensure continued development and implementation of advanced molecular tools for pre- and clinical molecular analyses. One joint development project with the Molceular Tools unit is the development of a multiplex isPLA that we aim to pilot as a service during 2023 or sooner.

There is a growing interest in the potential of exosomes and other extracellular vesicles as biomarkers. The Molecular Tools unit has developed a broad repertoire of technologies for sensitive and specific profiling and detection of exosomes, including PBA (Wu, *Nature Commun.* 10:3854, 2019), exo-PLA (Löf, Sci. Rep. 6:34358, 2016) and analysis of exosome contents with PEA (Larsen, *Mol. Cell. Proteom.* 16:1547, 2017), which we plan to make available as services at the facility.

The results from Olink's commercial 96x96 PEA panels are delivered as relative NPX values. There is an increasing demand from users, and also from reviewers of submitted papers, that protein levels measured by PEA are compared with results from other assays. If results could be delivered as weight per volume (w/v) or molarities this would facilitate meeting such requests. Absolute quantification can also simplify comparisons across studies and between batches of reagents, thereby stimulating clinical uptake of these assays. We have acquired equipment to run Olink's smaller customized 384x24 panels with absolute quantification and the first study with 10,000 patients was recently started, which hopefully will lay the foundation for a clinical routine diagnostics tool.

We have demonstrated that most proteins in samples dried on paper, unlike wet protein standards, retain detectability over many years (Björkesten, *Mol. Cell. Proteom.* 16:1286, 2017). Due to support via a development grant from SciLifeLab we are now ready to implement the analysis of dried protein standards as an option for scientists wishing to obtain protein results expressed in protein concentrations, rather than the relative NPX values, also for some 96x96 panels. After discovery studies, users often come back with requests for customized panels. Some of these inquiries can be met through the MesoScale platform but we can also conjugate antibodies to offer small, tailored PEA panels with standard curves. This is a function that is not currently available as a commercial service or provided by other service facilities using Olink panels.

Traditional blood sampling requires trained personnel and laboratory equipment, and the samples are typically stored as tubes frozen at –80°C, taking up considerable space in energy-consuming freezers. Using blood collected on paper cards (dried blood spots, DBS) offers several advantages over conventional blood sampling but their use in clinical research and diagnostics has been limited. Sensitive detection techniques such as PEA, PLA or MesoScale can be used for multiplex detection of proteins from the collected DBS. This has triggered an interest in analyzing already gathered sample sets in new ways but also in collecting larger sample sets on paper for future analysis. To punch out samples by hand is time consuming.

We are therefore setting up an automated service chain for the analysis of DBS in a 96-well format using a punch robot to meet this need and facilitate the forthcoming analyses.

Synergies, collaborations, and alternative providers

Most of the methods offered at the facility involve DNA-assisted affinity proteomics. We already use DNA sequencing as a readout for some of our technologies and foresee an increasing need to use DNA sequencing when implementing new technologies. With a close collaboration with the Genomics and the Bioinformatics platform we can ensure that Swedish researchers have accesss to the latest solutions for precision proteomics. We also discuss with the DDD Platform how our technologies could support their projects, and we are currently collaborating on developing methods to select binders from DNA encoded chemical libraries (DECL). We participate in beta-testing new commercial technologies that we consider offering as services, allowing us to validate the techniques and provide the companies with feedback that is beneficial both for our users and the company.

Several of the technologies offered remain unique for our facility in a world wide perspective, while the commercial multiplex PEA and MesoScale technologies are also available from other facilities and elsewhere. CBF was the first lab outside Olink to offer PEA panels as a service and the staff has aquired unique skills in optimizing workflows for both large and small studies, analyzing samples and interpreting PEA data. This professional mindset is also reflected in the MesoScale analyses and it is an important reason why new users join us and old users return. Core facilities focusing on exosomes are being established abroad as there is a demand for such services from the research community. We could offer a portfolio of technologies to study extracellular vesicles that are not yet available anywhere else in the world.

The facility's services have so far mostly been used by academia but also to a lesser degree by health care and industry. We anticipate that with our plans for expanding the services with advanced technologies for quantitative analyses of proteins, dedicated protein panels based on findings from the earlier large-scale biomarker screens, and other targets such as exosomes, the facility will continue and increase its attraction for domestic and international users.

Budget 2021–2024

The current user fee policy where academic users cover the reagent costs and parts of the costs for instrumentation will be continued. We request funding from SciLifeLab to cover salaries of all current personell at the two facilities to allow continued offering of current technologies with improvements and modifications described in plans for 2021-2024. Increased funding from SciLifeLab, to cover salary for one additional researcher and purchasing of some smaller instrumentation, will facilitate implementation of the new, world-unique methods for exosome analysis.

Costs	2020	2021	2022	2023	2024
Personnel (currently 4 FTE -> 8 FTE from 2021)	2 951	6 231	6 781	7 131	7 494
Operations	1 100	25 500	26 500	26 500	27 000
Premises	250	500	510	520	531
Instrument depreciations	150	800	800	800	800
Other	149	220	220	220	220
Sum costs (kSEK):	4 600	33 251	34 811	35 171	36 045

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	3 800	7 200	7 200	7 200	7 200
University funding	400				
User fees	400	26 395	27 895	27 895	28 895
Sum revenues (kSEK):	4 600	33 595	35 095	35 095	36 095

Table 1. Current budget (2020) and suggested budget 2021–2024

Mass Cytometry

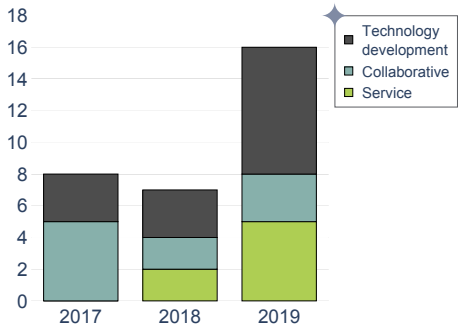
Read more: Web page, Publication Data Base

Basic Information

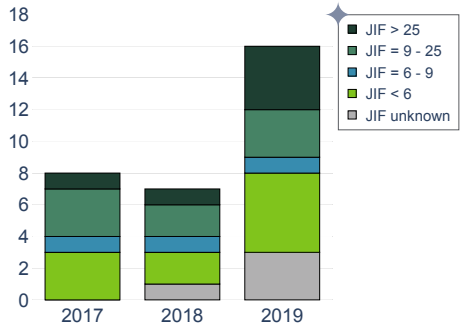
Facility director: Petter Brodin, Jan-Ingvar Jönsson
Head of facility: Lakshmikanth Tadepally, Jörgen Adolfsson
SciLifeLab facility since: 2015
Host University: KI, LiU
FTEs: 5.5
FTEs financed by SciLifeLab: 3.5

Funding 2020 (in kSEK)

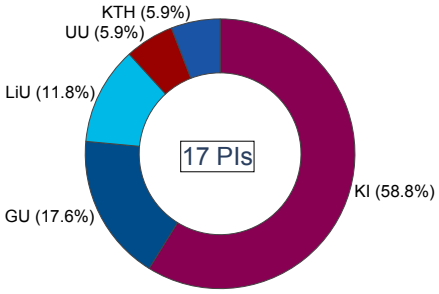
SciLifeLab: 6000
Total: 6800



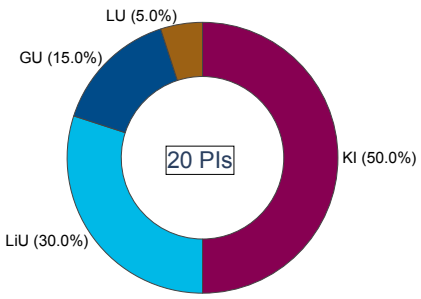
Publications by category



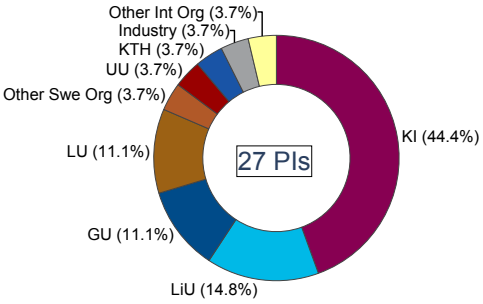
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

- Agilent, custom liquid handling robotics for automated sample processing and staining.
- Mass cytometry, cell phenotyping.
- Mass cytometry, cell functional response analyses.
- Mass cytometry, cell signaling analyses.
- Flow cytometric cell sorting and analysis.

New Technologies and Services 2021–2024

- Single-cell sectretomics, 45 cytokines secreted by single-immune cells (IsoLight™, IsoPlexis)
- Single-cell multiomics immune cell analysis + TCR/BCR-seq (BD Rhapsody™, BD)
- Blood immune response profiling (nCounter™, Nanostring) (Piasecka, et al, PNAS, 2018).
- VirScan, phage-library for profiling IgG against all viruses (Xu et al, Science, 2015).

Background

The Mass cytometry facility consists of two nodes, (Stockholm and Linköping). Project applications are managed via a common project portal (cytof.scilifelab.se) and LIMS system and distributed to these nodes. Customers send samples which are prepared, stained and acquired by facility staff with long experience. This is key for overall success given the complexity of such experiments. Sample handling is automated to reduce technical variation and improve data quality. The main bottleneck for Mass cytometry users is the specific data analysis methods required, which are quite specific. The facility currently employs a 0.5 FTE bioinformatician. There has been successful method development in the facility of a blood stabilizer solution (commercialized by Cytodelics AB), a miniaturized sample preparation (100 μL) for mass cytometry (Olin et al, Cell, 2018), as well as unique data analysis methods; ACCENSE (Shekhar et al, PNAS) and a recent deep-learning cell classifier method (manuscript in prep).

Plans for 2021–2024

New technologies/services planned for:

A broader offering in immunomonitoring will be our preferred focus for the coming years. This is a strong demand from clinical researchers studying cancer, inflammatory and allergic disorders where immunomonitoring today is essential. Many clinical trials involve immune-modulation and monitoring of samples from such trials require advanced immunomonitoring. Researchers are requesting the establishment of a facility to accommodate such needs and provide advanced immunomonitoring with necessary data analysis support. We currently have all necessary equipment and know-how to provide such service in the coming years.

Motivate how the technologies/services provided are nationally unique and internationally competitive:

State of the art immunomonitoring requires a multimodal approach. For example, we will offer TCR/BCR sequencing, both bulk and of single-cells, as well as phenotypic and functional analyses of antigen specific T- and B-cells using Mass cytometry or the recently procured IsoLight (IsoPlexis) instrument. For other projets, we will perform in vitro stimulation experiments and measure functional responses or signalling events using gene expression profiling (NanoString), or by targeting single-cell sequencing (BD Rhapsody) or CyTOF depending on the research question of interest. There are no other facilities offering all these different methods with expertise to choose optimal method and the appropriate bioinformatic pipeline to analyse such data individually, or in combination. The Brodin lab heading the Sthlm node of the current Mass cytometry facility, has all of these methods established. Leading institutions such as Mount Sinai, NY and Stanford University have established advanced immunomonitoring facilities (http://iti.stanford.edu/himc.html), and our proposed facility is competitive with these leading facilities.

Expected user base for 2021–2024 in terms of national spread, number of potential users and sector (academia, health care, industry and other governmental agencies).

We see a growing interest from clinical researchers with unique patient sample collections, but lacking laboratory resources or experimental expertise to choose optimal method, experimental design and perform analyses of the data.

How nation-wide user accessibility is achieved.

A broader national immunomonitoring facility is easier to communicate than the current Mass cytometry facility given that many researchers are unaware of Mass cytometry but understand immunomonitoring as a concept. We see this as a major benefit of the suggested broader offering of a future immunomonitoring facility.

How reproducibility, quality, and appropriate storage of data are ensured.

We will continue working with our existing LIMS and service portal system and extend this for additional data types. All generated data is stored in this database to ensure longterm storage, traceability and backup.

User fee model that will be applied for 2021–2024.

Full cost fee for international academic and all non-academic users. Priority is given to Swedish academic users and their projects will be subsidised as before.

Research environment and associated research groups that are contributing to the development of the facility/ unit.

The Brodin lab in Stockholm is a leading systems immunology lab with expertise in all technologies listed as future facility technologies above. The group is performing technology development of benefit for the entire facility, such as sample collection methods, experimental protocols and computational analyses. The Jönsson lab in Linköping are experts in murine hematopoiesis and brings important expertise in murine experimental methods etc.

Synergies and capability contributions: i) within the platform, ii) with other SciLifeLab platforms and facilities/units.*

With the proposed wider scope of the facility we see growing synergies with especially i) the plasma profiling facility, ii) Mass spectrometry-based facilities, as well as the iii) cell profiling facility and iv) NGI.

Collaborations with healthcare, industry and other national and international external organizations.*

Director Brodin is a paediatrician at the Karolinska University Hospital and his group is establishing diagnostic procedures for patients with inflammatory conditions and immunodeficiencies and these will be offered to all clinicians in Sweden from Q2, 2020.

There are also ongoing research collaborations with a number of pharma and biotech companies and these often involve broad, multimodal immunomonitoring assays.

Which alternative local/ national/ international facilities/ infrastructures and commercial providers are available to users? How is SciLifeLab funding of the facility/unit justified for technologies/services available elsewhere from a Swedish user perspective?

Many of our customers are clinical researchers lacking research labs. The services proposed here for the coming years will enable studies not possible currently, and no alternative facilties or CROs exist that can offer similarly advanced immunomonitoring services.

Budget 2021–2024

-The expanded budget is needed becasue of the broader immunomonitoring service with additional experimentl methods and a growing need for bioinformatic support. All the additional funds would be used to cover additional personell since instrumentation is already available in the facility and associated research labs.

Costs	2020	2021	2022	2023	2024
Personnel (5.5 FTEs)	3 600	4 500	4 500	4 500	4 500
Operations	2 100	2 500	2 500	2 500	2 500
Premises	800	800	800	800	800
Instrument depreciations	1 800	1 800	1 800	1 800	1 800
Other (indirect costs)	1 280	1 600	1 600	1 600	1 600
Sum costs (kSEK):	9 580	11 200	11 200	11 200	11 200

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	6 000	7 000	7 000	7 000	7 000
University funding	800	700	700	700	700
User fees	2 000	2 500	2 800	2 800	2 900
Sum revenues (kSEK):	8 800	10 200	10 500	10 500	10 600

Table 1. Current budget (2020) and suggested budget 2021–2024

Proteogenomics

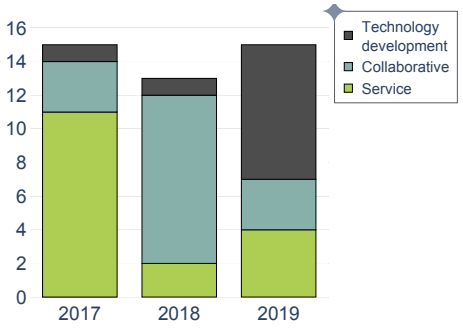
Read more: Web page, Publication Data Base

Basic Information

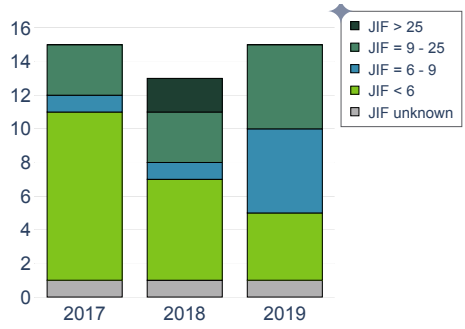
Facility director: Janne Lehtiö
Head of facility: Maria Pernemalm
SciLifeLab facility since: 2017
Host University: KI
FTEs: 8
FTEs financed by SciLifeLab: 1.5

Funding 2020 (in kSEK)

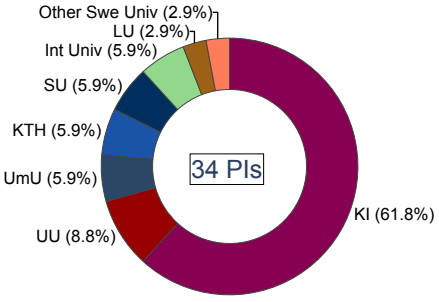
SciLifeLab: 3000
Total: 14025



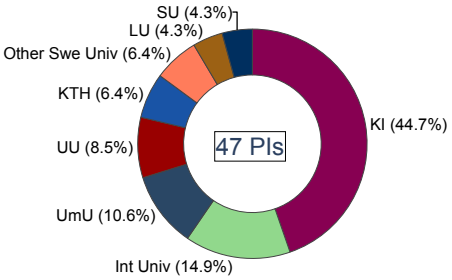
Publications by category



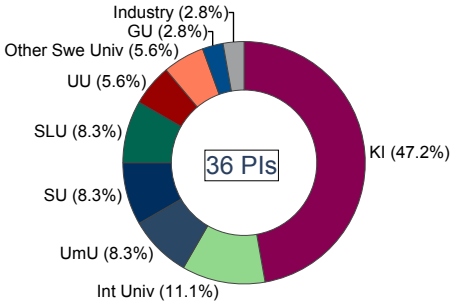
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

The facility offers state of the art mass spectrometry (MS) based proteogenomics analyses. As a core facility service, several of the services are unique in world wide scale.

- *Personalized proteogenomics:* Individual RNA/DNA sequence-based database generation for variant analysis at the protein level coupled with in-depth quantitative proteome analysis.
- *Unbiased proteogenomics:* Six frame translation of whole genome databases for protein coding genome annotation.
- *Disease state/Variant proteomics:* Database supplemented with all known SNPs and disease-causing genetic alterations. (Can be used when sample specific sequence data is not available.)
- *XenoProteomics:* Host-pathogen interaction studies, database construction with combined genomes.
- *Meta proteomics:* Proteogenomics analysis based on metagenomics database generation

New Technologies and Services 2021–2024

The facility vison and new services will be described in more detail below. All services are MS-based.

- Global plasma proteomics and plasma proteogenomics
- Clinical proteomics and proteogenomics analysis of large clinical cohorts
- High throughput proteogenomics validation based on Data Independent Analysis (DIA)
- Bioinformatics support to facility users
- Subcell spatial proteomics and proteogenomics

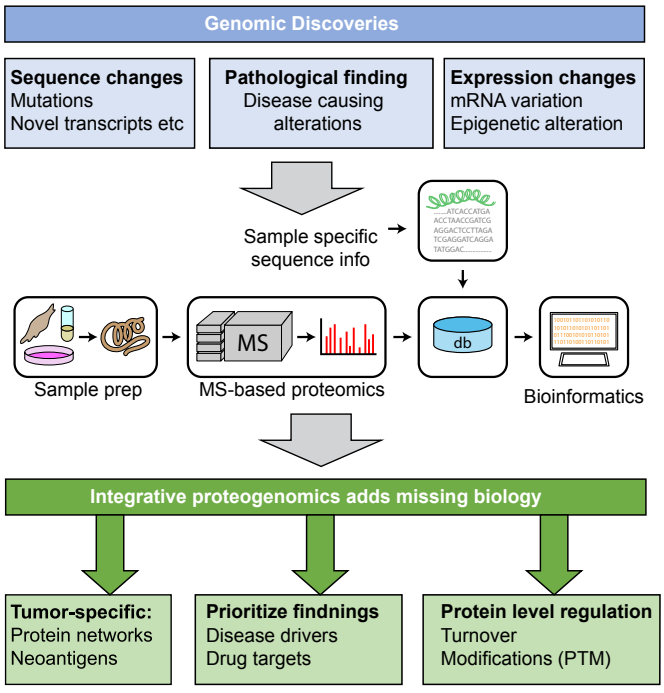


Figure 1. Protegenomics workflow and examples of proteogenomics applications

Background

MS-based proteomics fulfils the hallmarks of a national facility, with costly infrastructure, high demand of expertise and being a vital part of translational omics and systems biology capabilities.

In 2017, the joint Chemical Proteomics and Proteogenomics (CP and PG) facility was formed and entered the SciLifeLab proteomics platform, building on the complementary services from already existing cutting edge core facilities at Karolinska Institutet (CP), Karolinska University Hospital (PG) and the national infrastructure BioMS (www.bioms.se) (CP and PG). BioMS contributes with co-funding by the Swedish research council and the respective host universities. During 2017-2020 the two facilities have further developed their unique capabilities; the proteogenomics facility is closely connected to the proteomics, genomics and bioinformatics platforms at SciLifeLab; and the chemical proteomics facility has developed a close collaboration with the chemical biology and drug development platforms. Since 2019 the two facilities have reported separately to SciLifeLab and are now functioning independently of each other. Hence, the sections below will focus solely on the proteogenomics facility.

The Proteogenomics facility provides high level MS expertise in the area of proteogenomics and related clinical proteomics. Through integration with surrounding research groups and local efforts on genome medicine and precision medicine, clinical trial units, as well as with the regional Clinical Proteomics Facility (headed by Lehtiö, funded by Stockholm County council/Hospital research budget), the Proteogenomics facility has obtained a critical mass of instrumentation and expertise (total 8 PhD FTE; 1.5 FTE funded by SciLifeLab). Key technical developments include proteogenomics methods for plasma proteomics (Pernemalm eLife 2019), cellular localization (Orre LM Mol cell 2019), and a pipeline to generate proteogenomics data and accurate detection of variant peptides (Zhu. Nat comm. 2019). Moreover, we have developed the first integrated genome annotation workflow using peptide level data (Zhu Y Nucleic Acids Res. 2017), as well as novel clinical proteogenomics analysis combining transcriptomics and genomics data (Johansson H., Nature Comm 2019; Yang M. Nature Comm 2019). Several facility user-projects has also reached high impact journals including Wei B Nature Biotech. 2018, Srinivas V Nature 2018, Chan S Nature Microbiol 2017. The facility continuously take part in outreach activities both through SciLifeLab and BioMS and is for example invited to arrange a proteogenomics workshop in connection to the HUPO Annual Congress (HUPO2020).

Plans for 2021–2024

Part from increased biological proteogenomics analyses, clinical proteogenomics is a rapidly developing field taking advantage of the parallel developments in DNA/RNA sequencing, biological MS and bioinformatics. NCI funded a major cancer proteogenomics effort through its Clinical Proteomic Tumour Analysis Consortium (CPTAC) and follow up by International Cancer Proteogenome Consortium (funded by NIH and national initiatives). These large efforts and number of landmark publications has increased visibility of proteogenomics to the general scientific community, and thereby increased the demand for services. In parallel, key opinion leaders have raised the need of implementing proteogenomics as a part of clinical decision making in precision medicine (Zhang, Nat Rev Clin Oncol 2019). Our vision is to bring clinical proteogenomics available to the whole research community and therefore, we will introduce several new clinical MS-based technologies into the facility during next 4 years. Based on this vision the new technologies planned for within the facility are described below.

Global plasma proteomics and plasma proteogenomics

A novel method for global in-depth human plasma proteomics and proteogenomics enabling quantitative analysis of up to 2000 proteins to assist biomarker discovery has been developed in the group (Pernemalm eLife 2019) and is available as a service starting 2020.

Clinical proteogenomics analysis of large clinical cohorts

The purpose of this service is to boost molecular phenotype and biomarker research especially using biobanked material, and to facilitate use of proteogenomics in clinical trials and future routine analysis. This service includes proteogenomics in multilevel omics analysis and large-scale quantitative MS to take advantage of the cutting-edge instrument park and expertise to facilitate profiling projects out of reach for regional facilities.

High throughput proteogenomics validation based on Data Independent Analysis (DIA)

In contrast to global discovery proteogenomics Data Independent Analysis (DIA) rely on the targeted analysis of a specific set of proteins using MS spectral libraries. The method is highly suitable to define the molecular phenotype in clinical studies. The turnaround time for DIA project is substantially lower than traditional global in-depth proteogenomics, hence a key feature to transition to the clinical setting and for large validation studies. Will be piloted in the facility during 2022.

Bioinformatics service for facility users

Bioinformatics development is a crucial part of proteogenomics. In the proteomics and metabolomics platform, proteogenomics facility will pilot a new knowledge-transfer model with NBIS. A dedicated person from NBIS will be assigned to the facility to learn technology specific bioinformatics needed to assist in proteogenomics projects.

The proteogenomics facility has dedicated one internal bioinformatician to support the knowledge transfer and the facility will also offer bioinformatics support jointly with NBIS to users piloting in 2020 and starting in full scale in 2021.

Subcellular spatial proteomics and proteogenomics

The Subcell spatial MS-based proteomics workflow (www.subcellbarcode.org) allowing for accurate protein assignment to subcellular compartment (down to protein variant level) was published in 2019 (LM Orre, Mol Cell. 2019) and is requested frequently from users, thus will be incorporated as a service during 2020-21. This capability also strengthens the already existing synergy with the current Genomics platform and the spatial single cell analysis offered by Cell Profiling facility (Joshi RN Front Immunol 2019).

Clinical proteogenomics implementation

The Proteogenomics facility at SciLifeLab is in a unique position worldwide to develop high throughput MS based proteomics and proteogenomics towards clinical setting. Both the SciLifeLab's platform structure and surrounding strong research groups enable rapid development of clinical proteogenomics. As data implementation tool to guide clinical decision, the web based Molecular Tumor Board Portal (http://www.mtbp.org/) developed in the Lehtiö research group, is already in use for a large European genomics trial and can serve as pilot platform for implementation. To enable proteogenomics service development, the following *key steps are needed for implementation* of a clinical proteogenomics facility: *High capacity redundant instrument and data systems* for robust operation maintenance, *accreditation and dedicated personnel for sample preparation*, and *development of data handling pipeline of sensitive data.* Currently collaborations with NBIS and Research Institutes of Sweden (RISE) are ongoing for handling of data and development of AI algorithms for proteogenomics data-analysis. In parallel with the SciLifeLab embryo for clinical proteogenomics, there is a national development plan including the BioMS nodes in Lund and Gothenburg.

Budget 2021–2024

The increase of the technology portfolio of the facility during coming years demands more personnel, instrument investments as well more running costs. During our current budget (2020) we have 8 FTE and expect it to increase to about 12 FTE by 2024. We also expect to add 2-4 MS-instruments to our instrument park. This will need some increase in premises as well. We will continue to use our current user fee model for 2020–2024. The model is based on direct personnel time used for each experiment, costs of reagents and chemicals used in each experiment, cost for MS-time (based on depreciation cost). No other time, overhead time, INDI, or other costs are included in the price model.

Costs	2020	2021	2022	2023	2024
Personnel (8-12 FTEs)	7 181	7 900	8 800	9 600	10 000
Operations	3 927	4 400	4 800	5 300	5 700
Premises	1 006	1 040	1 100	1 400	1 400
Instrument depreciations	4 509	5 100	5 100	5 600	5 500
Other	600	600	650	700	750
Sum costs (kSEK):	17 223	19 040	20 450	22 600	23 350

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	3 000	4 500	5 500	6 000	6 000
Karolinska Institutet (BioMS co-financing)	1 950	1 950	1 950	1 950	1 950
Vetenskapsrådet (BioMS) through LU	3 800	3 800	3 800	3 800	3 800
KI/SciLIfeLab (Dyr utrustning)	900	900	900	900	
Karolinska University Hostpital (Clinical protomics)	3 175	3 200	3 200	3 300	3 500
KI/FoU (Dyr Utrustning)	1 200	1 200	1 200	1 200	1 100
Funding agency E					
User fees	3 200	3 500	3 900	5 500	7 000
Sum revenues (kSEK):	17 225	19 050	20 450	22 650	23 350

Table 1. Current budget (2020) and suggested budget 2021–2024

Glycoproteomics (candidate)

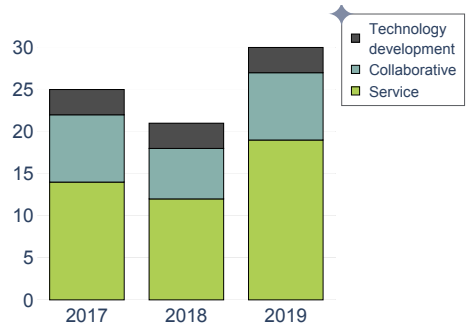
Basic Information

Facility director: Elisabet Carlsohn
Head of facility: Carina Sihlbom
SciLifeLab facility since: N/A
Host University: GU
FTEs: 2.5
FTEs financed by SciLifeLab: 0

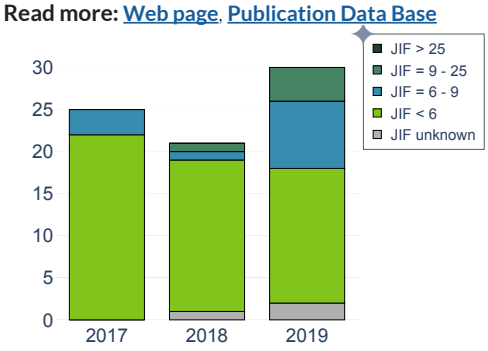
Funding 2020 (in kSEK)

SciLifeLab: 0
Total: 3500

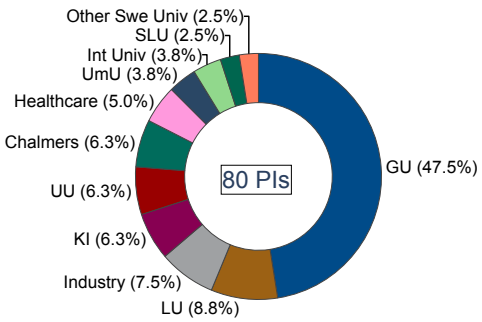
Read more: Web page, Publication Data Base



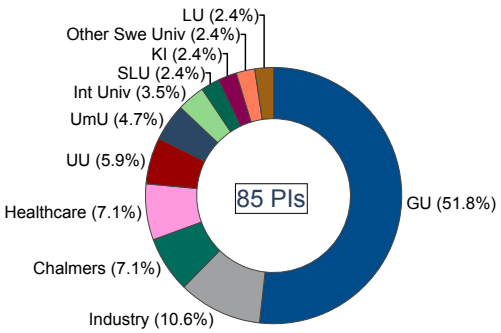
Publications by category



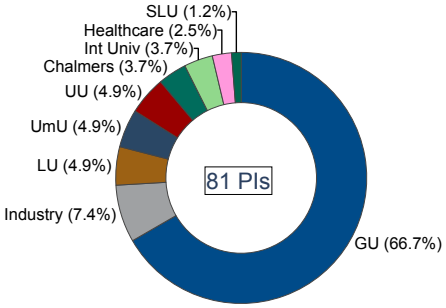
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

As part of the National Infrastructure (BioMS), CGG provides advanced analytical support for academic and industrial research in glycobiology and glycotechnology.

- LC-MS methods for analysis of glycopeptides in complex samples
- Analytical platforms for medium to large scale glycomics and glycoproteomic studies
- MS-based analytical platforms for glycans and glycolipid analysis
- Functional MS-assays to support studies of microbiota glycan degradation

New Technologies and Services 2021–2024

- Adopt analytical platforms to facilitate large scale glycomic and glycoproteomic studies
- Expand and further develop quantitative glyco-conjugate analysis
- Establish and provide glycoanalytical workflows for samples stored in biobanks
- Analysis of large glycans, with focus on glycos-aminoglycans and polylactosamine
- Analytical platforms for multiple PTM analysis to facilitate PTM cross-talk studies
- Support for biotechnological studies of specificity for glycobiosynthetic and biodegrading enzymes enabling functional assays of disease releated microbiome
- Validate and adopt new software tools for identifying and assigning glycoconjugates, statistical packages for quantitative glycomics and glycoproteomics.

Background

Carbohydrates are essential in all major biotechnological applications, i.e., development of renewable biomaterials, food, healthcare and personalized medicine. In spite of the large interest in glycosylation and growing awareness of its effect on protein function in health and diseases, glycoproteome remains severely understudied due to the demand for advanced and expensive analytical instrumentation and specially trained personnel. CGG is founded on the internationally recognized glycoanalytical research carried out at the University of Gothenburg since early 80's. The collected expertise in glycomic and proteomic fields, together with increased interest in the glycoscience, resulted in a facility providing advanced support for glycobiology and glycotechnology studies. The CGG became operational as part of the National Infrastructure BioMS in 2016 and has since then provided support to both national and international academic groups and to industrial partners.

The CGG is organized within the Proteomics Core Facility, a unit at the research infrastructure organisation, Core Facilities (CF) at University of Gothenburg. CF has its own dedicated budget and organisation and reports to the Academy board at the Sahlgrenska academy. The facility has 15 years of experience in developing MS-based proteomics

infrastructure and employs highly qualified and trained personnel. The majority of CGG employees have PhD degrees and many years of experience in MS-based method development, design and conclusion of research projects, as well as the knowledge within the glycobiology area. As a result, CGG is capable to offer research support at all levels: study design, sample preparation and analysis as well as data analysis and interpretation. Since the foundation in 2016, CGG established and provides methods for nanoLC-MS/MS detection and characterization of glycopeptides in complex samples using Q-Exactive HF and Orbitrap Fusion Tribrid MS. To facilitate structural analysis of glycoconjugates, CGG provides LC-MS methods for glycan and glycolipid analysis, including establishment of glyco-fragmentation libraries to facilitate data interpretation. As part of biotechnological support, functional MS-assays was developed to facilitate studies of microbiota glycan degradation.

Plans for 2021–2024

To address the needs of the glycoscience research community we aim to keep offering state of the art technical platforms for both *glycoproteomics* and *glycomics*. To facilitate the use of sample collections, we aim to work with Biobank Sweden (BIS) to establish various tissues and biological fluids compatible protocols. The established protocols will cover all structural aspects of protein glycosylation providing customer-fitted workflows capable to address the glycoproteome at different structural levels. We will adopt novel methodologies such as ion mobility for large scale glycoproteomic studies and middle-down proteomics for glycoproteoform profiling. We aim to expand and further develop our current analytical platforms to facilitate the analysis of large polymeric glycans, with focus on glucosaminoglycans and polylactosamines. Due to the frequent user-requests we will look into analytical platforms enabling multiple PTMs analysis, aiming to expand beyond established individual platforms to facilitate PTM cross-talk studies, especially those targeting glycosylation-phosphorylation cross-talks.

Our current data processing workflow for N- and O-linked protein glycosylation is based on widely used tools in LC-MS data, however, development of complimentary software tools for data validation was judged necessary and is initiated. CGG aims to adopt new software tools for assigning glycoconjugates and statistical packages for quantitation. CGG will continue to develop and sustain the internationally renowned UniCarb-DB, embedded in the infrastructure ELIXIR with developmental support from the Swiss Institute for Bioinformatics.

The complexity of glycobiosynthesis, a non-template driven process, presents a significant analytical challenge. Due to requirements for both advanced instrumentation and experienced researchers with know-how in glycoanalysis and data interpretation, there are only few dedicated facilities supporting glycoproteomic and glycomic studies worldwide. CGG is the only facility in Sweden offering broad and comprehensive glycoconjugate analysis to both academic and industrial research groups. University of Gothenburg has a strong tradition in glycoanalytics, represented by several prominent research groups that CGG works in close collaboration with to ensure the knowledge and technological transfer. To maintain and offer international competitiveness, CGG has continuous knowledge and technology exchange with leading international glycoscience centers: CBMS at Boston University, CCG at the University of Copenhagen and NRBT GlycoScience Group.

The user base for 2021-2024 is expected to grow with research groups from the six major cities in Sweden, Lund, Gothenburg, Örebro, Uppsala, Stockholm and Umeå that already use the infrastructure. CGG also expects to see an increased number of users due to the expansion of the support portfolio. The majority of the users are from life science sector including biological sciences, biomedical research, but other areas such as industrial biotechnology, chemical sciences, environmental sciences and agricultural sciences are also represented. The facility is reaching out to users through the web-site, the BioMS infrastructure and visibility at conferences and workshops. The user fee model will continue to be based on the costs for instruments service contracts, maintenance, consumables, investments for improvement and staff time. The user fees are subsidized for academic users while industry will be invoiced the full cost including depreciation, overheads, administration and VAT.

Synergies and capability contributions: Expanding the proteomic and metabolomic platforms with glycoproteomics and glycomics allows for incorporation of the main post-translational modification into the SciLifeLab portfolio. Altered glycosylation is a hallmark for many diseases such as cancer, autoimmune and age-related disease, with many disease biomarkers being glycoproteins. Using the glycosylation as a handle for PLA probes would allow for glycovariants of proteins to be measured. Accurate determination of glycosites and glycan structures will expand the capability of the PLA and biomarker proteomics platforms. For the protein expression and characterization facility, glycoproteomics would provide a new dimension by offering characterization of glycosylation generated in different expression system and facilitate glycoprotein production. The glycoanalytical data from cell lines provided by the cell profiling facility, including cell lines subjected to treatments affecting the glycosylation, would allow our users to go from glycobased discovery into cellular regulation enabling understanding of mechanism of pathological glycosylation alterations.

Glycoanalytics data includes site occupancy, type of glycosylation and microheterogeneity. To accommodate these data and to facilitate data translation into biological knowledge, a dedicated bioinformatic portal could be developed in collaboration with NBIS.

CGG is a unique facility providing state of the art glycoproteomic research as part of the Swedish BioMS infrastructure. Integration of glycoproteomics with existing SciLifeLab facilities would provide the means for funnelling glycobiological question in medicine and biology into systems glycobiology including genomics, transcriptomics, metabolomics and interactomics. With glycosylation being one of the main PTMs, adopting available SciLifeLab technologies for glycoapplications will enable Swedish researchers to access unique collection of tools to address glycobiology questions in health and disease. Compared to other world leading centers, providing open access glycoanalytics support for both industry and academia, CGG will have access to unique resources such as PLA techniques, antibody libraries, bioinformatics and mammalian cell production, all part of the same organisation within SciLifeLab, creating an edge for Swedish researchers to pursue global glycobiology reasearch. The inclusion of CGG in SciLifeLab will provide a flexible and affordable platform supporting early phase translational research and glycodiscovery.

Budget 2021–2024

Financial support from SciLifeLab will enable an expansion of CGG by increased personnel, in terms of technical experts with 1,5 FTE and analytical capacity by 1 high-end masspectrometry instrument.

Costs	2020	2021	2022	2023	2024
Personnel (2,5 FTEs 2020, 4,0 FTEs 2021-2024)	1 900	3 160	3 200	3 260	3 315
Operations	400	525	615	645	700
Premises	150	225	225	225	225
Instrument depreciations 1 new instrument from2020 + 1 from 2021	1 100	2 250	2 250	2 250	2 250
Indirect cost (OH)	600	975	1 010	1 025	1 050
Sum costs (kSEK):	4 150	7 135	7 300	7 405	7 540

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	-	2 000	2 000	2 000	2 000
University funding	1 100	1 900	1 900	1 900	1 900
Funding agency A (Research Council VR)	2 400	2 400	2 400	2 400	2 400
User fees	650	850	1 000	1 100	1 250
Sum revenues (kSEK):	4 150	7 150	7 300	7 400	7 550

Table 1. Current budget (2020) and suggested budget 2021–2024

Targeted and Structural Proteomics (candidate)

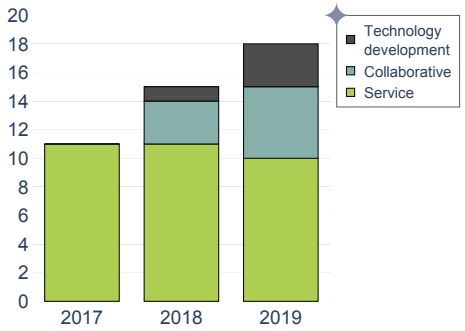
Read more: Web page, Publication Data Base

Basic Information

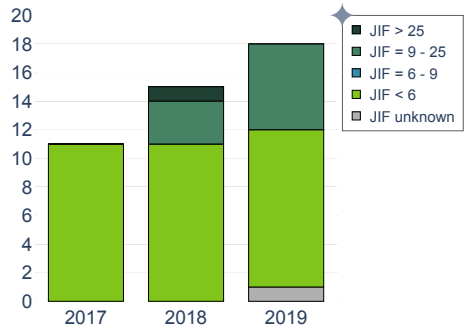
Facility director: Johan Malmström
Head of facility: Sven Kjellström
SciLifeLab facility since: N/A
Host University: LU
FTEs: 3.7
FTEs financed by SciLifeLab: 0

Funding 2020 (in kSEK)

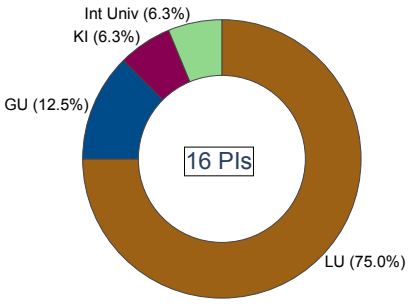
SciLifeLab: 0
Total: 11200



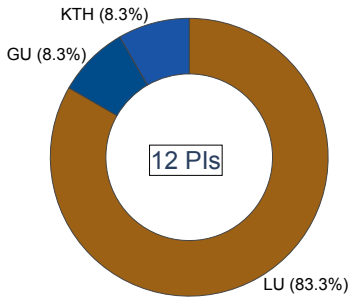
Publications by category



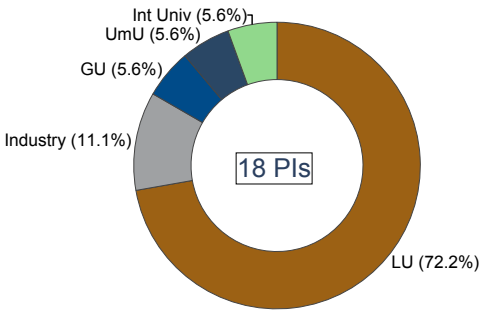
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

List of operational key technologies/services:

- Measure protein/ligand and protein/protein binding interfaces by hydrogen-deuterium exchange mass spectrometry (HDX-MS).
- Large- and small-scale mapping of protein-protein interactions in complex biological samples using affinity-purification mass spectrometry (AP-MS).
- Determine protein binding interfaces as well as the structure and composition of protein complexes using cross-linking mass spectrometry (XL-MS).
- Determine proteoform composition of endogenous proteins using intact weight mass spectrometry measurements.
- All service includes support for sample preparation, data acquisition and commercial and in-house solutions for data analysis support.

New Technologies and Services 2021–2024

List of planned technologies/services:

- Determine dynamics of protein interactions and protein interaction-networks by quantitative affinity-purification mass spectrometry (qAP-MS) as shown in recently published work.
- Determine quaternary protein structures in directly in bacteria, cells and tissues by targeted cross-linking mass spectrometry (TX-MS) as shown in recently published work.
- Strive towards integrative structural biological approaches by improved bioinformatics support in structural integration of mass spectrometry data with results from other structural biology techniques.
- Determine composition of sequence and post-translational modification status of proteins by top-down mass spectrometry

Background

The predominant goals of the Targeted and Structural proteomics facility is to i) support users to obtain information of protein-protein interactions, determine protein binding interfaces and to model protein structures of protein complexes ii) promote cross-facility support for integrative structural approaches and iii) strengthening the outcome of other national infrastructures in structural biology such as MAXIV, future ESS, the cryo-EM facility at ScilifeLabs and the NMR center at the University of Gothenburg. The facility is located at Lund University and was founded on the experience and research in mass-spectrometry based proteomics at Lund University. Currently, the facility is part of BioMS and aspires to become a SciLifeLab facility with a strong focus on developing our portfolio of offerings in structural mass spectrometry. BioMS is a nationally distributed scientific research

council (VR) financed infrastructure for biological mass spectrometry and proteomics with extensive experience in providing support at a national level. BioMS is hosted by Lund University with nodes at Lund University, University of Gothenburg, Chalmers University of Technology and Karolinska Institutet (for more information see https://bioms.se/about-bioms/).

The facility was established in 2016 and have since start provided support in structural proteomics. The main current operational technologies/services are listed in the section above, which have generated results for several publications (for examples see Puthia M et al Science translational 2020, Möller M et al Blood 2018 and Awad W et al Structure 2019). The facility is strategically located within a walking distance to MAXIV (https://www.maxiv.lu.se/) a Swedish national laboratory providing scientists with the most brilliant X-rays for research and ESS (https://europeanspallationsource.se/) which will upon the planned inauguration in 2023 greatly exceed and complement current leading neutron sources, enabling new opportunities for structural biology. The facility team includes director, head, four senior research scientists with more than 15 years experience each in proteomics and structural mass spectrometry, and one dedicated bioinformatician that will start spring 2020. In addition, the facility harbors four state-of-the art orbitraps, a robot for HDX analysis and several commercial and in-house developed software solutions. Over the next coming five years, the facility will double in size including both personnel and instrumentation. The facility is as mentioned part of BioMS that provides a portal for project requests at the national level and have the past years served many users resulting in several publications. Every project is evaluated and prioritized by the nodes according to the following preset criteria: feasibility, relevant research plan, national importance and synergies with other infrastructures or partners. BioMS is governed by a steering committee, a scientific director and the facility mangers found at https://bioms.se/about-bioms/.

A highlight the past years include several significant publications derived from the facility support. Importantly, the facility is embedded in an active research environment, which ensures technical developments as elaborated below. Another significant development is that many users aim at combining several structural mass spectrometry methods with other structural biology techniques such as x-ray crystallography, nuclear magnetic resonance spectrometry (NMR), single-particle electron cryo-microscopy (cryoEM) and small-angle X-ray scattering. These efforts clearly indicates that the field is moving towards more integrative structural biology approaches as previously proposed by Ward et al (10.1126/science.1228565). We believe that this is an increasing trend and that structural mass spectrometry will play an increasingly important role in strengthening the outcome of other national infrastructures.

Plans for 2021–2024

Our goal for the coming period is to further promote integrative structural biology projects. This will encompass establishing new technical developments, acquisition of new instrument types and to double the work-force. We plan to accomplish this goal by three predominant aims.

Firstly, we intend to transfer technical developments performed by affiliated research groups at Lund University to the facility by implementing targeted cross-linking mass spectrometry (TX-MS) recently published by Hauri et al 2019 (10.1038/s41467-018-07986-1) and quantitative affinity purification mass spectrometry (qAP-MS) using SWATH-MS published by Happonen et al 2019 (10.1038/s41467-019-10583-5). In TX-MS quaternary structure determination can be accomplished in biological samples using a combination of chemical cross-linking, high-resolution mass spectrometry and high-accuracy protein structure modeling. The approach relieves two predominant bottle necks in traditional cross-linking MS and enables modelling of large protein complex (>1MDa) directly in lysates of bacteria, cells and tissues. In qAP-MS, quantitative proteomics is used to determine dynamic protein interactions in biological samples. By qAP-MS it becomes possible to extend beyond static views of protein interaction networks to rather monitor the how different biological states alters the composition and connectivity of interaction networks. These two techniques will provide the users with new possibilities to more accurately determine the composition and binding interfaces of protein complexes.

Secondly, we aim to enhance our bioinformatics support and pipeline for integrative structural modelling techniques. We aim to in particular enhance our support in translating the MS-derived structural constraints from XL-MS and HDX to structural models of proteins. For this purpose, we use resources provided by SNIC and intend to form an active collaboration with the National Bioinformatics Infrastructure Sweden (NBIS). This will play an important role in further supporting user's ability to perform studies where data has been obtained from several structural biology techniques.

Lastly, we aim to strengthen the cross-facility support together with other large national infrastructures in structural biology. If our facility becomes an official ScilifeLabs facility we will explore the option of placing the facility at the Science Village Scandinavia strategically located between MAXIV and ESS to further promote users to adopt several structural biology techniques for their projects. The technical and bioinformatics developments are supported by neighboring academic research groups that have a particular focus on developing and applying structural mass spectrometry. Furthermore, the facility is discussing with LINXS to further promote an active participation from

the Lund Institute for neutron and x-ray science to support LINXS in their integrative structural biology efforts. We anticipate that the adoption of the planned new capabilities will be of increasing interest for the structural biology community which is widely spread across Sweden and of relevance for many research disciplines in life sciences. As the facility is associated with BioMS, the facility is already committed to serve users at a national level. The established project portal within BioMS ensures fair prioritization of user applications and there are established price models and data reporting strategies for the provided services.

We argue that establishing the facility in structural mass spectrometry as an official SciLifeLab facility will be of strategic importance. First, an official SciLifeLab facility will further complement the existing expertise and strengthen the efforts in connecting with other national infrastructures such as the cryo-EM facility at SciLifeLab and thereby provide a natural link between ScilifeLabs and MAXIV and in the future ESS both located in Lund. Second, the increased funding will promote the planned extension of our services and also support a potential move to the Science Village Scandinavia as mentioned above. Lastly, we think that the affiliation to SciLifeLabs will facilitate a stronger connection to scientists at a national level and to Swedish industry. The latter is of particular importance as there are few labs in Sweden that focus on structural mass spectrometry and we have noted that industrial partners are searching for such capabilities.

Budget 2021–2024

As shown in the budget table, the Targeted and Structural Proteomics facility receives funding from VR, Lund University and Region Skåne. The planned extra funding from SciLifeLab will be used to increase instrument capacity dedicated for structural biology related research projects. In addition, we plan to split the personnel cost between a one part time bioinformatics and a part time wet lab scientist that will predominately focus on the new technologies that we intend to adopt during 2021-2024. In addition, we will reserve part of the funding for relocating the platform to Science Village Scandinavia.

Costs	2020	2021	2022	2023	2024
Personnel (9 FTEs)	6 082	6 173	6 296	6 423	6 551
Operations, including material and services	1 500	1 600	1 700	1 800	1 900
Premises	205	210	215	220	225
Instrument depreciations	5 200	6 700	6 700	6 700	6 100
Other					
Sum costs (kSEK):	12 987	14 683	14 911	15 143	14 776

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	-	2 000	2 000	2 000	2 000
University funding	3 500	3 500	3 500	3 500	3 500
Region Skåne	500	500	500	500	500
VR	7 200	7 200	7 200	7 200	7 200
User fees	1 500	1 600	1 700	1 800	1 900
Sum revenues (kSEK):	12 700	14 800	14 900	15 000	15 100

Table 1. Current budget (2020) and suggested budget 2021–2024

Swedish Metabolomics Centre

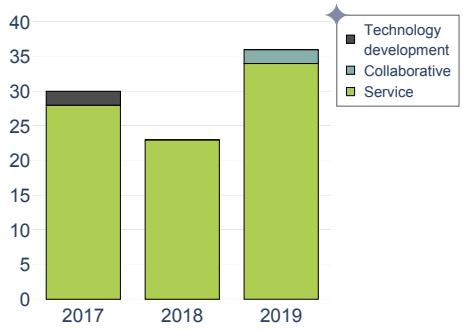
Read more: Web page, Publication Data Base

Basic Information

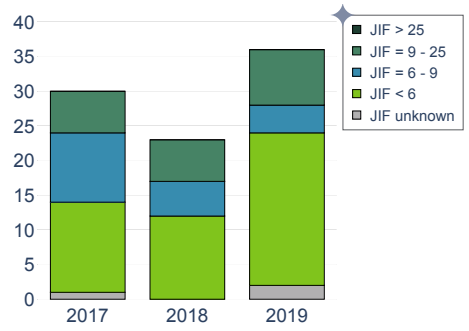
Facility director: Thomas Moritz, Anders Nordström
Head of facility: Annika Johansson
SciLifeLab facility since: 2017
Host University: SLU, UmU, Chalmers
FTEs: 6.5
FTEs financed by SciLifeLab: 1.2

Funding 2020 (in kSEK)

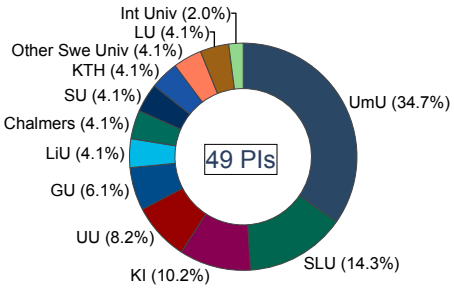
SciLifeLab: 3600
Total: 15660



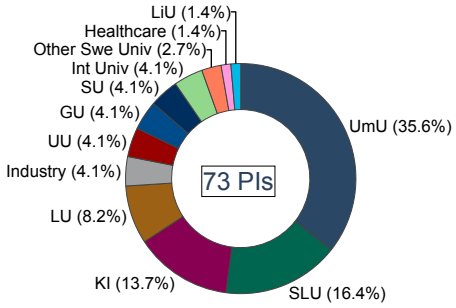
Publications by category



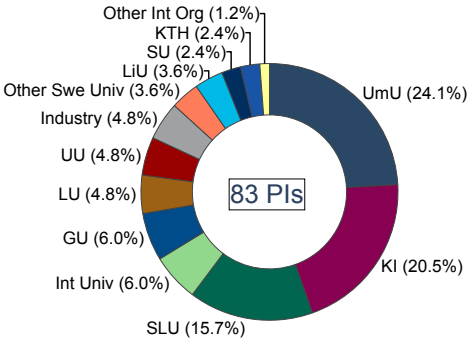
Publications by JIF



Users 2017



Users 2018



Users 2019

Current Technologies and Services

- Untarget metabolomics screening of plasma, cells or tissues
- Targeted analysis of specific metabolites/metabolite groups in biological matrixes
- Targeted lipid profiling and lipidomics
- Method development for metabolites/matrices of interest
- Study design support
- Open Access Lab (mass spectrometry instrumental rental per day for own applications)

New Technologies and Services 2021–2024

- Agilent Rapidfire system for library screening and large cohort metabolomics
- Fluxomics / Stable istope measurement of biochemical activity
- Large cohorts metabolomics
- Improved and increased target metabolite analysis portfolio
- Tools for connecting metabolite data to databases

Background

The Swedish Metabolomics Centre has, during 2017, 2018 and 2019, supported Swedish research groups through service, collaboration or open acess lab activities and enabled >80 peer reviewed publications. In total we are seven (7) full time staff associated with the facility. Day-to-day operations including client contact and support, run planning and instrument and staff coordination is lead by Head of Facility, Dr. Annika Johansson. Further, four PhD level staff, one MSc mass specialist and a lab technician constitute the core service organization. During this period Professor Thomas Moritz and Dr. Anders Nordstrom, representing SLU and UmU, respectively, have been director/co-director. All staff working at the centre have a PhD relating to metabolomics or multiple years of technical and conceptual experience covering technical, analytical or bioinformatics aspects of metabolomics and small molecule analysis using mass spectrometry. During this period a steady 60-80 projects per year have been processed as fee for service, with ~60% of these projects originating from Universities outside Umeå. The Swedish Metabolomics Centre's main achievement during this period is the broad user base and the large contribution in supporting Swedish researchers to publish their work. The publications supported in the period 2017-2019 include 5 x PNAS, 2 x Nat Comm, 1 x Nat Chem Biol, 1 x PLOS Genet, 1 x Cell Metab, 1 x Angew Chem. In 2019 a large collaborative project was also signed with a major biopharmaceutical company who intend to run samples in 2020.

Plans for 2021–2024

Technology

The metabolomoics landscape is changing rapidly. Commercial companies that are providing metabolomics service have entered the academic market during the period 2017-2019. The competitive edge provided by the Swedish Metabolomics Centre is our ability to adapt our methods to smaller projects concerned with special matricess. Nevertheless, for larger projects we can also provide services at a significantly lower cost which is beneficial to smaller research groups, and also in cases where the metabolomics not is the 'main street' of the specific project, but rather a 'higher risk avenue'. Furthermore, we provide a broader range of services than commercial metabolomics companies in the sense that we have a wide array of target metabolites (quantitiative) that we can measure in various sample matrixes. In addition we can measure untargeted (screening) analysis on the same sample. In general our edge is that we can rapidly adapt to the customer's need.

The main advantage, however, is our continuous exposure to different research questions and challenges. This ensures a continuous development in collaboration with clients and partners of the Centre, driven by actual needs of the community. Below are two examples of service we will initiate from 2021 that have no national or commercial availability as of today.

- We will introduce a RapidFire service for drug library activity screening using the Agilent RapidFire technology acquired with support from SciLifeLab. This technology enabales screening of 10.000-100.000 compounds in activity assays using mass spectrometry as read out. We are also developing this platform for screening of very large biological cohorts. Including but not limted to plant phenotyping and biobanked human samples.
- To enhance value of data for clients as collaborators, we will be rolling-out fluxomics as a service, both as stand-alone and in comjunction with standard quantitative metabolomics experiments; primarily in cell based studies, but also for animal studies using mice. Fluxomics, using stable isotope tracers, can aid in deciphering metabolic routes or relative kinetics of particular biochemical reactions.

Users

Since initiation of the Centre in 2013, the user base has been very stable with 60-80 projects completed per year. We do not expect a decrease in this, rather an increase. A majority of clients today are academic, and the proportion of industry partners is expected to increase. A major international biopharmaceutical firm has signed a large contract to run samples with the Centre in 2020. We will continue with a user-fee model rendering approx. 30% of full cost to be covered by users and 70% covered by grants from the universities and by the KAW foundation. For industrial partners we continue to use full-cost user fees model. The national coverage is wide with >60% of projects coming from outside Umeå.

Collaborations

We foresee that more projects will be carried out as collaborations, rather than as classical fee for service, over the next 4 years. This is in part driven by an observed need of us spending more time in the projects. Both for more challenging types of analysis such as fluxomics, but also for more time spent in dialogue back and forth with clients relating to interpretation and and implications of the data, including design of follow up experiments. It is very difficult to develop a "fee-model" for this kind of work, and the reward will rather have to be in the form of co-authorship.

There is today a growing number of collaborations with incoming projects. But also an established set of collaborations with Professor Thomas Moritz's old group at SLU, and new group at Novo Nordisk Center for Metabolic Disease in Copenhagen, as well as with Dr. Anders Nordstroms research group at Umeå University. Several collaborations are ongoing also with scientist at Umeå Plant Science Centre.

Budget 2021–2024

The base funding for the Swedish Metsaboolomics Centre is secured over the next 5 year period (2021–2025) through a KAW grant paired with support from the two host Universities, SLU and UmU. A portion of Scilifelab funding for the metabolomics centre (350 kSek) has been channeled to Chalmers. We are proposing to maintain the current ScilLifeLab funding level to Swedish Metabolomics Centre. The budget we are proposing here is based on a lower funding level which would mean 2650 kSek to Swedish metbaolomics Centre in Umeå and continue with 350kSek to Chalmers to maintain the collaboration. The funding going to Umeå will be marked for research and development using the SciLifeLab funded RafidFire instrumentation for 1.75-2 FTE postdoc or staff scientist. The somewhat reduced user fees are estimates based on more collaborative projects and fewer classical service projects. Operational costs are in addition to consumable costs (e.g. N2 gas dominating) and include service agreement contracts for 6 mass spectrometers at about 1500 kSek/year. Kempe funding is for a new mass spectrometer currently being acquired. Personel might vary a bit during the time period, with number of postdocs depending on collaborative projects. We believe that 1-2 postdocs will be funded through collaboration towards the end of the period.

Costs	2020	2021	2022	2023	2024
Personnel might vary, depending on # postdocs in collaborative projects	10 800	7 200	7 200	7 200	7 200
Operations	4 200	3 500	3 500	3 500	3 500
Premises	1 100	1 100	1 100	1 100	1 100
Instrument depreciations	3 330	3 600	3 300	3 100	3 100
Other					
Sum costs (kSEK):	19 430	15 400	15 100	14 900	14 900

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	3 600	3 000	3 000	3 000	3 000
University funding	4 000	4 000	4 000	4 000	4 000
KAW (approved extension 2021-2025)	7 000	5 000	5 000	5 000	5 000
SciLifeLab infrastructure 2018	500	500	500	500	
KEMPE	560	560	560	560	560
User fees	4 200	2 300	2 300	2 300	2 300
Sum revenues (kSEK):	19 860	15 360	15 360	15 360	14 860

Table 1. Current budget (2020) and suggested budget 2021–2024

Exposomics (candidate)

Basic Information

Facility director: Jonathan Martin
Head of facility: N/A
SciLifeLab facility since: N/A
Host University: SU
FTEs: 0
FTEs financed by SciLifeLab: 0

Funding 2020 (in kSEK)

SciLifeLab: 0
Total: 0

Read more: Publication Data Base

Current Technologies and Services

Services are not yet offered, this is a candidate facility seeking approval and support for 2021-2024.

New Technologies and Services 2021–2024

- High-Resolution Exposomics by HPLC-Mass Spectrometry with DDA/DIA workflow
- Training in exposomic data analysis workflows using commercial or open-source software
- High-Resolution Exposomics by GC-Mass Spectrometry

Background

The *exposome* is broadly defined as our lifetime exposure to all environmental factors, and today it is well recognized that health and disease are determined by the interaction between exposome and genome. Characterization of the chemical component of the exposome is termed exposomics, and this relies on exquisitely sensitive high-resolution mass spectrometers. The candidate facility in *Exposomics* will be globally unique and is leveraged by recent recruitment and ongoing investment in this field at Stockholm University, Department of Environmental Sciences (2018-2022, SEK 25M).

Professor Jonathan W Martin (Professor, SciLifeLab Faculty, and proposed Exposomics Facility Director) leads a research program in human and environmental exposomics, and research laboratories have already been developed at SciLifeLab to support this. Critical infrastructure already in place includes HPLC- and GC-Orbitrap mass spectrometers, and a positive pressure clean laboratory for processing of human biofluids or environmental samples. Current in-house technology that is ready for national application is the analysis of liquid samples (e.g. human biofluids, water) by HPLC with ultrahigh resolution mass spectrometry detection (Q Exactive HFX Orbitrap, Thermo Scientific) running parallel full-scan and MS/MS acquisitions in data dependent analysis (DDA) and data-independent analysis (DIA). This is a nontarget and semi-quantitative analytical method capable of unbiased chemical detection, but can also be adopted for quantitative targeted analysis in the same injection, depending on user needs. Various software (commercial and open-source) and computational power are available for analysis of the data.

New investment by SciLifeLab to form this National Facility (initially SEK 2M in 2021) will be used to hire a full-time staff (1 FTE) to be Head of Facility and to interact with clients (researchers, health professionals, government, and industry) to offer a tailored exposomics analysis. In addition to investment in full-time staff, the facility will invest in its mass spectrometry infrastructure, as well as in associated equipment to enable high throughput sample preparation and throughput, such as liquid handling robotics and centrifuges for sample preparation in 96-well format. The proposed Facility is nationally unique, in fact we are not aware that similar exposomics methods are offered for service anywhere in the world at this time.

The proposed National Facility in exposomics will grow to offer new services in 2022-2024 through local technology development. This will be enabled in part by internal technology development proposals, but also through general synergy with Dr Martin's basic research program in exposomics method development. The future vision includes integration of exposomics data into questions of systems biology by combining with local datasets in genomics, proteomics, and metabolomics with assistance of local bioinformatics expertise.

Plans for 2021–2024

As recently highlighted in *Science* (PMID: 31974245) the exposome paradigm has only recently come into scientific focus, and the chemical component of the exposome is increasingly accessible to scientists through mass spectrometry-based *exposomics*. These methods are highly specialized and currently only available in select research labs around the world. Highly sensitive ultrahigh resolution mass spectrometers are required, making the cost prohibitive to most laboratories. Moreover, careful sample preparation in a specialized clean-laboratory with positive pressure filtered air is recommended for quality control. Specialized workflows for data analysis which make use of databases and spectral libraries devoted to

environmental chemicals and chemicals in commerce are required. The methods are conceptually comparable to mass-spectrometry based metabolomics already offered by our Platform, but there are critical differences with respect to sample preparation, instruments, sensitivity and data processing which require a distinct National Facility in Exposomics.

Current research in exposomic methods is underway by GC-MS using a GC-Q-Exactive (Thermo Scientific). This development is necessary to expand small molecule coverage from ionic and polar analytes (HPLC-MS) to include non-polar analytes such as polycyclic aromatic compounds, brominated flame retardants, legacy organochlorine pesticides, polychlorinated dioxins, furans and polychlorinated biphenyls. We anticipate offering this method as a national service by 2023. This will be complimentary to the HPLC-MS methods, and some users will request both analyses. Other technology development will include transdisciplinary applications of exposomics and proteomics (serum profiling technology) which seek to understand the toxicological effects of the exposome in human blood.

We anticipate a wide user-base for 2021-2024 composed primarily of researchers at Swedish Universities and from Swedish research institutes where there are existing emphases on environmental health, occupational medicine, and environmental sciences. High-throughput (i.e. 1000s of samples) will likely be required to support highly-powered epidemiological investigations of human disease, such as environment-wide association studies (EWAS). Other users are anticipated from primary health care, and from government agencies tasked with monitoring of the environment or human blood, such as Swedish Environmental Protection Agency. We should also be prepared to work with industry due to increasing pressures for environmental sustainability and circular economy, which are increasingly concerned with chemicals and related impurities in commercial materials or new products.

Users of the facility will be prioritized if they are located in Sweden. Ensuring nation-wide accessibility is a priority, and users will be considered on a first-come first-served basis. An ad hoc advisory group composed of facility directors will be created if prioritization is required.

To maintain and ensure reproducibility and quality of the analysis we use several approaches including routine calibration, instrumental and procedural blanks, internal standard cocktails, internal reference samples and certified reference materials. These are injected many times throughout a sequence of samples to allow data normalization within a batch, and correction across batches. Sample preparation is conducted in a clean laboratory to prevent laboratory contamination and false-positives. All data are backed-up from the instruments to secure SciLifeLab servers at time of data collection.

User fees are budgeted to cover costs of standard sample-preparation consumables, analytical columns and reagents. User fees also account for costs of instrumental warranty, service and preventive maintenance plans. Department of Environmental Sciences owns the instruments and we pay daily user fees to offset their investments, resulting in higher prices for users in the private sector. Specialized chemical standards or unique analytical columns will need to be supplied by users, and method development for unique sample-types will be negotiated.

The research environment in which the proposed National Facility will evolve will lead to a high level of synergy, and also to rapid translation of new methods into delivery of unique service. Dr. Martin's research program is partly focused on technology development for exposomics in human and environmental samples, funded by national agencies including Vetenskapsrådet and Formas. Dr. Martin has an established reputation internationally for his research on mass spectrometry characterization of human and environmental samples, and many of his publications are highly cited (h-index 65). He also has collaborations with researchers in other SciLifeLab facilities and holds a grant to contribute serum exposomics analysis to the Swedish Scapis SciLifeLab Wellness Program (S3WP) which aims to integrate a wide range of omics data (genome, proteome, metabolome, exposome), clinical chemistry and other lifestyle factors in a longitudinal study of healthy adults. SciLifeLab is already well positioned to integrate exposomics data into broader questions of systems biology.

The technology and service offered are considered unique, thus we are not competing with alternative local, national or international facilities, nor with any commercial providers.

Budget 2021–2024

Salary and associated costs of the Facility Director (Prof Jonathan Martin) are covered by Stockholm University, Department of Environmental Sciences, and Dr Martin will dedicate 20% of his time to directing this new Facility. Salary is also budgeted (1.0 FTE) all years beginning in 2021 to hire a PhD-level Head of Facility; this person will be the only full-time staff in the first year because the initial user-base will take time to grow, and because the initial focus will be only on HPLC-Mass Spectrometry services. A second FTE will be required by 2022 as user base grows and to prepare for new services based on GC-Mass Spectrometry by 2023. There will be large demand on the time of both full-time staff for lab maintenance, sample analysis, data interpretation and communication with users. Existing mass spectrometers will be used in the first year (2021) but we will invest in sample preparation equipment

immediately. We will apply to the SciLifeLab internal call for expensive instruments in 2021, with hope of investing in a dedicated mass spectrometer by 2022. Rent for sharing of office and lab space has been budgeted. User fees shall cover all other costs, including sample storage, sample preparation, and costs of instrumental warranty and service plans. User fees do not include costs of specialized chemicals, which will be supplied by the users.

Costs	2020	2021	2022	2023	2024
Personnel (1.2 FTEs in 2021-2022, 2.2 FTEs in 2022-2024)		1 600	2 700	2 800	2 800
Operations		120	120	280	280
Premises		80	80	120	120
Instrument depreciations		700	700	1 000	1 000
Other (consumable costs of sample preparation, local user fees)		600	800	1 000	1 000
Sum costs (kSEK):		3 100	4 400	5 200	5 200

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding		2 000	2 400	3 000	3 000
University funding (20% salary, social and OH costs to Facility Director)		500	500	500	500
Scilifelab Internal Expensive Instruments Funding			700	700	700
User fees		600	800	1 000	1 000
Sum revenues (kSEK):		3 100	4 400	5 200	5 200

Table 1. Current budget (2020) and suggested budget 2021–2024

Swedish NMR Centre/Integrated Structural Biology

Basic information

Facility Director: Göran Karlsson, Gerhard Gröbner

Head of Facility: Cecilia Persson, Tobias Sparrman

SciLifeLab facility since: 2016

Host University: GU, UmU

FTEs: 11.9

FTEs financed by SciLifeLab: 3

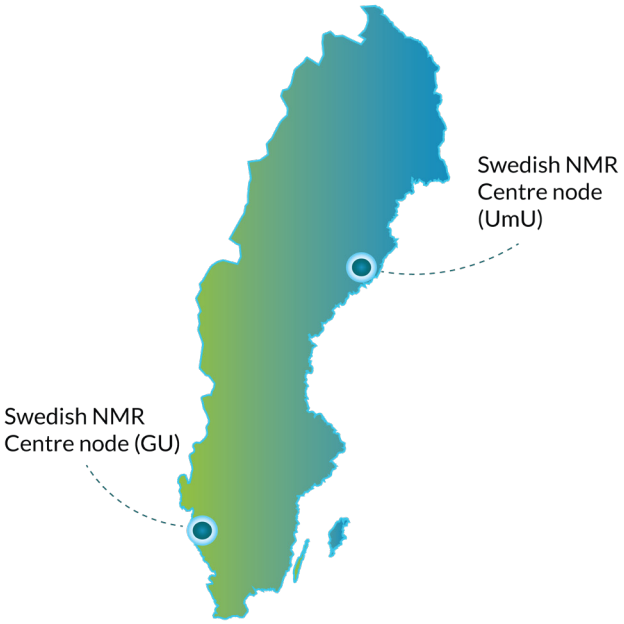
Vision:

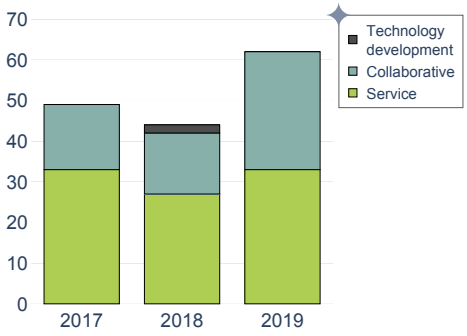
Establish an integrated Structural Biology (ISB) platform comprising the Swedish NMR Centre, the Cryo-Electron Microscope facility, the MAX IV laboratory, the H/D mass spectrometry facility and the European Spallation Source.

Mission:

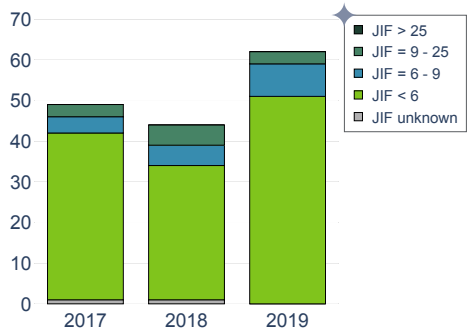
Provide access to state-of-the-art technology and comprehensive, cutting-edge expertise to users at all levels.

Geographical location of facilities

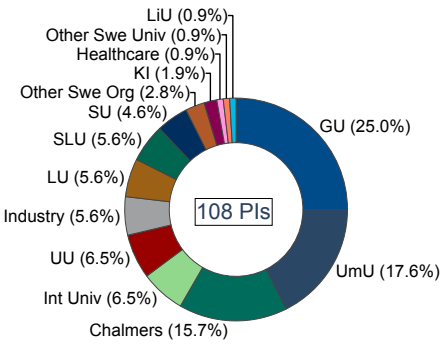




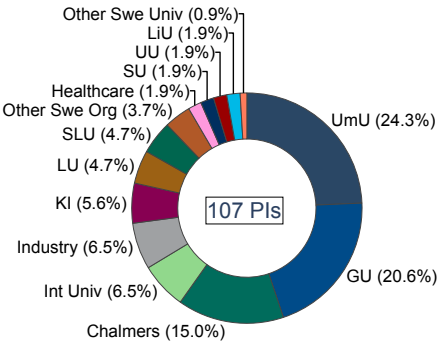
Publications by category



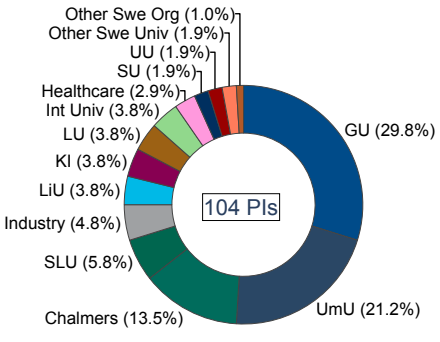
Publications by JIF



Users 2017



Users 2018



Users 2019

Read more: Web page, Publication Data Base

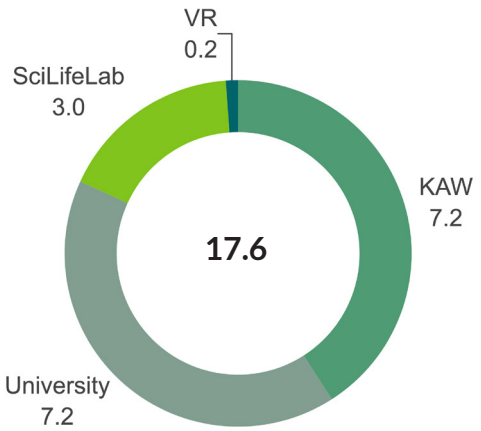
SciLifeLab funding 2020

Facility/unit	(MSEK)
Swedish NMR Centre	3.0
Total SciLifeLab funding	**3.0**

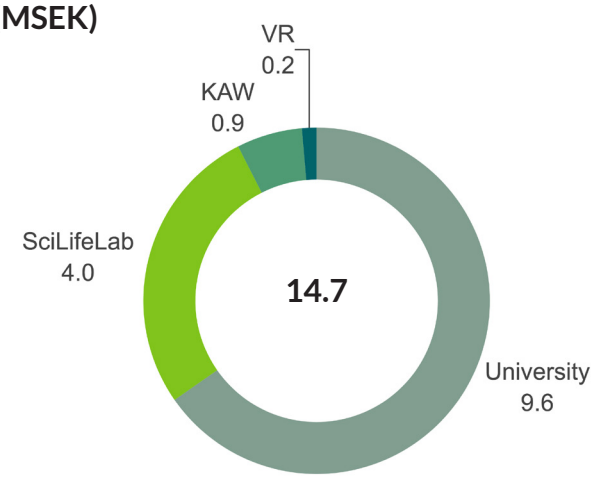
Suggested annual SciLifeLab funding 2021-2024

Facility/unit	(MSEK)
Swedish NMR Centre	4.0
Total SciLifeLab funding	**4.0**

Total funding 2020 (MSEK)



Total suggested annual funding 2021-2024 (MSEK)



Platform background

In recent years, a well developed and internationally competitive structural biology infrastructure emerged in Sweden based on the following major national cornerstones and their dedicated techniques:

- The Swedish NMR Centre (SNC) in Gothenburg and Umeå, for nuclear magnetic resonance
- Cryo-Electron Microscopy Facility (Cryo-EM) in Stockholm and Umeå
- H/D Mass spectrometry at the Targeted and Structural Proteomics facility in Lund
- The MAX-IV Laboratory in Lund, research infrastructure for X-ray crystallography and scattering
- The European Spallation Source (ESS), research infrastructure under development in Lund, for neutron scattering

These different techniques, based on inherent distinct physical principles, provide complementary structural and dynamical information, from atomic resolution level to insight into molecular assemblies, and covering time scales ranging from picoseconds to minutes and hours.

To exploit this huge potential on information in a synergetic and integrated way, these facilities should form a "virtual" Integrated Structural Biology (ISB) platform. The Swedish NMR Centre (SNC) was appointed by the SciLifeLab managing group to develop a successful strategy as further described here. The SNC will be the core of the ISB platform with its power in structural biology and further application areas within chemical biology, drug discovery and metabolomics; the other facilities will be virtually connected to it and all techniques will be synergistically bundled in this virtual ISB platform. Furthermore, the planned structure/organization will enable the ISB platform to be open for integration of novel technologies and initiatives such as LINXS (Lund institute of advanced neutron and x-ray science) and other emerging initiatives on a national/international (e.g. EU) level.

The Swedish NMR Centre (www.scilifelab.se/facilities/swedish-nmr-centre) with its two nodes at Gothenburg and Umeå, is a SciLifeLab facility since 2016. It has been successfully functioning on a national level in its key areas structural biology and metabolomics, complemented by small molecule NMR, chemical biology and (bio)materials analysis. The facility director (Karlsson, Gothenburg) and vice director (Gröbner, Umeå) report to the SNC steering group (8 members from academia and industry, appointed by VC of University of Gothenburg) which also approves budget and activity plans. The SNC employs ten senior staff scientists (PhDs with post-doc or industrial experience) all of them specialized in specific application areas; and together covering a wide range of NMR applications.

Plans for 2021-2024

We will establish a "virtual" integrated structural biology (ISB) platform centered around the existing liquid- and solid-state NMR (SNC GU/UMU facility) with Cryo-EM as a close SciLifeLab partner, Max IV and ESS virtually associated as national RIs and Targeted and Structural

Proteomics (SciLifeLab new candidate facility) as potential novel partners. The platform will provide comprehensive, cutting-edge expertise within structural biology. The integrated, synergistic approach will provide structural insights - at various size and time scales - into complex cellular processes in an unprecedented fashion. Moreover, through partnership with the national Lund Institute for Advanced Neutron and X-ray Science (www.linxs.se) and the common Integrative Structural Biology theme, the vision is to create an excellent resource both to the structural biology community as well as to the majority of users lacking this expertise; and it will be open for integration of new technologies and emerging research areas.

Establishment of a virtual ISB platform will confer a formalized interaction between SciLifeLab, MaxIV and ESS RIs. This matter needs handling by the MGs and the boards of each entity, though.

Overview of platform facilities and key technologies/ services planned for.

In recent years, the Swedish NMR, X-ray and Cryo-EM facilities have undergone tremendous methodological and technical developments; ideal to form the core foundation of a cutting-edge integrated structure biology platform (from 2021 onwards) and with ESS and H/D MS being associated in coming years. The technological development will focus on (1) combining these techniques in a synergistic way to provide support and solutions in all life science areas and (2) further development and purchase of state-of-the-art instrumentation, technologies and service for all core techniques, and maintain state-of-the-art access and support for included facilities and offered technologies.

NMR: The Swedish NMR Centre (SNC) is a SciLifeLab facility providing access and expert support to the most powerful liquid and solid-state NMR infrastructure in northern Europe. High-field instruments equipped with unique probes are used for biomolecular NMR, high-throughput robotic systems are used for drug screening and metabolomic profiling of bio-fluids and intact tissues. Successful structural biology projects include e.g. soluble intrinsic disordered proteins, insoluble membrane proteins in their native lipid matrix and amyloid fibrils. The facility supports yearly over 100 national and international PIs from academia and industry. It has been successful in the development and implementation of new methodology and technology (e.g. Non-Uniform Sampling, 3mm high-field cryoprobes) with major investments into novel methodological equipment being in the pipeline:

Ultra-fast solid state MAS NMR (850 MHz) will be installed in Umeå in 2020 to provide new analytical capabilities and insights into complex biological solids and materials (including tiny biopsies).

The first *Dynamic Nuclear Polarization (DNP) NMR* in Scandinavia will be installed in Gothenburg in 2020 in a collaborative project with AstraZeneca. The 400 MHz DNP system provides a dramatic sensitivity enhancement, particularly for surface/interface molecules and complex biomolecules.

Cryo-EM: The SciLifeLab Cryo-EM Facility (Stockholm and Umeå) became operational in 2016–2017 and has now reached full potential with six electron microscopes for screening, single-particle, sample preparation, and tomography support by very skilled facility personnel. For analysis of late image datasets, the computational infrastructure is established in collaboration with the cluster HPC2N, software is available and development ongoing. Major achievements have resulted in high-impact publications, and the facility is heavily used by researchers across Sweden. There is collaboration with other structure biology RIs like MAX IV and SNC, e.g., currently under way on a 1 MDa assembly, where NMR quantified 19F or methyl-TROSY dynamics are merged with single particle Cryo-EM structure data. This integrated approach enables functional understanding of biological systems otherwise and hitherto out of reach.

X-ray: MAX IV Laboratory is a Swedish national research infrastructure providing scientists with the most brilliant X-rays for research in structural biology and other areas. MAX IV, inaugurated in 2016, became recently fully operational at all beamlines with superb quality providing excellent service for hundreds of researchers; and already generating high profile publications in structural biology.

ESS: Neutron scattering research makes an increasing impact in structural biology, since it can provide unique insights into the organization of biological systems of varying complexity (e.g. biomembranes, protein assemblies). This technique will be available in Sweden via ESS from 2023 onwards and will then be highly beneficial across many applications in life- and materials sciences and medicine. Many collaboration with other neutron sources are ongoing to gain and develop expertise for ESS (e.g. close collaboration with ISIS neutron and muon source (UK) and Institute Laue-Langevin (F).

H/D MS Spectroscopy: Pioneered by Carol Robinson (Oxford, UK) this technique provides insight into protein structure, function and interactions using mass spectroscopy. One main focus is to study protein folding, and interactions with other proteins, cofactors, nucleic acids, small organic molecules including drugs and more. Unique is the study of proteins in a gas phase, ideal e.g. in the study of heterogeneous and dynamic protein assemblies. Johan Malmström established this H/D MS technique in Lund (https://bioms.se/technologies/hdx/) making it now available for Swedish structural biology researchers.

LINXS is an advanced study institute whose mission is to promote science and education focusing on the use of neutrons and X-rays, as well as complementary techniques. For the LINXS Integrative Structural Biology (LINXS ISB) thematic area this means the integration of synchrotron-based approaches (e.g. BioMAX, MicroMAX, CoSAXS), neutron diffraction, NMR, single particle Cryo-EM, MicroED, MS-based structural biology etc. The ISB thematic at LINXS already has four active working groups. Partnering with LINXS ensures a dynamic generation of related working groups, a program for reaching out to user communities, and a connection to international networks.

Importance and impact of the platform 2021–2024

Swedish research (academia, industry) will significantly profit from a national integrated structural biology platform, ideal to integrate information from atomic to cellular scales and a vast range of time scales, and tailored for biological systems of increasing levels of complexity; information not accessible by a single method. The open access to the full portfolio of structure biology techniques enables researchers to address not only fundamental questions in life sciences but also to generate new knowledge and technology needed in pharmaceutical/medical industry. This capacity to translate research and technology into societal benefit is essential in combating successfully the huge challenges humanity is facing today: health, food and environment-sustainability. As a cross-disciplinary platform, we can provide molecular information in each of these areas. In the health sector the focus will be on cancer, diabetes, aging and drug resistance; all key areas of many Swedish companies and SciLifeLab units (e.g. Drug Discovery and Development platform). This way, the ISB platform will generate not only basic knowledge about disease driving molecular mechanisms, but also enable development of novel therapeutic strategies and novel drug candidates. There will be numerous new opportunities for innovations, especially for research driven companies such as AstraZeneca, Nouryon, and other healthcare companies and spin-offs, with especially smaller ones heavily relying also in the future on easy access to state-of-the-art infrastructure and expertise on a national level.

Importance of SciLifeLab funding of the platform as a national resource

Availability of this advanced research infrastructure for top-level structural biology is essential for researchers for being at the forefront in their research areas. While e.g. access to national large-scale units is affordable without major costs, university funded facilities like NMR (SNC) and Cryo-EM are very expensive and often a high barrier for researchers not familiar with NMR and its potential. To provide national access to these technologies via SciLifeLab will a) reduce this burden via affordable (moderate user fee contribution) access to equipment and

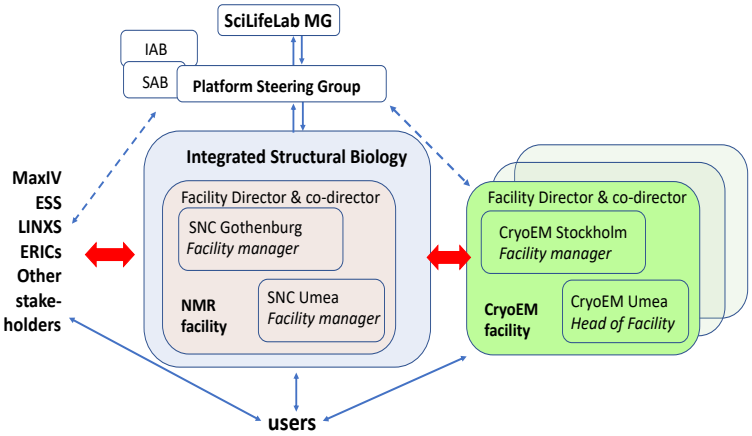


Figure 1. Governance and organization of the ISB platform

specialized expertise, b) attract challenging (risky) projects to this platform with affordable fees and expert support, c) be an invaluable source to scientists familiar e.g. with NMR to get easy access to state-of-the-art equipment (and expertise) not available at their home university) expand structural biology techniques (NMR mainly) to research areas where these techniques are not routine, e.g. plant- and environmental sciences, biogeochemistry, environmental archaeology, medicine, and, e) expand into novel research areas emerging at the horizon.

Benchmarking of the platform in an international perspective

Various national RIs (research infrastructures) in structural biology exist. In Europe, a range of RIs emerged where the main structural biology technologies are available like Francis Crick Institute (UK), French Infrastructure for Structural Biology (FRISBI), and many more. In most cases these RIs offer access to the whole portfolio of techniques, with high-end NMR and Cryo-EMs on site while access to large synchrotron and neutron facilities is often separately managed. These infrastructures differ in size, funding and equipment, something to be taken in account when comparing with the SciLifeLab ISB platform. However, the SNC, Cryo-EM, Max IV and ESS have in last years emerged as word-class facilities with increasing international reputation and output in form of high-profile papers, recruitment of international researchers and invitations to international conference in structure biology.

Future plans for governance and organisation of the platform

The platform steering group will sort directly under the SciLifeLab MG, in accordance with the governance model for SciLifeLab, and will directly report and be accountable to the MG (Figure 1). The steering group may appoint a scientific advisory board (SAB) and an international advisory board (IAB) for independent advice and quality control. The platform steering group members are leading scientists on a national or international level, from universities, RIs or industry. The main task for the steering group, apart from approval of budget and activities, and

defining the long-term strategy, is to oversee availability of access and support for the user community to facilities within the SciLifeLab organization and to provide guidance and support in the interaction with the external RIs Max IV and the ESS, e.g. through a scientific committee. The set-up facilitates interaction with ERICs on the European level, and could serve as a contact point in a strategic process, aiming for Sweden to become INSTRUCT partner.

Overall platform plans to ensure that the most relevant technologies in the field are provided as services to users in Sweden

The described technologies provide structural information on atomic or near-atomic resolution, and together form the core of the ISB platform. Each area is characterized by fast technology and methodology development. A strategy to keep technologies at the forefront relies on four main points:

- Participation of facility directors and staff scientists at international conferences in structural biology and on specific technologies, and facility and company user meetings to ensure that technology and methods developed in these areas can get implemented in Sweden.
- Regular meetings with other facilities and SciLifeLab management to evaluate the need for upgrades or purchase of new equipment and which novel services should be offered on a national level.
- In cooperation with national science foundations and local universities ensure the purchase of the necessary state-of-the art equipment (e.g. in NMR 1.2 GHz for ca. 120 MSEK) and ensuring open, and affordable access to all researchers to this novel equipment inclusive expert support.
- Recruiting leading research PIs in novel/developing technologies and research topics.

NMR facility: nationally unique and internationally competitive

The NMR facility provides access to one of the most powerful liquid and solid-state NMR infrastructures in the Nordic countries for all academic and industrial researchers across Sweden. The facility includes expertise and support by highly trained NMR staff, which allows to provide state-of-the-art NMR service to the majority of researchers not experts in NMR. High-field instruments are equipped for biomolecular solution NMR, robotic sample preparation and high-throughput metabolomics of bio-fluids. This SNC offers unique liquid and solid-state NMR capabilities at 850/900 MHz for studies e.g. of soluble intrinsic disordered proteins, insoluble membrane proteins, amyloid fibrils, metabolomics on complex biofluids and intact tissues, materials- and environmental sciences. Fragment-based screening is also offered as national support for CBCS and DDD, including comprehensive substance libraries. The DNP instrument and the Ultrafast MAS equipment are unique in Sweden and at the forefront of technological development on the European level.

Synergies: i) within the platform, ii) with other platforms and facilities/units

Due to the focus on structural biology the synergy within the ISB platform is very good, especially when measures for cross-disciplinary coordination of research projects are fully implemented. This would also allow future integration of Targeted and Structural Proteomics facility (H/D MS) into the SciLifeLab platform and seamless virtual integration of the independent RIs Max IV and ESS.

The different facilities provide highly complementary, structural data on an atomic level. The establishment of an integrated structural biology platform offers a unique opportunity to Swedish scientists for support to access all major structural biology technologies from a single point of entry. The platforms for drug development, “Chemical Biology and Genome Engineering” and “Drug Discovery and Development platform”, would have strong synergies; NMR and crystallography are techniques widely used in modern pharma industry (e.g. AstraZeneca).

The NMR facility, in parallel, massively contributes to metabolomics, due to outstanding reproducibility, quantitation and the possibility to directly analyze complex biofluids (urine, serum/plasma). On the analysis side, there is exchange of expertise and advanced data analyses with Swedish Metabolomics Centre at “Proteomic and Metabolomics” and the BINS bioinformatics platform.

Collaborations with healthcare, industry and other external organizations

The need of Swedish industry for access to this type of platform is reflected by the large number of life science/medical company users. There are many ongoing collaborations between companies of varying size and the public structural biology facilities, with many smaller companies essentially relying on this open access for their survival. The related LINXS activities are engines for linking the platform to the international community, not the least via international guest researcher programs and via the guidance of the LINXS international SAB. The installation of the DNP-NMR instrument is part of a long-term collaborative project between the Swedish NMR Centre and AstraZeneca with a focus on pharmaceutical development. Together with BIS (Biobanks Sweden) the use of NMR for QC of biobanked samples is investigated. The Swedish NMR Centre is partner in infrastructure applications (EU Horizon 2020, NordForsk).

Which alternative infrastructures are available to users?

There is no competing ISB platform on the national level. Between 2012-2016, SNC and MAXLab were part of the research council supported RI SwedStruct. On the European level, a small number of Swedish users have obtained access at the Diamond and ISIS facility in the UK or ESRF/ILL in France. Other, in principle open, facilities in Europe are large NMR centers via Instruct-Eric, but time is very limited and for small number of users only. Within the SNC facility, the combination of high-field (≥700 MHz magnets) and various cryoprobes are unique in a national setting, as is the access to the ISO-certified metabolomics methodology. The joint competence and expertise within the group of staff scientist is difficult to match also on an international level.

How data-driven science will be promoted by the platform

Data driven science is a central component for the ISB platform as well as for the SNC facility. The different structural biology techniques generate increasingly large data volumes for processing and analysis. The central concept of the ISB platform presumes the merger of complimentary data during processing an analysis, including modeling of drug interaction, based on *in-silico* or empirical data.

NMR-based metabolomics provide a snapshot of the state of an organism. Combining genome wide association studies (GWAS) with targeted metabolomics and lipoprotein profiling will become increasingly important in precision medicine. Efficient data handling is required, but also harmonization with existing principles for data sharing (FAIR and GDPR). Data from environmental research at SNC on eco-systems and climate change are used to model plant climate interactions on century time scales.

Budget 2021–2024, user base, data quality and user fees

The SNC is mostly faculty funded (Gothenburg and Umeå). SciLifeLab funding (~25%) is an important fraction. Permanent staff FTE:s is the same. Running costs decrease from 2021 due to the installation of a helium liquification unit at SNC. The upgrade of the RI instrumentation continues, but at a slower pace compared to the KAW funded major upgrade during 2013-2020.

The already *existing* user base comprises many more than 100 PIs from all major Swedish universities, several university hospitals and regions, and users from research institutes and industry, including e.g. AB Volvo, RISE, Medivir and AstraZeneca. Per year, the facility provides more than 40 000 hrs of spectrometer time on high field instruments to national and international users. The total need for all science areas to access to state-of-the art NMR instrumentation and expertise is much higher. The availability of DNP and ultrafast MAS NMR will further broaden the user base in areas of biosciences, chemical engineering, materials- and environmental sciences.

Nation-wide user accessibility is achieved through a continuous reach-out process. This comprises local discussion groups and invited presentations at other universities, arrangement of, and participation in national and international workshops, symposia, meetings and conferences, including SciLifeLab reach-out, science and facility forum events. The Swedish NMR Centre has organized national NMR meetings 2014, 2016 and 2018, and organizes the Nordic NMR Conference in 2020. The facility co-organized the Structural Biology (SBnet) meeting in 2016, and the Swedish Metabolomics conference in 2018.

NMR is intrinsically a quantitative method with inherent reproducibility. Standard routines are applied to ensure reproducibility over time. In metabolomics, an ISO-certified procedure is applied and a QC algorithm detects variations in sample and spectrometer performance. Spectrometer raw data is backed continuously on two levels. Special routines apply for metabolomics data, in accordance with the GDPR.

The user fee model for academic users is based on actual running costs excluding depreciation. A combination of staff support, remote access and automation makes the facility available 24/7. Current user fees are displayed at the facility web page. For structural biology applications, a reduced user fee will be applied, in order to harmonize with cost models for similar national and international services, e.g. MaxLAB for x-ray diffraction, the SciLifeLab EM facility for cryo-EM data, iNEXT (the EU H2020 consortium for integrated structural biology), etc. For metabolomics, a sample based user fee is applied.

The facility is embedded in an environment of NMR research groups at the University of Gothenburg (Karlsson: metabolomics, NMR-optimized cell-free expression; Orekhov: Non-Uniform Sampling, pulse sequence development; Burman: membrane proteins, IDPs) and Umeå (Gröbner: biological solid-state NMR; Schleucher: environmental NMR; Wolf-Watz: Protein function), respectively. This highly complementary expertise drive the translation of biomolecular NMR methods into new areas.

Costs	2020	2021	2022	2023	2024
Personnel (11 FTEs)	9 084	8 450	8 600	8 750	8 900
Operations	3 500	2 100	2 200	2 300	2 400
Premises	2 384	2 420	2 455	2 490	2 525
Instrument depreciations	4 140	4 576	3 700	2 950	2 400
Sum costs (kSEK):	19 108	17 546	16 955	16 490	16 225

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	3 000	4 000	4 000	4 000	4 000
University funding	7 200	9 600	9 600	9 600	9 600
Funding KAW	7 200	1 900	1 200	500	-
Funding VR-RFI	200	200	200	200	200
User fees	1 500	1 800	2 000	2 200	2 400
Sum revenues (kSEK):	19 100	17 500	17 000	16 500	16 200

Table 1. Current budget (2020) and suggested budget 2021–2024

Diagnostics Development Platform

Basic information

Platform Director: Richard Rosenquist Brandell

Vice Platform Director: Lucia Cavelier

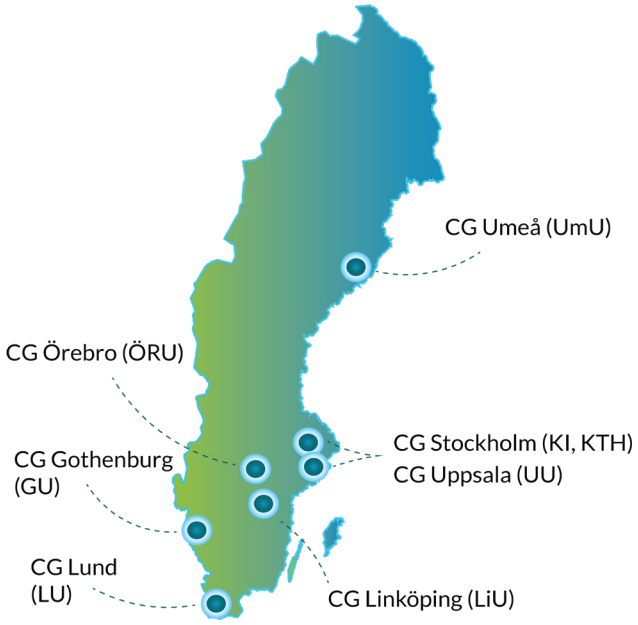
Platform Vision:

To operate as a key research infrastructure for translation of new high-throughput technologies into clinical utility

Platform Mission:

1. To provide world-class, end-to-end service and support to translational research projects and clinical studies/trials across Sweden.
2. To perform proof-of-concept demonstrations, adapt and optimize new technologies enabling precision medicine.
3. To provide a direct societal benefit through translational and diagnostic activities.

Geographical location of facilities



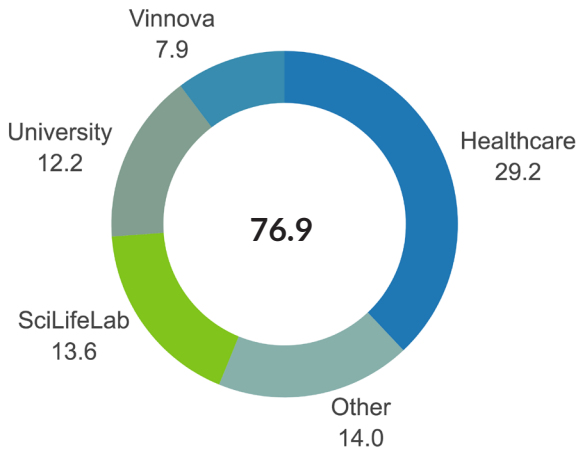
SciLifeLab funding 2020

Facility/unit	(MSEK)
Clinical Genomics Gothenburg	2.2
Clinical Genomics Linköping	0.3
Clinical Genomics Lund	2.2
Clinical Genomics Stockholm	5.5
Clinical Genomics Umeå	0.3
Clinical Genomics Uppsala	2.7
Clinical Genomics Örebro	0.3
Platform Coordination	0.0
Platform New Initiatives	0.0
Total SciLifeLab funding	**13.6**

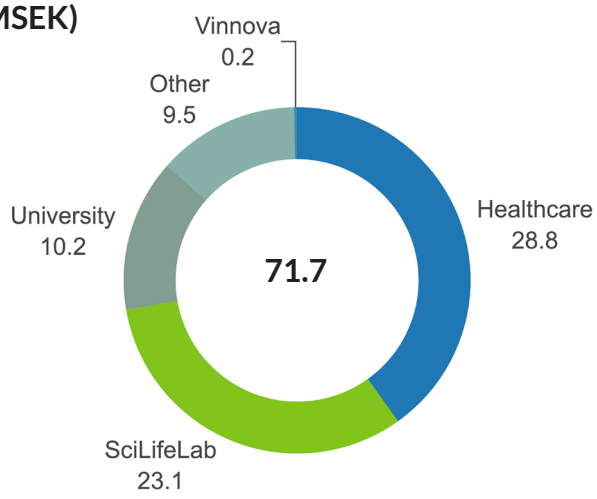
Suggested annual SciLifeLab funding 2021-2024

Facility/unit	(MSEK)
Clinical Genomics Gothenburg	2.2
Clinical Genomics Linköping	1.5
Clinical Genomics Lund	2.2
Clinical Genomics Stockholm	5.5
Clinical Genomics Umeå	1.5
Clinical Genomics Uppsala	2.7
Clinical Genomics Örebro	1.5
Platform Coordination	1.5
Platform New Initiatives	4.5
Total SciLifeLab funding	**23.1**

Total funding 2020 (MSEK)



Total suggested annual funding 2021-2024 (MSEK)



Background

The Diagnostics Development platform (DD platform) was established in 2014 from three facilities, i.e. Clinical Genomics in Stockholm and Uppsala and Clinical Biomarkers[1] in Uppsala. The platform expanded in 2016 by including Clinical Genomics in Gothenburg and Lund and since 2019 reached national coverage by establishing Clinical Genomics facility nodes in Linköping, Umeå and Örebro. Hence, the platform now covers and operates at all universities with a medical faculty and at all university hospitals in Sweden.

The purpose of the platform is to serve as a key research infrastructure for the development, validation and implementation of new high-throughput technologies for clinical and translational research projects, clinical trials and diagnostics within healthcare. We provide a unique end-to-end service, i.e. from sample preparation and analysis to clinical interpretation. As a translational platform within SciLifeLab, we actively collaborate with biobanks, healthcare and industry, and provide cutting-edge technologies and services to enable individualized patient care and precision medicine at a national level.

Key achievements of the DD platform include:

- Provision of expertise and service to >150 PIs in 2019. The services encompassed analysis of >15,000 samples for research and clinical trials, as well as development and application of a wide range of high-throughput technologies.
- Implementation of high-throughput diagnostic tests for rare diseases, cancer and infectious diseases. As a prime example, Sweden was one of the first health-care systems to implement whole-genome sequencing (WGS) in clinical routine. In 2019, >15,000 patient samples were analyzed with tests developed by the platform, including 2,600 whole genomes, 1,400 exomes and 6,400 gene panels.
- Initiation of Genomic Medicine Sweden (GMS), a national effort to coordinate implementation of precision medicine in Sweden. As the technological basis of GMS, the DD platform has for example developed national broad gene panels for solid tumors and hematological malignancies for translational research and clinical diagnostics.

Plans for 2021-2024

Organisation and internal synergies

The DD platform consists of Clinical Genomics facility nodes that provide service at all seven medical faculties and university hospitals in Sweden. The facility nodes are formally organized at each medical faculty in close collaboration with the respective university hospital. The platform is governed by a platform director and a vice platform director that lead the platform management board consisting of seven facility directors (ordinary members) and seven heads of facility (substitute members). Management board meetings will be held monthly, and meetings with the whole platform will be arranged 1-2 times per year.

The multidisciplinary facility teams consist of molecular biologists, bioinformaticians, software developers and other IT professionals, clinical molecular geneticists and medical doctors. We thus combine technical expertise in assay development, including bioinformatics and software engineering, with clinical expertise in assay needs and performance. We provide access to a unique research and development environment, and enable new types of translational and clinical research projects that cannot be managed without the close connection to clinics and biobanks.

The national coverage of the platform is a key uniqueness and leads to a multitude of excellent synergies. For example, national coordination facilitates harmonisation of new technologies, reduces development costs and accelerates implementation of novel tests in healthcare, since method development can be carried out at one or a few sites in collaboration followed by a rapid rollout across all healthcare regions. We plan to collaborate around increased automation in the laboratories, optimized sample flows between facility nodes to reduce turnaround times (TAT) as well as a joint framework for data storage and sharing.

Key technologies and services

An important mission task of the platform is horizon scanning within life sciences and information technology to identify new techniques that can be used in pre-clinical and clinical applications. Technology development and adaptation is carried out as a service to researchers and clinical laboratories, or as internal projects that can serve as proof-of-concept for further establishment of new services and clinical implementation.

Development of new diagnostic tests often starts with collaborative pilot projects to optimize laboratory and bioinformatic workflows, and is followed by a careful validation process, whereby the performance is evaluated with respect to specificity, sensitivity, reproducibility, TAT and cost. The validated assays that we offer to researchers follow quality assurance standards ensuring high precision and quality; selected analyses are ISO accredited, and we are preparing for the changes required by the upcoming European In Vitro Diagnostic Regulation. Once a clinical routine test is validated, GMS or healthcare personnel take over the operations for clinical samples (Figure 1).

[1] The Clinical Biomarker facility is now included in the Proteomics and Metabolomics platform.

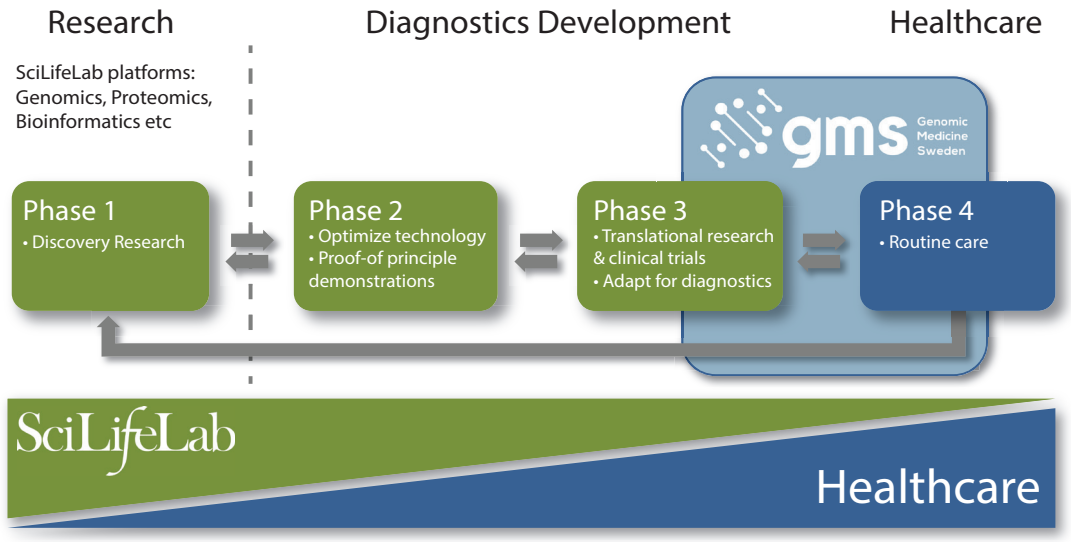


Figure 1. The DD platform operates in phase 2 and 3 as a 'bridge' between research and healthcare.

While we focus most of our current activities on rare diseases, cancer and infectious diseases, we will expand our services to pharmacology, complex diseases and immunology, in collaboration with GMS.

Our current key technologies include short- and long-read sequencing, transcriptome analysis, single-cell sequencing, and ultrasensitive variant detection (Figure 2). In contrast to other SciLifeLab platforms, a large proportion of the technologies/services offered by the platform have been harmonized between the facility nodes in order to ensure equal access for translational/clinical researchers and healthcare across Sweden (Table 1). That said, different facility nodes offer unique techniques and services as outlined in the respective facility plans. Our basic technologies are complemented with diagnostic and medical expertise within the focus areas, bioinformatics expertise, and access to clinical validation cohorts, to enable end-to-end service for the users.

A unique asset for the platform is *clinical bioinformatics* that includes analyzing, storing and organizing biological data that supports patient management and care, and is an essential, integrated part of all translational and clinical applications. The DD platform devotes significant resources to develop bioinformatic pipelines and IT systems tailored for translational research and diagnostics. Out of a total staff of 75 FTEs, 38 work with bioinformatics, software development or system administration.

During 2021-2024, we plan to develop new services in the following areas:

Long-read sequencing. We have previously developed a clinical test for detection of resistance mutations in the *BCR-ABL1* fusion gene in chronic myeloid leukemia using long-read sequencing, in collaboration with the SciLifelab Genomics Platform. We plan to implement services in three additional areas: i) In rare disease diagnostics short-read WGS already has a dramatic impact today, but >60% of the cases remain unsolved. Long-read sequencing enables identification of structural variants in repetitive regions and facilitates phasing of variants potentially increasing the diagnostic yield. ii) Cancer diagnostics often require a battery of different methods to retrieve the essential genetic markers. We will evaluate the potential of long-read techniques to replace current laborious chromosome analysis methods. iii) In clinical microbiology, long-read sequencing facilitates assembly of complete microbial genomes and offers shorter TAT compared to current culture-dependent methods for species identification, antibiotic resistance prediction and epidemiological surveillance.

Clinical transcriptomics. To increase our ability to identify disease-causing variants from targeted sequencing or WGS in rare diseases, we will set up complementary analyses of the transcriptome (RNA-seq). This will also

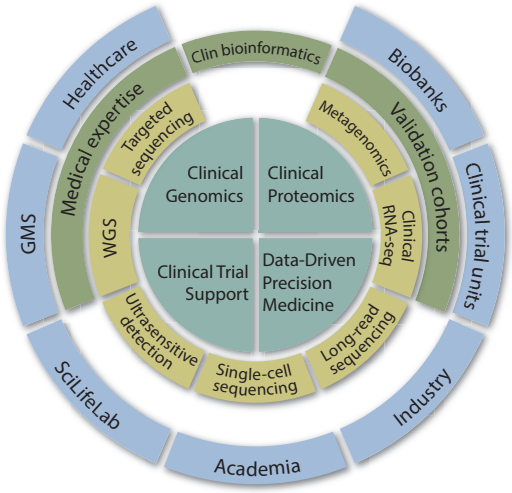


Figure 2. Technologies, services and collaborators of the DD platform. The circles show, starting from the outermost, our collaborators (blue), our competences and resources (dark green) and our current technologies (light green). In the center, current and planned capabilities are depicted.

Technologies/services	Gothenburg	Linköping	Lund	Stockholm	Umeå	Uppsala	Örebro
WGS							
Exomes/gene panels							
Targeted or global RNA analysis							
Targeted or global long-read seq							
Ultra-sensitive detection							
Single-cell sequencing							
SNP or methylation array analyses							
Microbial WGS or resistance typing							
Metagenomics							
Bioinformatics support							
Clinical interpretation support							
Instrument availability for researchers							

Table 1. Technologies and services currently available at the Clinical Genomics facility nodes (indicated in green).

Technologies/services	Gothenburg	Linköping	Lund	Stockholm	Umeå	Uppsala	Örebro
Clinical transcriptomics							
Novel applications of long-read sequencing[1]	micro			rare	rare	cancer	micro
Novel applications of ultra-sensitive detection							
Single-cell diagnostics							
Spatial transcriptomics							

Table 2. Coordinating nodes for new applications (indicated in orange).
[1] Different nodes will coordinate the three pilot projects in rare disease, cancer and microbiology.

improve understanding of non-coding variation through identification of altered transcript isoforms and expression changes. We currently evaluate RNA-seq in acute leukemias and pediatric oncology to confirm expression of pathogenic variants, identify fusion genes that are relevant for prognosis or treatment, and enable expression-based classification and prognostication. NanoString-based expression analysis, which e.g. classifies breast cancer patients into treatment groups or predicts prognosis of lymphoma patients, will be offered as a service.

Ultra-sensitive variant detection. Ultra-sensitive assays for identification of low frequency mutations are of importance for diagnosis, prognosis and response to therapy in cancer. We have developed and implemented diagnostic tests using liquid biopsies (i.e., detection of variants in circulating tumor DNA) for lung cancer and we currently support a large clinical study where patients with myelodysplastic syndrome are followed longitudinally using digital PCR after stem-cell transplantation to predict early relapse and optimize treatment. There is, however, a need for sensitive follow-up methods also for other diagnoses, and we plan to implement new cutting-edge technologies, such as deep-sequencing with unique molecular identifiers and super rolling circle amplification.

Single-cell diagnostics and spatial transcriptomics. Single-cell sequencing holds potential to significantly improve clinical diagnostics. We have already experience of setting up methods such as single-cell RNA-seq, ATAC-seq, and CITE-seq for research purposes, and we now plan to establish diagnostic single-cell sequencing in collaboration with the SciLifeLab Genomics platform. Potential pilot projects include single-cell analysis for improved diagnostics, prognostication and follow-up of hematologic malignancies, for diagnosing cancers of unknown primary origin, and for monitoring the T-cell response following immune checkpoint blockade. Spatial resolution of gene expression is important for the understanding of subclonal development in heterogenous tumors as well as the interactions between tumor cells, stromal cells and the immune cell environment. We plan to evaluate clinical applications of spatial transcriptomics in collaboration with the SciLifeLab Spatial Biology infrastructure.

Our working model is that one to two nodes lead the development of each new application (Table 2). Once a method is established, the technology will be transferred to the remaining nodes if there is a high local demand. This will ensure national harmonization and maximized utilization of resourses and impact on clinical research and healthcare.

Capabilities

The DD platform has developed a number of key capabilities in collaboration with different healthcare units and other SciLifeLab platforms (Figure 2). Our main capability is **Clinical Genomics,** which comprises most of our current technologies as well as our services in adaptation, validation and implementation of methods for clinical diagnostics. During 2021-2024, we will continue

developing novel applications within clinical genomics, and in addition work to establish the following capabilities:

Clinical proteomics. Large-scale proteomics holds potential to strongly contribute to diagnostics of various diseases, and we expect proteogenomics to be part of the core diagnostic repertoire in five years. We aim to establish clinical proteomics as a capability within the DD platform, in collaboration with the SciLifeLab Proteomics and Metabolomics Platform. Pilot projects will be initiated in hematologic malignancies where integrative genomics and proteomics (WGS, RNA-seq and proteomics) will be used to investigate if this approach can improve disease stratification.

Clinical trial support. The clinically validated assays developed by the DD platform are available to academia and industry as support for clinical trials. Our services include e.g. rapid detection of therapeutic biomarkers on DNA or RNA level and monitoring treatment response by ultra-sensitive assays. During 2021-2024 we will establish special tracks to support clinical trials in need of genomics-based biomarker assays, as we expect a high demand for this service. As part of this, we envision enhanced collaboration with clinical trial units, Clinical Studies Sweden and the Centre for Advanced Medical Products to promote innovative clinical trials in Sweden for rare diseases and cancer.

Data-driven precision medicine. The goal of precision medicine is to move towards individualized diagnosis and treatment based on e.g. biometrics, genetics and imaging. To achieve this, data from a large number of patients and from a multitude of systems need to be collected longitudinally. This requires comprehensive systems and dynamic tools for storing, organizing and analyzing large amounts of data. To realize data-driven precision medicine we need to define national data standards for storage and sharing of genomics data, patient health information and other metadata, which will be essential for future advanced analytics. The DD platform will play a key role in this process, in collaboration with e.g. GMS, AI Innovation of Sweden and Global Alliance for Genomics and Health.

External collaborations and synergies

The DD platform maintains a large network in the national and international research communities, organizations and industries, where our close connections to the health-care system makes us a particularly valuable partner for technology development and testing.

SciLifeLab infrastructures. The DD platform collaborates with the Genomics platform, with synergies concerning shared instrumentation and joint technology development. Additional collaborative projects within long-read and single-cell sequencing will be initiated during 2021-2024. We currently work on a WGS cancer pipeline suitable for both research and diagnostics in collaboration with the Genomics and Bioinformatics platforms. We also foresee enhanced collaborations with the Bioinformatics platform and the SciLifeLab Data Center, in order to realize data-driven precision medicine. We plan to collaborate with the Proteomics and Metabolomics platform to enable clinical proteomics, and the Drug Discovery and Development platform concerning biomarker assays for newly developed drugs. In these collaborative projects, the DD platform will contribute with expertise in test development and implementation, clinical know-how on data interpretation, personnel for coordination and development, sample cohorts, and to some extent instrumentation. Importantly, we will be a link to the healthcare system at a national level.

Healthcare. The Clinical Genomics facility nodes are present at all Swedish medical faculties, and are integrated with all seven university hospitals, thus providing a strong link between SciLifeLab and healthcare. We have close relations with Regional Cancer Centers and Centers for Rare Diseases, ensuring that novel diagnostic methods developed by the platform can be introduced into national care programs, and we actively collaborate with clinical trial units to support clinical trials. We also play a key role as trainers and teachers for healthcare professionals and clinical researchers in the field of genomic medicine/precision medicine.

Genomic Medicine Sweden. The national precision medicine initiative Genomic Medicine Sweden (GMS) was initiated by the DD platform in 2017. GMS has the ambition to secure access to NGS-based diagnostics for all patients in Sweden in order to introduce individually adapted therapies and follow-up strategies within healthcare. GMS focuses on developing assays for uniform molecular diagnostics over the country and building a national infrastructure for computation and secure data storage, to structure genomic data and linked metadata to enable for example disease-specific variant databases. The Clinical Genomics facility nodes provide the technological basis and serve as a 'test bed' for new technologies within GMS. Importantly, the strong link between the DD platform and GMS ensures that projects, technologies and assays can be carried from basic and translational research projects, through implementation projects, to clinical routine (Figure 1).

Biobanks. The DD platform has close connections to Biobank Sweden, a national biobanking infrastructure with the same steering group as GMS. Biobank Sweden has centers at the university hospitals and provides access to high quality samples for research as well as rare samples needed for validation purposes.

Innovation and collaboration with industry. The market within genomics-based precision diagnostics, an area where our platform possesses key capabilities, is rapidly expanding. During 2021-2024, we will work with the

innovation offices at our host universities to enable new methods and products developed within our platform to reach the market. We also provide service to the industry and have several past and present collaborations with biotech and pharmaceutical companies, such as Bristol-Myers Squibb, Illumina, and Incyte. Our role in these collaborations is to test new products, develop innovative diagnostic methods, or characterize patient material as part of clinical studies and trials.

International collaborations. The DD platform actively takes part in several international initiatives, including the Nordic Alliance for Clinical Genomics, the Global Alliance for Genomics and Health, the European '1+ Million Genomes' Initiative, several European Reference Networks for rare diseases and ICPerMed. Through participation in these networks we liaise with Nordic and European peers to facilitate cross border learnings, harmonisation of processes, quality assurance of analyses and data sharing, to support discovery and diagnostics.

Challenges 2021-2024

A challenge during 2021-2024 will be to keep up-to-date in terms of instrumentation for high-throughput technologies. We will apply for upcoming calls within SciLifeLab for expensive equipment and also coordinate investments with the Genomics platform to secure state-of the art instrumentation within our focus areas. Similarly, we will continuously perform technology development projects together with research groups, other SciLifeLab platforms, and industry, to be able to offer cutting edge techniques. In order to effectively coordinate activities between our facility nodes we will employ a national coordinator and an administrative coordinator that will assist the platform management board. We will also stimulate and promote competence development of staff and national collaboration by offering site visits and exchange of personnel between nodes, as well as organize joint workshops about relevant topics. A final major challenge relates to data storage and sharing; here we will work closely with the SciLifeLab Data Office and GMS to set national standards for data storage/sharing, thus paving the way for data-driven precision medicine.

Uniqueness, user base and importance

The DD platform is a key translational infrastructure uniquely positioned between academia and healthcare, hence leveraging one of SciLifeLab's key mission statements - societal impact. Our comprehensive support, including understanding of clinical needs, technical assay development including wet lab and bioinformatics, software development, quality assurance, and clinical interpretation, provides a unique service for our end-users and collaborators. The presence of Clinical Genomics nodes at all medical faculties ensures national accessibility for researchers and healthcare and enables close and personal support. As a result, there is a high and increasing demand for the expertise and services provided by the platform. In addition to researchers and healthcare, we serve governmental agencies including the Swedish Medical Products Agency, the Swedish National Veterinary Institute, the Swedish Food Agency, and the Public Health Agency of Sweden. With the recent expansion of three new nodes, the user base is expected to increase in the next few years. We also expect increased number of users as a result of new technologies and services being introduced, the planned expansion to new disease areas, and a larger demand of genomic characterization as part of clinical trials. In summary, the DD platform is in a position to make a significant contribution to medical research and to promote precision medicine at a national level, well inline with the ambition of the Swedish Life Science strategy to become internationally leading in precision medicine.

Budget 2021-2024

The majority of the funding within the DD platform originates from other sources than SciLifeLab national platform funding, which in 2019 only constituted 13% of the total DD platform budget (including user fees). Considering the high demand for the DD services and the expansion to nation-wide coverage, we believe that an increase of the SciLifeLab funding to the requested level is well justified.

The budget includes dedicated funding for each facility node, and funding for coordination and development projects that currently remain on the platform level. The internal distribution of the funding will be decided when the overall platform budget for 2021-2024 is known.

Clinical Genomics Gothenburg

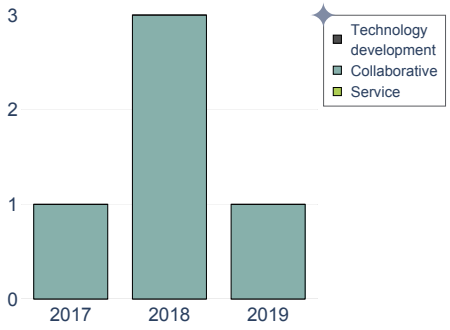
Read more: Web page, Publication Data Base

Basic Information

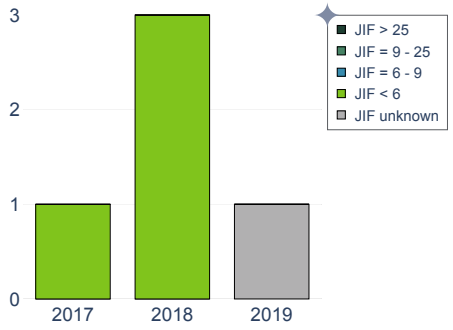
Facility director: Tommy Martinsson
Head of facility: Per Sikora
SciLifeLab facility since: 2016
Host University: GU
FTEs: 8.2
FTEs financed by SciLifeLab: 3

Funding 2020 (in kSEK)

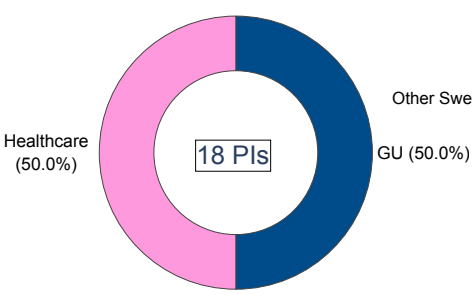
SciLifeLab: 2200
Total: 6170



Publications by category



Publications by JIF



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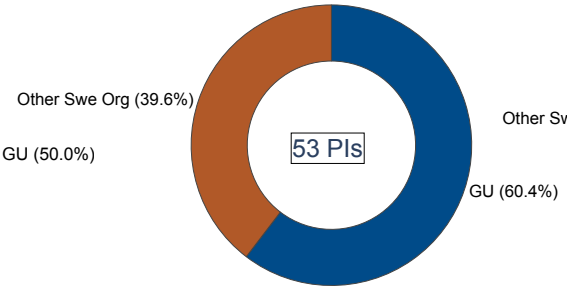
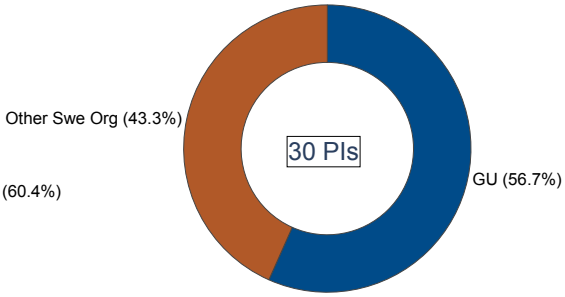


Users 2018



Users 2019

For an overview of current technologies and services at each Clinical Genomics facility node, see Table 1 in the DD platform report.

New Technologies and Services 2021–2024

- New computational techniques in life science
- Long-read sequencing for novel applications (coordinating node for the DD platform)
- Expanded single-cell analysis
- Further developments in ultra-sensitive methods (coordinating node for the DD platform)
- Proteomics/proteogenomics service to be offered together with the Proteomics Core Facility at the Sahlgrenska Academy.

Background

Clinical Genomics Gothenburg (CG Gothenburg) combines support in high profile translational research projects with clinical development and sequencing for Region Västra Götaland (VGR) and Sahlgrenska University Hospital. The facility is governed by a steering group consisting of representatives from both VGR and the University of Gothenburg and facility personell is employed through either one of the host organisations.

Since its inception in 2016 the facility has seen steady growth and an expanding user base. We now have 6 bioinformaticians and 4 laboratory personell, this number will be expanded by a new laboratory hire early 2020 and a new bioinformatics hire at the end of 2020.

We have expanded our operations with a number of instruments funded in part or in full by Sahlgrenska University Hospital, including a 10x Chromium and perhaps our largest investment, a NovaSeq 6000. The facility has access to 3 MiSeqs, a NextSeq and 2 S5 XL machines. The facility manages its own compute cluster of ~650 cores with 500 Tb of attached short term storage, as well as links to the VGR Datalake for long term storage. We have developed and validated multiple techniques for clinical use, including gene panels for hematology and solid tumours, various viral resistance panels, bacterial WGS, human WES and clinical metagenomics. From summer 2019 we are offering whole-genome sequencing with a clinically validated bioinformatics workflow and clinical interpretation to researchers. The goal is to accredit the WGS workflow by the end of 2020. We are also working closely with local research groups at the Wallenberg Center for Translational Medicine (WCTM) to introduce ultrasensitive detection of cell-free DNA for cancer treatment monitoring.

Currently, we are analyzing ~1000 human samples using WGS, 500 samples with RNA-seq and 1500 microbial samples per year including metagenomics, viral resistance typing and bacterial whole genome sequencing. Approximately 80% of WGS samples and 95% of microbial samples are from healthcare. Furthermore, we are now implementing our new LIMS system that will go online first

half of 2020 and we are actively working on automation of routine tasks in the lab. Finally, the facility is now working close with Genomic Medicine Sweden and the University of Gothenburg to develop the next generation of IT-infrastructure for data storage, large-scale data analysis and data organization with an early pilot finishing in 2020.

Plans for 2021–2024

The facility focus for the years of 2021-2024 will be on improved automation of the laboratory as well as traceability and accountability of the lab flows. Laboratory protocols will be accredited at the earliest possibility. Furthermore, the IT infrastructure will be shifted to a hybrid-cloud structure where data is housed either on-premise or inside the VGR datalake. The facility will work in close collaboration with a new research group in quantum computing for life science being established in cooperation with Sahlgrenska University Hospital and the Wallenberg Center for Quantum Technology at Chalmers (WaQT) as well as AI-innovation of Sweden and ChAIr, the Chalmers AI research infrastructure. Initial investment includes two PhD positions in life science quantum computing where one applicant will come from physics/computer science and one from bioinformatics/biology. The team will be managed by one PI within Sahlgrenska University Hospital and one within WaQT with the CG Gothenburg Head of Facility acting as co-PI. Intial focus will be on applied quantum algorithms to accelerate and improve classification of metagenomics samples and development of theoretical algorithms for future applications. These methods can then be used in the existing clinical metagenomics pipeline (PaRCA) established by the facility.

Laboratory techniques that will be implemented during 2021-2024 include long-read technology as a complement to existing short-read sequencing. Oxford Nanopore is the first choice but solid state nanopore manufacturers will likely come to market soon, broadening the applications significantly. Another technique that is rapidly evolving is single cell/in-situ transcriptomics and the facility is watching development in this field closely. We will also start the move from on-premise data analysis to a cloud-based solution, reducing costs and increasing flexibility and overall computational power. Finally, we are in discussions with the Proteomics Core Facility at the Sahlgrenska Academy in order to coordinate their offerings with that of CG Gothenburg and facilitate testing of proteomics as a complement to genomics in the clinic.

Budget 2021–2024

The facility applies a combination of hourly fees for bioinformatic development and support and a 10% surcharge for sequencing services to researcher that gets reinvested into the facility.

Costs	2020	2021	2022	2023	2024
Personnel (8.2 FTEs 2020, 9.2-11.2 FTEs 2021-2024)	5 120	5 660	6 380	6 380	6 920
Operations[1]	1 300	250	250	350	350
Premises	920	920	920	1 200	1 200
Sum costs (kSEK):	7 340	6 830	7 550	7 930	8 470

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	2 200	2 200	2 200	2 200	2 200
University funding	1 470	1 470	1 470	1 470	1 470
Hospital funding	1 600	1 600	1 600	2 000	2 000
Vinnova (GMS)	900				
User fees	1 600	2 000	2 200	2 500	2 800
Sum revenues (kSEK):	7 770	7 270	7 470	8 170	8 470

Table 1. Current budget (2020) and suggested budget 2021–2024.
[1] Increased operational expenses during 2020 are due to projects executed in collaboration with GMS.

Clinical Genomics Linköping

Basic Information

Facility director: Peter Söderkvist
Head of facility: Tobias Strid
SciLifeLab facility since: 2019
Host University: LiU
FTEs: 2
FTEs financed by SciLifeLab: 0.3

Funding 2020 (in kSEK)

SciLifeLab: 333
Total: 3033

Read more: Web page, Publication Data Base

For an overview of current technologies and services at each Clinical Genomics facility node, see Table 1 in the DD platform report.

New Technologies and Services 2021–2024

- Clinical transcriptomics (coordinating node for the DD platform)
- Methylation / Epigenetic analysis of brain tumors
- Long-read sequencing
- Ultra-sensitive detection methods on Liquid Biopsies

Background

CG Linköping was incorporated under the SciLifeLab umbrella during 2019. CG Linköping will be managed by a steering group headed by the Dean of the Medical Faculty, Linköping University (LiU), board members from the departments and representatives from the University Hospital and the industry. CG Linköping operates as a branch of the core facility within the Medical faculty, LiU, and in tight collaboration with the Genomic Medicine Center (GMC) South East to support preclinical and clinical research in Linköping. Together with the clinical NGS-platform the core facility for molecular biology will constitute the foundation of CG Linköping. CG Linköping will aid in the implementation of molecular tests of clinical relevance and provide service to researchers in Linköping, the south-east healthcare region and nationwide. CG Linköping has access to 2 Illumina MiSeq, 2 Illumina NextSeq500 and two Qiagen GeneReaders for sequencing. During 2020 we will upgrade one of the NextSeq500 to 550 to enable Illumina array reading possibilities for e.g. methylation arrays, invest in Nanopore long read sequencers and invest in a 10X single cell isolator to complement the BioRad droplet single cell isolator already in use. In a longer perspective and if demanded, CG Linköping and GMC-South East may consider to invest also in a high capacity short and long-read sequencer.

The core facility for molecular biology has been operational for more than 20 years and has offered next-generation sequencing to the Linköping research community since 2013. One bioinformatician (1 FTE) shared by LiU and the SciLifeLab Bioinformatics platform (NBIS) and placed at the core facility has been serving local scientists analyzing mainly sequencing data as well as participating in the NBIS national services. A user group (chaired by Peter Söderkvist) has been responsible for keeping the facility operational and updated. At present we do not offer end-to-end project service for on-demand projects, but this is one of the main priorities during the current transformation to a fully operational SciLifeLab CG facility node.

Plans for 2021–2024

During 2021-2024, as a CG facility node, we will extend the personnel with at least onemolecular biologist (PhD level), one biomedical scientist and a bioinformatician to be able to provide end-to-end services to clinical research projects and on demand assays, but also by offering clinically established analyses to the research community. To promote our services we will perform outreach activities, starting locally, to inform researcher and clinicians about current and upcoming services.

There is however, already an immense interest from several clinical departments to launch different sequencing projects with the aim of improving diagnosis to be included in clinical decision making. Together with the Department of Rheumatology the core facility is establishing agene panel for autoinflammatory diseases and together with Department of Surgery a gene panel for adrenal tumors. An NGS/epigenetic analysis for brain tumors is also highly demanded, since methylation profiling improves the diagnostic resolution. Transcriptome microarray and RNA-sequencing analysis on formalin fixated paraffin embedded samples, single cells and liquid biopsies are highly interesting in several cancer forms e.g. lung tumors. Rapid molecular genetic mutation analysis on needle biopsies of the thyroid using digital PCR to guide surgery is under development. The CG Linköping facility will be helpful in planning, performing and interpreting the results of offered molecular analyses.

CG Linköping will also boost molecular and genetic research in preclinical and technical science, areas of particular importance for the recent investments at LiU in the Wallenberg Center for Molecular Medicine and Center for Social and Affective Neuroscience. In addition, CG

Linköping will boost the already successful scientific and clinical collaboration between the Medical and Technical Faculties in e.g. the Center for Medical Imaging and Visualization. As the treatment strategies in healthcare becomes standardized in accordance with the activities of Regional Cancer Centers (RCC), the collaboration with the regional Biobanks and RCC is expected to intensify and increase the role for CG Linköping to facilitate the transfer and adaptation of research findings to implementation and use in the clinic.

Budget 2021-2024

Costs	2020	2021	2022	2023	2024
Personnel (2-6 FTEs) [1]	1 800	3 500	3 500	4 500	5 000
Operations [2]	200	500	700	800	1200
Premises [3]	0	0	0	0	0
Instrument depreciations [4]	420	420	420	420	420
Other	20	60	60	100	100
Sum costs (kSEK):	2 440	4 480	4 680	5 820	6 720

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	330	1 000	1 000	2 000	2 000
University funding	1 800	1 800	1 800	2 000	2 000
Vinnova (GMS)	900				
Planned grant applications	0	200	500	600	800
User fees	300	600	800	1000	1 500
Sum revenues (kSEK):	3 330	3 600	4 100	5 600	6 300

Table 1. Current budget (2020) and suggested budget 2021–2024.

[1] To be able to offer end-to-end services we expect to expand our personell to at least 6 FTEs.
[2] Approximate numbers. Reagents are currently purchased by each individual researcher. This will be transformed into a user fee during 2020.
[3] Cost for premises are currently fully financed directly by ALF-means not specified in the budget.
[4] Estimation based on current and future instrument purchase.

Clinical Genomics Lund

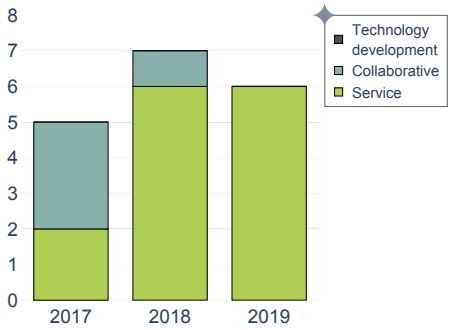
Read more: Web page, Publication Data Base

Basic Information

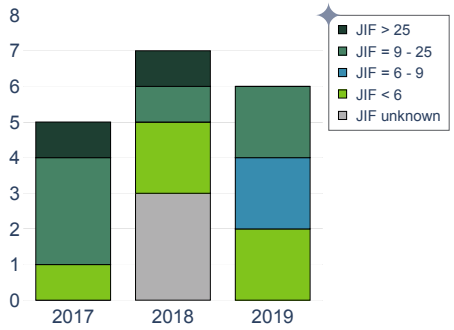
Facility director: Thoas Fioretos, Åke Borg
Head of facility: Markus Heidenblad, Ingrid Wilson
SciLifeLab facility since: 2016
Host University: LU
FTEs: 11
FTEs financed by SciLifeLab: 3

Funding 2020 (in kSEK)

SciLifeLab: 2200
Total: 11850



Publications by category



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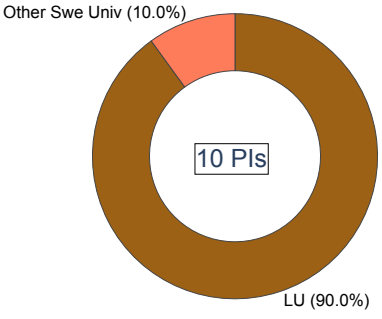

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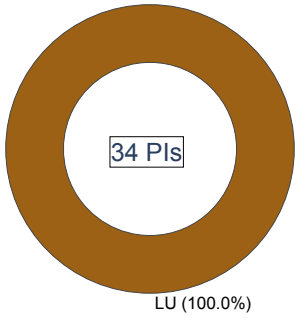

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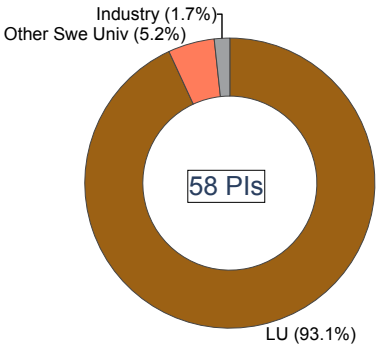


Users 2019

For an overview of current technologies and services at each Clinical Genomics facility node, see Table 1 in the DD platform report.

New Technologies and Services 2021–2024

- Clinical transcriptomics (coordinating node for the DD platform)
- Single-cell diagnostics (coordinating node for the DD platform)
- Novel long-read sequencing and ultrasensitive dignostics applications

Background

Clinical Genomics Lund (CG Lund) consists of two closely linked expert core facilities; the Center for Translational Genomics (CTG) at the Medical Faculty of Lund University and the Center for Molecular Diagnostics (CMD), part of the regional healthcare (Region Skåne). Whereas CTG focuses mainly on high-profile clinical and translational research projects, CMD is responsible for all NGS-based diagnostics for the southern healthcare region. CG Lund is governed through the respective organizations, but coordinated through largely overlapping management groups and share robotics and sequencing instruments (NovaSeq 600). Also at the operative level several key people are partly employed at the two units.

Through CTG, researchers are offered not only standard targeted and global short-read sequencing assays of bulk samples, but also front-line research methodologies, such as long-read and single-cell applications. The majority of projects are handled as service projects, but also more customized solutions can be provided, and collaborations established around strategically important projects (e.g. with potential future clinical utility or around novel promising technologies). At CMD, diagnostics has been developed for wide variety of clinical needs (e.g. non-invasive prenatal testing, and various assays for profiling of different tumor types, rare diseases, and microbes). The close link between CMD and CTG, allows a seamless translation of newly developed diagnostic assays into healthcare.

Since the start, CG Lund has processed more than 15,000 research and clinical samples (about 8,000 in 2019 alone; note that only research projects/resorces are shown in the statistics above). From the research perspective, a particular focus lies on cancer, where CG Lund was early in the implementation of research-promoting sequencing-based diagnostics (e.g. somatic WES and global RNA-seq) and in several cases based on methods translated from local research groups. An example of an ongoing strategic collaboration aims at establishing RNA-seq (expression profiling) as a diagnostic tool for improved stratification of

solid tumors and hematologic malignancies. CG Lund has also led a coordinated DD platform procurement of three NovaSeq 6000 instruments now implemented at CG nodes in Lund, Gothenburg and Stockholm, respectively. Apart from the Illumina platform, CG Lund also posesses instruments for Ion Torrent- and Oxfort Nanopore Technology-based sequencing and has recently also established a single-cell sequencing platform for research purposes. To process the massive amounts of data generated, CG Lund has established a dedicated HPC cluster at the Lund University super-computing cluster LUNARC.

Plans for 2021–2024

During 2021-2024 a number of new technologies and services will be implemented and/or translated into healthcare. Apart from implementing nationally harmonized best-practice and research-promoting diagnostics as part of the national Genomic Medicine Sweden (GMS) collaboration, where many of today's clinical assays will be replaced, CG Lund aims to participate in several collaboration pilots around important technologies for tomorrow's diagnostics. Particularly, CG Lund will focus at the implementation of clinical transcriptomics and single-cell diagnostics, respectively, where research services were offered early on and where strategically important collaborations have been established, e.g. with Åke Borg's lab around the national SCAN-B project, aimed at implementing RNA-seq as a diagnostic tool for breast cancer, and with Göran Karlsson's and Thoas Fioretos' labs around novel single-cell applications and leukemia diagnostics.

To meet the increasing demands of services and diagnostics, large efforts will be made to automate and streamline both laboratory and data processing steps further, necessitating the need to recruit new competences in automation, bioinformatics and software development. The latter will, moreover play an important role in improving variant interpretation and decision-making support tools for healthcare purposes (for clinical scientists, laboratory physicians, and clinicians) and to support research groups that are lacking bioinformatics resources. Other challenges that need to be addressed are upscaling of computation and data storage needs. In the short-term perspective, IT needs will be handled locally, but in a longer perspective - once legal and other more practical aspects around data sharing have been addressed – as a part of the national Genomics Medicine Sweden initiative.

Budget 2021–2024

The budget below is restricted to the research services for CG Lund, that is services provided through CTG. The clinical operations at CMD are fully financed through the regional healthcare system and handled separately, with an overall budget of 36 MSEK in 2019, and expected to grow in the coming years. Because several of the backbone funds for CTG (mainly from Lund University, Region Skåne and SciLifeLab) are time-bound for 1-3 years, there are large uncertainties in the long-term budget below. The budget is based on prolongation of current funding levels.

Costs	2020	2021	2022	2023	2024
Personnel (11 FTEs)	8 227	8 392	8 560	8 730	8 905
Operations	1 196	1 220	1 244	1 269	1 294
Premises	1 800	1 800	1 800	1 800	1 800
Instrument depreciations	1 781	1 768	983	203	-
OH, travel exp	2 000	2 000	2 000	2 000	2 000
Sum costs (kSEK):	15 004	15 180	14 587	14 002	13 999

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	2 200	2 200	2 200	2 200	2 200
University funding (MedFak, Lund University)	5 250	5 250	5 250	5 250	5 250
Funding FoU (Region Skåne)	2 000	2 000	2 000	2 000	2 000
Vinnova (GMS)	600				
Funding ALF for rent	1 800	1 800	1 800	1 800	1 800
User fees	2 310	2 541	2 795	3 074	3 382
Sum revenues (kSEK):	14 160	13 791	14 045	14 324	14 632

Table 1. Current budget (2020) and suggested budget 2021–2024.

Clinical Genomics Stockholm

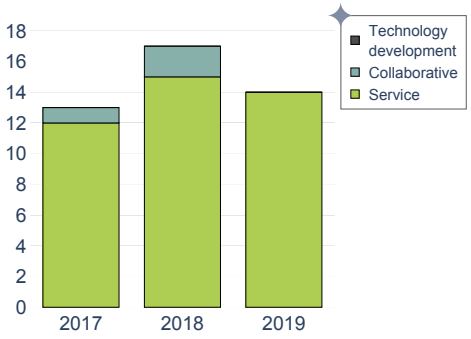
Read more: Web page, Publication Data Base

Basic Information

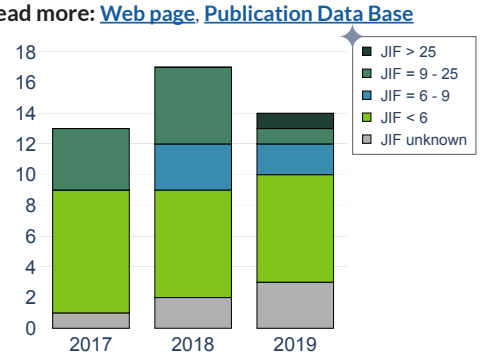
Facility director: Valtteri Wirta
Head of facility: Valtteri Wirta
SciLifeLab facility since: 2014
Host University: KI, KTH
FTEs: 30
FTEs financed by SciLifeLab: 3

Funding 2020 (in kSEK)

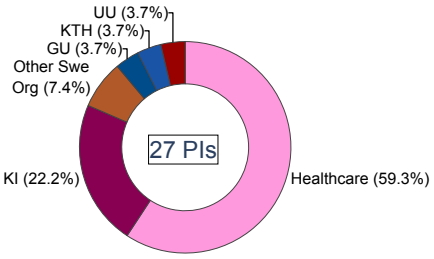
SciLifeLab: 5500
Total: 24300



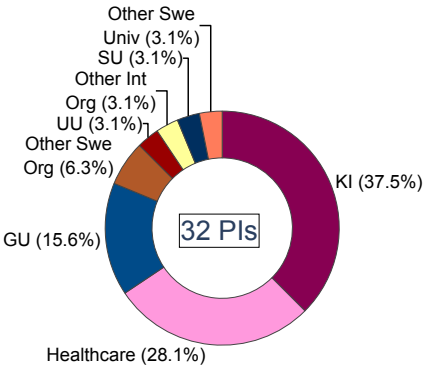
Publications by category



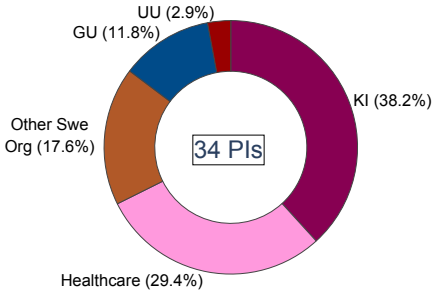
Publications by JIF



Users 2017



Users 2018



Users 2019

For an overview of current technologies and services at each Clinical Genomics facility node, see Table 1 in the DD platform report.

New Technologies and Services 2021–2024

- Single-cell sequencing
- Spatial genomics and transcriptomics (coordinating node for the DD platform)
- Long-read sequencing (coordinating node for the DD platform)

Background

Clinical Genomics Stockholm (CG Stockholm) is affiliated to KI and KTH, and is linked to the Karolinska University Hospital through Genomic Medicine Center Karolinska. The majority of the staff work on data and information management activities such as bioinformatics and software development. The laboratory engineer team has strong expertise in methods and assay development and is supported by a state-of-the-art technical infrastructure, including 3 NovaSeq 6000 sequencers, 4 large-scale liquid handling systems and an on-premise high-performance computing system with 1.5 Pb of storage. The disease focus areas include rare diseases, cancer and infectious diseases. Development projects for new assays or services are based on user needs; the driving principle of prioritisation is the broader applicability of the developed assay or service within the research and diagnostic community across Sweden.

Key achievements include the development and implementation of WGS based testing for rare disease diagnostics (one of the first large-scale implementations globally); to date more than 6,000 genomes have been analysed through this workflow. Other achievements include the implementation of WGS based microbial typing in diagnostic and surveillance settings in collaboration with healthcare and several other governmental agencies. In collaboration with several research groups, the facility has developed targeted cancer assays that are now being used in clinical trials. The majority of the analyses provided by CG Stockholm are ISO accredited according to ISO 17205 standard.

Plans for 2021–2024

CG Stockholm plans to provide new services in close collaboration with other infrastructures at SciLifeLab. The key knowhow contributed by CG Stockholm will include bioinformatics and software development to ensure usability of the results in the intended settings, including diagnostic settings. For data generation, the collaboration models may include either outsourced data generation, or collaborations on data generation using joint investments into infrastructure and recruitment of personnel to work in an embedded setting at the collaborating facility. Planned bioinformatic development work includes a move towards a systems biology approach through integration of multiple data layers, with combined DNA and RNA layers as a first

step. This approach will be valuable both for rare disease diagnostics, as well as for several cancer applications. As a next step, CG Stockholm will also be engaged in establishing capabilities for advanced data mining using AI-based approaches.

To provide ability to interrogate the repetitive part of the genome and to provide phasing between variants, CG Stockholm plans to implement *long-read sequencing/* optical mapping as a service. This work will be done in close collaboration with other CG facility nodes, the Genomics platform and expert research groups. Finally, future service plans also include establishing *single-cell assays* as well as analyses retaining the *spatial resolution* of the tissue specimen. The latter is planned in collaboration with the emerging facility for Targeted Spatial Omics.

Within the DD platform CG Stockholm provides support in large-scale sequencing (e.g., WGS), software development (e.g., Scout clinical interpretation solution, bioinformatic workflows) and wet-lab protocol development (e.g., SOP for the national cancer panel). Cross-platforms collaborations include long-term collaboration with NGI (shared sequencing infrastructure) and sequencing services to the Eukaryotic Single-Cell Facility. Towards healthcare CG Stockholm provides a unique opportunity to develop, optimize and implement NGS-based testing in diagnostic settings.

CG Stockholm has strong links to several research groups and healthcare entities in the Stockholm region. These groups are both users of the facility node and collaborators on technology development; examples of strong research environments linked to CG Stockholm include the research groups of Professor Anna Wedell (KI, expert on WGS, inherited metabolic diseases and clinical implementation of NGS), Associate professor Anna Lindstrand (KI, expert on detection of structural variation using short and long-read NGS and optical mapping), Professor Richard Rosenquist Brandell (KI, expert on hematological malignancies and clinical implementation of NGS), Assistant professor Johan Lindberg (KI, senior researcher and head of cancer genomics at MEB, expert on method development and clinical trials), Professor Jan Albert (KI, expert on HIV and clinical implementation of NGS), and Professor Christian Giske (KI, expert on antimicrobial resistance).

CG Stockholm operates a *user fee model* where projects are categorised either as 1) as a translational or clinical research project or a clinical trial where 70-80% of the costs are covered using user fees, or 2) as diagnostic projects where data is used as part of the patient's care and where a full cost pricing model is applied. The facility node is primarily funded through user fees (85%), with the proportion of user fee-based funding gradually increasing.

Budget 2021–2024

Costs	2020	2021	2022	2023	2024
Personnel (30 FTEs 2020, 34-23 FTEs 2021-2024)	24 302	28 501	24 544	20 200	20 200
Operations	29 448	24 000	24 000	24 000	24 000
Premises	3 249	3 249	3 249	3 249	3 249
Instrument depreciations	5 750	5 000	1 600	600	500
Other	-	-	-	-	-
Sum costs (kSEK):	62 749	60 750	53 393	48 049	47 949

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	5 500	5 500	5 500	5 500	5 500
SciLifeLab (instrument)	1 000	1 000			
University funding	2 750	2 750			
Region Stockholm	5 000	5 000	5 000	5 000	5 000
Norwegian Research Council	900				
Vinnova (GMS)	2 500	600			
Barncancerfonden	900				
Planned grant applications		3 000	2 000	2 000	2 000
Surplus distributed over five years (total 23700 kSEK)	9 750	8 000	4 850	600	500
User fees	35 000	36 000	36 000	35 000	35 000
Sum revenues (kSEK):	63 300	61 850	53 350	48 100	48 000

Table 1. Current budget (2020) and suggested budget 2021–2024.

Clinical Genomics Umeå

Basic Information

Facility director: Richard Palmqvist
Head of facility: Per Larsson
SciLifeLab facility since: 2019
Host University: UmU
FTEs: 3.5
FTEs financed by SciLifeLab: 0.3

Funding 2020 (in kSEK)

SciLifeLab: 333
Total: 3524

Read more: Web page, Publication Data Base

For an overview of current technologies and services at each Clinical Genomics facility node, see Table 1 in the DD platform report.

New Technologies and Services 2021–2024

- Novel diagnostic areas (microbiology and immunology).
- Broader screening tests for cancer and inherited diseases, incorporating new diagnostic markers.
- Ultrasensitive mutation detection methods for liquid biopsies of cell-free DNA.
- Long read sequencing for rare diseases (coordinating node for the DD platform).

Background

Clinical Genomics Umeå (CG Umeå) is a joint venture between Umeå University and clinical laboratories at Umeå University Hospital. It operates in a tight collaboration with Genomic Medicine Center North and is an integrated part of the Department of Medical Biosciences, Umeå University. As CG Umeå is a new entity with a steering group representing the university, the hospital and industry the organization and founding of the facility still is a work in progress. The department of Medical Biosciences, Umeå University and the cliniclal laboratories for molecular biology and sequencing at Umeå University Hospital has, however, collaborated tightly for more than 20 years.

CG Umeå offers NGS sequencing on an Illumina MiSeq or NextSeq 550, single cell sequencing with the Nanopore system and microarray analyses on the Illumina platform. Further, instrumentation for Sanger sequencing, digital droplet PCR (BioRad) and real time PCR (BioRad), as well as QuantStudio 6 Flex Real-Time PCR (ThermoScientific), multiplex microscope, are available for preclinical and clinical research. Until now the facility has operated as a network of collaborating research groups and laboratory medicine at the University Hospital rather than a core facility.

The collaboration between Umeå University and Umeå University Hospital has been vital for adapting and implementing telomer length analysis and four NGS panels including one for fusion gene analysis in clinical routine. During 2017-2019 the number of clinical samples analyzed with tests implemented in collaboration with the university has increased from approximately 400 to approximately 1400 in 2019. All tests developed for clinical use are offered as a service to researchers and the facility is involved in several clinical trials.

Plans for 2021–2024

New services are planned in close collaboration with researchers and other infrastructures at SciLifeLab where possible. The collaboration models may include nationwide research projects or outsourced data generation to the collaborating facility to optimize use of costly equipment. Investments into a dedicated infrastructure will only be made if the sample volumes reach sufficient levels or if there are other strong reasons, such as turnaround time or accreditation. Within the time period we foresee a need to expand our ability for single-cell sequencing as well as to be able to provide long-read sequencing at the facility.

The facility has ongoing discussion together with the sections Clinical Microbiology and Clinical Immunology at Umeå University Hospital regarding how to integrate these diagnostic areas in CG Umeå.

To meet the increasing numbers of analysis there is a strong need to further automate both lab and data processing steps. Apart from the challenges this puts on the laboratory this is a necessary endeavor in the work with simplifying the process in which we can offer end-to-end support to researchers. Large-scale sequencing projects where we primarily can offer preanalytic, bioinformatic and clinical support are planned to be performed in collaboration with other SciLifeLab infrastructures.

For service projects to researchers, user fees include reagent costs and salaries for experimental work and bioinformatics. The overhead is normally 21%. For development of diagnostic tests for healthcare, the funding is project-based and need to be discussed with Umeå University Hospital to ensure funding for further technology development needs.

Building 6M at Umeå University strategically accommodates the laboratories for Clinical genetics, Clinical pathology,

Microbiology and Clinical chemistry at Umeå University Hospital, and more than 20 translational research groups at Umeå University. The focus of their scientific research is genetic diseases, microbiology, neurological diseases and viruses. Examples of research groups at Umeå University and Umeå University hospital include: Professor P Andersen (expert on amyotrophic lateral sclerosis), professor T Brännström (expert on amyotrophic lateral sclerosis and brain tumors), associate professor I Golovleva (expert in genetics and hereditary eye diseases), associate professor F Aguilo (expert in stem cell biology, epigenetics and epitranscriptomics), associate professor M Hultdin (expert on hematology and telomere related diseases), associate professor S Degerman (expert on epigenetics and telomere biology in hematological malignancies), associate professor M Johansson (expert in oncology and cancer research), professor R Palmqvist (expert in pathology and cancer research), Professon M Landsröm (expert in pathology and cancer research), Professor A Sjöstedt (expert in microbiology).

Budget 2021–2024

Costs	2020	2021	2022	2023	2024
Personnel (3.5-5 FTEs)	2 394	2 394	3 420	3 420	3 420
Operations	200	300	400	500	800
Premises [1]	-	-	-		
Instrument depreciations	400	400	400	400	400
Sum costs (kSEK):	2 994	3 094	4 220	4 320	4 620

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	330	1 000	1 000	2 000	2 000
University funding [2]					
Region Västerbotten to development group at Laboratoriemedicin	2 394	2 394	2 394	2 394	2 394
Vinnova (GMS)	800				
User fees	200	200	300	300	300
Sum revenues (kSEK):	3 724	3 594	3 694	4 694	4 694

Table 1. Current budget (2020) and suggested budget 2021–2024.
[1] Premises so far paid by ALF but is under discussion
[2] Under discussion

Clinical Genomics Uppsala

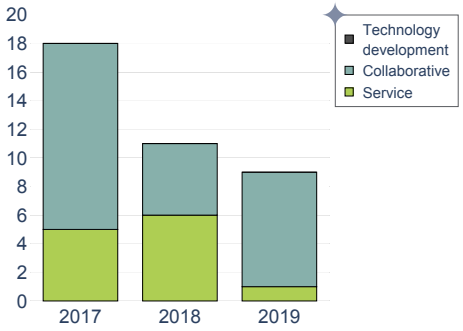
Basic Information

Facility director: Lucia Cavelier
Head of facility: Malin Melin
SciLifeLab facility since: 2014
Host University: UU
FTEs: 14.9
FTEs financed by SciLifeLab: 4.7

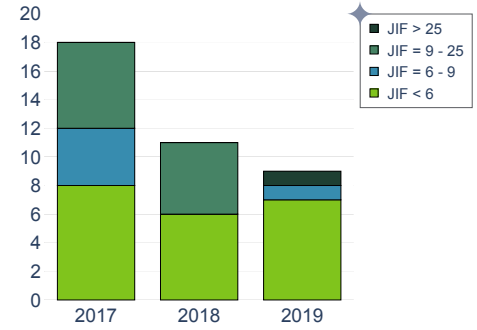
Funding 2020 (in kSEK)

SciLifeLab: 2700
Total: 13858

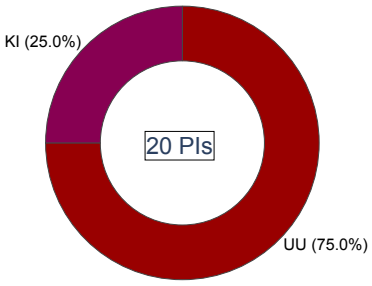
Read more: Web page, Publication Data Base



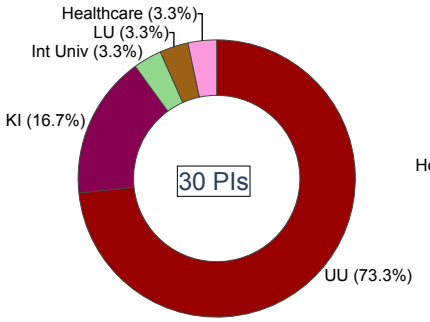
Publications by category



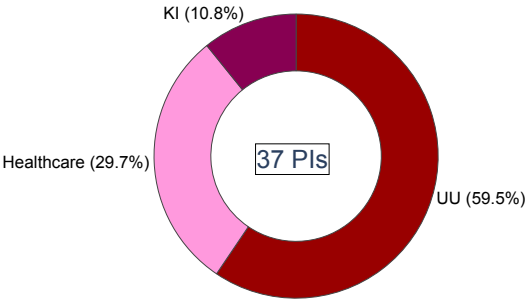
Publications by JIF



Users 2017



Users 2018



Users 2019

For an overview of current technologies and services at each Clinical Genomics facility node, see Table 1 in the Diagnostics Development platform report.

New Technologies and Services 2021–2024

- Novel methods and applications of ultrasensitive detection (coordinating node for the DD platform)
- Novel cancer applications of long-read sequencing (coordinating node for the DD platform)
- Novel diagnostic areas (microbiology, immunology and pharmacogenomics)
- Single cell and spatial sequencing/characterization

Background

Clinical Genomics Uppsala (CG Uppsala) is jointly set up by Uppsala University, Uppsala University Hospital and SciLifeLab, with a steering group representing all parties. CG Uppsala is fully integrated with the sections Clinical Genetics and Clinical Pathology at the hospital. This setup provides several synergies in terms of efficient utilization of competence, instruments and localities. Our team includes molecular biologists, bioinformaticians, clinical molecular geneticists and medical doctors, thus combining technical and clinical expertise. We provide researchers with access to a range of clinically validated molecular analyses within our current focus areas solid tumors, hematology and rare diseases. We also develop diagnostic tests as a service to healthcare, and have so far implemented 32 different clinical tests into routine diagnostics. We were for example among the first in the world to establish a clinical test based on long-read sequencing in 2015. We have a wide range of state-of-the-art instruments, including 4 Illumina MiSeq, 3 Illumina NextSeq, NanoString nCounter, BioRad digital PCR and 2 liquid handlers. We collaborate with the National Genomics Infrastructure for access to Illumina NovaSeq 6000, 10X Genomics, PacBio and Oxford Nanopore instruments. We operate our own secure calculation cluster and integration with hospital IT ensures that all clinical samples are handled in accordance with clinical requirements.

Key acheivements of CG Uppsala during 2017-2019 include:

- Analysis of 1,335 R&D samples in 2019 (65% increase since 2016)
- Analysis of 3,007 clinical samples in 2019 (105% increase since 2016)
- Increase in user fees with 152% comparing 2016 to 2019
- Engagement in several major service and collaborative projects with researchers and industry (e.g. Bristol-Myers Squibb, Incyte)

Plans for 2021–2024

Services. CG Uppsala has established liquid biopsies and digital PCR for ultrasensitive variant detection, and we plan to complement with super rolling circle based detection and ultradeep sequencing. Applications include analysis of

cell-free DNA for early detection of relapse and longitudinal analysis of cancer variants. We will also evaluate the clinical utility of long-read sequencing for characterization of cancer genomes, in collaboration with the Genomics platform. Further plans are to expand our operations to microbiology, immunology and pharmacology, where there is an imminent need for new services and diagnostic tests. Pilot projects include microbial whole-genome sequencing, with focus on fungal genomes, detection of resistance mutations in RNA viral genomes and analysis of fetal RH in maternal blood using digital PCR. We also continuously develop new cost efficient gene panels for different types of sporadic and hereditary cancer and broad screening tests for both cancer and inherited disorders. In concert with the DD platform, we will evaluate clinical applications of single-cell and spatial sequencing in hematology and solid tumours.

Capabilities. CG Uppsala will participate in the development of the Clinical trial support and Clinical proteomics capabilities at the DD platform. We already contribute to clinical studies (e.g. NMDSG14B, MEGALiT and SCANALL), and will increase our collaboration with the Clinical Research and Development Unit at Uppsala University Hospital. Furthermore, we will have a major role in the integration of clinical data to quality registries in collaboration with the Regional Cancer Centers.

Collaborations. CG Uppsala frequently engages in collaborative projects with researchers, SciLifeLab platforms and industry, which provide opportunities for advanced method development and novel services for the Swedish research community. Research collaborations include: Assoc. prof. Lucia Cavelier (UU), Assoc. prof. Johan Botling and Prof. Marie-Louise Bondeson (UU), experts on clinical diagnostics and clinical implementation of our current three focus disease areas hematology, solid tumors and inherited disease, Prof. Eva Hellström-Lindberg (KI) and Dr. Panagiotis Baliakas (UU), experts on myelodysplastic syndrome and hereditary hematological malignancies, respectively, Prof. Ulf Landegren (UU), expert on development of novel innovative methods and Prof. Lars Feuk (UU), expert on long-read sequencing methods.

User fees. For service projects to researchers, user fees include reagent costs and salaries for experimental work and bioinformatics. For development of diagnostic tests for healthcare, CG Uppsala gets 10% of the income later received by the clinics when running these tests. This funding is used for further technology development.

Budget 2021–2024

The presented budget includes cost and revenue both at the university and the hospital. In addition, premises and instrumentation are partly funded by the hospital (not included in table). The SciLifeLab funding is set to the current level, however the distribution of the DD platform funding is yet to be decided.

Costs at Uppsala University	2020	2021	2022	2023	2024
Personnel (10.3 FTEs 2020, 11-13 FTEs 2021-2024)	10 200	11 200	11 400	12 400	12 700
Operations	5 100	5 300	5 400	5 500	5 600
Premises	230	230	240	240	250
Instrument depreciations	500	500	500	500	500
Sum costs (kSEK):	16 030	17 230	17 540	18 640	19 050
Costs at Uppsala University hospital (4.6 FTE)	4 300	4 800	4 900	5 000	5 100
Total sum costs	20 330	22 030	22 440	23 640	24 150

Revenues at Uppsala University	2020	2021	2022	2023	2024
SciLifeLab funding	2 700	2 700	2 700	2 700	2 700
SciLifeLab SFO	500	500	500	500	500
SciLifeLab TDP	1 212	-	-	-	-
ALF infrastructure	3 000	3 000	3 000	3 000	3 000
Funding for depreciations (ALF and other sources)	500	500	500	500	500
Vinnova (GMS)	781	-	-	-	-
Vinnova (ultasensitive detection project)	600	-	-	-	-
Funding for service costs	65	65	65	65	65
Planned grant applications	-	2 000	2 000	2 000	2 000
User fees	6 500	7 100	7 800	8 500	9 300
Surplus distributed over five years (total 4000 kSEK)	200	1 400	1 000	1 400	-
Sum revenues (kSEK):	16 058	17 265	17 565	18 665	18 065
Revenues at Uppsala University hospital	4 300	4 800	4 900	5 000	5 100
Total sum revenues (kSEK):	20 358	22 065	22 465	23 665	23 165

Table 1. Current budget (2020) and suggested budget 2021–2024.

Clinical Genomics Örebro

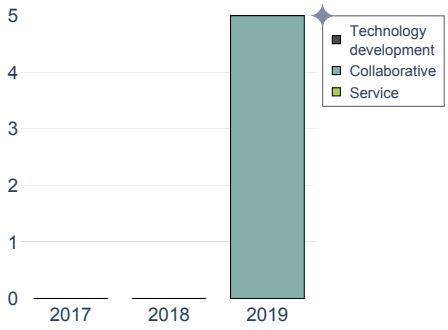
Read more: Web page, Publication Data Base

Basic Information

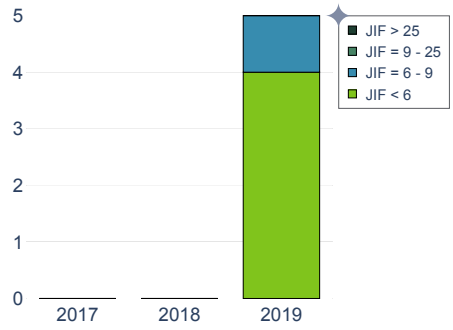
Facility director: Gisela Helenius
Head of facility: Bianca Stenmark
SciLifeLab facility since: 2019
Host University: ÖRU
FTEs: 5
FTEs financed by SciLifeLab: 0.3

Funding 2020 (in kSEK)

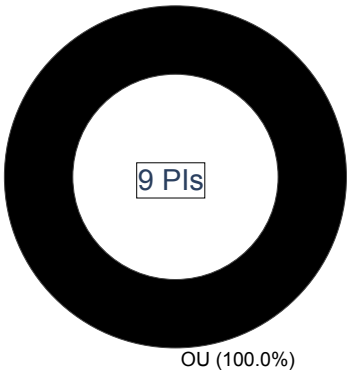
SciLifeLab: 333
Total: 10139



Publications by category



Publications by JIF



Users 2019

For an overview of current technologies and services at each Clinical Genomics facility node, see Table 1 in the DD platform report.

New Technologies and Services 2021–2024

- Rapid typing and characterization of microbial genomes with long-read sequencing (coordinating node for the DD platform)
- Shotgun metagenomics short-read/long-read sequencing

Background

Organization

Clinical Genomics Örebro (CG Örebro) is a collaborative effort between Region Örebro län and Örebro University. From Region Örebro län, the Department of Laboratory Medicine and Clinical Research Centre contribute to the facility node. The Clinical Research Centre includes the Clinical Research Laboratory, which supports clinical/translational researchers and constitutes an important part of CG Örebro with shared personnel. CG Örebro is physically located at the Department of Laboratory Medicine at the University Hospital Örebro, but belongs formally to the School of Medical Sciences, which provides strong bioinformatics expertise linked to the facility. Molecular biologists, lab technicians and bioinformaticians from all the contributing partners will be working in the facility node.

CG Örebro has organized its services around the focus areas cancer, rare diseases, complex diseases and infectious diseases. The facility node has long experience and expertise in molecular characterization of microbes, both for clinical use and research. Additionally, sequence-based molecular diagnosis for pathology is used in clinical routine since several years. In the coming years, the facility node will, together with local research groups, serve several projects regarding complex diseases, such as inflammatory bowel diseases.

Current technologies/services offered

CG Örebro is integrated in the molecular diagnostics lab at the Department of Laboratory Medicine where sequencing is performed on the Illumina (NextSeq and MiSeq), Thermo Fisher (Ion S5 Prime) and Oxford Nanopore (MinION) platforms. Various systems for automated library preparations and QC are available as well as storage and software infrastructure for bioinformatics analysis.

Outreach

An outreach afternoon will be held on the 31st of March 2020 were researchers at Örebro University and University Hospital Örebro will be invited to a symposium presenting the new facility node in Örebro.

Plans for 2021–2024

New technologies/services

CG Örebro will continue to focus on new technologies for microbial whole-genome sequencing such as typing, resistance identification, surveillance, and epidemiological typing. Future plans include shotgun metagenomics with both long-read and short-read sequencing as culture-independent techniques for concomitant detection and typing of microbial pathogens, e.g. in patients with sepsis, sexually transmitted infections and prosthetic joint infections. Long-read sequencing techniques will also be used to provide services to investigate the relationship between the bacterial genome, transcriptome and methylome.

Associated research groups

CG Örebro collaborates with several research groups that contribute to the development of the facilty. Examples of research groups at Örebro University and Örebro University Hospital include: Assoc Prof Magnus Unemo, director of the WHO Collaborating Centre for Gonorrhoea and other sexually transmitted infections. Professor Dirk Repsilber (Örebro University), expert in functional bioinformatics. Assoc Prof Paula Mölling, expert in *Neisseria meningitidis* and sepsis. Professor Bo Söderquist, expert in staphylococci and prosthetic joint infections. Assoc Prof Torbjörn Norén, expert in *Clostridioides difficile*. Professor Mats G Karlsson, expert in pathology and cancer research. Assoc Prof Gisela Helenius, expert in circulating biomarkers for cancer. Assoc Prof Gabriella Lillsunde-Larsson, expert in human papilloma virus induced cancer. Professor Ola Nilsson, expert in rare pediatric endocrine disorders.

User fee model

For academic or healthcare research projects, we are adapting to the model for user fees that is used in Region Örebro län. The user fee is based on time for project meetings and laboratory work together with costs for materials and reagents. For industrial research projects, full cost mode will be applied. Projects for implementation into clinical molecular diagnostics are covered by the Department of Laboratory Medicine.

Budget 2021–2024

Costs	2020	2021	2022	2023	2024
Personnel (5 FTEs 2020, 6-7 FTEs 2021-2024)	4 000	4 800	4 800	5 600	5 600
Operations	750	1 000	1 100	1 200	1 300
Premises	1 339	1 339	1 339	1 339	1 339
Instrument depreciations	1 120	1 120	1 120	1 120	1 120
Sum costs (kSEK):	7 209	8 259	8 359	9 259	9 359

Revenues	2020	2021	2022	2023	2024
SciLifeLab funding	330	1 000	1 000	2 000	2 000
University funding	400	400	400	400	400
ALF (instrument)	2 200	500	500	500	500
Region funding Region Örebro län Laboratory Medicine	5 609	5 859	5 959	6 059	6 159
Region funding Region Örebro län Clinical Research Centre	800	800	800	800	800
Vinnova (GMS)	800				
User fees	1 000	1 100	1 200	1 300	1 400
Sum revenues (kSEK):	11 139	9 659	9 859	11 059	11 259

Table 1. Current budget (2020) and suggested budget 2021–2024.

Drug Discovery and Development Platform

Basic information

Platform Director: Per Arvidsson

Co-Platform Director: Kristian Sandberg

Platform Vision:

To be an essential part of the Swedish innovation infrastructure by providing high quality drug discovery programs that are globally competitive for funding and clinical development

Platform Mission:

- Turn Academic Discoveries into Innovations
- Provide technologies and training for state-of-the-art Drug Discovery & Development

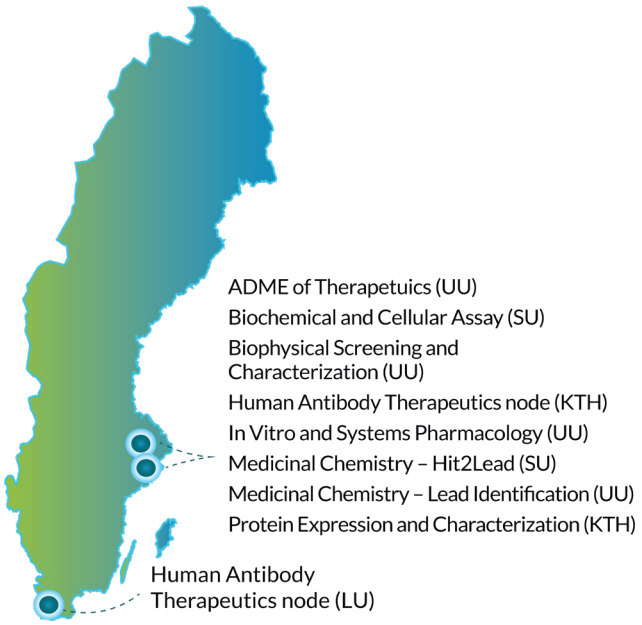
SciLifeLab Platform since: 2014

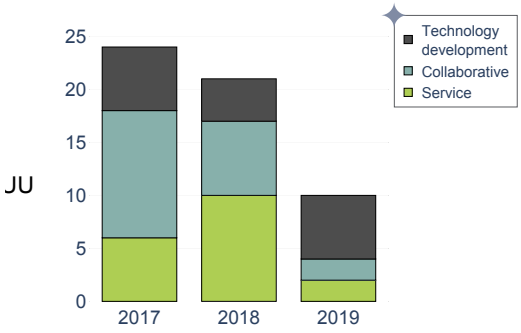
Host Universities: KI, KTH, LU, SU, UU

FTEs: 42

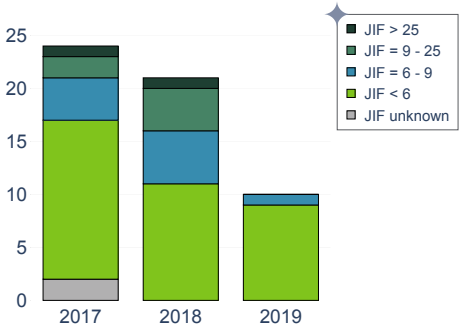
FTEs financed by SciLifeLab: 41

Geographical location of facilities

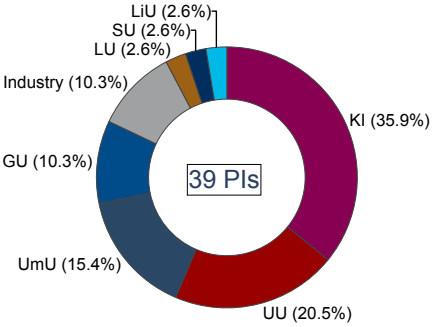




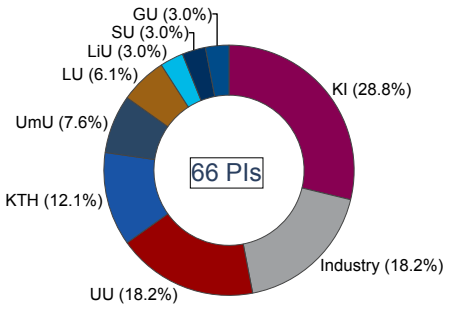
Publications by category



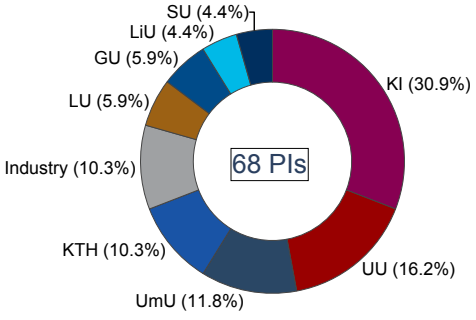
Publications by JIF



Users 2017



Users 2018



Users 2019

Read more: Web page, Publication Data Base

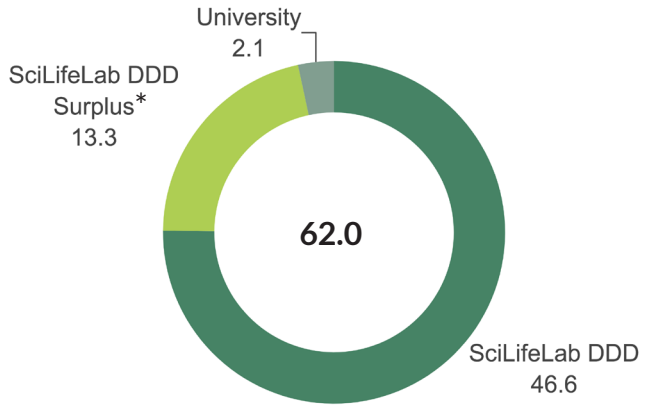
SciLifeLab funding 2020

Platform	(MSEK)
Drug Discovery and Development	46.6
Total SciLifeLab funding	**46.6**

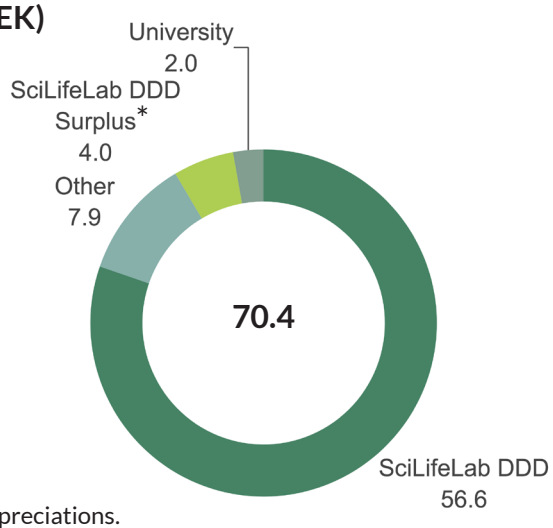
Suggested annual SciLifeLab funding 2021-2024

Platform	(MSEK)
Drug Discovery and Development	56.6
Total SciLifeLab funding	**56.6**

Total funding 2020 (MSEK)



Total suggested annual funding 2021-2024 (MSEK)



* Revenues from surplus accumulated 2013/2014 are fixed to ongoing depreciations.

Background

The SciLifeLab Drug Discovery and Development (DDD) Platform was established within SciLifeLab through a strategic Swedish governmental initiative in 2013. Earmarked funds were allocated to establish a national platform for supporting academic research projects with a potential to result in new therapeutics (Research and Innovation bill 2012/13:30 and 2016/17:50). DDD offers industry-standard infrastructure, service, and expertise to progress academic discoveries towards pre-clinical proof-of concept, followed by guidance for further development. The dedicated DDD funding reflects the government´s ambition that Sweden should remain a leading life science nation, building on a proud history of collaboration between industry and academia, which resulted in companies like AstraZeneca, Pharmacia, and others. Given the global shifts in research strategy seen in major pharmaceutical companies with decreased investment on internal R&D efforts, academic researchers need to be more actively engaged in the discovery of novel therapeutics. The governmental DDD investment should be seen as a way to narrow the gap in the well-known "Valley of Death" by making drug discovery programs more attractive for the seed funding and private capital required to initiate development of new medicines.

Hence, the mission for DDD is to be instrumental in successfully turning academic findings into early drug development programs through providing an environment for scientific collaborations of the highest international standard, competence, and advanced infrastructure in the area of drug discovery. Two major specific objectives are:

1. To provide industry standard drug discovery services to academic scientists in Sweden that allows their programs to be globally competitive for further (clinical) development.
2. To provide education, training, and expertise in drug discovery to academic scientists and actors in the Swedish innovation system.

Currently, the DDD platform is staffed by >40 researchers with industrial experience and engage 10 university professors in the management team. DDD offers integrated drug discovery support primarily to Swedish academia. An external steering group carefully reviews programs entering the platform and monitors progression biannually. Upon approval for entering the DDD platform, the staff works together with the principal investigator (PI) to add industrial drug discovery quality and expertise to the programs. Importantly, also projects that are not accepted are given valuable feedback through the process that raises awareness of the requirement needed for a competitive drug discovery program. DDD is versatile and has broad competence in that the drug-leads that we work with can be either small molecule drugs, human antibodies or new modality approaches for therapy. In accordance with the Swedish teacher´s exemption law (or Professor´s privilege law), the academic scientist retains all intellectual property rights and ownership of discoveries made during this process. Carefully set exit criteria and collaboration with the universities' innovation offices pave the way for spinouts, or partnerships with established pharma or biotech companies. Comprehensive descriptions

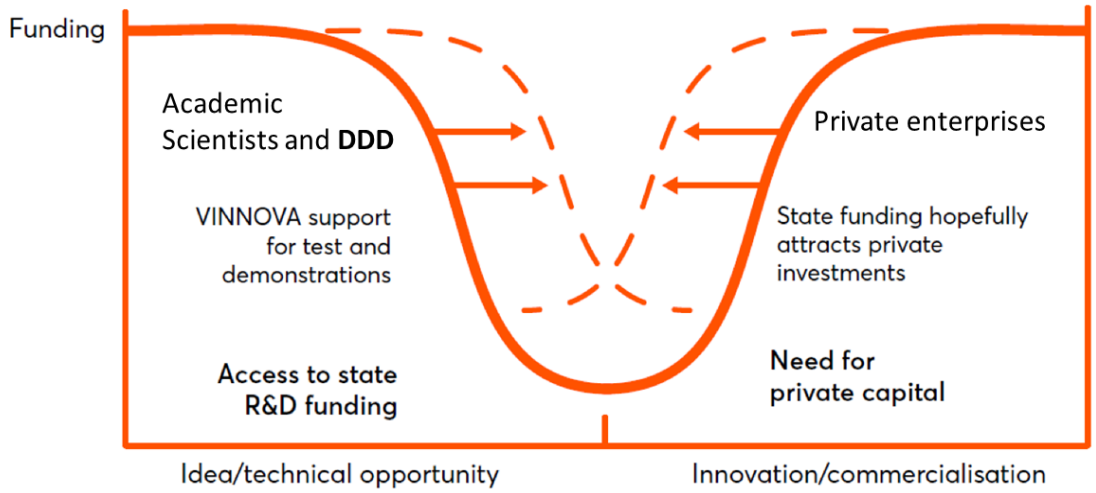


Figure 1. Positioning of DDD to bridge the gap of the "Valley of Death". Figure adapted from Arntzeb et al. Testing innovation in the real world – real-world testbeds. 2019

of the rationale for creating a national drug discovery infrastructure and the special considerations needed in the Swedish innovation landscape can be found in Drug Discovery Today and Future Science.

DDD was formed to reflect the fact that drug discovery programs are interdisciplinary and require multiple competences that work together *simultaneously* in collaboration with the PI to progress a drug discovery program. That means that the whole platform is regarded as one unit to deliver on the core activities, and that the SciLifeLab concept of individual facilities is misleading for the DDD operation. Nevertheless, nine facilities, distributed to five universities, offer services with the following expertise that covers much of the spectrum of capabilities required to take academic discoveries to commercial drug development starts.

- Protein Expression and Characterization (PEC), KTH Royal Institute of Technology - producing recombinant proteins and engineered cells in transient systems
- Human Antibody Therapeutics (HAT), KTH Royal Institute of Technology and Lund University – selections from five in-house generated phage-display libraries SciLifeLibs 1-5; and DNA Encoded Chemical Libraries (DECL)
- Biochemical and Cellular Assays (BCA), Stockholm University - with the responsibility to set up and run primary assays for the projects
- Two facilities for medicinal, combinatorial and computational chemistry (MCH2L and MCLI), Stockholm University and Uppsala University

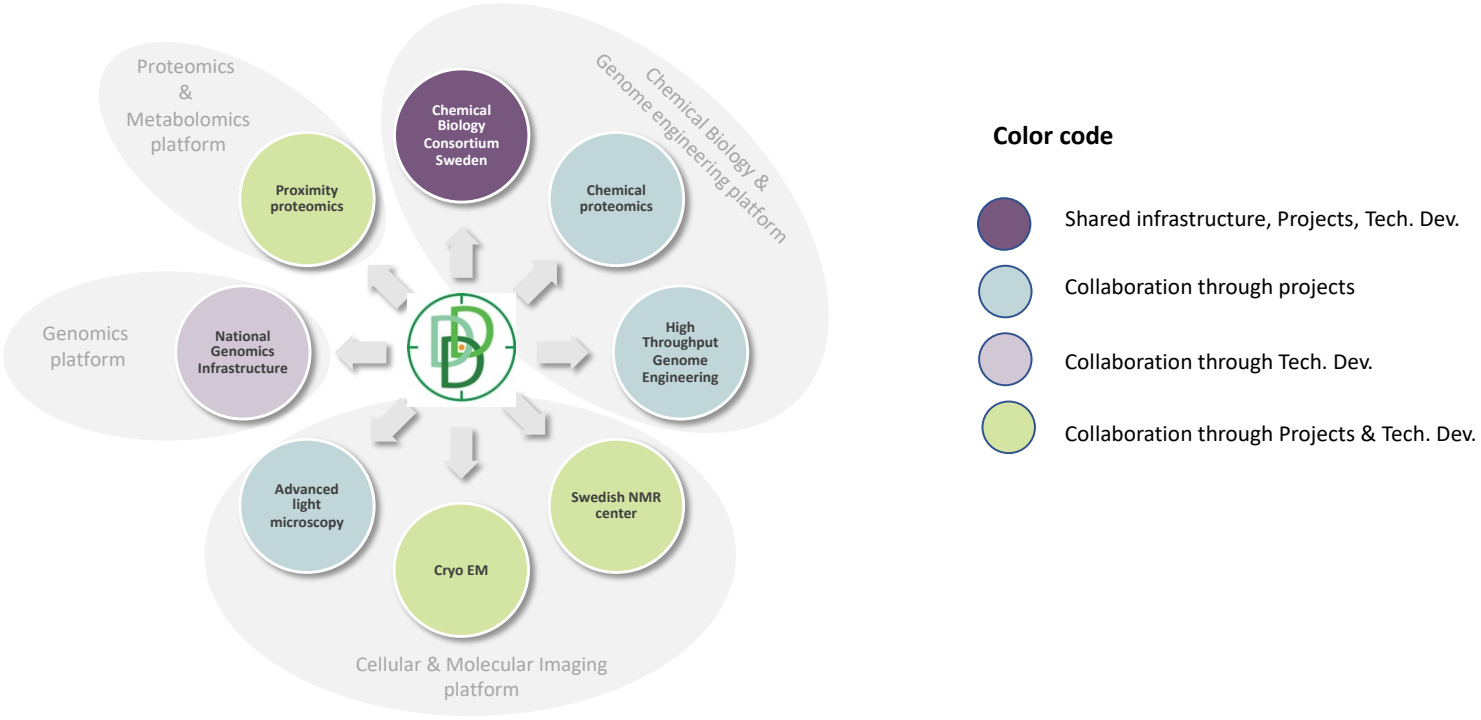


Figure 2. DDD centric illustration of interactions with SciLifeLab facilities. Collaborations with facilities in other platforms are normally mediated via the project owner, but increasingly via technology development projects. Collaborations with SciLifeLab faculty and SciLifeLab Operations Office and Data Center are even more abundant but is not shown.

Year	Programs*	First meetings	Proposals that are rejected by steering group	Programs returned to explorative research	Programs partnered for commercial development
2014	4	47	1	0	0
2015	10	60	0	0	1
2016	17	56	0	0	3
2017	17	26	2	3	1
2018	18	43	2	3	2
2019	16	31	1	3	2

Table 1. Evolution of the project portfolio at DDD for 2014-2019. *Number of active programs December 31, 2019.

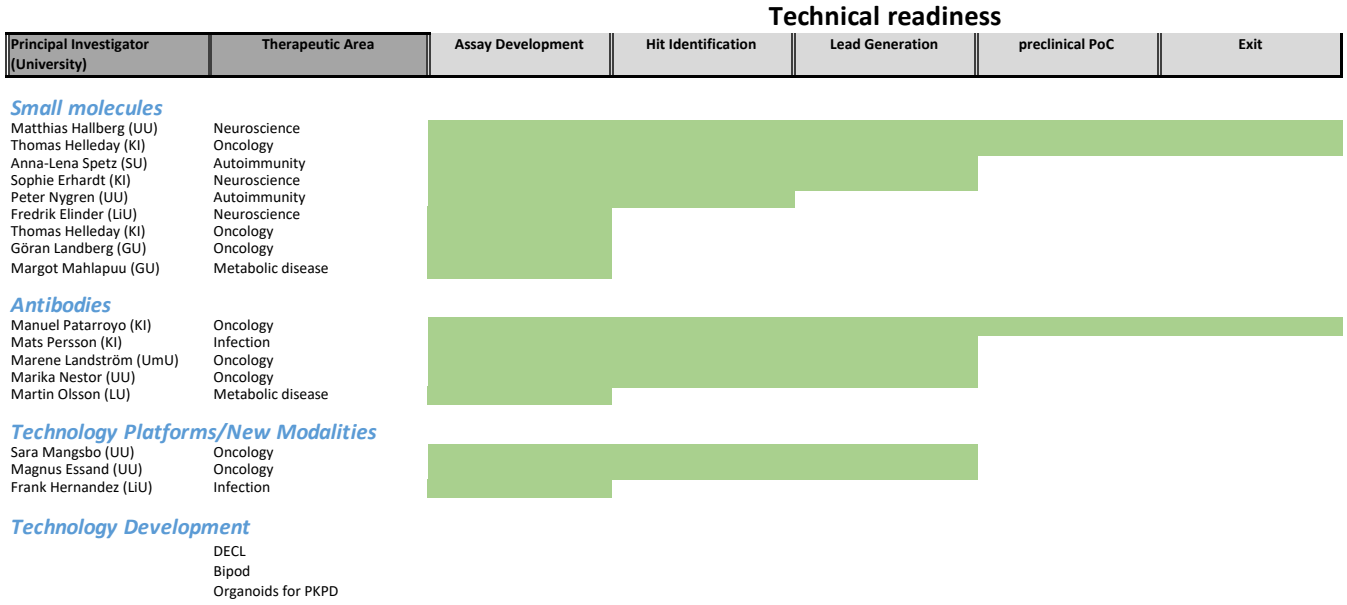


Figure 3. Current DDD portfolio divided into small molecule-, antibodies-, new modalities-, and internal technology development programs. In addition to these large programs, which are externally reviewed and resourced every six months, DDD annually supports some 30+ smaller projects from academia and SMEs.

- ADME of therapeutics facility, Uppsala University - supports with in vitro and in vivo data on drug metabolism, pharmacokinetics and pharmacodynamics, including also PKPD and PBPK modelling
- In Vitro and Systems Pharmacology (IVSP), Uppsala University - gives access to clinical material, mechanism of action studies and identification of putative pharmacodynamic biomarkers
- Biophysical Screening and Characterization (BSC), Uppsala University - supports with biophysical and structural studies to demonstrate and understand ligand to target interactions
- Target Product Profiling and Drug Safety Assessment (TPP&DSA), Karolinska Institutet and Uppsala University - runs the DDD office; gives support to users of the platform to prepare their projects before entrance to and exit from DDD; and provide design support for pharmacological studies in vivo to secure that data of relevance to investors and industry is captured from these studies

Compound management of DDD synthesized small molecules, preparation of assay ready plates, and the SciLifeLab compound collection are accessed through the Compound Center (CC) operated by the Chemical Biology Consortium Sweden (CBCS) facility within the CBGE platform.

Additional capabilities that are utilized less often are accessed from other SciLifeLab facilities, academic labs outside of SciLifeLab, CROs or international infrastructures. Recent examples on how DDD interacts with SciLifeLab resources is illustrated in Figure 2, e.g. use of the Swedish NMR center for fragment screening, Cryo EM-mediated structural determination of membrane receptors, Hydrogen-Deuterium Exchange Mass Spectrometry (HDX-MS) by the Chemical Proteomics facility for epitope mapping, and joint projects and sharing of infrastructure with the CBCS facility, etc. Increased cross-platform research collaborations are taking place through central SciLifeLab funding through Research Community Programs (RCPs) and Technology Development Programs (TDPs) (*vide supra*).

Since the start in 2014, DDD has established an efficient, but slim, organization with a critical mass to provide support in-line with the tasks given by the government. DDD is now recognized as a key resource for the Swedish life science ecosystem, and the organization, competence, and capabilities are attracting increased attention from

industrial and academic stakeholders around the globe. From a national Swedish perspective, this investment has been productive at *Turning academic discoveries into innovations*, as illustrated in Table 1. After five years of operation, >250 potential drug discovery projects have been evaluated with an admission rate of 10-15%; two programs have reached phase 1 clinical studies; three programs have been licensed by international pharmaceutical companies, and four programs have contributed to the foundation of new Swedish companies. DDD supported programs are also more competitive in grant applications for translational science/innovation, e.g. Swelife and Innovation verification grants.

DDD currently supports a portfolio of 17 programs and runs three technology development projects (Figure 3). All projects represent "first in class" drug entities and some projects have the potential of developing into new platform technologies for drug discovery. Two projects have recently been described at the SciLifeLab website; example 1 & example 2. In addition, flexible use of platform resources enables support to >30 small service projects (e.g. in vitro ADME profiling of compounds, in vitro systems profiling, SPR-analysis, access to instruments and training, etc.).

Technologies for state-of-the-art drug discovery

As an example of the objective "*Provide technologies and training for state-of-the-art drug discovery and development in Sweden*", DDD has expanded its offerings and has, in addition to small molecules and antibody therapeutics, supported cell therapy and vaccination approaches. Currently DDD runs three "new modalities" programs: a bispecific antibody program; a CAR-T program and; an oligonucleotide targeting technology. An important aspect is that the expertise available within the PI-team joins forces with the drug discovery expertise at DDD, thereby resources complement each other.

The portfolio also harbours three larger internal technology development projects that are run together with other SciLifeLab facilities and external PI's – outlined in more detail in the "Plans for Technology Development" section below.

Benchmarking of DDD

Globally, a recent publication highlighted DDD as one of thirteen academic drug discovery centers with competence and capacity to move drug discovery to the clinic. The placement within the larger SciLifeLab infrastructure and environment was seen as unique as it offers programs access to complementary technologies. It should be noted that DDD´s role models for "academic" drug discovery centers such as LifeArc (the former MRCT) UK; Cancer Research UK; Lead Discovery Center at the Max Planck Society, Germany; Scripps Institute; Broad Institute, and others in the US, have vastly different prerequisites for holding and negotiating intellectual property rights than what is presently possible in Sweden (see reference 1 for a detailed discussion).

From an international perspective of related activities, DDD has four important features:

- DDD is a translational drug discovery center, *not* a HTS / screening center
- DDD works with small molecules, biologics as well as cell therapies
- Focus is on pharmacological effect of drugs (PK/PD)
- The operation is run under the unique Swedish professor´s privilege law

The SciLifeLab International Advisory Board (IAB) made a detailed evaluation of DDD in 2019, and concluded: "*DDD is unique in Scandinavia and will certainly raise the success rate of translational programs and the impact of basic biomedical research carried out in Sweden.*"

DDD is unique in the Nordics and essential for Sweden

The user survey undertaken by DDD in 2019 clearly shows that nothing similar to DDD exists in Sweden or in the other Nordic countries. A combination of different national and international CROs could offer some of the technical services offered by DDD, but the use of CROs is not an option for academic researchers at this early stage of development for two reasons: 1) prohibitively large costs and; 2) knowledge about what services to request. Many PI's, and innovation offices, lack an insight about required studies (what to do and when). This in turn leads to suboptimal use of governmental "innovation" grants, and projects spun-out as new start-ups without enough relevant data to attract funding and/or partnerships. DDD generated data-packages are known to sustain project funding for further product development. DDD support also ensures more efficient use of scarce resources for contracting competences within contract research organizations (CROs) at the later stages of preclinical development, e.g. large-scale protein production, in vivo studies, IPR, analysis of commercial potential, valuations, etc. As illustrated in this movie, DDD is also seen as an essential technology and expertise provider for small medium sized enterprises (SMEs) acting in Sweden.

DDD has new legal proxy status

Since April 2019, DDD has secured a legal office at Uppsala University that acts as a contractual entrance point (proxy) and signing party for all operations at DDD. The SciLifeLab board and principals for the host universities supported this solution. The new contractual status of DDD allowed three industrial contracts to be signed in 2019 and allowed the infrastructure to be members of EATRIS. The ability to sign contracts is a prerequisite for most external interactions outlined below.

Plans for 2021–2024

During 2019, DDD has worked together with the DDD national steering group and the SciLifeLab management to formulate a long-term strategy for the platform. The ambition for 2021-2024 is to develop the DDD platform further as a public-public/public-private national consortium addressing major unmet therapeutic needs and as an engine to bring new drugs and new therapeutic modalities towards clinical trials. This work can be facilitated by transforming the "passive" service operation which DDD largely represents today into an organization that proactively engages to initiate dedicated drug discovery programs in academia (input) and offer access to venture capital funded or pharma-linked consortia that can bring such discoveries forward (output). DDD, as embedded within SciLifeLab, could in particular address biomarker-defined subsets of patients and thereby contribute to the precision medicine strategy of SciLifeLab. In order to provide additional steps in taking candidate molecules into clinical use, DDD could also support and facilitate studies at specific, highly advanced, in-vivo mice model centers to establish molecular mechanisms. However, most importantly, the DDD needs to stay focused on delivering high quality, drug discovery programs.

In depth interviews with stakeholders of DDD were carried out by an external expert in late 2019. The stakeholders represented PIs and other academic scientists, Technology Transfer Offices (TTOs), industry, CROs, universities, and the broader Life Science Community in Sweden. Irrespective of stakeholder, there were four common opinions about DDD:

1. DDD meets a great need. The contributions are appreciated and involvement of DDD constitutes a recognized "seal of quality" for translational projects
2. DDD is an essential part of the Swedish innovation system
3. The DDD working model enables dissemination of drug discovery concepts and procedures, secures data quality and reproducibility, and has become a joint platform for collaboration between academy, innovation systems and industry
4. DDD should continue to evolve interactions with additional actors in the life science arena to strengthen its role as a Swedish hub for drug discovery

SciLifeLab has included a budgetary request for DDD to take a more proactive role in establishing and maintaining research consortia involving external stakeholders. Hence, the overarching strategy is as follows:

- *Delivery of DDD programs must remain the core business for the platform.* DDD Programs directly support Swedish academia and build value through experimental studies and clear development plans.
- *A key deliverable for DDD is to perform pharmacological studies.* This includes design of in vivo studies, selection and bioanalysis of suitable pharmacodynamic biomarkers and modelling of pharmacokinetics and pharmacodynamics data (PKPD). This support would ideally be made accessibe to more academic scientists for the benefit of improved publications, not only to dedicated DDD programs.
- *DDD should promote closer interactions with TTOs and research funding organizations* to reinforce innovation aspects acted on by academic scientists (i.e. input). In parallel, principals should give DDD a clear remit to support TTOs with drug discovery expertise and wet lab resources. Establishment of public-private partnerships in defined areas is also a future opportunity.

Delivery of DDD programs requires securing current operations

As outlined in the introduction, DDD currently has nine facilities at the four host universities for SciLifeLab offering cross-facility services that represent the core capabilities for successful academic drug discovery. In addition, DDD has support from the Lund University core facility U-READ (Unit for Rapid Engineered Antibody Development) that complements and increases competence and capacity of the HAT facility at KTH. Also, an agreement between the Karolinska Institute and Research Institutes of Sweden AB (RISE AB) provides access to expertise in drug safety assessment.

In order to deliver on the strategy outlined above, DDD, as one unit, has the right competence for the coming five years. However, the resource allocation between facilities might need to be balanced depending on the nature of the therapeutic modalities requested by the users. There is also a constant need to evolve the technology offerings from the facilities. Examples of this evolution are: increased focus on early identification and validation of relevant pharmacodynamic biomarkers at the in vitro and systems pharmacology (IVSP) facility; setting up capacity for selection from DECLs at the human antibody facility (HAT); building competence and capacity for combinatorial chemistry and DECLs at the MCLI facility; assuring access to in-house dosing for in vivo PK studies with accompanying bioanalysis at the ADME facility, etc.

Communication enables a pharmacological mindset

Outreach activities are important to engage with new partners in Life Science and make the DDD offer more accessible. To align and communicate interests from the multitude of stakeholders, DDD distributes an external newsletter at times, and more frequently releases news on the DDD social media channel on LinkedIn. DDD made an

effort 2019 to improve public awareness and these attempts need to be further strengthened 2021-24 – preferably by stronger support from the SciLifeLab Operations Office.

An important way to position DDD as a hub for academic drug discovery is the organization of two annual "free of charge" symposia. These are often arranged in collaboration with external organizations. Examples are: "Biomarkers in Drug Discovery – How to Predict for Success in the Clinic" in collaboration with AstraZeneca, "Biologics – Bridging the Gap" in collaboration with the Testa Center & GE Healthcare, and "Formulation – Friend or Foe" in collaboration with three pharmaceutical formulation consortia funded by the Swedish innovation agency. Beginning 2017, DDD also organizes recurrent Drug Discovery Seminars where invited scientists can present their science applied to drug discovery. DDD is occasionally arranging short courses in drug discovery technologies and has also been engaged in leading an externally funded research school in drug discovery and development. Interestingly, the curriculum of this research school was picked up by A-STAR in Singapore in 2019 after looking at YouTube.

Arguably, the most important communication is the face-to-face interactions with scientists when their projects are discussed with representatives from DDD and the need for solid pharmacological studies of a potential therapeutic is made clear. The in-depth interviews with PI's in 2019 indicated that these interactions were very valuable for them. This has eventually, by "word of mouth" spread the view that DDD is a trustworthy organization to work with to their fellow scientists. One outcome from these interviews was that many of our academic customers volunteered to act as "ambassadors" for DDD at their university. This concept is now under evaluation. Based on above, *more focus is now directed towards the direct interaction with all of our customers (academic scientists as well as TTOs, research grants organizations, industry) in order to enforce that pharmacological, rather than phenomenological, studies are required for drug discovery as well as conclusive scientific publications.*

Increased support to TTOs and research funding organizations

The innovation environment in Sweden is globally unique due to the "Professors privilege law". The law gives the academic PI ownership of all data generated through public funding, meaning that the PI him-/herself is both free and obliged to chose commercialization path; i.e. TTOs do not play the same role in Sweden as in other countries. DDD does not offer business development support for projects in its portfolio, but instead require that the PIs engage their local TTO. These interactions are usually well functioning, e.g. a representative from the host TTO takes part in project meetings and utilizes DDD expertise for evaluation of local projects. However, the mandate of the TTO in the Swedish system, with its professor´s privilege, is challenging. TTOs can support the project owner with public funding for e.g. IP analysis/filing, business plan preparations and market analysis. This relatively modest funding is typically exhausted when it is time to present the project for investors and the PI is often left alone in the complex process of negotiation, due diligence etc. The situation is improved when a holding company or incubator is involved. Unfortunately, a large number of projects are closed in the process, despite substantial investments in e.g. verification and patent costs. In addition, from our experience, there is still a huge and largely untapped source of potential drug targets in the academic sector that never come to the attention of the innovation system or DDD. *An improved Swedish model to proactively identify and* resource *interesting drug target opportunites is warranted and we believe that DDD could contribute to this.*

SciLifeLab, DDD, and several actors within the innovation systems in Sweden acknowledge these shortcomings in the life science innovation ecosystem. SciLifeLab has therefore proposed additional funding from the next research and innovation bill to use SciLifeLab and DDD as one hub to improve the situation. DDD has also initiated work with the university incubators to approach consortia of investors for novel funding mechanisms for early pharmaceutical programs that suffer from long and expensive development timelines.

In summary, DDD currently holds a very strong national role as a trustworthy, efficient and professional joint arena for various stakeholders in drug discovery and drug development and impacts on the Swedish life science research community and society. Given the short time the infrastructure has existed, and the trends seen among the many stakeholders, i.e. PIs, TTOs, funding agencies, etc, it is anticipated that DDD has the potential to solidify its role as the primary hub for academic drug discovery & development in Sweden, if supported by the necessary funding and mandate. As a final note: the SciLifeLab IAB visit in 2019 commented that "*The expertise in the DDD group is important for Sweden to exploit the opportunities that arise from the substantial research base across the country.*"

Governance to leverage the legal proxy status of DDD

In 2018, new steering documents for DDD were approved by SciLifeLab director Olli Kallioniemi ("SciLifeLab Drug Discovery and Development (DDD) Platform Terms and Conditions for Funding") and by the DDD platform steering group ("SciLifeLab Drug Discovery and Development (DDD) platform Rules of Procedure") that clearly state responsibilities for key functions within the platform and

for the DDD steering group. In short, the DDD steering group should be composed of four leading academic (medical) scientists and three representatives from industry and the innovation system or funding agencies. The steering group is responsible for strategic decisions of the platform and gives input on the budget distribution before formal approval by the SciLifeLab board. All larger investments in instrumentation and personnel are decided by the steering group. Most importantly, the steering group is also responsible for prioritization of DDD programs and technology development, and the bi-annual prioritization process determines to which projects DDD allocates resources. Decisions and priorities are then implemented by the two platform directors and the DDD management team. The mandate of the DDD steering group assures that DDD resources are distributed in a transparent process across the country and no changes to this governance process are suggested.

Maintaining the DDD legal proxy status and the Governance structure, as outlined above, that allows DDD to sign agreements and execute joint projects with external partners is essential for the future development of the platform. Preferably also Lund University should accept this arrangement before the next funding cycle 2021-2024.

Plans for technology development

Despite being a conservative business with long development cycles, the pharmaceutical industry is undergoing a fast transition into new therapeutic strategies that have been instigated by academic science. In addition to cell and gene therapies, (supported by other governmental initiatives), an increased volume of new therapeutic entities such as peptides, nucleic acids, conjugated molecules are entering clinical trials. Targeted protein degradation through Protac molecules is progressing extremely rapidly, and their potential to offer a completely new therapeutic principle (event-driven rather than occupancy-driven pharmacology) is supported by recent phase 1 data from the first Protac molecule. Similarly, new technologies, such as DNA encoded chemical libraries and artificial intelligence systems, drastically change how certain parts of the early stage drug discovery process has accelerated. Likewise, analytical and prognostic biomarkers need to be implemented earlier in the drug discovery process to increase success in later stages of development.

As stated already before, DDD benefits from sourcing targets and projects from the entire academic life science / health science profile. In order for DDD to provide the most relevant technologies and molecular entities to Swedish academia and industry, a number of internal "Technology development projects" have been initiated. Current technology development and implementation projects are "DECL" – the set up and dissemination of large DNA Encoded Chemical Libraries and "Bipod" – the exploration of novel E3 ligase binders for development of Protacs, and "Organoids for PKPD modelling" – evaluation of in vitro and in vivo hosted organoids combined with measures of drug exposure and identified biomarker response. Other new technologies that are being implemented 2021-24 involve: MS-based bioanalysis of biological drugs, and complementation of the SciLifeLab compound libraries to facilitate identification of hits amenable for lead generation. These technology development projects occupy approximately 10% of available resources at DDD (excluding specific university funding to DDD for these projects). As a comment, SciLifeLab policies states that not more than 20% of the platform resources should be spent on technology development.

DDD benefits greatly from being part of the vibrant SciLifeLab infrastructure, which offers the project owners access to new complementary technologies and expertise that are seldom available even at large pharma companies. This integration also allows cross-facility and cross-platform collaborations through SciLifeLab sponsored RCPs and TDPs. DDD is involved in the Biophysical interactions RCP and the following TDPs: "BIPOD" led by Dr. Mikael Altun (KI) aiming to develop novel tissue specific Protacs, "Mammalian protein production" led by SciLifeLab fellow Alexey Amunts (SU) aiming to develop medium-sized protein expression capability, and "RIF-Seq: RNA isolation free RNA sequencing" led by Prof. Mats Nilsson (SU). Likewise, the DECL project is a close collaboration between DDD, and the SciLifeLab facilities NGI, single cell proteomics & PLA, Data Center and external PI's Ulf Landgren (UU), Ola Spjuth (UU) and Göran Landberg (GU). Ideally, as for projects and targets, new technologies that may have a direct impact on the practical execution of drug discovery projects could be increasingly sourced from the whole national Swedish research community with help of dedicated funding.

It is important to stress that the DDD platform does not only offer technologies useful for drug discovery. Equally important, some would say even more important, is the general expert competence DDD offers to Swedish drug discovery programs and innovation systems. The perpetual competence required to advance a drug discovery & development program through the strongly regulated process is available at DDD. DDD therefore aim to prioritise collaborative efforts and direct interaction with TTOs, industry, funding agencies and regulatory bodies in the coming years.

The legal proxy status of DDD also facilitates collaborative research with other organizations; technology development for year 2021-2024 is therefore expected to be increasingly performed in direct collaboration in research consortia, funding agencies and industry. The strategy is therefore to actively seek up and inform about the opportunities in collaborating "inside DDD".

Collaborations with healthcare, industry and other national and international organizations

It is important to stress that not only Swedish infrastructures are considered when searching for the best way to progress a drug discovery program; rather, the national Swedish infrastructures, like DDD and CBGE, should serve as a link and facilitate access to other European infrastructures. In this regard, programs at SciLifeLab are making use of the screening services offered by the IMI program ESCulab-European Lead Factory – two DDD programs will conduct screening there in 2020 after initial assay set-up and validation locally in Sweden; similarly, ESCulab expects DDD, together with the PI, to continue to work on the hit-to-lead and lead development part of these small molecule programs.

The DDD infrastructure is active in three IMI projects (ENABLE, ULTRA-DD and Conception) and the legal office of DDD in 2019 allowed us to become a member of the European Infrastructure for Translational Science (EATRIS). This year DDD was involved as reviewers in the SPARK Norway innovation program. These international commitments are important to maintain knowledge of the frontline in research, to build networks, and to access new technologies when they emerge.

As outlined above, the strategy for 2020-2024 will be to actively identify and inform external organizations about the opportunities to use the DDD infrastructure for attracting external funding. Ongoing discussions are already ongoing with TTOs, Venture Capital funds and industry. *Importantly, this strategy relies on the current slim organization remaining with regard to competence (FTE) and access to instruments. Based on this basal capacity DDD can leverage partners and collaborator's programs upon request.*

DDD assures quality, reproducibility, and data driven science

The fact that 50-90% of preclinical biomedical data is non-reproducible is a large reason for why DDD is highly valued as an independent quality assurance vehicle for programs seeking further national funding or being exposed to due diligence by international pharma and VC companies. Data generated by DDD is based on validated assays and all data generated by DDD is kept in electronic lab journals. Updates on program progressions and new plans are written and externally evaluated twice yearly; formal decision points exist for each major study/milestone in the programs. Likewise, a system of both internal and steering group approved check-points assures that the right data is available for decision making at the right time. Examples includes checkpoints to assure that validated assays are at hand before starting extensive chemistry programs, input from the DDD "in vivo design team" to ensure that relevant pharmacological data are produced in animal experiments, and that an "industry-like" candidate target product profile is available upon exit of the program from DDD.

Budget 2021–2024

Two essential factors to secure current operations of DDD are: 1) to maintain the critical mass of expertise in our facilities and; 2) to replace instruments that are essential for day to day activities. Most of the available instruments where purchased up front 2013/2014 and now need to be replaced. Analysis of required instrument investments for the period 2021-2024 indicates that the target for annual depreciation level should be 9-11 MSEK. Surplus accumulated from 2013/2014 (in the start-up phase of the platform) has also been used to hire temporary personnel 2015-2020. Temporary personnel have been used to adjust for resource demands and to understand the critical mass of resources that are required to run the platform.

From 2021, we need to secure some of these resources to maintain the functionality of the platform as we see it today. The legal framework for DDD is critical and allows us to build public-private and public-public partnerships that enables us to expand activities in areas of common interest. This could involve to increase support to SMEs and work with users to secure joint funding for personnel, etc. A current example of the "DDD inside" strategy mentioned previously is DDD as co-applicant to the Swedish Foundation for Strategic Research (SSF) for the project "UPGRADE: An incubator of hits and leads for anti-bacterial drug discovery programs". If granted, DDD will offer flexible resources over a 5-year period in exchange for full cost coverage of personnel and reagents from the consortium.

Hopefully, the outcome of this strategy will be that the mission of DDD as a translational infrastrucute that supports Swedish academic DDD programs will continue at the same level as today, whereas development and implementation of new technologies as well as exploration of new target classes or focused efforts on certain diseases could be driven primarily from joint projects with industry and "DDD inside" grants. Although we will not know the total SciLifeLab/DDD budget until Nov 2020, we have asked for more funds to increase support to the innovation systems - this is captured in the budget posts Personnel and "Other".

Costs	2020	2021	2022	2023	2024
Personnel (FTEs on running budget + FTE paid by surplus and extra TDPs) [1]	(35+7)	39	39	40	40
Personnel [2]	38 493	41 000	41 000	42 000	43 000
Operations	18 066	18 861	19 061	19 261	19 461
Premises	4 576	5 000	5 400	5 800	6 200
Instrument depreciations [3]	6 170	10 459	11 154	8 713	3 702
Other [4]	-	1 061	1 061	2 061	2 061
Sum costs (kSEK):	67 305	76 381	77 676	77 835	74 424

Revenues	2020	2021	2022	2023	2024
Distributed SciLifeLab DDD Funding	46 593	46 593	46 593	46 593	46 593
University SFO funding (UU) [5]	2 008	2 000	2 000	2 000	2 000
DDD surplus accumulated from 2013 [6]	13 306	5 811	5 075	3 384	1 640
Suggested increased funding to DDD 2021-2024 [7]		5 000	8 000	12 000	15 000
Required additional funding to maintain current level of operations and to give support to the Innovation systems		10 977	9 908	7 658	2 891
User fees [8]	5 398	6 000	6 100	6 200	6 300
Sum revenues (kSEK):	67 305	76 381	77 676	77 835	74 424

Table 1. Current budget (2020) and suggested budget 2021–2024.

[1] Immediate need to get funding for 4 FTE for personell currently on temporary positions paid by surplus generated 2013-2014

[2] Cost for 35 FTE year 2020 is 36056 KSEK. In the budget for year 2020 is 7 FTEs paid by surplus 2437 KSEK at DDD and Technology Development grants given to universities for collaboration with DDD

[3] Steady state costs estimated to be 9-11 MSEK to maintain instrument park. Costs include for planned replacements were done 2019

[4] Increase of "Other" is to allow for focused support to the innovationssystems

[5] Absolute requirement for DDD project coordination and DDD office function

[6] Surplus used for depreciation of instruments 2021-2024, upfront payment.

[7] Comments made by SciLifeLab to the 2020 Research and Innovation bill

[8] Reagents plus part of service costs

Data Centre

SciLifeLab Data Centre

Research data is one of the most definitive and lasting products of SciLifeLab operations and is key to securing a high scientific impact of our services. With this in mind, the Data Centre (DC) was established in 2016 as a central support function to the infrastructure, serving primarily the technology platforms but also management and the Operations Office. The primary goal of the DC is to maximize the scientific impact of SciLifeLab generated data, through providing expertise and services for facility needs on IT and research data management, and by promoting Open Science, responsible data sharing, and facilitating that SciLifeLab produced data follows the FAIR principles (Findable, Accessible, Interoperable, and Reusable). The Data Centre will have an important role in the next phase of SciLifeLab, with a strong focus on data-driven life science. With the ability to both provide services and to help shape SciLifeLab data policies and data related conditions for facilities, the Data Centre is also supports SciLifeLab in the shift towards Open Science.

National context

As a major data producing life science research infrastructure, SciLifeLab is heavily reliant on services for IT and data management (Figure 1). IT is central to SciLifeLab operations through all phases of the data life cycle from data production, data sharing in projects, to publishing and data re-use. The IT needs range from bread-and-butter support for licenses, workstations and network infrastructure to high performance compute and storage, services for human sensitive data, and cloud services.

In Sweden, compute and storage for active research projects are provided by the Swedish National Infrastructure for Computing, SNIC. The universities are responsible for long term storage and archiving of data, as well as for legal requirements on data protection and public access to information. It is also their duty to protect the governance of generated data to fulfil these legal requirements, and secure access for their own researchers to their data. In practice, few solutions exist today in Sweden for long term storage and archiving of large-scale life science data even at the universities. Another e-infrastructure, SND (Swedish National Data Service), is a main driver for FAIR data and has established a network of university-based Data Access Units that provide local research data support, primarily regarding FAIR and meta data services.

SciLifeLab has therefore currently a limited mandate, and limited funding, to operate large scale base IT resources that would broadly serve researchers. Instead, it relies on efficiently gathering the needs of its units and find the right service providers. The Data Centre has a central co-ordinating role to communicate with platforms about their IT and data management needs, and through them also to be informed of the needs of the platform user. DC will then find efficient solutions from different service providers – often university IT divisions, national e-infrastructures,

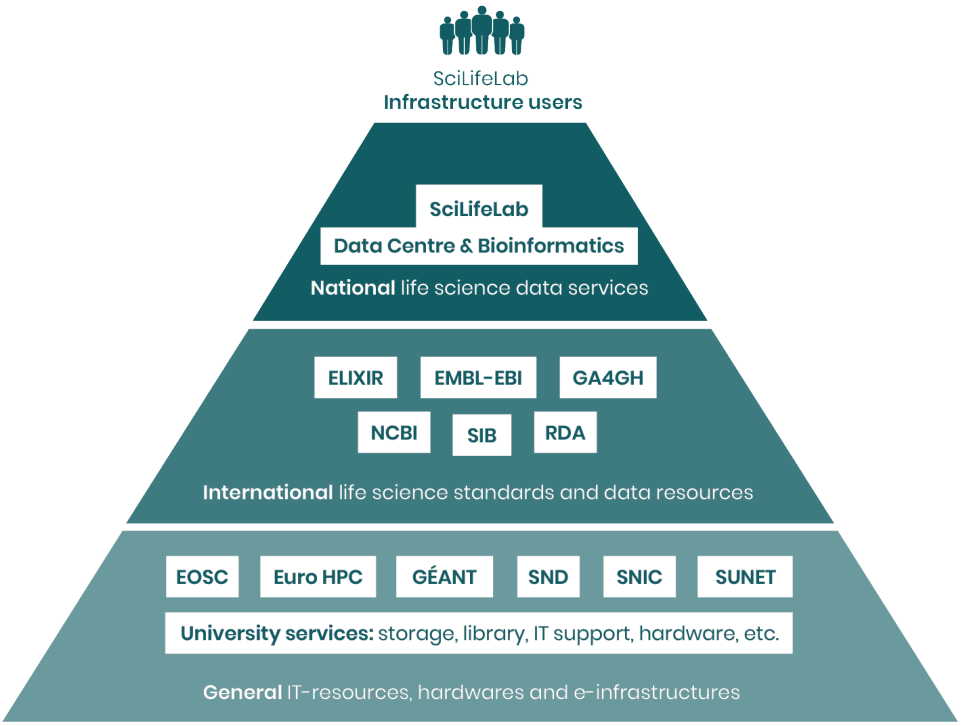


Figure 1. SciLifeLab provides life science specific services to its infrastructure users primarily by utilizing national and international general IT services and e-infrastructures (bottom level) and international life science data resources and standards (second level).

commercial providers, or through own development efforts. Support to individual research projects are primarily carried out by the SciLifeLab Bioinformatics Platform (National Bioinformatics Infrastructure, NBIS) which also is the Swedish ELIXIR node.

In 2018, the Swedish Research Council (VR) together with the Universities' Reference Group for Infrastructure (URFI), commissioned an international expert panel for an in-depth study on the state of Swedish e-infrastructure. In its report [https://www.vr.se/analys/rapporter/vara-rapporter/2019-02-14-an-outlook-for-the-national-roadmap-for-e-infrastructures-for-research.html] the panel concludes that Sweden has a fragmented landscape of e-infrastructures and IT service providers for academic users, with " ... unclear, sometimes seemingly overlapping mandates, gaps of services and confusion among e-infrastructures, universities, and also within the Swedish Research Council". Regarding data publishing, the panel found that there is "...currently no coherent national solution for data publishing, archiving, and long-term storage, or data preservation for research in Sweden". The report is currently followed up by work by the Swedish Research Council and the universities, and may lead to a re-organization of national e-infrastructure. For Swedish life science, this means a period of uncertainty regarding how today's issues with for example long term storage and data publishing will be resolved. In light of this, SciLifeLab through its Data Centre and Bioinformatics Platform (NBIS) will be providing certain broader services to address needs of its users and platforms, that are not provided by other actors. This will be done in careful coordination with universities and e-infrastructures, and as part of SciLifeLab's infrastructure services towards users in its specific scientific field.

Data Centre Background

The initiative for a Data Centre to maximize the scientific impact of generated data came in 2016, after major investments in the Genomics platform had increased the capacity to produce sequencing data, but the IT capacity required to manage this data and the ability to assess its scientific impact were not fully matching. This also co-incided in time with the government's research proposition in 2016, assigning the Swedish Research Concil to coordinate the drive towards open access to research data [https://www.vr.se/english/mandates/open-science/open-access-to-research-data.html]. "The FAIR guiding principles for scientific data management and stewardship" [Wilkinson et al, Scientific Data 3, 160018 (2016)] had been published earlier same year. The SciLifeLab Data Centre was therefore one of the earliest units in the country to focus on research data support primarily towards data producers, with the idea that by supporting the FAIR principles already at the stage of data production, it would greatly facilitate reproducibility and transparency further downstream the data flow and help researchers publish high quality, re-useable data.

The DC currently employs seven staff – one head of unit, one coordinator, and five system developers and data engineers. Another data engineer will be recruited in 2020. The unit is now considered a permanent part of the organization.

Services

The Data Centre provides a number of different services, primarily with SciLifeLab facilities as users. Sometimes, access to services is also given to research projects in a collaborative format, if it supports the development of new DC services, or projects with a wide national impact. In general, researchers that require support to their specific projects are primarily served by the SciLifeLab Bioinformatics Platform, NBIS (Figure 2).

The DC operates a small number of servers to host its own developed services, and computational services developed by facilities, including a new Kubernetes cluster with both CPU and GPU nodes. It also operates a SciLifeLab institutional general data repository hosted by Figshare,

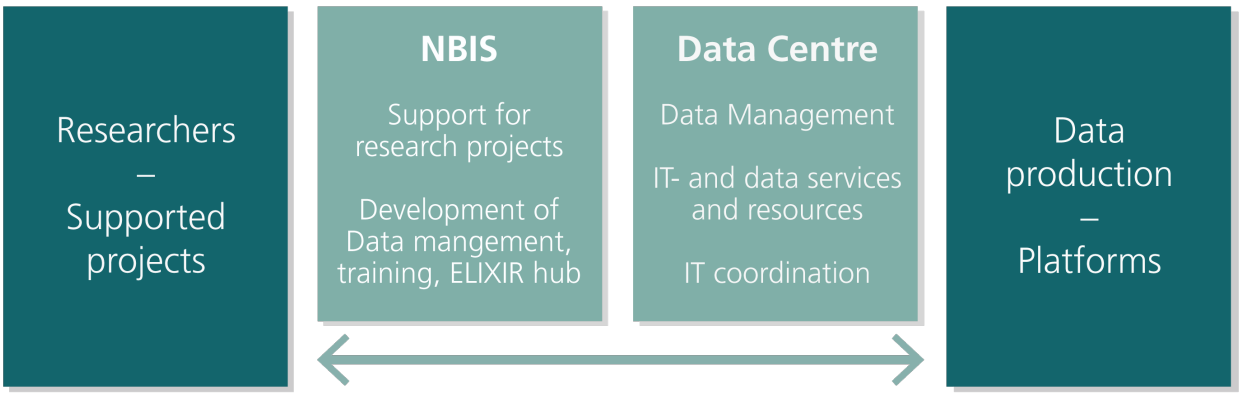


Figure 2. The SciLifeLab Data Centre (DC) provides services primarily to the technology facilities, which in turn supports user projects. In particular, DC supports data generating facilities, whereas NBIS, the Bioinformatics platform, primarily supports individual user projects. DC and NBIS work in close collaboration.

a service available for all platforms and SciLifeLab affiliated researchers. This service will be launched on March 1, 2020. DOI minting is provided using a Datacite account in collaboration with the Bioinformatics Platform, and using Figshare for data publishing.

The Data Centre communicates with all facilities across Sweden through a helpdesk or through its many regularly scheduled face-to-face- or video meetings to listen to data- or IT-related issues and needs. We always look for the most suitable solutions, that also are cost efficient and could be extended to serve several facilities with similar needs. Sometimes, such solutions can be provided through national e-infrastructures, sometimes through university IT departments, sometimes through commercially available solutions, but sometimes we believe custom developed software is the right choice. All Data Centre software are Open Source and freely available at Github.

Services to platforms and facilities

Examples of services provided to the infrastructure today include:

Helpdesk: The Data Centre operates a Zendesk powered helpdesk with ticketing system at datacentre@scilifelab.se.

SciLifeLab Order Portal: This is a web-based form management system individually configurable for the facilities to handle both contacts with their users. The system is currently used by a number of facilities, including the SciLifeLab Genomics platform (National Genomics Infrastructure, NGI) and the National Microscopy Infrastructure (NMI) where facilities in the SciLifeLab Imaging platform are participating. A demo version is available at https://orderportal.scilifelab.se.

Publication Database: This is a service for SciLifeLab associated publications. It serves as a system for facilities to report publications resulting from their services, but also publications from researchers. A web-based search and browse interface is provided, as well as an Application Programming Interface (API) and JSON data exports. Today, publications from facility users and SciLifeLab affiliated researchers are located in two separate instances, https://publications.scilifelab.se and https://publications-affiliated.scilifelab.se. The Publication Database is used for bibliometric analyses in for example annual reports and to prepare for evaluations. The Data Centre has recently secured access to raw, publication level, bibliometric impact data from Web of Science (Clarivate) for all publications in the database, and access to manually curated bibliometric data in collaboration with KTH library. This data will be used to further develop the bibliometric services to facilities and management.

Data Delivery Portal: The DC is developing a cloud-based system for delivery of data from facilities to users. Currently, data transfer from SciLifeLab's 40 facilities to their more than 1,300 users is handled individually by each facility. The Data Delivery Portal will provide a single interface to a storage system linking all users with all facilities, where data will be delivered to "buckets" in the cloud storage, from which users can retrieve the data, move it to storage near compute services, or, if appropriate, submit data directly to a repository for publishing. It contains data protection measures such as on-the-fly encryption and anonymization provided by an innovative AI anonymization engine, VEIL.AI, in collaboration with FIMM and with funding from EIT Digital. The portal will be opened for beta testing in June 2020.

Data Tracker: Facilities are now required to uniquely identify projects and datasets. A goal for the Data Centre is to link user projects at facilities with produced datasets, published articles, and published data. Today, not all facilities have well developed systems to track data, and the Data Centre is currently building a central database for SciLifeLab users, projects and datasets that will be central for improving tracking of impact and ease of access for users, in particular for cross-platform projects.

Data management plans (DMPs): Structured plans for data management in research projects are becoming increasingly important and the Swedish Research Council (VR) requires that supported projects maintain DMPs already from 2020. The Data Centre participates in the VR-led national coordination group for DMPs, and works closely with the Bioinformatics Platform (NBIS) and research data offices at host universities to provide DMPs for users. The Data Centre hosts the Data Stewardship Wizard, an ELIXIR-developed web-based tool for storing and maintaining DMPs. In this way, SciLifeLab will be able to guarantee that supported projects that use our DMP templates fulfil VR requirements. We consider DMPs to be central in planning resource allocation in the future, and plan to require facility supported projects to establish DMPs.

Service hosting: Some facilities and research groups develop their own web services, in support of publications or projects, or service operations. It is today a relatively complicated procedure for such users to set up both the infrastructure needed and the service itself, even if a long-term plan for service maintenance may exist. SciLifeLab Data Centre will support such work by setting up a small Kubernetes cluster for hosting such services, where the developing team will be required to provide the service as a Docker container and commit to three years of software updates, security patches and user support. The cluster supports both CPU- and GPU-compute services. This service is being piloted in 2020.

Facility management systems: The Data Centre is strongly encouraging SciLifeLab facilities to use facility management systems to keep track of their operations. At two Swedish universities, such a software system has been

procured with the Data Centre as an active partner to secure availability and requirements by SciLifeLab facilities. The procured system, Agilent iLab, helps facilities to track user projects, manage user lists, plan consumables, handle scheduling of instruments and staff, handle pricing and invoicing, including integration with university economy systems. It will greatly facilitate cross-platform activities between facilities using the same system.

Legal and ethical issues: The Data Centre supports facilities and administration to increase compliance with the EU General Data Protection Regulation (GDPR) specifically in issues relating to sensitive data handling. A service is also provided to handle data access requests and the corresponding legal processes for PIs that want to share genomic datasets. This work is done in collaboration with the Centre for Research Ethics and Bioethics in Uppsala and with legal departments at the host universities. Making health data more often available for research is an important future goal, and we have close interactions with for example Genomic Medicine Sweden (GMS) that will build data infrastructure on the health care side.

DC also provides a number of scientific resources of national interest that are openly accessible to anyone. Among these are the Swedish allele frequency database, SweFreq (https://swefreq.nbis.se), developed by the Bioinformatics Platform (NBIS), and data access services for large scale genomic data from SciLifeLab supported sequencing projects. DC hosts an Omero server (https://openmicroscopy.org) to store imaging data for facilities.

Support to Operations and Management

The Data Centre also supports SciLifeLab central management and the Operations Office, for example with bibliometric data, analysis and visualizations for reports and presentations. DC also takes part in the writing of reports, official policies, terms and conditions for facilities, etc. The Data Centre has also developed a dedicated system, Anubis, for proposal submissions and review handling, first used in this present evaluation.

Coordination and collaboration

The Data Centre coordinates its activities closely with several other organizations in Sweden and abroad. We meet regularly with SNIC management to coordinate issues regarding compute and storage, and with SND and VR to discuss FAIR and Open Science. As research data offices has started at a number of universities hosting SciLifeLab units, we have established contacts and also hosted workshops focused on life science specific data support in Sweden. DC also regularly meets infrastructures that are part of NeIC, the Nordic e-infrastructure consortium, and particularly interacts actively with CSC in Finland regarding handling of sensitive human data, and other issues. The DC has also a collaboration with RIKEN Data Centre regarding life science data suitable for AI research projects. As we plan to establish pipelines to support automated submissions of project data to suitable archives at the European Bioinformatics Institute (EMBL-EBI) in Hinxton, UK, we aim to establish closer interactions there and will visit Hinxton in March 2020.

Outreach

Every year since 2017, the Data Centre has organized a one-day workshop focused on scientific data with international speakers for a broad scientific audience. In 2019 a workshop on "Reproducibility and data re-use in life science" was organized and broadcast live on Youtube, in a collaboration with the journal eLife. In 2020, a two-day workshop will be held on September 23-24, with the tentative title "Data driven life science". The Data Centre has also held seminars on GDPR and a jamboree for linking datasets to publication records in the SciLifeLab Publication Database.

Plans for 2021-2024

In its recent Roadmap for 2020-2030, SciLifeLab has identified Data-Drive Life Science (DDLS) to be its primary area of activity. In the Roadmap, a strategic objective is for SciLifeLab to create a national framework for life science data. The shift towards data driven science has of course already started, but we expect increasingly stronger demands for services that support all stages of the data life cycle (Figure 3). The Data Centre will be an important central function both to coordinate this work, listen to users and assess needs, and communicate with potential providers. The DC will also be central to data driven collaborative projects with industry or health care, as well integrating expertise in legal and ethical issues regarding data handling. SciLifeLab should be a leader in Open Science, and strive towards fully open data, code, protocols and results.

We strongly believe that SciLifeLab benefits from providing coordination, common data policies and central services for data and IT through its Data Centre, for reasons of efficiency but also, for example, quality and ease of access for users to cross platform services.

A number of areas for future work have been brought up in the Roadmap 2020-2030, and the future plans for the Data Centre is closely linked to how these strategic goals are approached, and a continuation and scale-up of its operations beyond 2020.

Strengthening IT for data production

Swedish universities and e-infrastructures already provide IT services, including compute and storage solutions for individual researchers. In order to provide IT solutions that SciLifeLab's data-producing platforms require, we will efficiently utilize existing resources and push for new

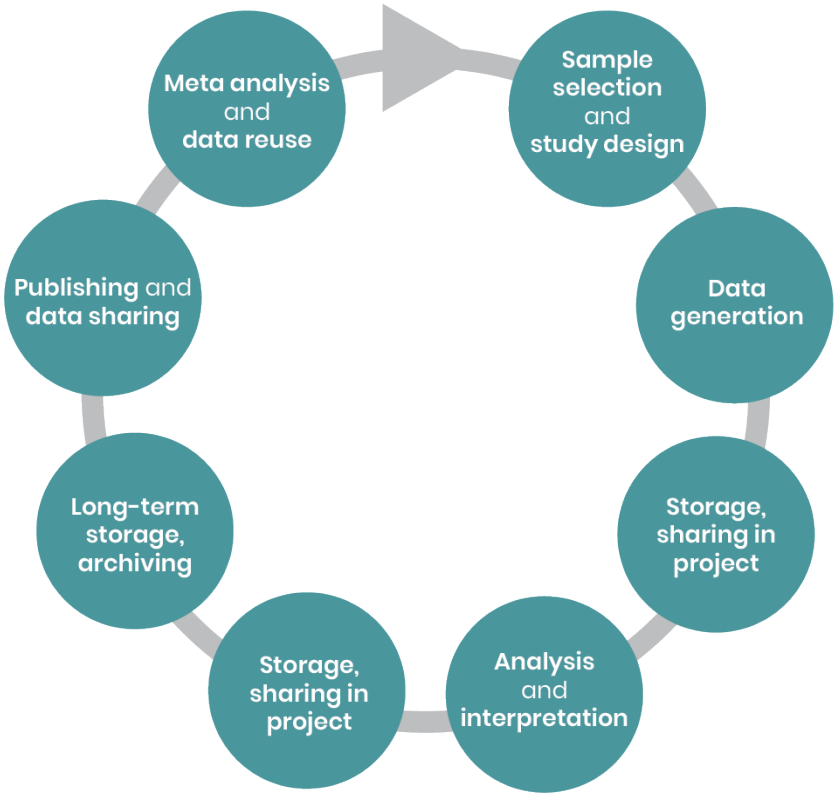


Figure 3. The flow of data in a cycle from production to analysis, sharing in projects, publication and re-use to initiate new studies characterizes data-driven life science.

IT development that is aligned with the requirements that we expect will develop within the SciLifeLab infrastructure. This will be done together with Swedish universities and national e-infrastructures and aligns with Nordic and international standards, as exemplified in the Nordic Commons digital data infrastructure proposed by NordForsk.

For 2021-2024, the Data Centre plans to address this by securing access to dedicated compute and storage infrastructure, both through on-premise HPC and cloud services, that can efficiently serve the needs of the facilities for data collection, internal preprocessing pipelines and user collaborations. The processes for handling IT issues within facilities will also be improved, and we envision a dedicated SciLifeLab IT function towards facilities to handle technical support issues, software systems, and compute and storage access.

Providing services and infrastructure for data-driven life science

Data produced at SciLifeLab will be governed by the university or the organization that hosts a research project. SciLifeLab will provide additional data stewardship, services and infrastructures that enable large-scale, complex and high impact data-driven projects that would otherwise not be possible. This will include hosting of data repositories, added-value databases that include visualization and analytics, meta-data services through interaction with SciLifeLab data stewards, and facilitation of data publishing in international repositories using automated pipelines. Researchers will also need support and services to comply with international standards for data sharing, such as the FAIR principles and GDPR, and to improve the reproducibility of published results.

The ability to access and re-use data is central to data-driven science. In particular, this is of high importance for cross-disciplinary research such as the development and application of new AI-based methods. This will require high quality reference datasets and establishment of collaborative opportunities and relationships with national AI initiatives such as AIDA, WASP and AI Innovation of Sweden.

SciLifeLab Data Centre has a range of activities planned for 2021-2024 to support this drive towards data-driven life science. In particular, we will build data services that enable data sharing in collaborative projects while ensuring the universities' requirements on data governance and security. To provide increased availability to the data generated by SciLifeLab, we will expand access to repositories for raw and processed data. In addition to expanding the general data repository hosted by Figshare, we will (when suitable) build automated pipelines from data producing facilities to the appropriate international repositories at for example EMBL-EBI. Already today, certain facilities, such as Cryo-EM, have set up such pipelines and we believe this can be expanded to many other data types. Such submission pipelines will require greater care for proper meta-data

generation at the facility level, and to a certain degree require users to provide sample meta-data.

Added value databases are resources that provide deeper insight in datasets, including visualization and tools for data mining, filtering and extraction of different data subsets. The Data Centre will during 2021-2024 greatly enhance the capability of SciLifeLab to host such resources in dedicated data infrastructure, and work actively with facilities to identify and develop such services. In particular, the Data Centre can provide a common platform for compute and storage needs for such services, and train facilities to develop them.

We will improve our support to users in data management issues by employing data stewards. This will be done both at the Bioinformatics platform (NBIS) to support research projects, and at the Data Centre to support facilities and data production. In order to raise the quality and scientific value of produced data, we will develop systems to manually curate (where suitable) produced data within our service projects. Integrating international standards, both ontologies for meta-data and technical standards used in the development of services, will be imperative.

Developing services for sensitive data

SciLifeLab will build on our already strong international network of services and infrastructure providers such as EMBL-EBI, ELIXIR, Global Alliance for Genomics and Health, and many others to develop services and resources for sensitive or confidential data. Such data, including for example whole genome sequencing data from humans, have special demands on access control and data protection. Increased effort for sensitive data will support promoting applications in health care and industrial collaborations in a safe, secure, ethical and responsible way. In particular, this will be required for our efforts in data-driven precision medicine and to support large scale initiatives like the 1+ Million Genomes Project, where Sweden is one of 20 European nations committing to large scale human sequencing to improve health. SciLifeLab will also engage in the development of national health data repositories as being developed within Genomic Medicine Sweden (GMS) and act as a federated source for international initiatives such as the Nordic Commons digital infrastructure development and the European Open Science Cloud (EOSC). There are also important international research efforts on de-identifying data while still retaining sufficient information to perform research; this is critical for a number of machine-learning applications, and SciLifeLab is the natural national organization to support such applications in Sweden.

In 2021-2024, SciLifeLab Data Centre will build services that in particular enable data sharing in collaborative projects on health data or human sensitive data. In genomics, this will be done in close collaboration with GMS. In particular, we will increase our expertise and collaborations in ethical, legal and social issues (ELSI) issues to, for example, provide advice on ethical applications and consent forms to enable data sharing while protecting individual integrity, as well as legal issues concerning data protection. Our ambition is to be able to act as a broker for Swedish life science data sets that require access control, connecting applicants with data access committees, and host services that guarantee transparent processing of access applications, secure data transfers, and support data access committee (DAC) work. We will also increase our technical expertise on data protection and integrate new mechanisms for this in SciLifeLab data management systems.

Simplifying access to services through data-centric integration

Researchers should be able to access SciLifeLab services and infrastructure in simple ways that best serve their research projects, without needing to know the details of SciLifeLab infrastructure organization. Using a data-centric approach for infrastructure operations and a common project portal, the Data Centre will improve how researchers can store, track and edit information and data from all their SciLifeLab projects, at any platform. Support efforts will be linked in the most efficient way, based on the whole research project design. This is a fundamental change in how users approach SciLifeLab as a national infrastructure, and this shift is planned to start in 2021.

SciLifeLab will also develop a data policy that sets out requirements on openness and transparency on users, and support for FAIR data production for the facilities. We expect to fully require that datasets produced by SciLifeLab facilities are made openly accessible, except when prevented by legal, ethical or contractual obligations.

Notes


SciLifeLab

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