► 2019 | Appendices

International Advisory Board

SciLifeLab

Karolinska Institutet

KTH Vetenskap och Konst

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Appendix A.

SciLifeLab responses to the International Advisory Board (IAB) comments from 2017

(Originally approved by the SciLifeLab Board in 11/2017, then updated 11/2018 for discussion and version approval at the board meeting on Feb 2019)

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Global context

1. SciLifeLab is a major strategic initiative and its operations need to be optimized to maintain the competitiveness of Sweden and the "Mälardalen" (Greater Stockholm) region in molecular life sciences.

Re: SciLifeLab is first and foremost financed as a national infrastructure, designed to benefit researchers in the whole of Sweden, but also aspires to create a powerful research environment between the host universities. SciLifeLab needs to balance these focuses and make its infrastructure, research, training and collaboration activities also benefit academia, industry and societal sectors nationally. The government sees SciLifeLab as one of the three major infrastructures in Sweden, along with MAX-IV and ESS, and SciLifeLab is the only one dedicated exclusively to life science.

SciLifeLab complements Swedish universities by addressing technological challenges that universities cannot tackle alone and by avoiding unnecessary redundancy. To optimize the operations of SciLifeLab our goal is to synchronize SciLifeLab funding with that of universities and external funders. During the last two years, we have strengthened the coordination with the host universities in a number of ways, including regular meetings between management and the host university rectors, heads of departments and SciLifeLab committees. Our research environments have been further strengthened by research community programs (RCPs), technology development programs (TDPs) and improved coordination of the SciLifeLab Fellows program, in coordination with the SciLifeLab committees and the host universities. Additional funding provided to the Data Center is aimed to design and implement cross-university procedures and policies for sustainable and long-term data management and to promote research integrity. Finally, we have extended our involvement with non-host universities outside the Uppsala-Stockholm region to further enhance the national engagement.

Challenges facing SciLifeLab

2. The IAB advocates the combined model of both national infrastructure provider and major research center in order to fulfil the new vision and mission statement and to enable SciLifeLab to compete with forefront international centers in Europe and elsewhere.

Re: This recommendation is in accordance with our ambitions, and aligns with the new mission and vision statements for SciLifeLab. Although the infrastructure and research missions are independently funded, we believe a successful model of mutual benefit has been achieved for maintaining cutting-edge infrastructure embedded within excellent research environments. To encourage and support this development further, we have granted funding to TDPs, for updating our infrastructure, and RCP aiming at bringing researchers together for utilizing and strengthening the infrastructure. SciLifeLab also needs to achieve balance and clarity in communication and branding of both the national infrastructure mission, and its Stockholm-Uppsala focused research center mission.

3. However, if the universities are unable to take the further steps necessary in terms of integration in support of SciLifeLab then the creation of the SciLifeLab with its own legal personality remains the only way forward.

Re: SciLifeLab is a collaborative effort across the four host universities, a model that has major advantages in e.g. resource commitment from the host universities, flexible collaboration platforms across the host universities, and host university support for SciLifeLab in HR, purchasing, financial and IT matters. However, this model also presents practical challenges, such as administrative and legal complexity internally, and the lack of a contractual ability to engage external stakeholders under the SciLifeLab name. The organizational restructuring of the SciLifeLab management in 2017 now facilitates much improved joint decisions and interactions between SciLifeLab stakeholders. Other developments are underway in 2018-2019, including the launch of a dedicated external relations office for SciLifeLab, as well as a review together with the host universities regarding the legal representation of SciLifeLab.

Governance and structure

4. There should be increased coordination between the four universities not only at the Rectors' level but at all levels (including Departmental Heads and other faculty levels) to support SciLifeLab's mission.

Re: This is an excellent recommendation. There are indeed already multiple levels of coordination in place between SciLifeLab management and the host universities. The new organizational structure of SciLifeLab launched in 2017 introduced the role of Integration Directors (IDs) at each host university as the crucial link between SciLifeLab management and host universities. IDs facilitate links with the SciLifeLab committees of each host University that make decisions about SFO funding as well as links to the multitude of departments associated with SciLifeLab at each host University. SciLifeLab Management Group meeting is arranged 2-3 times per semester together with the IDs to facilitate this coordination. In addition to the IDs, the host university representatives in the board provide a link to the host universities, to complement discussions with the Rectors. The host universities indeed undertake many critical responsibilities and services for SciLifeLab by providing resources for e.g. HR, legal, financial, communication, procurement, etc. More than 30 university departments are now linked to SciLifeLab, and it is a challenge to connect to them all, taking their differences into account. Some departments employ 100s of scientists and facility staff at SciLifeLab, and hence have a keen interest to follow the developments of SciLifeLab. Other departments have only limited commitments in SciLifeLab, and therefore the level of engagement, interest and knowledge about SciLifeLab varies widely among the individual departments and their leadership. The management group arranged two joint meetings for all department heads and their representatives in 2018. These meetings have been positively received and have contributed to the clarification of collaborative relations, and will continue bi-annually. In addition, department heads are regularly informed about important decisions involving facilities where they have staff employed. We have also updated a "Facility Agreement and Terms & Conditions for Funding" (Appendix H), containing general guidelines about governance and policies for the facilities, which is signed by the host university department to which the facility belongs.

5. The IAB considers the possibility of having formal agreements between the universities to enable one university (presumably KTH) to be in a position that it can rapidly endorse such matters as agreements between SciLifeLab with industrial partners or to sign international research collaboration memoranda without undue delay or bureaucracy is an important matter for consideration by the SciLifeLab Board.

Re: This is an important issue to SciLifeLab and to the host Universities and initial steps are now being taken to explore and solve the problems. The host universities recognize that it is their responsibility to provide an efficient handling of legal matters and will do so, in close collaboration with the SciLifeLab Management.The purpose of a detailed review of the topic is to catalogue the specific challenges that prevail today and seek solutions to problems that need to be addressed (see 3 above).

KTH is the overall coordinator for SciLifeLab and submits the annual report for SciLifeLab to the government each year. However, KTH is as such not responsible for execution of the functions of SciLifeLab at other host universities and does not represent SciLifeLab staff or facilities from other universities. Pan-SciLifeLab agreements with external parties therefore have required negotiation and approval from all parties independently, and on a case-by-case basis, a complicated and time-consuming process. Steps have now been taken in certain cases to simplify the process regarding access to the individual infrastructure platforms. Thus, in 2018 the SciLifeLab Board agreed to allow UU to serve as a central legal "host" for the SciLifeLab DDD platform (representing four other universities). Similarly, the Bioinformatics platform (NBIS) uses UU as their node for platform coordination across the seven universities included in that platform. Agreements regulating this NBIS arrangement are currently being drafted. The Genomics platform (NGI) uses KTH as a proxy based on the template of a long-running VR grant for this infrastructure collaboration between KTH, SU and UU. In the Diagnostic Development Platform, each node has a bi-modal agreement with the local health care region (e.g. KI and the Karolinska University Hospital). A single university can thus assume functional responsibility for coordination within individual platforms, but this has now resulted in a host of different arrangements to each case. These cases serve, however, as useful examples in developing a general model for handling SciLifeLab-wide legal issues that go beyond one platform and beyond the management of funding and access to infrastructure networks.

6. There has to be more devolved authority for the senior management (under the SciLifeLab Board), with the Director having greater control of personnel issues, finance and physical space and laboratories.

Re: The Director of SciLifeLab reports to the SciLifeLab Board on matters relating to national funding and can exercise a coordinating role in such matters via the selection and operation of national facilities. However, in most research-related issues and in aspects related to e.g. personnel, HR, finance, space and legal issues, each host university exercises independent authority. The SciLifeLab Board, Director and the SciLifeLab Management Group (MG) can promote collaborations, joint programs and interactions, but no single individual or group can dictate matters across university boundaries.

In Stockholm, the three Stockholm host universities jointly share the responsibility for decisions relating to Campus Solna, such as space allocation, entry and exit of group leaders, SciLifeLab Fellows, staff, work safety, IT and so on (Appendix G). These decisions are formally under the Campus Solna Committee that has representatives (3 SDs and 3 IDs) from the three Stockholm Universities and the Infrastructure Director of SciLifeLab. The Campus Solna Manager takes care of practical facility issues, but since 2017, the responsibility for coordination rests jointly with the Campus Solna Committee represented by the three host Universities. To promote community building practices and address forthcoming space allocation challenges facing Campus Solna, the possibility of a strategic and scientific review of Campus Solna has been discussed.

In Uppsala, most of the scientists and infrastructures are located within the space of individual departments, but the Navet building is governed by the Administrative Center for SciLifeLab at Uppsala University.

7. There needs to be common policies, procedures and decisions with regard to appointment and tenure procedures (SciLifeLab Fellows), to innovation procedures and practices to ensure research integrity.

Re: Common policies, SciLifeLab Fellows' matters, innovation or research integrity issues are all managed independently by the host universities. The management and the board can try to coordinate such procedures and promote harmonization, but many issues are deeply embedded in established procedures, or laws, in the Swedish university systems, and SciLifeLab only has limited capacity to influence this.

Although we have worked to increase harmonization between host universities of the SciLifeLab Fellows' program, recruitment, appointment, tenure evaluation and career policies ultimately remain under the control of each host university. A document describing the minimal requirements and conditions for SciLifeLab Fellows has been constructed in close dialog with the host universities. National regulations from the government regarding tenure-track appointments are now in force and will thus also shape the future profile of the SciLifeLab Fellows program. These rules apply to the recruitment of young group leaders within a maximum of 5 years after obtaining a PhD, meaning many accomplished applicants have been classified as "too experienced" to be nominated as SciLifeLab Fellows under this new rule. Several of the previously nominated fellows at KTH, SU, UU and KI have now received tenure or long-term positions, clearly proving the SciLifeLab Fellows program is meeting its goal of bringing new international faculty to the host universities. At KI, where a formal tenure system is not in use, the continuation of appointments of SciLifeLab Fellows are handled in competition with all other young group leaders, but SciLifeLab Fellows have so far scored at the top in these rankings.

Innovation practices are in general quite difficult to coordinate in Sweden due to the "teacher's exemption" (or "professors' privilege") legislation which allows "researchers" (there are some variations between universities on how this is applied for e.g. technical staff) to independently develop and commercialize IPR related to their discoveries. Therefore, both Swedish universities and their respective innovation offices do not own or have the ability to transfer IP, and more so focus on guiding scientists in commercializing their innovations. As each of the host universities house innovation offices, and own the data upon which IP is developed, SciLifeLab does not engage in tech transfer or innovation processes, nor do we currently have the resources to establish our own innovation office. DDD addresses IPR within their platform further in Appendix F.

The issues of research integrity are discussed in detail in Appendix C. White Paper – Research Integrity.

Platforms

8. Platforms should be open to the community at large, with a transparent, merit-based prioritization process and with a special provision for access for SciLifeLab Faculty and Fellows. The IAB recommends to the SciLife-Lab Board that there should be a provision of approximately 20 percent of the total SciLifeLab resource to these 'internal' users (both Fellows – highest priority - as well as Faculty) who, beyond this allocation, would bid for open access alongside other users within the national infrastructure provision.

Re: This comment has been extensively discussed with the SciLifeLab Board and the host universities. As national infrastructure funding requires an equal access policy to infrastructure services based on scientific merit, granting priority to internal users, even SciLifeLab Fellows, is difficult. Here, there is a clear discrepancy between SciLifeLab and other international comparable centers, that maintain core facilities exclusively for internal use. Additionally, the turn-around time for analyses at some national infrastructure facilities is often not as fast as in local core facilities making them less suitable for experimental research requiring rapid-turn-around time to plan the next experiment.

It is important to support the SciLifeLab Fellows and all affiliated researcher as much as possible in order to maximize both the impact and excellence of the SciLifeLab research environment. Therefore, the national mission for research infrastructure, and the facility support to internal research needs to be balanced between national and SFO funding. Obviously, access to the SciLifeLab infrastructure is a key motivation for SciLifeLab Fellows to join SciLifeLab, and this should be promoted by local arrangements in Stockholm and Uppsala. Thus, clear communication is key to avoid mismatch of expectations on what SciLifeLab can or cannot provide in terms of national infrastructure access and core facility capabilities. There are a number of actions that are being taken to address matters with the SciLifeLab Fellows program and their research environment, such as:

- *Each national facility can use up to 20 percent of their annual budget for internal research and development, and facilities are incentivized to engage in collaborations with SciLifeLab Fellows. Some SciLifeLab Fellows that are closely associated with SciLifeLab technologies benefit greatly from this opportunity, while others benefit less as their research may be less associated with technology development in general.*
- *The RCPs and the TDPs were both specifically meant to foster new close collaborations between scientists and infrastructures. Some SciLifeLab Fellows successfully raised collaborative funding through these programs, while others were not successful and felt that the funding was mostly allocated to senior PIs in the SciLifeLab community. In the first round of these calls, networks where SciLifeLab Fellows participated did not receive as much funding as one could have hoped, an aspect for consideration in future calls. Future SciLifeLab postdoc funding mechanisms may also help here.*
- *Host universities and departments should clarify (preferably already at the recruitment stage) how SciLifeLab Fellows can align with the national infrastructures. The potential needs for national infrastructure services of new SciLifeLab Fellows needs to be mapped at the start of their careers.*
- *SFO and host university funding may be needed to secure SciLifeLab Fellows' infrastructure needs if this issue is not otherwise sufficiently resolved. It is possible that the host university (e.g. SFO funding) could be applied to "buy time" from facilities and their equipment for this purpose. Arrangements could also include off-hours availability of instruments.*
- *SciLifeLab Fellows also need better access to "standard" laboratory equipment, particularly in the SciLifeLab space in Stockholm, where SciLifeLab Fellows are separated from their host departments (see below). As with national infrastructures, an inventory of such needs should be performed for each new SciLifeLab Fellow in the beginning of their term to avoid problems arising from a mismatch of expectations. The first recruited SciLifeLab Fellows experienced the most challenges, mainly as the Alpha and Gamma buildings at Campus Solna at that time were new and did not even have the basic infrastructure or equipment. In the early years in Stockholm, particularly at some universities, SciLifeLab Fellows were selected exclusively based on the interests of the host universities, without much reflection on how would their research will fit with the SciLifeLab community or facilities.*
- *SciLifeLab representatives (SDs and IDs of each host university) are now actively involved in the recruitment of future SciLifeLab Fellows and can thus communicate the role of the organization and the details of the SciLifeLab Fellows Program. SDs and IDS are also the contact points and responsible persons for addressing the needs of the SciLifeLab Fellows at each host university.*

9. Platforms should be, unambiguously, core parts of the SciLifeLab program and should report and be under the general direction of Director of SciLifeLab.

Re: This is usually the case but MG needs to focus more effort towards ensuring that all platforms are more clearly branded under the SciLifeLab name. Many platforms have, for a variety of historical or practical reasons, their own nomenclature for their own national networks (e.g. NGI, NBIS, CBCS, Bio-MS, NMI). VR-funded infrastructure networks are sometimes identical to the ones that SciLifeLab funds, while more often the VR-funded networks include partners that are not SciLifeLab national facilities. Therefore, in the future SciLifeLab funding cycle, we will need to make greater efforts to integrate both the SciLifeLab-funded and VR-funded parts, as well as other regional and local networks in this cycle. Executing SciLifeLab-driven steering of platforms is challenged by funding arrangements, conditions, and expectations from other sources. For some national facilities SciLifeLab provides <5% of the total funding while, in the other extreme, some facilities get almost 100% of their core funding from SciLifeLab national funding, but most facilities are somewhere in between. For example, VR and KAW exercise their own policies for steering of the facilities they fund. A pre-condition for VR infrastructure funding is matching host funding of 50 percent. Thus, the basic funding from SciLifeLab often ends up being used as VR co-funding. Discussions are underway with VR to better coordinate national facilities, but VR is only a funding body and the coordination needs to take place with the host university of each network making full coordination difficult. Overall, the agreement that SciLifeLab signs for each facility/platform is key to the control of the use of the national funding and can be used to spell out the conditions, including branding of SciLifeLab.

10. SciLifeLab should perform an analysis of which projects use multiple platforms, with the data forming a "Venn diagram" to show the added value and links of SciLifeLab platforms and provide easy mechanisms for cross-platform access.

Re: This is a good recommendation which has been executed (see infrastructure section of report). Cross-platform access is one of the major aspects that makes SciLifeLab truly unique, both nationally and internationally. This could increasingly be exploited for the comprehensive understanding of life, such as in in systems biology, and systems medicine studies, as well as in biomarker discovery opportunities. The number of publications that have made use of more than one SciLifeLab platform is currently about 13%, and is showing an increasing trend. We are contemplating that cross-platform use should become one of the key performance indicators for SciLifeLab facilities and platforms as well as a metric for SciLifeLab as a whole. Efforts will be initiated to make it easier for users to analyze their samples using multiple platforms as well as dealing with the integrated data.

11. The IAB endorses the SciLifeLab plan for a steady evolution of the platforms with the establishment of life cycle planning in a transparent and simplified system, with an ongoing program of peer reviews and evaluations.

Re: SciLifeLab management and stakeholders thank the IAB for this positive comment. This policy will be continued and refined, and the 2019 IAB site visit will focus on discussing the principles on how the next SciLifeLab infrastructure evaluation should be performed. The promotion of a fully national development of the infrastructure services will be a priority, engaging the user community, host and non-host universities, the NSC and RCP/TDP communities in the process. We also envision that future development, and the next evaluation of SciLifeLab infrastructure, will happen at the level of the platforms, and not the individual facilities.

12. The IAB will focus on the Drug Discovery platform at its next meeting (See also Appendix F).

Re: The MG will present the Drug Discovery and Development (DDD) platform during the 2019 IAB site visit. It is important to emphasize that DDD has a dedicated budget and mandate from the government that is separate from the rest of the SciLifeLab infrastructure. The management will work together with the DDD platform management to discuss future plans and also emphasize the unique angle of DDD as compared to similar industrial and academic drug discovery pipelines elsewhere. For example, the link to the capabilities of other SciLifeLab platforms is a potential unique perspective for DDD in the future.

13. There needs to be a continuing need for an assured long-term funding commitment for the Bioinformatics platform.

Re: In the era of "big data", the national role of SciLifeLab as a coordinator of data and bioinformatics cannot be overestimated. SciLifeLab also has a large and experienced community in this field. For example, out of all fields where SciLifeLab publications are published, computational biology has the strongest relative citation metrics (see Appendix I. SciLifeLab bibliometric analysis). The bioinformatics platform is perhaps the best example of how SciLifeLab has fully integrated, with its truly national platforms with members all over the country at all major universities. At the same time, the need for bioinformatics support from the national research community is so great that it is impossible to fully satisfy and meet these needs. The Bioinformatics platform has been awarded the same four-year funding commitment from SciLifeLab as the other platforms (2017-2020). The platform has also received a major three-year funding from VR (in a competitive call for 2018-2020), and is now applying for yet another for the period 2021-2024. In addition, a substantial long-term funding commitment (until 2025) was also received from KAW foundation to WABI long-term bioinformatics support. In addition, the platform is co-funded by all the participating universities. Efforts to support bioinformatics training have been important and will continue to be so. Moreover, SciLifeLab Data Center (see below) was launched and funded in 2017. Taken together, these commitments represent a major shift towards a data-centric SciLifeLab operation, a process that is planned to be continued during the next four-year funding period (see section Future plans for SciLifeLab in the main report).

In addition, it is important to point out that many SciLifeLab platforms and facilities also engage their own bioinformaticians to help with analyzing the data they produce. For example, the DD platform devotes significant internal resources for supporting bioinformatic analysis of clinical sequencing data. The SciLifeLab Data Center will try to integrate the bioinformatics and data handling needs, and capabilities of the various wet-lab infrastructure platforms. Overall, the total number of computational staff and resources to bioinformatics is much bigger than the fraction of funding devoted to the bioinformatics platform and the SciLifeLab Data Center. Bioinformaticians at other platforms can be affiliated with the bioinformatics platform for knowledge exchange and improved coordination. During 2018, contacts with other platforms have been improved; for instance, other platforms are invited to bioinformatic retreats for strategic planning, and we have started a joint seminar series. An even stronger Bio-IT community at SciLifeLab is desired, though this is already one of the most highly cited research fields at SciLifeLab.

14. SciLifeLab needs to develop a clear strategy for the data generated by the platforms and the tools used to access and re-use data in line with overall data stewardship policies (FAIR).

Re: SciLifeLab has a two-pronged approach to FAIR data, where the Bioinformatics Platform supports and provide tools for end users in research projects, while the SciLifeLab Data Centre supports and provides tools for the service platforms that produce the data. The two units work in close coordination. We will increase requirements for utilizing common processes addressing FAIRness of produced data, and rewarding good practices. The SciLifeLab Data Centre provides systems for the platforms that helps SciLifeLab to track data and results, such as: an order portal system, a publications database with cross references to published datasets, an IT/data helpdesk for the facilities, and processes for facilities to report IT and data management needs. A common platform for data delivery is also under development, and tools for facilities to support users with plans for data management.

The Bioinformatics platform is the Swedish node of EU-ELIXIR, thus takes part in several European activities to address FAIR data, such as: technical interoperability standards, development of the local EGA database for sensitive data and tools and standards for data management plans. Starting 2019, SciLifeLab also requires service platforms to uniquely identify projects and produced data objects, to facilitate tracking and availability. The Human Protein Atlas database is a key Swedish contribution to ELIXIR. While SciLifeLab does not yet systematically maintain its own data repositories, a public database of past SciLifeLab projects and datasets will be released in 2019.

We agree that a clear strategy for FAIR data needs to be further developed, and utilize work recently published by VR on assessment criteria for FAIR data.[1]

[1] https://www.vr.se/5.ad27632166e0b1efab1ce0.html

15. There needs to be a clear and rational charging logic within the Bioinformatics Platform for short-term and long-term support – at a later stage a joint application to the Wallenberg Foundation for both support services could be undertaken.

Re: The MG has encouraged the facilities in the Bioinformatics platform to gradually increase and harmonize their user fee structures. However, the principles of user fees, or lack thereof, also depend on the policies of other major funders of these facilities (VR for short-term and KAW for long-term bioinformatics). Indeed, SciLifeLab provides only a small co-funding to the WABI program, and the WABI platform has already applied and received substantial long-term follow-up support from KAW with an extension of the current contract until 2025. The MG will continue discussions with the Bioinformatics platform, KAW and VR aiming at to harmonizing user-fee principles for the platform in the long-run. In late 2018, the Bioinformatics platform added a new support model - Partner Projects - for larger projects (> 50% bioinformatics support for at least 2 years), which will enable long-term commitment and, in some cases, also co-funding of bioinformatics resources in grant applications. In a Partner Project, the user pays the salary cost of the platform expert(s).

16. A long-term plan for the Bioinformatics Platform hardware should be part of SciLifeLab strategy.

Re: SciLifeLab does not currently have the funding, nor the mandate to operate its own IT systems on a national scale, since this would conflict with systems provided by SNIC and SUNET, the two major national research infrastructures for IT, supported by VR. Therefore, SciLifeLab has set up processes to identify IT needs by platforms, and to coordinate these with SNIC and SUNET. This is mainly done via the Compute & Storage facility at the Bioinformatics platform and via the SciLifeLab Data Centre. The hardware and deployment procedures are currently working but the ever- increasing volumes of data will pose serious challenges in the future if not considered now. SciLifeLab is in a unique position to map the demands from the life science community and communicate these demands to the national providers.

NBIS already has the mandate, and budget from VR, for publishing sequence data and we are setting up a local EGA-SE node in the federated EGA landscape early 2019. NBIS is also providing user support in data management, and data publishing, while the SciLifeLab Data Centre supports the facilities regarding IT and data management.

Specifically, we plan to:

- *Estimate the current investments and future needs (FTEs, costs and PB storage) for data processing, internal back-ups, data delivery, and general IT for the production of data at SciLifeLab.*
- *Estimate the current and future needs from SNIC (FTEs, costs and PB storage) for computation and storage of active research projects in life science.*
- *Estimate the current and future needs from universities (FTEs, costs and PB storage) for data publishing and archiving for legal reasons and reproducibility in life science.*
- *Evaluate the needs and place them in perspective of the current budget at SciLifeLab for IT. What can be offered by SNIC, and what can be offered from the universities. Can the needs in life science be met over the next five year-period?*
- *Ensure communication, planning and regular follow-up with SNIC and universities regarding strategic questions related to data management and make sure to get clear commitments from universities and SNIC regarding their roles and contribution.*
- *Continue the communication, planning and regular follow-up meetings between the Compute & Storage facility at SciLifeLab with SNIC and other actors regarding technical implementations, user support and information*

Research

17. The IAB continues to recommend the development of major national research projects, which are in the national interest, and take advantage of the Swedish data infrastructure and the national investment in the SciLifeLab in terms of both facilities and brainpower.

Re: Following recommendations by the IAB, the first call for SciLifeLab National Research Programs (RCPs) was launched in 2018. Seven out of 32 RCP applications were funded with 1 MSEK/yr each (combined National and SFO funding) for three years and will be launch in 2019. The RCPs do not fund research activities per se, rather provide a coordinative capacity between experts across the nation in a given area, to collaborate closely with infrastructure platforms. Therefore, the RCPs will form an excellent incubational space for discussing grand challenge initiatives, with the ambition to source the majority of their funding through external grants. Besides the seven RCPs, we will also present nine examples to the IAB of different ongoing major research programs at SciLifeLab that already have either national interest or excellent grand challenge potential, or both.

18. Such national projects may also be seen in an international context in which Sweden and SciLifeLab can lead in developing international consortia.

Re: The vision that the SciLifeLab RCPs should strive to be at the top of their fields globally, seek joint research support nationally and internationally, and indeed could lead international consortia will be expressed. We also hope to illustrate to the IAB that the seven RCPs and nine major research programs that are underway at SciLifeLab, are often in close international collaboration. SciLifeLab is closely linked to several international networks in genomics, proteomics, single cells and translation, as quantified and visualized in the network of high-profile co-publications (see Figure 21b in Main report).

19. In developing future major research projects, the SciLifeLab Board should engage with the funders such as VR, the Wallenberg Foundation and the Science Academies, in their foresight activities for science planning and should develop its own Strategic Research Plan to clarify the near-term and long-term visions and mission priorities.

Re: Long-term priorities for SciLifeLab associated research are being planned. This will be done in dialog with host universities, considering SciLifeLab Fellows' research areas, RCP topics and future RCP calls. It is also necessary to engage in meetings with funding agencies, such as: VR, KAW, FORMAS, Vinnova, and SSF, to establish joint interests, ensuring that SciLifeLab research, but also the infrastructure areas and capacities, align with major national research priorities and research programs in progress elsewhere.

20. The SciLifeLab Board should develop processes for evaluating proposals for national research projects through a 'bottom-up' call within the host and other universities based on assembling critical masses with SciLifeLab Faculty and Fellows being involved.

Re: See above, this suggestion has been executed during 2018, and the first seven RCPs will start in January 2019. The RCPs will present their plans during the IAB site visit in March and after initial feedback and experience, we will launch a second round of RCP programs. As mentioned, SciLifeLab only fund coordination of the RCPs as well as assembling of a community, while the research will need to be funded otherwise.

Non-biomedical life sciences

21. Environmental life sciences, biodiversity, agriculture and forestry continue to be an area that is under-represented and needs to be encouraged and given priority.

Re: It is true that the environment part of the SciLifeLab mission continues to be underrepresented and further efforts are needed. One of the seven RCP programs funded represents non-biomedical research (Aquatic Microbiome Research Initiative).[2] In addition, today, there are already several SciLifeLab Fellows appointed in non-medical research areas.[3] Furthermore, many of the top publications featured on the SciLifeLab website arise from non-medical research areas, and we continue to strive towards a more inclusive overall research profile in these under-represented fields. Also, we think the combination of health and environmental profiling will be a key strength of SciLifeLab for defining the human "exposome" and its impact on health.

22. Calls for major national projects in the non-biomedical life sciences could be used to stimulate this area by combining top-down encouragement with a bottom-up response.

Re: The call for RCPs specifically encouraged applicants from non-biomedical research. However, despite of this the number of applicants from other fields was low, and only one application passed the evaluation in this first round. We will continue the RCP program in the future and will launch calls again to even more prominently fund new initiatives, and initiatives outside of the biomedical arena. Besides national programs, it is also important that the future research profile of Campus Solna research center includes a stronger representation of non-medical topics.

[2] https://www.scilifelab.se/RCPs/
[3] https://www.scilifelab.se/research/fellows/

SciLifeLab Fellows program

23. The IAB recommends to the SciLifeLab Board and to the host Universities that the Fellows' appointments should be the six-year norm that applies in most other parts of the world with special action needed to resolve the dilemma faced by current Fellows due to start-up delays.

Re: Initially the SciLifeLab Fellows program was not optimally coordinated between the host universities and the SciLifeLab management, nor within Campus Solna. Focus was primarily on hiring truly excellent researchers, with not enough emphasis on establishing mentors and supportive research environments for facilitating the start-up of SciLifeLab Fellows' groups. Thanks to the increased awareness of these issues, the career tracks of future SciLifeLab Fellows will be better coordinated. The host universities dictate the length and localization (in Stockholm) of its SciLifeLab Fellows' appointments. For example, KTH offers four plus four-year appointments, Uppsala four plus two years, while the new government regulations suggest up to a six-year term for tenure track. The SDs and IDs from the four host universities have now developed guidelines for the minimal expectations for a SciLifeLab Fellow across all the host universities, with the ambition of explicitly defining SciLifeLab Fellows' conditions from the beginning of their terms. The complex environment of SciLifeLab, with its national infrastructure role, has now also been better communicated via an information package to new SciLifeLab Fellows at the start of their appointments.

24. The IAB strongly recommends to the SciLifeLab Board that the Rectors appoint a single, common appointment and tenure committee for the SciLifeLab Fellows which can apply commonly agreed transparent criteria and whose decisions will be accepted by the constituent institutions.

Re: The host universities have indicated that this recommendation is not possible. The formal appointments are made by the universities, which have their own appointment and tenure committees. The universities also take the legal and financial long-term responsibility for personnel appointed. The funding of SciLifeLab Fellows is achieved through SFO funding independently controlled by each of the host universities. However, as indicated above, work will continue within the spirit of this recommendation to increase clarity and transparency of the SciLifeLab Fellows program procedures as much as possible. See also point 26.

25. The IAB recommends to the SciLifeLab Board that a Senior Research Coordinator be appointed for the Fellows program. The appointee should develop procedures for senior mentorship of SciLifeLab Fellows as a matter of high priority.

Re: The SciLifeLab Fellows' program is much better coordinated today than it was a year ago, but there is still room for significant improvement. This program also includes peer-mentoring aspects and in some cases the established SciLifeLab Fellows have volunteered to assist new SciLifeLab Fellows to adjust to the SciLifeLab environment. Mentoring of SciLifeLab Fellows is also now one of the key responsibilities of the SDs and IDs at each host university. This will ensure not only mentoring according to Swedish procedures and policies, but will also pay attention to and advice towards university-specific regulations. Mentorship by individuals who are not in the same host university has proved not to be optimal, since procedures and policies vary between the different universities.

26. The IAB strongly recommends to the SciLifeLab Board and to the host Universities that there has to be a coordinated approach to the recruitment policy regarding Fellows, who should be at the core of major national programs. In addition, it is recommended to develop a national science framework for their tenure prospects and to embed their own research interests and meet the strategic needs of the overall program.

Re: The SciLifeLab Fellows Program is funded and individually coordinated by each of the host universities. Therefore, we will not be able to achieve a completely aligned SciLifeLab Fellows Program, rather we must aim for four programs that are slightly different at each host university, including individual processes for recruitment, appointment, and tenure evaluation. Individual departments have a major role here in e.g. selecting the fields for recruitment based on their own interests. However, SciLifeLab management has been involved in the recruitments (usually SD or ID or both) and this ensures alignment with the SciLifeLab profile in the future at the time of recruitment, mentorship and tenure, to the extent possible.

27. The IAB encourages the SciLifeLab Board to consider introducing an EMBO -'EIPOD'-like competitive post-doctoral fellowship scheme, in which a project and post-doc is jointly supervised by two PIs, each with a different complementary skill (e.g. wet and dry). This could be an international program across SciLifeLab to encourage interdisciplinary research and provide excellent training for the researchers of the future.

Re: This is an excellent recommendation, and based on the host university summaries for the IAB this recommendation will be prioritized. Many of the host universities have already supported internal post-doc positions for SciLifeLab faculty within their own university (with their SFO funding), and sometimes shared between researchers and facilities. In the future, this could be accomplished in joint calls for post-docs, leading to collaborations across the host universities, as well as across facilities and research groups in the same manner as the RCP and TDP calls executed in 2018. Collaborations between facilities and researchers could also be co-funded by national infrastructure funding.

SciLifeLab Faculty

28. There should be some form of common definition of SciLifeLab Faculty without this being too rigidly or narrowly defined and who, with the Fellows, have priority access to the Platforms.

Re: The concept of SciLifeLab "faculty" or "group leaders" (faculty is not an appropriate term due to the mixup with the host universities' faculty), will need to be harmonized between Stockholm and Uppsala and across all host universities. If there are special benefits (and expectations) with being a SciLifeLab-affiliated group leader, we will have to formulate very clear definitions, so that we create clear selection criteria. A complicating factor has been the different methods by which SciLifeLab-affiliation has been defined historically in Stockholm (physical localization to campus Solna) and Uppsala (identification of relevant research areas). Therefore, we are considering two levels of engagement for group leaders. "Core" faculty with a close relationship with SciLifeLab platforms and whose capabilities would have all their publications affiliated with SciLifeLab, and "associated" or "affiliated" faculty who would have less involvement and would only be required to affiliate some of their publications with SciLifeLab depending on context. The benefits and responsibilities of group leaders in both these scenarios are now being discussed and we hope to present a firm recommendation for the IAB at the site visit in March 2019. For reasons outlined in recommendation nr 8, it is, however, not possible to give internal faculty priority access to the platforms with the benefit of the national funding. Though, both other ways of providing access, and other benefits of faculty are being considered (e.g. post-doc programs). Finally, it is important to also consider the concept "SciLifeLab Research Community", which would be more broadly defined and also involves other stakeholders, such as users of platforms. The large community of around 1300 users annually also contributes significantly to the expertise, technology development and collaborations with the platforms.

Research integrity (See also Appendix C)

29. It is necessary that SciLifeLab management engages with the employing institutions to ensure that all those conducting research in SciLifeLab have had appropriate training in integrity, research ethics and the responsible conduct of research. Therefore, the IAB recommends to the SciLifeLab Board that a protocol be established between SciLifeLab and the four host universities to ensure that researchers have appropriate education and training and that there are robust and commonly agreed procedures for investigation should incidents occur.

Re: Appendix C. White Paper - Research Integrity, will discuss these issues from the angle of the SciLifeLab community as a whole, with a broad view on good infrastructure practice, also involving data handling and research reproducibility. Issues on research integrity are formally the responsibility of the host universities, and only the host universities can take any actions if scientific misconduct is discovered. SciLifeLab neither has the legal status, nor the mandate to take any formal role in this process. There are unique aspects of SciLifeLab operations, such as the facilities receiving national infrastructure funding, SciLifeLab Fellows, and users of national infrastructure funding, where SciLifeLab could engage in preventive and educational activities, as well as promote good scientific and infrastructure practices. These recommendations will all be considered in planning future training events for staff, faculty and SciLifeLab Fellows.

30. Provision has to be made for data management planning, data collection, storage and archiving. The ongoing efforts of SciLifeLab of both the Bioinformatics Platform and the SciLifeLab Data Office need to be reinforced as a matter of priority.

Re: This is a major aspect for SciLifeLab in its quest towards a data-centric mode of operation. Please see detailed responses earlier to points 14 and 16. The newly-created SciLifeLab Data Center will focus on these priorities, but this will not be sufficient to deal with all the various data types and data sources, nor with long-term storage requirements or sensitive healthcare data. Consequently, the Bioinformatics platform, other SciLifeLab platforms, the host universities and the national computational infrastructure SNIC, are other key stakeholders in this question. However, there is also a continuing challenge to keep up with the availability of short-term data storage space to handle the massive amounts of new genome sequences produced. The users of SciLifeLab facilities and their home universities are ultimately the ones formally responsible for long-term storage of data, but typically they lack the capabilities and resources to do so. Discussions are thus underway to address these challenges in the future, but will take time and resources from the entire scientific community. SciLifeLab has helped by raising awareness of these challenges to its stakeholders. Finally, there are particular challenges with sensitive data from clinical sequencing for healthcare units. In these cases, the healthcare providers should be ultimately responsible as users, but typically they also lack the infrastructure and skills to handle the massive amounts of data produced. This question continues to be a major challenge, not just for SciLifeLab, but for society as a whole.

31. Such protocols should be extended to the researchers using SciLifeLab facilities from other universities and from collaborating organizations.

Re: Procedures and policies for research integrity and data management will be created for the national facilities when dealing with users from both host universities, as well as users from other parts of Sweden. Other issue to consider are legal and ethical liabilities associated with clinical diagnostic procedures, as well as possible ethical issues, financial details and conflicts with companies. A related, but equally important goal is how SciLifeLab can help to address the burning reproducibility issues in biological and biomedical science during the project prioritization process for facilities. Data management plans and ensuring FAIRness of data work towards these aims are discussed elsewhere in the IAB report.

Human resources

32. A coordinated procedure is needed to address career development and related human resource issues especially for the staff involved in platforms and infrastructure service.

Re. This is an excellent recommendation. HR policies linked to research careers are the responsibility of the host universities, but are a priority for SciLifeLab. Our committed, trained and motivated staff remains the most valuable assets of SciLifeLab. Often, e.g. the Heads of Facilities' careers are totally invested in maintaining technological capabilities to support the infrastructure services provided, thereby working for the benefit of other researchers. However, in the traditional university systems, most career and reward structures aim exclusively towards a PI career. The MG strongly desires coordinated efforts to boost the careers of its entire professional infrastructure staff, from technicians to senior scientists and Heads of Facilities. This topic was discussed at the Facility Forum in Uppsala in October 2017 and at the SciLifeLab Board Strategy Meeting in May 2018. While career path policies change slowly at the universities, and may also need legislative changes at the ministry-level, the SciLifeLab Board has approved a budget of 2 MSEK/yr to help with career development programs, meetings, training, mini-sabbaticals, lab visits and other support for the SciLifeLab infrastructure staff. We are preparing to open such a call in the spring of 2019.

Branding

33. In terms of branding, SciLifeLab has to take account of its founding framework and build this into a new and more efficient model.

Re: Indeed, more efforts are needed to boost the SciLifeLab brand: at the host universities, nationally, in the government, in media, industry, healthcare and also internationally. There has been a significant effort to further profile and brand SciLifeLab as a research resource to the entire Swedish research community. In 2018, SciLifeLab hosted a dedicated workshop and a one-day satellite symposium targeted specifically towards industry during the Nordic Life Science Days (NLSDays), northern Europe's largest life science industry and partnering meeting. [4] We have also been a prominent voice for clinical life science research through engaging in the launch and development of Genomic Medicine Sweden (GMS), and for the past three years SciLifeLab has had a continual presence at Almedalen week, Sweden's largest and most important annual political networking event.

[4] https://www.nlsdays.com/

34. IAB suggests branding SciLifeLab as an entity linked to the four universities and indicating its role as the national life sciences hub. Such branding has to cover all SciLifeLab related activities.

Re: This is a good recommendation. The SciLifeLab name is often invisible since legal contracts and other agreements are primarily, often exclusively, carried out in the name of the host universities. Therefore, we will need continued collaboration with our host universities to really promote the SciLifeLab name and brand in these national and international collaborations, towards the government, and with the public to boost continued and expanded support for the SciLifeLab funding and its national role. The primary and strongest branding of SciLifeLab is in its status as a national infrastructure, from which we are continuing to build on to create an equally strong brand for associated research centers, as well as for collaborative communities. In the future this will require a much more proactive engagement of our research community, a community which is constantly growing through increased infrastructure activity at non-host universities, and through growing numbers of users nationally. Securing the acknowledgement and the voice of researchers across Sweden will help to solidify the role of SciLifeLab as a truly national life science community and a Swedish research hub.

35. SciLifeLab and its Board should look at opportunities to promote its brand not just in Sweden but worldwide.

Re: There is an increasing international interest in SciLifeLab, and SciLifeLab is more proactively being branded as a unique research endeavor also towards foreign audiences thus increasingly has dialogs with other international life science centers. One example being the ongoing collaboration, seminar series and postdoc program SciLifeLab has with RIKEN in Japan which has been very successful. In addition to the growing number of global corporations that express an interest to engage collaboratively with SciLifeLab, public, private and governmental life science advocates and branch-organizations are increasingly using SciLifeLab to promote Sweden's strong academic life science sector. This is apparent through the dozens of delegations and dignitaries from various countries around the world that have visited SciLifeLab over the past few years. As an example, the Japanese confederation of enterprises, Keidanren, recently visited Sweden with a large delegation represented by some of the largest corporations in Japan. SciLifeLab was the only academic organization that was visited by this delegation, a testament to its international visibility and attraction. The SciLifeLab model per se has also raised considerable international attention from emerging international regions (e.g. in South America, Africa, China and Eastern Europe) as a pioneering way to coordinate limited resources within life science to create regional strength in research and infrastructure.

Profiling SciLifeLab internationally has been successful in raising awareness and there lies considerable opportunity not only for SciLifeLab and the host universities, but also for Sweden in general. Though, concrete collaborations or long-term commitments are still difficult in the multi-university context of SciLifeLab as each host university has their own internationalization agenda and strategy, with different partners and regions of interest and preference, and it is exceedingly difficult to align SciLifeLab's international partnering opportunities with the ambitions of all four host universities.

36. The existing major Keystone Conferences could be supplemented by other major conference on molecular life sciences, possibly in cooperation with the Nobel and Wallenberg Foundations.

Re: Such opportunities will be explored

Innovation and industrial collaboration (See also Appendix D)

37. The IAB recommends that a formal and innovative policy for industrial engagement is needed and it asks for a paper by SciLifeLab for Board consideration and review. The next IAB review will put special emphasis on industrial collaboration and innovation.

Re: The MG and SciLifeLab Operations Office have prepared a white paper about industrial collaborations and associated policies for the SciLifeLab Board (Appendix D), and will also use this as a basis for the IAB review. Each of the host university have their own innovation offices and external relations offices with established procedures for industrial collaboration, hence it will be important to work together. Importantly, SciLifeLab is launching its own external relations office in 2019, with the help of a four-year grant from VR that will considerably accelerate the capacity of SciLifeLab to proactively engage with the industrial sector.

38. Industry should be invited to be significant partners in major national research projects with companies being encouraged to second researchers to the platforms.

Re: This recommendation is interesting and will be considered when the SciLifeLab external relations office will start in 2019. Our RCP call in 2018 was already open to the participation of companies, but very few applications with company participation were received. However, several major industrial collaboration agreements are already underway. (Appendix D).

39. A renewed effort is needed to create a system of "Common IP Exploitation" which the IAB recognizes as not an easy or simple task but a very necessary one.

Re: This is indeed important, but not an easy goal given the Swedish legislation on one hand, our multi-university setting on the other, in addition to the lack of a legal entity/representation for SciLifeLab. The first and foremost obstacle for a common SciLifeLab IP policy is the "teacher exemption" at Swedish universities, which provides researchers the freedom to own and control the IP generated from most academic research projects. This has been discussed in the section on DDD, whose operations closely relate to this aspect. Thus, the IP policy is not only dependent on different universities, but also on the investigators themselves. Additionally, SciLifeLab does not have neither the ability, nor the mandate, to handle IP by itself. The major route for IP coordination would be through the innovation offices that already exist at the four host universities, but they have mostly an advisory role and do not participate directly in IP formation, securing or licensing. Technology transfer has in most cases worked well, and many spinoff companies have been launched in the SciLifeLab environment. In the future, harmonization of IP policies across host universities are needed, including discussions and collaboration about exploitation of IP, as described in the text on the DDD platform.

Clinical collaboration (See also Appendix E)

40. The IAB asks that a paper on clinical collaboration be produced by SciLifeLab for review by the SciLifeLab Board and the IAB will put a special emphasis on this aspect of SciLifeLab activities at its next review.

Re: The MG has produced a white paper on clinical collaboration (Appendix E). There are already major efforts underway within this domain at SciLifeLab, particularly at the Diagnostics Development platform which was expanded in 2019 to involve all the universities with a medical faculty with links to the associated health care regions. The Genomics Medicine Sweden program strives to take genome sequencing to the clinical routine, with collaboration across genomics facilities at the various universities and the hospital based diagnostic units. A major effort on standardization of bioinformatic processes will be aimed for. SciLifeLab has also funded a RCP that will form a national research community in clinical genomics.

Future reviews

41. The IAB proposes that its next review should be held towards the end of 2018 with a significant focus on users and partners.

Re: The SciLifeLab Board and MG agree that IAB meeting every two years is appropriate. The next meeting is set for March 13-15, 2019.

42. Whilst also addressing such issues as the formulation of national research ('flagship' programs, the roles of SciLifeLab Fellows and Faculty and areas of concern including the Drug Discovery Platform, links with clinical research, development of life sciences areas other than biomedicine and industrial collaboration, the IAB will also wish to examine the triad of relationships: between the universities; between the universities and SciLifeLab; and between university departments and SciLifeLab.

Re: These relationships will be described at the next site visit by ways of with writeups and stakeholder meetings. It is also a wish from the host universities to bring up these relationships for discussion during the next IAB site visit.

Appendix B.

List of stakeholders, committees and participants at the site visit

Contents

SciLifeLab International Advisory Board

Name	Affiliation	Role
Jan Ellenberg	EMBL Heidelberg, Germany	Chair
Søren Brunak	Technical University of Denmark and University of Copenhagen, Denmark	Board member
Yoshihide Hayashizaki	RIKEN Omics Science Center, Japan	Board member
Sirpa Jalkanen	University of Turku, Finland	Board member
Janet Jansson	Pacific Northwest National Laboratory, USA	Board member
Jonathan Knowles	FIMM, University of Helsinki, Finland	Board member
Svante Pääbo	MPI for Evolutionary Anthropology, Germany	Board member
Aviv Regev	Broad Institute, MIT, USA	Board member
Sarah Teichmann	Wellcome Sanger Institute, UK	Board member
Jo Bury	VIB, Belgium	Board member
Stephanie Alexander	EMBL Heidelberg, Germany	Secretary

SciLifeLab Board

Name	Affiliation	Role
Carl-Henrik Heldin	Uppsala University	Chair
Margareta Olsson Birgersson	Roche Sweden	Industry representative
Sophia Hober	KTH Royal Institute of Technology	KTH representative *until March 31, 2019*
Annika Stensson Trigell	KTH Royal Institute of Technology	KTH representative *from April 1, 2019*
Karin Dahlman-Wright	Karolinska Institutet	KI representative
Anders Karlhede	Stockholm University	SU representative
Stellan Sandler	Uppsala University	UU representative
Gunilla Westergren-Thorsson	Lund University	External university representative *until March 31, 2019*
Göran Landberg	University of Gothenburg	External university representative *from April 1, 2019*
Fredrik Elinder	Linköping University	External university representative
Marianne Sommarin	Umeå University	External university representative *until March 31, 2019*
Katrine Riklund	Umeå University	External university representative *from April 1, 2019*

SciLifeLab Management Group (MG)

Name	Affiliation	Role
Olli Kallioniemi	Karolinska Institutet	Director
Siv Andersson	Uppsala University	Co-Director
Annika Jenmalm Jensen	Karolinska Institutet	Infrastructure Director
Peter Nilsson	KTH Royal Institute of Technology	Scientific Director (SD)
Janne Lehtiö	Karolinska Institutet	Scientific Director (SD)
Mats Nilsson	Stockholm University	Scientific Director (SD)
Ulf Gyllensten	Uppsala University	Scientific Director (SD)

Host University Rectors' Council

Name	Affiliation
Sigbritt Karlsson	KTH Royal Institute of Technology
Ole Petter Ottersen	Karolinska Institutet
Astrid Söderbergh Widding	Stockholm University
Eva Åkesson	Uppsala University

KTH SciLifeLab Committee

Name	Affiliation	Role
Mathias Uhlén	KTH Royal Institute of Technology	Integration Director (ID) *until December 31, 2018*
Amelie Eriksson Karlström	KTH Royal Institute of Technology	Integration Director (ID) *from January 1, 2019*
Sophia Hober	KTH Royal Institute of Technology	Committee member and SciLifeLab Board member
Kevin Smith	KTH Royal Institute of Technology	Committee member
Peter Unsbo	KTH Royal Institute of Technology	Committee member
Peter Nilsson	KTH Royal Institute of Technology	Committee member and Scientific Director (SD)

KI SciLifeLab Committee

Name	Affiliation	Role
Stefan Eriksson	Karolinska Institutet	Integration Director (ID)
Janne Lehtiö	Karolinska Institutet	Committee member and Scientific Director (SD)
Lars Engstrand	Karolinska Institutet	Committee member
Katja Petzold	Karolinska Institutet	Committee member
Anna Falk	Karolinska Institutet	Committee member
Vicente Pelechano Garcia	Karolinska Institutet	Committee member and Fellows representative

SU SciLifeLab Committee

Name	Affiliation	Role
Ylva Engström	Stockholm University	Integration Director (ID)
Henrik Cederquist	Stockholm University	Committee member
Barbara Wohlfarth	Stockholm University	Committee member
Lennart Bergström	Stockholm University	Committee member
Tom Britton	Stockholm University	Committee member
Sören Nylin	Stockholm University	Committee member
Joakim Edsjö	Stockholm University	Committee member
Katariina Kiviniemi Birgersson	Stockholm University	Committee member
Jesper Norell	Stockholm University	Committee member
Yuan Guo	Stockholm University	Committee member

UU SciLifeLab Committee

Name	Affiliation	Role
Mats Larhed	Uppsala University	Integration Director (ID)
Eva Tiensuu Janson	Uppsala University	Committee member
Margareta Hammarlund-Udenaes	Uppsala University	Committee member
Anna Qvarnström	Uppsala University	Committee member
Peter Lindblad	Uppsala University	Committee member
Hanna Johannesson	Uppsala University	Committee member
Karl Michaelson	Uppsala University	Committee member
Mia Phillipson	Uppsala University	Committee member
Carolina Wählby	Uppsala University	Committee member
Staffan Svärd	Uppsala University	Committee member
Aris Moustakas	Uppsala University	Committee member
Jenny Alfredsson	Uppsala University	Committee member and Vice Head of Operations
Ulf Gyllensten	Uppsala University	Committee member and Scientific Director (SD)

Campus Solna Committee (CSC)

Name	Affiliation	Role
Annika Jenmalm Jensen	Karolinska Institutet	Infrastructure Director
Peter Nilsson	KTH Royal Institute of Technology	Scientific Director (SD)
Mathias Uhlén	KTH Royal Institute of Technology	Integration Director (ID) *until December 31, 2018*
Amelie Eriksson Karlström	KTH Royal Institute of Technology	Integration Director (ID) *from January 1, 2019*
Janne Lehtiö	Karolinska Institutet	Scientific Director (SD)
Stefan Eriksson	Karolinska Institutet	Integration Director (ID)
Mats Nilsson	Stockholm University	Scientific Director (SD) and Chair
Ylva Engström	Stockholm University	Integration Director (ID)
Fredrik Sterky	KTH Royal Institute of Technology	Campus Solna Manager and Head of Operations

SciLifeLab Operations Office Management

Name	Affiliation	Role
Fredrik Sterky	KTH Royal Institute of Technology	Head of Operations
Jenny Alfredsson	Uppsala University	Vice Head of Operations

National SciLifeLab Committee (NSC)

Name	Affiliation	Role
Gunilla Westergren-Thorsson	Lund University	Chair and member of SciLifeLab Board
Lisbeth Olsson	Chalmers University of Technology	Committee member
Jan Stenlid	Swedish University of Agricultural Sciences	Committee member
Lena Carlsson Ekander	University of Gothenburg	Committee member
Mikael Sigvardsson	Linköping University	Committee member
Those Fioretes	Lund University	Committee member
Maria Fällman	Umeå University	Committee member
Tommy Olsson	Wallenberg Centers for Molecular Medicine	Committee member

SciLifeLab Platform Directors

Name	Affiliation	Platform
Bengt Persson	Uppsala University	Bioinformatics, Director
Erik Lindahl	Stockholm University	Bioinformatics, Vice Director
Hjalmar Brismar	KTH Royal Institute of Technology	Cellular and Molecular Imaging, Director
Göran Karlsson	University of Gothenburg	Cellular and Molecular Imaging, Vice Director
Anna-Lena Gustavsson	Karolinska Institutet	Chemical Biology and Genome Engineering, Director
Johan Ledin	Uppsala University	Chemical Biology and Genome Engineering, Vice Director
Richard Rosenquist Brandell	Karolinska Institutet	Diagnostics Development, Director
Ulf Gyllensten	Uppsala University	Genomics, Director
Per Arvidsson	Karolinska Institutet	Drug Discovery and Development, Director
Kristian Sandberg	Uppsala University	Drug Discovery and Development, Vice Director
Jochen Schwenk	KTH Royal Institute of Technology	Proteomics and Metabolomics, Director
Masood Kamali-Moghaddam	Uppsala University	Proteomics and Metabolomics, Vice Director

Drug Discovery and Development Platform Steering Group

Name	Affiliation	Role
Håkan Billig	University of Gothenburg	Chair
Lars Lannfelt	Uppsala University	Academic representative
Maria Jenmalm	Linköping University	Academic representative
Mef Nilbert	Lund University	Academic representative
Anna Sandström	AstraZeneca	Industry representative
Kjell Sackariassen	KellSA	Industry representative
Charlotte Edenius	Allmora Life Science	Industry representative

National Genomics Infrastructure (NGI) Platform Steering Group

Name	Affiliation	Role
Marju Orho-Melander	Lund University	Chair
Niklas Dahl	Uppsala University	Steering group member
Cecilia Williams	KTH Royal Institute of Technology	Steering group member
Erik Larsson	University of Gothenburg	Steering group member
Kajsa Paulsson	Lund University	Steering group member
Erik Johansson	Umeå University	Steering group member
Gonçalo Castelo-Branco	Karolinska Institutet	Steering group member

National Bioinformatics Infrastructure (NBIS) Board

Name	Affiliation	Role
Ulf Gyllensten	Uppsala University	Chair
Leif Andersson	Uppsala University and Swedish University of Agricultural Sciences (SLU)	Board member
Laura Elo	Turku University, Finland	Board member
Peter James	Lund University	Board member
Inge Jonassen	University of Bergen, Norway	Board member
Tanja Slotte	Stockholm University	Board member
Therese Sörlie	Oslo University Hospital, Norway	Board member
Helena Westerdahl	Lund University	Board member

SciLifeLab Fellows

Name	Affiliation
Magda Bienko	Karolinska Institutet
Simon Elsässer	Karolinska Institutet
Claudia Kutter	Karolinska Institutet
Vicente Pelechano	Karolinska Institutet
Paul Hudson	KTH Royal Institute of Technology
Ilaria Testa	KTH Royal Institute of Technology
Adil Mardinoglu	KTH Royal Institute of Technology
Lucie Delemotte	KTH Royal Institute of Technology
Marc Friedländer	Stockholm University
Tanja Slotte	Stockholm University
Alexey Amunts	Stockholm University
Kristina Jonas	Stockholm University
Oskar Karlsson	Stockholm University
Jens Carlsson	Uppsala University
Sebastian Deindl	Uppsala University
Fabien Burki	Uppsala University
Daniel Globisch	Uppsala University
Mikael Sellin	Uppsala University
Erika Comasco	Uppsala University
Olof Eriksson	Uppsala University
Aleksej Zelezniak	Chalmers University of Technology
Sari Peura	Swedish University of Agricultural Sciences (SLU)

RCP coordinators

Name	Affiliation	Name of RCP
Alexey Amunts	Stockholm University	Biology of Molecular Interactions
Mathias Uhlén	KTH Royal Institute of Technology	The Human Protein Atlas
Richard Rosenquist Brandell	Karolinska Institutet	Large-scale Clinical Genomics and Complex Diseases
Joakim Lundeberg	KTH Royal Institute of Technology	The Human Developmental Cell Atlas
Stefan Bertilsson	Uppsala University	Aquatic Microbiome Research Initiative
Oscar Fernández-Capetillo	Karolinska Institutet	Phenotypic Drug Discovery in Human Disease
Kristian Pietras	Lund University	Swedish Tumor Microenvironment (STorM) Program

Participants at the Meeting with selected Head of Departments of the host universities

Name	Department	University
Karin Forsberg Nilsson	Department of Immunology, Genetics and Pathology	Uppsala University
David Van der Spoel	Department of Cell and Molecular Biology	Uppsala University
Nils-Göran Larsson	Department of Medical Biochemistry and Biophysics	Karolinska Institutet
Susanne Nylén	Department of Microbiology, Tumor and Cell Biology	Karolinska Institutet
Stefan Ståhl	Department of Protein Sciences	KTH Royal Institute of Technology
Peter Unsbo	Department of Applied Physics	KTH Royal Institute of Technology
Lena Mäler	Department of Biochemistry and Biophysics	Stockholm University
Per Ljungdahl	Department of Molecular Biosciences	Stockholm University

Participants at the parallell session about Drug Discovery and Development

Name	Affiliation	Role
Per Arvidsson	Karolinska Institutet	Drug Discovery and Development, Director
Kristian Sandberg	Uppsala University	Drug Discovery and Development, Vice Director
Håkan Billig	University of Gothenburg	Chair and member of DDD steering group
Anna Sandström	AstraZeneca	Member of DDD steering group

Participants at the parallell session about Executing SciLifeLab's national mission

Name	Affiliation	Role
Fredrik Sterky	KTH Royal Institute of Technology	Head of Operations
Jenny Alfredsson	Uppsala University	Vice Head of Operations
Lars Hammarström	KTH Royal Institute of Technology	Strategic Relations Officer
Johan Rung	Uppsala University	Head of Data Centre
Bengt Persson	Uppsala University	Platform Director, Bioinformatics
Björn Nystedt	Uppsala University	Head of facility, Bioinformatics Long-term Support

Appendix C.

White paper – Research Integrity: Good infrastructure practice and risk management (draft)

Contents

Executive summary

Although SciLifeLab is not legally accountable for research integrity issues, there are strong incentives to establish and maintain coherent guidelines for risk management of concerns such as fraud, adhering to contracts, ethical standards, data integrity, IP breach, conflicts of interest, and reproducibility of science. This white paper presents an overview of identified risk areas and actions being taken or planned by SciLifeLab to mitigate these risks.

Introduction

During its last visit in 2017, the IAB encouraged SciLifeLab to consider aspects of research integrity and requested a white paper on this topic from the SciLifeLab perspective.

SciLifeLab is governed as a joint venture where the formal responsibility for employees and activities remain at the four host universities. Therefore, SciLifeLab is not legally accountable for the integrity of research performed, nor does it have the mandate to investigate misconduct or implement specific policies to address integrity concerns. However, this does not mean that SciLifeLab should not be concerned nor consider these issues seriously. All national facilities and research endeavors supported by SciLifeLab should be of the highest standard in terms of research integrity, ethics, reproducibility and documentation. Crisis management and communication procedures are essential if any incidents happen, but preventative actions and educational efforts are also important.

This document presents a broad view of research integrity and risk management from the SciLifeLab's perspective, including issues related to governance, ethical operational principles, code of conduct, good infrastructure practice, conflicts of interest, reproducibility, documentation and research data integrity. SciLifeLab's future success is dependent on retaining its reputation and brand as a world-class research community working according to the highest quality, ethical and legal standards. Thus, SciLifeLab needs to be proactive in addressing aspects of research integrity together with the host universities.

Risk assessment

We have identified areas where research integrity issues may arise and created a list of *potential* risks below. When the word SciLifeLab is used, unless otherwise specified, it refers to all operations nationally associated with SciLifeLab, not just facilities within the host universities.

National mission of SciLifeLab

The brand of SciLifeLab is strong not only regionally, but also nationally and internationally. Serving the national perspective responsibly and enabling transparent and open selection of funded facilities, projects (e.g. RCPs, TDPs, instruments) and allowing broad access for users on equal terms is the responsibility of the SciLifeLab Board and management. Misconduct of this responsibility can severely harm the reputation of SciLifeLab.

The SciLifeLab multi-university model and accountability

While the roles and responsibilities of the host universities are well defined, responsibility for SciLifeLab brand integrity as a national infrastructure organization remains complex and represents a potential vulnerability. On a practical level, particularly at Campus Solna, legal responsibilities that bind one host university (e.g. MTAs, DTAs, CDAs, IPR, ethical permits, consents and other legally binding agreements) may be inadvertently be assumed to cover personnel resources from another university which are not legally engaged and breach of these agreements is a risk.

Data management

SciLifeLab generates a considerable fraction of the life science research data produced in Sweden - the collection, storage, archiving and processing of which represents a major challenge. This is particularly challenging in a multi-university system with numerous parties responsible for IT. The formal responsibility for long-term storage of data generated at SciLifeLab lies with the users and their home institutions, but often they lack the capabilities, knowledge and resources to do so in a sustainable manner and at a big data scale. In addition, the new GDPR directives introduced 2018 present major storage and data-sharing challenges for sensitive personal data such as human genetic sequencing or clinical data. Coordination of these issues requires education and interaction with scientists, as well as IT and legal departments at universities. Until a sustainable framework for this is developed, maintaining data integrity remains a vulnerability.

Mentoring and training, particularly of young scientists and international recruits

SciLifeLab needs to ensure that all its resident scientists, especially international recruits, are aware of Swedish university regulations and policies. Such scientists, often in their early career stage, may come from different scientific traditions and practices when it comes to research integrity issues. Especially at Campus Solna, where SciLifeLab faculty are geographically "isolated" from their home university departments, there is a risk that personnel are not informed and do not act in compliance.

Ensuring good infrastructure practice

MG has created a Terms and Conditions for Funding document for national SciLifeLab facility operations (Appendix H). These aim to avoid SciLifeLab facilities being utilized in unethical, poorly constructed, or irreproducible scientific practices. However, as SciLifeLab carries out 3000-4000 projects annually, detailed scrutiny of individual projects is often beyond its capability. Regardless of precautions, ethical issues and irreproducibility may arise, due to technical faults, errors in sample data or labels, faulty sample storage, delayed release or loss of data, or incorrect analysis. Disagreements and research integrity issues may also arise from the determination of authorship rights based on contributions from national infrastructure services, despite international norms according to the Vancouver principles.

Reproducibility in science

Reproducibility is a major challenge in life science and SciLifeLab must always strive to promote high reproducibility of data produced, through stringent scientific, infrastructure and data practices. However, many pre- and post-analytical steps (e.g. sample prep) are beyond the control of SciLifeLab and leave a risk that data cannot be reproduced, despite our best efforts.

Ethical permits and research practices

SciLifeLab users are responsible for securing the relevant ethical permits required to perform their research and protecting identities of patients and background data before analyses are undertaken. Due to the volume of projects handled at SciLifeLab, ensuring that all ethical permits are in place is a challenge. SciLifeLab needs to ensure that its facilities are not used for unethical research purposes, such as lack of patient consents, ethical permissions or misuse of data. Recent developments

have made this concern even more relevant, given increased recent media attention to fake research and research publications and major concerns on unethical research practices, such as germline CRISPR editing.

Incidental findings in research and omics diagnostics

Incidental findings are potentially significant unanticipated findings that arise from research or diagnostic procedures and that may impact on the health of the participants. A key ethical question is as to whether they should be communicated to the research subject and how? These arise particularly in genomics, but may increasingly be found in other fields, such as plasma biomarkers. In genetics, there are international recommendations on such practices, and often these policies are typically already addressed in ethical permissions. However, in some cases these questions may come back to SciLifeLab when new investigational technologies are used.

IPR and Commercialization

SciLifeLab infrastructure services may create patentable discoveries and assets. The right to commercially exploit these discoveries belongs to the researcher who made the discovery by Swedish law. As retaining IPR is often a prerequisite by users to utilize SciLifeLab services, SciLifeLab facilities require the capacity to transfer and regulate IPR and confidentiality. This is particularly important within the DDD platform. IP may also be generated as a result of technology development within SciLifeLab facilities or by group leaders associated with facilities. Licensing or commercialization of such technologies to third parties or spinoffs backed by investors may create situations where technology developed in the SciLifeLab community may no longer be available to be applied in research services if the underlying technology belongs to a private entity. This ultimately may affect the freedom to operate SciLifeLab has to offer services to the national life science community.

Personal conflicts of facility and research staff: research vs. infrastructure funding

Many facilities arise out of individual research groups that have developed or adapted new technologies that are broadly useful to others. These scientists often continue to combine an appointment (or directorship) at a facility with a research position as a group leader or a professor. This is a very successful model and allows for innovation and technological development of the infrastructure. However, this model also has the typical risk that funding for infrastructure could theoretically create a conflict, or appearance of a conflict, that the facility funding benefits the affiliated PI's research instead of or more than external users. The converse is also true that some directors of facilities have faced a liability to their role as a PI of academic grants. When facility funding has decreased, their host departments have insisted that they should now employ facility personnel with their personal research grants. Given the size of some of the national facilities, up to 20-50 people in some cases, this is not an acceptable situation for PIs acting in research infrastructure. This liability has in some occasions made them give up serving as a facility director.

Personal conflicts of facility and research staff: academia vs. industry

There may be occasions when a scientist at a national facility has set up a spin-off company or has a personal conflict with a company providing equipment, reagents or services to the SciLifeLab facility. This is particularly likely to create problems in Sweden where the teacher exemption gives individual PIs right to exploit commercialization of findings at their institution.

Crisis management

No matter what precautions are taken for securing quality, integrity, and ethical priority in its activities, situations may occur where SciLifeLab activities in a specific project or even as a whole are questioned. This may be of direct or indirect causes, for example by misconduct of a user, a facility, a spinoff company or with any researcher with a connection to SciLifeLab. Although the main responsibility always lies on the host university of the person concerned, SciLifeLab's brand and image may be irreversibly damaged. SciLifeLab may become the victim of different types of crises for many reasons, ranging from physical accidents in lab environments, to research fraud by a facility or external user, or public reactions to controversial research projects or actions.

Mitigating integrity risks within SciLifeLab

We have identified key actions and preventative measures that are important for SciLifeLab to maintain high research integrity, good infrastructure practice and minimize risks. These are outlined below under the same headings as above. Action items are numbered.

The SciLifeLab multi-university model and accountability

The multi-university model for SciLifeLab is strong but also complex and there is need to further clarify the responsibilities between the SciLifeLab Board and SciLifeLab host universities. Also, the role of KTH as primary host university needs to be considered in case integrity issues associated with the SciLifeLab name and brand arise.

1) The SciLifeLab Board will discuss and clarify its role in relation to KTH and other host universities to define responsibility regarding crisis management and perception of SciLifeLab as a national infrastructure.

2) SciLifeLab is considering setting up a multidisciplinary, cross-university working group to address good infrastructure practices, preventive measures and practical risk and brand management in the SciLifeLab community.

3) The planned investigation on legal representation of SciLifeLab should also explore research integrity and risk management practices across the entire SciLifeLab community, including academia, health care and industry.

4) SciLifeLab will arrange discussions and information on working in a multi-university context such that the staff understands the complications and risks associated with university-specific regulations, particular towards external parties (MTAs, DTAs, CDAs etc.)

National responsibility of SciLifeLab

SciLifeLab needs to maintain the operations of its national life science infrastructure responsibly. Priority of funding and strategies need to be done in an open, transparent and fair manner. SciLifeLab has a four-year facility funding cycle including an international mid-term evaluation to assure integrity of this process.

5) Involve the national community in reviewing current infrastructure deliverables and planning the next phase of each of the SciLifeLab infrastructure platforms. Continue transparent operations, decision-making and communication about new calls and decisions on funding.

Data management

SciLifeLab adheres to international FAIR data principles (Findable, Accessible, Interoperable and Reusable) and fosters good data practices amongst users and the life science community in general to minimize risks with handling sensitive data.

6) Engage the SciLifeLab Data Centre to assist and educate facilities, users and their home universities in long-term solutions for responsible data management, including storage, processing, FAIRness and GDPR.

7) Data Centre has a mandate from the SciLifeLab board to represent SciLifeLab towards host universities, SNIC and other parties in issues regarding IT and data management, and to promote better coordination of the data infrastructure of life sciences in Sweden.

8) The SciLifeLab Bioinformatics platform (NBIS) will create an agreement so that UU can serve as a central host for processing and analysis of all human (genome) data from any university in Sweden to enable GDPR compliant national data analysis infrastructure.

9) SciLifeLab will define expectations of data handling for national facilities and include these in facility agreements, but also facilitate such arrangements by providing systems, software, training and guidance.

Mentoring and training, particular of young scientists and international recruits

10) SciLifeLab will continue to arrange courses and training events, including on GDPR and will include other aspects of research integrity on the agenda.

11) SciLifeLab Campus Solna introduction material will be revised to include paragraphs on research integrity, data management and risks of the multi-university environment.

12) Although all universities in Sweden have the same legal responsibilities and similar policies and regulations, SciLifeLab has to make sure that all personnel are aware of these.

Ensuring good infrastructure practice

The MG requires facilities to adhere to the *Terms and Conditions for Funding* guidelines (Appendix H) in order to be funded as a national facility, including good infrastructure practice so that facilities can set up their technologies, select projects, perform high-quality service, keep necessary logs and handle data responsibly.

13) SciLifeLab will continue to systematically define guidelines for good facility practice when it comes to research integrity issues as well as data handling. Every year, a meeting is held with all facilities where the current challenges or needs for new guidelines are assessed. Therefore, the facilities are also involved in creation of new and improved guidelines.

14) The SciLifeLab facility agreement will also include an expectation that conflicts of interest need to be communicated and resolved, particular for personal conflicts with companies that are collaborating with the facility.

15) SciLifeLab facilities need to ensure that their services do not infringe on patent rights, commercial interests, or compete unfairly (with government subsidies) with the private sector. This is particularly critical when serving non-academic customers, such as health care and industry.

16) Co-authorship between the user and SciLifeLab staff should be clarified preemptively to avoid potential conflicts. In some facilities, co-authorships are rare, while in others intellectual contributions meeting the criteria of authorship often belong to the nature of the service. Guidelines for this process are outlined in the Terms and Conditions for Funding document and adhere to Vancouver principles (Appendix H).

Ethical permits and research practices

All facilities supporting projects requiring ethical permits must clearly communicate that the responsibility for securing the necessary permits lies with the user. However, the facility must also accommodate the requirements stated by the permit, which is especially important for generation of clinical data. SciLifeLab has actively informed facilities about consequences relating to GDPR legislation, in addition to the new guidelines to adjust to GDPR requirements from the host universities.

17) Human genome sequencing operations at SciLifeLab take place in access-controlled environments. Human genome sequence data are delivered to a dedicated IT system at SNIC, the so-called Bianca server (in 2018-2019) where it can be analyzed in a safe and secure manner.

18) When possible, raw RNA/DNA sequence data will be converted to e.g. gene expression counts or lists of (somatic) mutations that are not be considered as sensitive data.

19) SciLifeLab facilities clearly indicate in their user agreements that users are responsible for securing required ethical approvals, patient consents, animal experiment permissions (when relevant), and that human data are handled responsibly and in a GDPR-compliant manner. The facility agreement will clearly indicate that that neither the SciLifeLab board nor host universities will allow for unethical research to be carried out at the national facilities.

Incidental findings in research and omics diagnostics

20) SciLifeLab expects that users follow standard international recommendations, ethical guidelines, and patient consents on how to deal with incidental findings.

IPR and Commercialization

SciLifeLab does not develop, own or transfer intellectual property. SciLifeLab service agreements with users typically transfer results and IP to the users of the facility. This prevents SciLifeLab (or the host universities) in dictating commercialization principles for its researchers. However, universities have dedicated innovation offices to assist researchers in the commercialization process.

21) SciLifeLab needs to secure the best possible prerequisites for innovation and commercialization to occur within its boundaries. This includes securing the possibility for confidentiality. The DDD has built best practices here that can be applied elsewhere within SciLifeLab.

22) As SciLifeLab's host universities are public authorities, SciLifeLab is subject public disclosure legislation that can jeopardize protection of IP-sensitive data and results. SciLifeLab has been and will be in active dialog with the government to ensure better protection of confidentiality within academia. Using SciLifeLab service should not impact on researchers risking their confidential background, sideground, and foreground data or IP.

Personal conflicts of facility and research staff: research vs. infrastructure

23) SciLifeLab expects that all national funding provided to facilities is managed in accounts that are separated from the facility directors' own research accounts as a PI. SciLifeLab facility funding cannot be used for a PI's research funding, nor can missing funding to a facility to be compensated for from a PI's research grants. This is indicated in the Terms and Conditions for Funding document (Appendix H).

Reproducibility in science

The quest to secure quality and reproducibility of research is common to scientific organizations globally and a topic of considerable current debate. SciLifeLab has established high-quality, sometimes accredited, lab procedures that promote reproducibility in science. This problem is however not limited to generation of data but also relates to pre-analytical steps, study design and the interpretation of data that are often not in the control of service facilities.

24) SciLifeLab has a responsibility to inform the users on limitations of data interpretation, an area where SciLifeLab's dedicated facility staff play a crucial role. SciLifeLab also provides professional support for data analysis via the Bioinformatics platform and other functions. SciLifeLab regularly holds workshops and training on aspects of data integrity, reproducibility, and related topics.

Crisis management

25) A proactive crisis management plan both for physical risks or public/media situations is necessary. SciLifeLab is putting together a crisis management plan with two tightly linked sections (physical accidents and media-based crisis communication). Such plans have been available at Campus Solna and in Uppsala but as SciLifeLab grows, this need to cover all national activities including non-host universities. The new plan aims to also clarify communication strategies in alignment with the universities. It is very important for SciLifeLab to speak with a unified voice in such a situation, while primary communication often will be directed by one of the host universities.

Conclusion

Given the volume and scale of SciLifeLab activities, with a community of over 1000 affiliated scientists from many universities, 3000-4000 service projects carried out annually at SciLifeLab facilities, with 10,000s of samples analyzed, terabytes of data being produced, stored and analyzed per year, with both commercial and health care links increasing, the likelihood of some issues arising on research integrity, research reproducibility or other risks is almost inevitable in due course. While we have not had a major crisis at SciLifeLab over the past 9 years, some concerns have certainly already touched the SciLifeLab community and have been handled at the host universities according to internal guidelines. The 25 actions indicated here are meant to proactively decrease research integrity issues, improve research infrastructure services and reduce risks for the SciLifeLab and its host universities when it comes to brand, recognition, profile and funding. Some of these actions are underway and incorporated into the Terms and Conditions for Funding document, while others will be acted upon the approval of this document at the SciLifeLab board.

Appendix D.

White paper – Industrial Collaboration (draft)

Contents

Executive summary

Collaboration with industry represents an important facet of SciLifeLab's operations, which the government would like to promote and expand. Service activities to the industrial sector account for about 5% of total SciLifeLab facility resources, but the practical impact of industrial engagement is much larger, creating a foundation for technology co-development and transdisciplinary collaboration. Expanding and supporting increased collaboration with industry is dependent on i) dedicated resources and activities with an industrial focus, ii) creation of better organisational pre-requisites for establishing and maintaining industrial collaboration, and iii) clarification of the mission of SciLifeLab in the Swedish life science ecosystem. These challenges are currently being addressed through investment in staff, strategic development of methods for industrial interaction, communication and branding, and dialog with governmental and university stakeholders for alignment of SciLifeLab's mission and funding base for the future.

Introduction

In its meeting on March 8-9, 2017, the IAB requested a white paper on the topic of industrial collaborations. SciLifeLab already has several different types of interactions with the industrial sector including: i) companies providing technologies and methods for the platforms and facilities ("vendors"), ii) private sector users of facilities, iii) industry use of facilities as testbeds for developing new technologies in collaboration, iv) strategic research collaborations, and v) spin-off companies arising out of SciLifeLab-associated research. Industry engages with SciLifeLab in different fields of research, such as diagnostics, pharma/biotech, med-tech, contract services, ITC, environmental science and other fields nationally and internationally.

Sweden's life science industry has a strong heritage and maintaining close ties with this sector is important to SciLifeLab's future development. Industry provides the majority of the total annual R&D funding in Sweden and a recent report from the Confederation of Swedish Enterprises [1] identifies access to qualified personnel and strong academic environments as the most important factors governing where corporations choose to invest their research activities.

In addition to the benefits of interacting with industry for the purpose of collaborative research, there have also been expectations on increasing the availability of SciLifeLab's infrastructure services to industry partners. The governmental research proposition of 2016 (2016/17:50 – Kunskap i samverkan) has stated specifically that there needs to be a greater accessibility and utility of national research infrastructures for the broader scientific community in Sweden:

"…industry access to research infrastructures such as SciLifeLab, MAX IV and ESS should be further developed and strengthened… It is desirable that the use of existing research infrastructures be broadened by providing business and public sector players with the opportunity to conduct outstanding research and development at the facilities. It is important that existing legislation and governance models do not exclude researchers working outside academia and are in line with the government's overall ambition of increasing accessibility of research infrastructures in order to meet our social challenges."

The government's ambitions are in line with SciLifeLab's vision to develop into a national hub for life science, supporting biomolecular research across disciplines and sectors, and enabling science that would not otherwise be possible in Sweden. We believe that SciLifeLab could be more effectively promoted as a key component of the overall Swedish life science ecosystem, as a tool for attracting visibility, international investment, clinical trials, talent and research efforts to Sweden. SciLifeLab could be a key vehicle for societal growth, innovation and industrial collaboration - and has already shown potential in attracting funding, visibility and expertise to the country. Thus, significant interest is currently focusing towards using SciLifeLab as a preferred national collaboration partner for industry, for NGOs and for international networks.

[1] Görnerup, E. "Näringslivet och akademin", Svenskt Näringsliv, (2018) 1-12

Problem statement

Although there is growing interest in SciLifeLab from the industrial sector, the relative utilization of SciLifeLab infrastructure by industry has remained relatively constant at <5% of total over the period 2014-2017 (Figure D1).

SciLifeLab is funded by the Ministry of Education & Research and hence its primary efforts have been to develop a framework for supporting the academic user community. Thus, services and underlying technologies are not primarily tailored for industrial needs. Preliminary investigation has however indicated that there are clear hurdles that could be addressed in order to increase awareness, availability and access of non-academic users to SciLifeLab:

1. Communication, branding, and collaboration management: SciLifeLab lacks both sufficient dedicated resources for promoting its activities, expertise and capabilities, and also clarity of its mission and responsibility, particularly to the non-academic sector in Sweden and abroad. The individual scientists and over 40 facilities within SciLifeLab, spread across 10 universities nationally, are today supported with only one dedicated person in charge of promoting/branding the use of SciLifeLab in non-academic contexts, international exposure, and coordination of collaborations with external parties. During 2017, the SciLifeLab External Relations Forum (SERF) was established, consisting of representatives from host university external relations and/or innovation offices together with the SciLifeLab Strategic Relations Officer. SERF is intended to build a more consistent dialog between host universities and SciLifeLab's strategic management and allow alignment of partnering and collaboration strategies between industry and academia. This effort has created a better dialog and flow of information on efforts within each organization. It is, however, critical that SciLifeLab secure dedicated resources specifically allocated to support part-

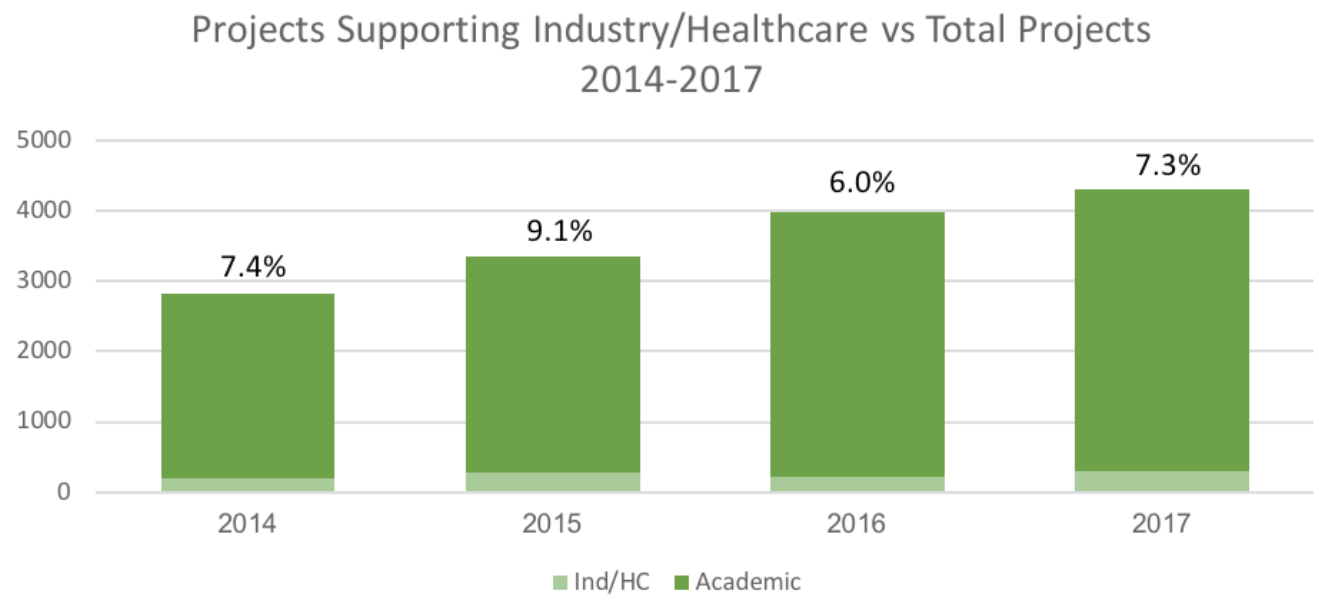

Figure D1. Figure illustrating number of projects supporting industry (Ind) and healthcare (HC) as a portion of total number of projects performed within all SciLifeLab facilities during the period 2014-2017. 2014: 195/2632 (7.4%), 2015: 279/3077 (9.1%), 2016: 226/3754 (6.0%), 2017: 294/4003 (7.3%). Based on reported activities from all SciLifeLab facilities to management through facility reports 2014-2017.

nering and collaboration with external entities. In addition, the role of SciLifeLab can be expanded to be part of national and international endeavors and networks, beyond the scope of single university engagements. How SciLifeLab positions itself towards these initiatives needs further clarification in dialog with the host universities and other key stakeholders.

2. Legal representation and contracting: As SciLifeLab is a distributed infrastructure not represented by a dedicated legal entity its organization, personnel and facilities span over 10 universities and dozens of departments nationally. Although this diversity underlies the dynamic environment of SciLifeLab - coordinating these assets and resources within the scope of a collaboration with external parties is a considerable challenge. SciLifeLab is dependent on each host university legal department to independently support contracting and partnering initiatives as no dedicated legal resources are available within SciLifeLab. Thus, formalization and execution of agreements and contracts can in many cases take a very long time, particularly when more than one university is participating in a collaboration. As SciLifeLab extends its organization further beyond the host universities nationally and also engages more readily with external parties, the challenges to its legal representation will likely increase.

3. Policies and practices for access to infrastructure: In general, all qualified academic researchers have equal access to the SciLifeLab infrastructure. If demand is greater than resources can accommodate, prioritization of projects based on scientific excellence (usually by an external advisory group) is applied. Increasing industrial usage presents several challenges to this policy that need to be addressed:

a. Prioritization of industrial users is difficult utilizing the same process as for academic researchers. Often, industrial utilization is not focused on open science principles with a goal of publishing, rather highly specific and confidential research. For this reason, facility personnel may be less incentivized to work with industrial projects. Therefore, academic and industrial users cannot be triaged against the same scale of priority and in often oversubscribed facilities, the prioritization remains a challenge.

b. Many facilities have long queues for access; if industrial projects are not prioritized, waiting times may become too long to be practical.

c. Due to principles of public disclosure, to which all Swedish universities are bound, it can be difficult to preserve the adequate confidentiality and IPR protection acceptable for industry.

d. SciLifeLab infrastructure facilities need to charge full cost for industrial access to infrastructure. In several areas, this may render the services expensive and hence uncompetitive for private sector users, particularly in comparison with dedicated contract research organizations (CROs) internationally. On other occasions, full-cost pricing has led to claims that SciLifeLab fees are too low and hence could interfere with pricing in the private sector. Obviously, as a publicly funded initiative, SciLifeLab needs to avoid direct competition with the private sector.

In order to facilitate the transition of SciLifeLab into a hub and a resource for the entire life science community in Sweden, dedicated resources and a clear strategy are required to increase SciLifeLab's availability and accessibility for sectors outside of academia. We believe that there is a need to invest more into the organizational management and branding of SciLifeLab, with the purpose to specifically addressing the limitations listed above.

So, what is an optimal level of industrial engagement? We do not believe that it is appropriate to aim for a specific percentage, as this will be self-regulating, or to require a certain ratio of industry users on a facility level, as the relevance to industry varies within the infrastructure. We do, however, believe that we should aim for creating the best pre-requisites possible for industry to be informed, empowered, and capable of utilizing SciLifeLab as a resource, in an open and efficient manner.

Solution

Reaching the aforementioned goal is based on securing strategic resources, funding and organizational development of SciLifeLab during the next 5-year period.

Dedicated coordinative resources: SciLifeLab External Relations Office

In November 2018, the Swedish Research Council approved SciLifeLab's application to establish a dedicated External Relations Office within the scope of its call "Increased Access to National Infrastructures". SciLifeLab was granted 8 MSEK over the period 2019-2022, allowing the recruitment of a dedicated industry/clinical liaison, to support the Strategic Relations Officer in engaging with organizations and individuals from these sectors in a proactive manner. The Office will also be complemented with a legal coordinator with the task of coordinating the legislative and legal complexities between SciLifeLab and host universities, assist with drafting of agreements, identification of funding opportunities etc. These resources will supply a critical complement to the Operations Office, supporting SciLifeLab infrastructure and research community with increased access to engaging with the industry and healthcare sectors (Figure D2).

Branding strategies/events/communication

SciLifeLab has made dedicated efforts over the past two years to increase its exposure to the industrial sector. This has been done primarily through increased dialog with potential partner industries, who frequently visit SciLifeLab to discuss collaboration possibilities. Examples of companies that have visited SciLifeLab during the period 2017-2018 include Aprea, AstraZeneca, Beactica, BGI, Bioneer, Bioreparia, Bristol Meyer Squibb, Ferring Pharmaceuticals, GE Healthcare, HighRes Bio, IBM, Johnson & Johnson, Labcyte, Lexogen, Merck, Microsoft, Olink, Pelago, PExA, Roche, Samsung, Scienion, Syncona, Takeda, ThermoFisher Scientific, and UCB Pharma. Securing additional resources dedicated to maintaining these relationships and further developing them into fruitful collaborations will be an important step to increasing industrial collaboration across SciLifeLab. Increased resources allow a more preemptive approach to industrial partnering, reaching out towards external parties of strategic interest to SciLifeLab in a proactive manner. A particular need is to increase the awareness of SciLifeLab outside the health/pharma/biotech sector and branch to other areas of life science, e.g. the environmental and biotechnology sector.

Often it is not only the SciLifeLab technologies and infrastructure that attracts users per se, but the joint capability to make use of the latest technologies with research experts, health care, biobanks etc. Therefore, we plan therefore to focus on promoting such joint research collaborations.

During 2017-2018 SciLifeLab has taken an active role in

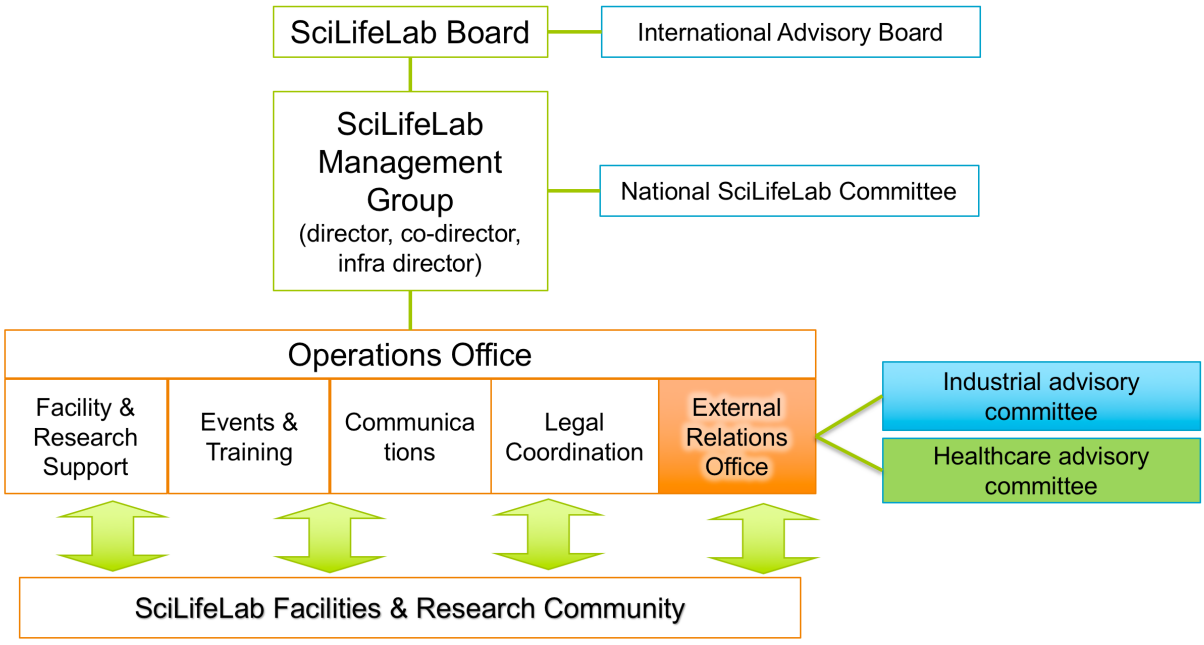

Figure D2. Organization of the External Relations Office within the national SciLifeLab Operations Office. Complementing the current capabilities (communications, events, training, infrastructure support etc) with external relations capacity will create a link to external users and collaborators for the infrastructure.

several national and international conferences, symposia, workshops and events specifically catering to the industrial sector. SciLifeLab continues to be an active contributor to AIMdays, recurring thematic workshops with a specific focus on a research area of high current interest to both academic researchers and industry. In September 2018, SciLifeLab helped to co-organize the annual Nordic Life Science Days (NLSdays) which were held in Stockholm. NLSdays is represented by over 1300 delegates each year, primarily from both the Nordic region and elsewhere in Europe. Participant groups range from industry scientists, management, business development, VCs, service providers and regional trade associations. SciLifeLab hosted a one-day satellite symposium to NLSdays, where industry delegates from over 90 organizations attended to learn more about SciLifeLab. In addition, a dedicated SciLifeLab workshop was arranged, featuring emerging technologies being developed within SciLifeLab that can be of interest to industry. A more proactive approach and increased resources would allow for even greater exposure at additional national and international events with a focus on industrial life science research and technology, such as BioEurope and SLAS.

National/international funding and networks

Both major national and international grant calls focused on industry-academic collaboration (VINNOVA, H2020, IMI, etc) are increasingly dependent on participation of considerable infrastructure components for guaranteeing feasibility of proposed project plans. Here, SciLifeLab can play an important role in securing infrastructure access to Swedish and international consortia. Today, SciLifeLab's individual facilities are often included in such calls, under their respective host university names, but such collaborations can then incorporate only one university at a time (given that typical EU collaborations cannot have multiple partners from a single country). An improved and coordinated ability for the SciLifeLab community to apply for international funding would be beneficial to both the host universities and Sweden as a whole. This would enable SciLifeLab to join and proactively participate in international networks or infrastructure consortia, such as EU-Life, ESFRI programs, IMI calls, international Precision Medicine initiatives etc.

Review of SciLifeLab's legal representation

An issue that restricts collaborating broadly with industry is the de-centralized legal status of SciLifeLab's individual components. SciLifeLab is not a legal entity, rather an integrated part of the host universities. As such, SciLifeLab cannot enter into legally binding contracts under its own name, seek national or international funding as an entity, jointly procure critical instrumentation between different parts of the infrastructure, or take an active part or membership in international networks or collaborations.

The infrastructure facilities are legally localized within one of the four host universities and several SciLifeLab platforms host facilities from multiple universities. Hence, industrial users/collaborators wishing to access multiple facilities require contractual engagement and negotiation with multiple universities, which can be costly, slow and complex. During 2018, both DDD and NBIS have initiated activities to formally place their respective platforms legally under Uppsala University to avoid this dilemma. It is, however, not sustainable or a holistic solution to create a SciLifeLab organization where individual platforms have their coordinating "homes" under different universities.

Today, the possibility to create pan-SciLifeLab collaborations with industry are complex and thus most collaborations are restricted to individual facilities (or PI:s) through their respective host university departments. The role, name and brand of SciLifeLab are thus absent from the context of the collaboration and often SciLifeLab management may not even be aware of such collaborations. This is a challenge for the expected role of SciLifeLab to be a key component of the industrial interactions.

The issue of SciLifeLab's future legal representation has been debated since the launch of SciLifeLab, and resolving this issue is beyond the scope of this document. There is, however, a strong consensus that SciLifeLab's scientific identity should remain tightly interlinked with the host universities. SciLifeLab management and the host universities are currently planning a review of the legal issues of relevance to industrial interaction during 2019. This review and potential avenues forward will be presented to the SciLifeLab Board and the rectors of the host universities for consideration in late 2019.

Dedicated facility resources and funding for industrial utilization

If there is a continued demand for services from industry, it would be possible to set up a full-cost services system that operates independently from the academic user base. This approach has been successfully implemented by the Clinical Genomics facility, the overwhelming majority of which is dedicated to full cost service towards the healthcare sec-

tor (see Appendix E. White Paper - Clinical Collaboration). Healthcare utilizes >80% of the Clinical Genomics services and the facility has thus been optimized for this process. In facilities with much lower (and infrequent) levels of full-cost utility, maintaining a critical mass of resources is more difficult. In order to not drain resources from the personnel dedicated to the academic sector, complementary public funding and complementary methods for industry access would need to be secured. These options have been introduced to the government and will be part of SciLifeLab's roadmap when applying for continued funding during 2019.

Conclusion

In summary, industrial engagement is critically important for the future of SciLifeLab as an organization as well as for fulfilling the government's expectations for the major national infrastructures. Setting up a strategy for the next 5-10 years requires clarification of both the role that SciLifeLab is expected to play towards industry as well as how it should interact with the health care sector as well as the international arena. These will all depend on how SciLifeLab's role is perceived and if and how it is expected and mandated in practice to function as a hub for life science collaborations in Sweden. The recent success in gaining additional dedicated resources for industry engagement will help this development.

Appendix E.

White paper – Clinical Collaboration (draft)

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Executive summary

SciLifeLab works actively with clinical and translational reseachers as well as the healthcare sector to enable research on human health and to facilitate transfer and clinical adaptation of new technologies. It is thus important that SciLifeLab develops increasingly holistic sample-to-data solutions and pipelines for clinical and translational research within its facilities. SciLifeLab could also play an important role in national initiatives for precision medicine and future health care, currently being developed by Sweden's Life Science Office. The recently launched national precision medicine initiative, Genomic Medicine Sweden (GMS), is an example of SciLifeLab's contribution to healthcare, and presents a path that the SciLifeLab community can utilize to bring additional advances from research towards clinical application.

Introduction

Applications of research in healthcare represent aspects of SciLifeLab's operations with perhaps the greatest direct impact on society. Several SciLifeLab facilities (eg Clinical Genomics, Proteomics, Plasma Profiling and Mass Cytometry) have substantial research collaborations at the clinical research interface. A considerable number of SciLifeLab scientists also have dual affiliations with university departments and hospitals and thereby serve as a natural bridge between SciLifeLab and healthcare. This has led to a steady increase in clinical collaboration and co-publication with clinical researchers and the healthcare sector over the past few years, now accounting for over 30% of all publications from SciLifeLab. [1] However, research in healthcare is complex and highly regulated at the level of ethical, legal and data practices. Ensuring effective and secure interoperability of data and samples between the clinic and SciLifeLab's academic environment is thus critical.

Interactions between SciLifeLab and healthcare have grown significantly in the past few years, and as of 2018, healthcare made up 8% of the users of SciLifeLab services. This is to a large extent mediated through the Clinical Genomics facilities within Diagnostics Development (DD), providing healthcare units at major university hospitals access to state-of-the-art sequencing capacity for diagnostic and clinical research purposes. Increasingly, however, clinical and epidemiological research, clinical trials, diagnostics development, clinical biomarker discovery, and precision medicine efforts could also benefit from the multitude of additional omics, imaging, functional and translational technologies that SciLifeLab hosts. We thus hope to utilize the lessons learned from the Clinical Genomics efforts towards catalyzing the transfer of new technologies into the clinic.

The newly instituted Governmental Life Science Office is developing a life science strategy for Sweden, heavily focusing on clinical research and medical innovation, where *precision medicine, data handling* and *future healthcare strategies* are prioritized areas where SciLifeLab can and should play an important role. In addition, there have been considerable governmental and regional investments in establishing biobanks, facilities for production of biological therapeutics or utility of artificial intelligence, all areas that have considerable potential for SciLifeLab to collaborate with and many such interactions are already underway.

This white paper will focus on two topics: i) the potential of evolving SciLifeLab's organizational and collaborational role in clinical research and future healthcare in alignment with the national life science strategy for Sweden and ii) the practical steps that SciLifeLab can do to further enhance that its platforms are useful to clinical researchers, clinical trials and healthcare.

We hope that SciLifeLab can be seen as an emerging life science hub in Sweden through its extensive network of affiliations and connections as well as a host of capabilities for reserch on human health. We believe that there resides significant potential in building further on this network and fully capitalizing the SciLifeLab model for the benefit of the future of healthcare in Sweden.

[1] Based on PubMed analysis of SciLifeLab publications co-authored by hospital-affiliated researchers during 2015-2018.

The national life science strategy for Sweden

In February of 2018, the Governmental Life Science Offices of Sweden were established, with the aim of forming a bridge of dialog between the ministries of Enterprise & Innovation, Research & Education and Health & Social Affairs. The offices have set three preliminary priority areas for Sweden as a life science nation:

1. *Utilization of digital healthcare data* – The growing digitalization of patient-healthcare interaction is poised to generate massive quantities of data from disparate sources. Collecting, integrating and utilizing these data for the benefit of patients, healthcare providers and researchers in Sweden requires the appropriate legislative and technical pre-requisites, integration of biobanks and registries, and interoperability of data.

2. *Precision medicine:* future diagnostics, treatment and cures – There is a rapid development from "one size fits all" healthcare to an individualized patient approach for preclinical and clinical research, healthcare and medicine in general. Sweden hosts a range of capacities that can put us at the international forefront, but requires alignment in order to be utilized efficiently. Appropriate legislative and reimbursement models need development, and access and sustainability of the appropriate infrastructures hosting necessary omics and computing technologies need to be secured.

3. *Future healthcare:* integration of research and development – The development of next-generation healthcare requires an integration of R&D activities into medical practice, incorporating innovation into healthcare activities through cultural and structural evolution. This requires increased dialog and proactive collaboration of the academic and industrial sectors with healthcare, an increase and prioritization of exploratory clinical trials in Sweden, and the regulatory requirements necessary to efficiently enable access to the most innovative medicines to patients.

Although these priority areas are still being further elaborated, SciLifeLab can play a significant role in all of them. SciLifeLab has had initial dialog with the government in this regard, highlighting our potential contributions, which will benefit the long-term funding and sustainability of SciLifeLab. Concomitantly, it is apparent that in many aspects universities, health care organisations and the government are not fully aware of the capabilities that SciLifeLab can provide to e.g. precision medicine. Therefore, further education, profiling and branding of SciLifeLab as a contributor to this field of development is necessary. It is therefore our plan to take the base of this writeup and develop a dedicated white paper to the government and funding agencies detailing SciLifeLab's potential and future contributions to precision medicine.

Many of the fundamental challenges faced in dealing with healthcare collaboration are common with those presented on industrial collaboration, i.e. dedicated resources, exposure/branding, and legal ability. Strategies to address these are presented in Appendix D and will not be revisited here. The development of future healthcare and precision medicine in Sweden is a long-term complex program and requires coordination with a nation-wide network of universities, public healthcare regions, hospitals, regulatory authorities and hence the role of SciLifeLab in this process needs to be defined carefully and clearly. It is not the role of SciLifeLab to carry out medical diagnoses or become a routine health care service partner, rather it aims to facilitate the translation of such capabilities to the clinic.

Utilization of digital healthcare data

Unraveling the molecular complexities of human disease requires a broad array of technologies generating vast amounts of data from diverse sources. Human research data, often sensitive in nature, is one of the most valuable products of SciLifeLab services, and it is important to extend the availability of both technology platforms and data resources to non-academic and healthcare users. Securing adequate e-infrastructure for interoperability, security, storage and sharing of this data requires the collective efforts of the entire life science community, including industry and healthcare, but also a regulatory and ethical framework to enable sharing. Handling data from patients or individuals participating in research requires elaborate and interoperable IT systems and data management. Today, these data resources are scattered within the 23 independent healthcare regions in Sweden which have full authority and exclusive responsibility for handling data from their patients. Thus, interoperability and data sharing are challenging and The Life Science Office sees digital healthcare data transformation as one of the major focus areas for the nation.

SciLifeLab can contribute to building technologies and enabling capabilities for translational molecular research data in Sweden. SciLifeLab's Clinical Genomics facilities within the DD platform have laid the groundwork in implementing inter-sectorial data-pipelines for real-time diagnostic genomic analysis of patients with rare genetic diseases and cancer. This initiative is now being further developed within other indications and on a national level with the launch of GMS. To date, Genomic Medicine Centers (GMCs) are under establishment at all seven university hospitals and remain linked with the DD platform of SciLifeLab. GMS will have a strong focus on uniting all healthcare regions through a common ethical, legal, technical and analytical framework. Legal representatives from the healthcare regions have started discussions on the legislative aspects of data sharing within healthcare, between healthcare and academia, and with industry, aiming to make joint interpretations and recommendations for data sharing and storage. The GMS informatics team is working closely with NGI and NBIS to develop a common IT-infrastructure for genomic data sharing and storage. These data analysis, interpretation, storage and sharing modules will constitute a new type of national resource at the intersection of healthcare and academia. Future initiatives within other omics technologies will require similar centralized data support in order to maintain interoperability – an initiative requiring national coordination.

To fully utilize the increase in data volume and complexity that we expect as a result of closer interaction between research and healthcare, a greater coordination of technical as well as legal work on the national level between universities, infrastructures, healthcare, and other stakeholders is required. Improved support functions for IT processes and data management are needed to translate the generated data to new scientific results with truly societal benefits, and SciLifeLab will take a leading national role in this work.

Precision medicine and Genomic Medicine Sweden (GMS)

Precision medicine

In the emerging precision medicine era, the prevention, early diagnosis and treatment of diseases become increasingly individualized, and hence diverse and complex (Figure E1). While precision medicine will eventually involve multi-omics approaches, most current efforts under this name are heavily focused on genome sequencing and linking such data with healthcare outcomes. The biggest efforts so far in the EU have happened in UK, Germany and France (e.g. Genomics England's 5 Million Genomes project). In addition, an EU level program to develop a shared sequence resource (with associated demographic, clinical and follow-up data) for 1 M people is currently being planned.

Launch of GMS

Sweden's efforts in Precision Medicine are heavily focused around Genomic Medicine Sweden (GMS, Figure E2), which has its roots in the SciLifeLab DD platform. This effort, originally developed for allowing rapid-real time NGS-based diagnosis of rare inherited diseases and cancer, has since 2017 become a nation-wide effort to implement and utilize NGS as a routine clinical diagnostics tool also for other indications. The effort recently received 40 MSEK stage-2 project funding from Sweden´s Innovation Agency, Vinnova, for expanding the initiative to all seven major university hospitals in Sweden during 2019-2020. The ultimate aim of GMS is to integrate findings from next-generation sequencing into individual patient electronic healthcare records and registries enabling personalized management and care, and to provide a unique resource for population-based, cross-disciplinary research projects within the field of precision medicine. Clinical whole-genome sequencing has already been established for rare inherited diseases in 2015 and today over 3000 such diagnoses are done annually. Over 5000 cancer samples undergo panel sequencing today across Swedish hospitals.

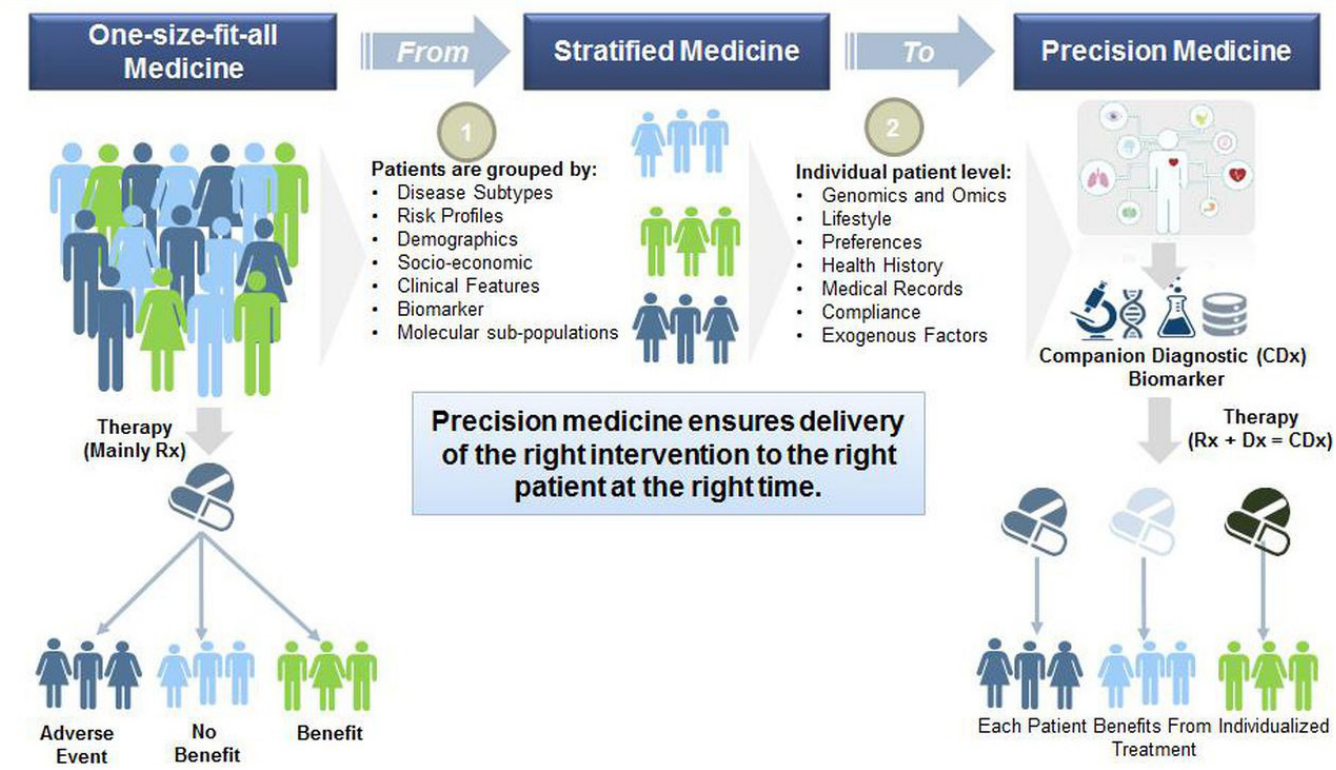


Figure E1. The paradigm shift of precision medicine (Frost & Sullivan).

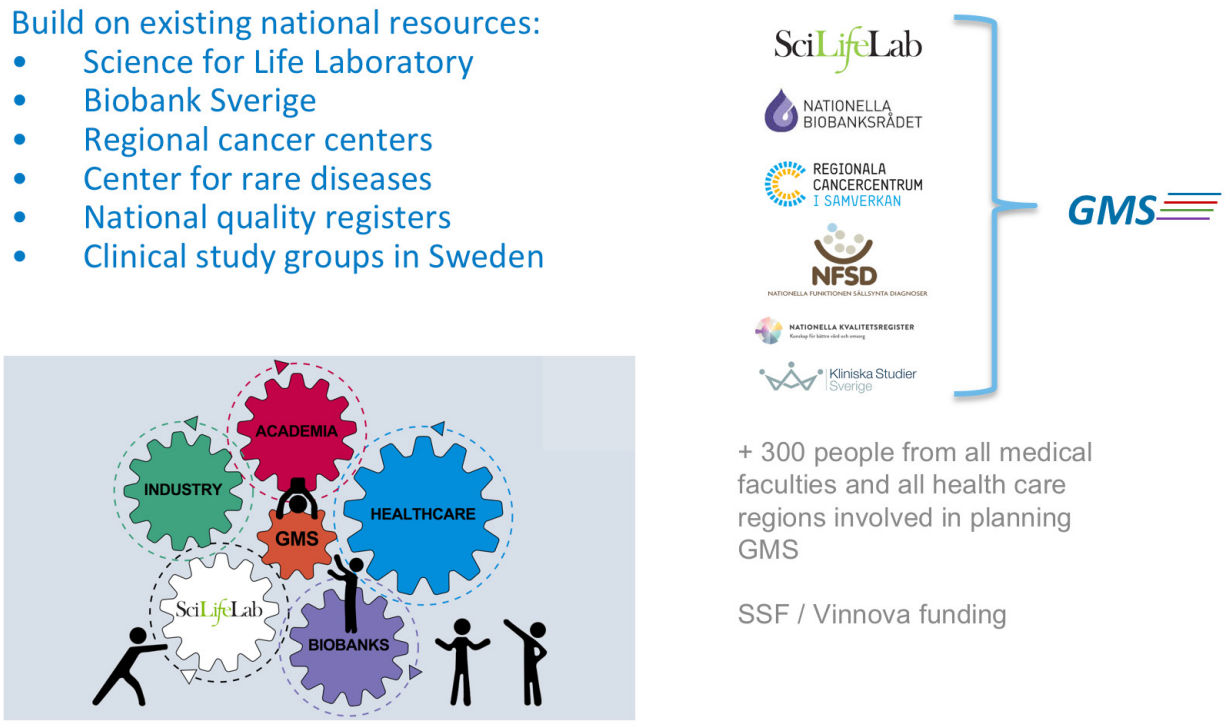


Figure E2. The Genomic Medicine Sweden effort: summary of partners and goals.

GMS and SciLifeLab relationship evolves

The primary disease focus areas of GMS are rare inherited diseases and cancer (both solid tumors and hematological malignancies) as well as infectious diseases/microbiology. The next phase will also encompass addressing complex diseases, pharmacogenomics and health economy aspects, partially through one the SciLifeLab RCPs. To extend the GMS initiative nationally, regional Genomic Medicine Centers (GMCs) will be established at all university hospitals (Lund, Gothenburg, Linköping, Örebro, Stockholm, Uppsala, Umeå).

The SciLifeLab Clinical Genomics facilities at these sites play a key role as established facilitators between academia and healthcare, assisting to set up and establish the new GMCs. Therefore, SciLifeLab continues to be a major indirect contributor to GMS through DD. Contrary to research core facilities with services targeted for academic research projects, the Clinical Genomics facilities focus on clinical needs and demands in terms of sample processing times, lab certification and accreditation, and clinical interpretation of analytical results. The DD platform will adapt, mature and transition methods and data analysis tools towards clinical routine diagnostic use, and provide genomics services for clinical trials.

International Cancer Core Europe Collaborations

On the international arena, SciLifeLab groups (e.g. Janne Lehtiö at KI) have played a major role in setting up bioinformatics infrastructure to provide a molecular tumor board capabilty for Cancer Core Europe (https://www.cancercoreeurope.eu), a legal entity consisting of a collaboration across 7 major cancer centers in Europe. This capability will enable interpretation of cancer genome data and serve as an EU-wide center facilitating interpretation of cancer genome sequencing and matching patients with CCE-driven clinical trials.

Future healthcare: integration of research and development

The transition of new technologies and diagnostic tools from academic research to widespread utilization in clinical practice is a long and winding road, passing through multiple iterations of development and maturation, and can take up 10-15 years for full implementation. In order to facilitate this process of clinical innovation, dynamic testbed-environments, such as the DD and DDD platforms of SciLifeLab provide, are needed at the interface of university and hospital (Figure E3). Through interaction with university hospitals, healthcare regions, medtech and ICT companies, there is great promise in further developing SciLifeLab as a common testbed for technologies at the interface between academia and healthcare - advancing additional omics technologies into routine clinical practice. For example, discussions and meetings between SciLifeLab and the Karolinska University Hospital Laboratory (KUL) have identified several novel technologies beyond genomics that can be envisioned to have clinical utility in the near future, such as proteomics, metabolomics, microbiome research and imaging technologies. Discussions on such interactions will continue. Also, the close link of SciLifeLab with the GMS project will also enable us to test-drive and implement other diagnostic capabilities in a translational research setting, with full integration with national biobanks and national health care players.

SciLifeLab's capacity for close interaction with healthcare has positive effects also on our capacity for industry collaboration. An example is the Microbial Research Centre at KI/SciLifeLab which is supported by a major grant from Ferring Pharmaceuticals. It is based on SciLifeLab technologies, KI research expertise, national and local biobanks and clinical sample acquisition opportunities that together form an attractive milieu for industry to collaborate with. Similar infrastructure-academia-healthcare-industry collaborations are underway in e.g. nanoscale drug development and immunological monitoring of patients undergoing clinical trials for evaluating new therapies.

Another path to clinical implementation arise through SciLifeLab-community developed technologies being further developed by startup companies, eventually entering clinical practice as diagnostic tools. An example of such capabilities include the use of the Proximity-Extension Assay (PEA) technology developed in Ulf Landegren's laboratory at UU and diagnostic tools based on this technology by the spin-out company O-Link. Another example is the development of the Spatial Transcriptomics diagnostic technology by, amongst others, Joakim Lundeberg of SciLifeLab. This technology has been commercialized by the spin-out company Spatial Transcriptomics, recently acquired by 10X Genomics.

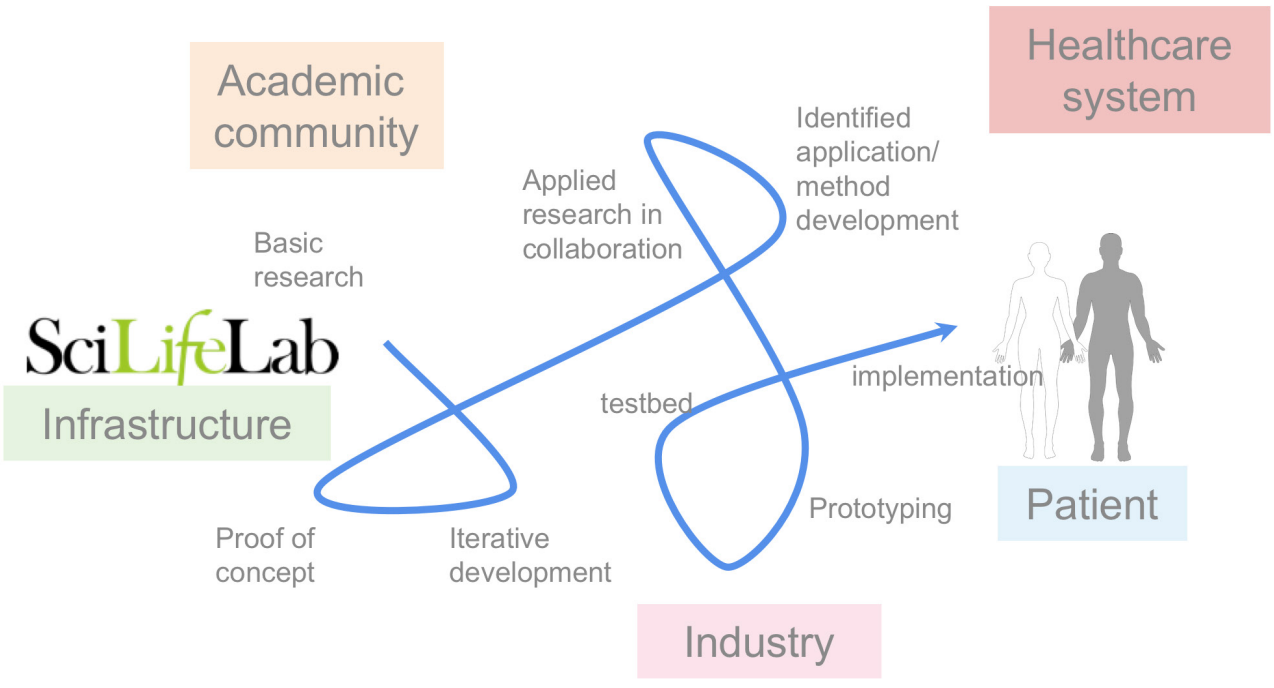


Figure E3. Pipeline transition of basic research findings to clinically implemented methods and treatments in healthcare, passing through several iterative intermediate stages.

Enhancing SciLifeLab platform use to clinical researchers, clinical trials and healthcare

The discussion above highlights the key role of the Diagnostic Development (DD) platform and the GMS network, which remain the cornerstones of the SciLifeLab interactions with healthcare. This DD platform is, however, predominantly focusing on direct healthcare applications, often by analyzing and interpretation of one sample at a time. Furthermore, this platform mostly covers genome sequencing. Thus, on the clinical research side, many capabilitis need to be also developed for clinical research. With the DD platform, GMS projects and the associated nation-wide networks well developed, the path to the next clinical breakthroughs will hopefully will be faster and cheaper.

Full-service from sample to insights

In order to facilitate a broad application of all SciLifeLab platforms by clinical researchers, biobanks, translational and hospital-based researchers, it is necessary to create systems and workflows that are better applicable and accessible towards the clinical research field. For example, most of the current users of SciLIfeLab do have enough basic biological knowledge to find and negotiate sample analyses and data analysis strategies, but for many busy clinical researchers, these need to feature a full-service from sample acquisition and handling to analysis and data interpretation and data handling (including storage, analysis and GDPR compatible data handling). Thus, such seamless services are being producted now. Similarly, we will need a hotline and advice on how to profile samples and what technologies and data analysis strategies to use. Ideally this could be built together with the Bioinformatics platform and Data Center, the SciLifeLab infrastructure coordination office and the new External Relations Office could together set up such functions in a pilot mode.

Integration with bioinformatics and data handling

Related to above, it is essential for clinical researchers and the clinical trials to feature a real-time data analysis and interpretation service. This is also being developed and has enabled a Cancer Core Europe -based molecular tumor board to be launched from SciLifeLab for local and European users. Clearly many more efforts are needed for high-quality integration to the diagnostic frameworks at all hospitals across the country. The clinical researchers will also need much more support to handle data storage, analysis and interpretation, including safe data handling and GDPR implementation.

Involve clinical researchers in the SciLifeLab Community

Of the current research community programs (RCPs), only one had a strong clinical focus. In the next RCP call, we will plan to undertake and nominate more such efforts, helping to bring together a community of researchers in selected topics.

The National Molecular Medicine Fellows Program (NMMP)

The NMMP is a collaboration between SciLifeLab and the Wallenberg-funded centers for Molecular Mecicine in Umeå, Gothenburg, Lund and Linköping. Together, these centers are hiring now up to 80+ young PIs in molecular medicine, half of whom are expected to be clinical researchers, ideally young practicing clinicians. This joint program provides a major avenue for SciLIfeLab to engage in collaborations with the next-generation of Swedish clinical researchers and establish strong links with this progressive and promising community.

Develop DDD plans for new drugs and precision medicine

DDD platform is engaged in supporting the development of new drugs from academic inventions all the way towards first-in-man testing. Phase I has already been reached in some projects, and it is likely that DDD will in the future become a major force in the translation of drug discovery leads to precision therapeutics, via licensing the discoveries to startups, biotechs, and big pharma.

Clarify and communicate SciLifeLab's capabilities in clinical research, trials and diagnostics

A common theme of this white paper is that SciLifeLab houses a diverse set of capabilities that it is difficult to effectively communicate to external entities and stakeholders. Thus, further propagation and branding of such capabilities are necessary. Communication materials highlighting specific capabilities, e.g. immunology, AI-based image analysis, systems biology, pharmacology, drug discovery, disease models, wellness profiling, diagnostics and biomarker discovery need to be produced tailored to specific audiences.

Conclusion

In summary, SciLifeLab presents a unique platform to help Swedish healthcare develop its technology base towards future healthcare challenges and also a dynamic research environment within which clinical and diagnostic breakthroughs can be achieved. SciLifeLab achieves this by aligning its activities with those of the Swedish life science strategy. In addition, we will undertake specific steps to advance the practical limitations on SciLifeLab accessibility for clinicians and clinical researchers. We will undertake concrete actions for improved access and utility of clinical data from research through the Data Center and national bioinformatics platform, further elaboration of the national precision medicine initiative Genomic Medicine Sweden through aligned development of the DD platform nationally, and an integrated approaches to enabling transition of future healthcare technologies by close collaboration of SciLifeLabs facilities with R&D units of university hospitals.

Appendix F.

SciLifeLab Drug Discovery and Development (DDD) Platform Report

Contents

Outline of Documentation

This appendix F is divided into three parts. The document starts with a SWOT analysis of the present position of SciLifeLab DDD and raise a number of questions to the IAB based on the presented plans and strategies.

In the second part, we present the background, development, and deliveries of the SciLifeLab DDD operation since the start in 2013.

In the third, main part, we outline plans and developments.

For clarity, both these sections are divided into the same four main themes:

DDD Programs – the most important work is to offer drug discovery expertise and infrastructure to the Swedish academic system.

Technology Developments – development and implementation of new technologies that will allow us to offer state-of-the-art drug discovery capabilities in the future.

Life Science Community building and education – an important role for SciLifeLab DDD since the start has been to promote drug discovery research and to educate the next generation of drug discovery professionals – especially in light of the closure of "powerhouses" such as Pharmacia and AstraZeneca.

Organization – The organization of SciLifeLab internally, within SciLifeLab, and in relation to host universities.

Abbreviations

3D-QSAR	Three dimensional - Quantitative Structure–Activity Relationship
AD2C	Academic Drug Discovery Consortium
ADME	Adsorption Distribution Metabolism and Excretion facility
BCA	Biochemical and Cellular Assays facility
BSC	Biophysical Screening and Characterization facility
CBCS	Chemical Biology Consortium Sweden
CC	Compound Center facility
CDTP	Candidate Drug Target Profile
CP	Checkpoint
CRISPR/CAS9	Clustered Regularly Interspaced Short Palindromic Repeats -associated Cas9 gene
DECL	DNA Encoded Chemical Library
DDD	Drug Discovery and Development platform
EATRIS	European infrastructure for translational medicine
Fab	Antigen binding fragment of an antibody
FTE	Full Time Employment
GMP	Good Manufacturing Procedures
HAT	Human Antibody Therapeutics facility
HDX-MS	Hydrogen deuterium exchange mass-spectrometry
IAB	International Advisory Board
IMI	Innovative Medicines Initiative
IP	Intellectual Property
IPR	Intellectual Property Right
IVSP	In Vitro and Systems Pharmacology facility
IT	Information Technologies
KI	Karolinska Institutet
KTH	Royal Institute of Technology
LCMS	Liquid Chromatography-Mass Spectrometry
LU	Lund University
MAX-4	The European synchrotron radiation facility in Lund
MCH2L	Medicinal Chemistry Hit to Lead facility
MCLI	Medicinal Chemistry Lead Identification facility
MS	Mass-spectrometry
NIH	National Institute of Health
PBPK	Physiologically Based Pharmacokinetics
PEC	Protein Expression and Characterization facility
PKPD	Pharmacokinetics Pharmacodynamics
PI	Principal Investigator
Protac	Proteolysis Targeting Chimera
RCP	Research Community Program
ScFv	Single-chain Variable Fragment
SGC	Structural Genomics Consortium
SME	Small and Medium-sized Enterprises
SPARK	Stanford Medicine SPARK Translational Research Program From Bench to Bedside
SPR	Surface Plasmon Resonance
SU	Stockholm University
TDP	Technology Development Program
TPP&DSA	Target Product Profiling & Drug Safety Assessment facility
TTO	Tech Transfer Office
UU	Uppsala University

SciLifeLab DDD SWOT Analysis January 2019

Strenghts (internal)

- Strong track record
- Accepted & attractive "business" model for Swedish academia
- Embedment in the Universities builds trust among academic scientists
- Operation under the teachers' exemption law protects academic science from exploitation by internationally active organizations like e.g. LifeArc
- DDD offers a critical mass of operation
- Flexibility for target and drug modality
- Dedicated and skilled personnel

Weaknesses (internal)

- Sub-optimal exit model and collaboration with TTOs
- Bureaucratic environment surrounding SciLifeLab partly dependent of being a collaboration between different organization (Universities)
- Support to SMEs requested but options unclear due to legal obstacles
- Competitive instinct between Universities restrains initiation of programs which is indicated by few programs originating from Lund and Gothenburg

Opportunities (external)

- Large interest to have DDD as partner for national grant applications
- Reputation of quality "on the rise" both nationally and internationally
- Access to state-of-the-art (high-risk-high reward) technologies
- If entrepreneurial behavior is encouraged is a large pool of academic science available to "mine" innovations
- DDD becomes an essential part to build a seamless line of progression of innovative ideas from lab bench to the clinic. This require intensified interactions with innovation systems (including grants, expertise in regulatory requirements and IP) and healthcare.

Threats (external)

- Personnel leaves or become unmotivated because the career ladder is based on teaching and publications
- Dependent on few funding streams for operation, investments, and technology developments
- Funding available to PI decrease and are not prioritized for DD
- Competitive offers from international organizations could emerge (if current model changes too much)
- Global recession makes biotech investments less attractive (affects exits)

Questions to IAB on the Future Strategy of SciLifeLab DDD

1. How should SciLifeLab DDD help bridge the Valley of Death by building a seamless line of progression of innovative ideas from lab bench to the clinic?
2. How can the whole SciLifeLab build on opportunities and expertise that SciLifeLab DDD offers, and vice versa?
3. Which new technologies do you find particularly relevant for SciLifeLab DDD to put in place?
4. How important is it for SciLifeLab DDD to engage in formal training, i.e. offering courses that is included in the examination for students etc.? Do you agree that the informal training, seminars, workshops and other non-formal education should remain at the same level as is?
5. Many principal investigators declare that the first meeting with a confidential outside experienced view and the pre-project phase at DDD is very valuable for them as academic scientists. Some use DDD only for help in project planning and continuous feedback on their own work. Do you have any suggestions for how DDD could get credit from this "soft" input?
6. Should SciLifeLab venture into new opportunities with industry, with VC funded projects for specific drug discovery programs
7. What is your opinion on resources to spend on DDD Programs versus Technology Development?

Background

The Drug Discovery and Development (DDD) Platform was established in 2013 through a specific Swedish governmental initiative with earmarked funds within SciLifeLab to establish a national platform to support 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 platform, expertise, and strategic support to promote progress of projects towards pre-clinical proof-of concept and a strategy for further development. The special DDD funding in the 2012 and 2016 Research and Innovation Bills stem from the global challenge of the pharmaceutical industry that few new drugs reach patients despite a continued unmet medical need across many disease areas. It is becoming clear that university researchers need to take a step forward and more actively engage in the discovery of novel therapeutics. Such a development could be seen as a natural further development of ongoing efforts in translational medicine, and SciLifeLab was considered a suitable host for this new national platform. Hence, the mission for SciLifeLab DDD is to transfer basic research to early drug development programs, and to build an environment for scientific collaborations of highest international standard, competence, and advanced infrastructure in the area of drug discovery. Two major specific objectives are:

1. To increase the reproducibility rate in academic life science by providing an industry standard infrastructure tailor made for drug discovery research and;
2. To provide expertise knowledge and training in drug discovery.

Currently, the SciLifeLab DDD platform is staffed by 10 university professors and >35 scientists with industrial experience. SciLifeLab DDD offers integrated drug discovery support primarily to the Swedish academic research community. The national platform steering group carefully reviews programs entering the platform and monitors progression biannually. Upon approval, the platform staff works together with the researcher to add industrial drug discovery quality and expertise to the programs. The drug leads 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 rights and ownership during this process. Carefully set exit criteria and collaboration with the universities' Innovation Offices pave the way for spinouts, or partnerships with pharma or biotech companies.

Ten facilities at five universities offer services with the following expertise:

- protein expression and characterization (PEC)
- human antibody therapeutics (HAT)
- biochemical and cellular assays (BCA)
- two facilities for medicinal and computational chemistry (MCH2L and MCLI)
- drug metabolism and pharmacokinetics (ADME)
- in vitro and systems pharmacology (IVSP)
- biophysical screening and characterization (BSC)
- Compound Center (CC) (run in close collaboration with the Chemical Biology Consortium Sweden)
- Target Product Profiling and Drug Safety Assessment (TPP&DSA) facility (run in close collaboration with the RISE Research Institutes of Sweden AB)

From an international perspective, SciLifeLab DDD has four distinguishing features:

a. The operations run under the Professor´s privilege law
b. SciLifeLab DDD is a drug discovery center, not a screening center
c. SciLifeLab DDD works with small molecules, biologics as well as cell therapies
d. Focus is on pharmacological effect of drugs (PK/PD)

Comprehensive descriptions of the SciLifeLab DDD platform can be found in Drug Discovery Today [1] and Future Science. [2]

[1] Arvidsson, P.I. et al. Open for collaboration: an academic platform for drug discovery and development at SciLifeLab. Drug Discovery Today (2016). https://www.sciencedirect.com/science/article/pii/S1359644616302446?via%3Dihub

[2] Arvidsson, P.I. et al. Institutional profile: the national Swedish academic drug discovery & development platform at SciLifeLab. Future Science (2016). https://www.future-science.com/doi/full/10.4155/fsoa-2017-0013

Financial aspects of SciLifeLab DDD

The funding of both SciLifeLab and SciLifeLab DDD come directly from the government´s Department of Education and Research to KTH – the Royal Institute of Technology. Funding is then distributed to host universities in accordance with SciLifeLab Board decisions. Notably, the funding for SciLifeLab DDD is "earmarked" in the sense that at least 40 MSEK/year (2013-2016) and 50 MSEK/year (2017-2020) are to be used for drug discovery and development operations. Per Arvidsson was recruited and charged with the task to establish the infrastructure in March 2013. The first operational plan for SciLifeLab DDD was worked out with Tom Meyerson Goldschmidt and Karin Forsberg Nilsson at Uppsala University, and approved by the SciLifeLab board in late 2013. The objective was to establish SciLifeLab DDD as a national infrastructure for academic drug discovery and development, by building capabilities at the four SciLifeLab host universities. Recruitment of staff, procurement of instrumentation, and building of the infrastructure were complete in May 2014 – which can be considered the first operational date of SciLifeLab DDD. Kristian Sandberg was recruited as co-platform director and responsible for the operations at Uppsala University in March 2015. Starting in 2017, the funding increased from 40 to 50 MSEK/year, and then the human antibody therapeutics facility (HAT) expanded their operation to also include personnel and infrastructure at Lund University (at an institution with large experience in antibody drug discovery).

The budgeted funding and expenses of SciLifeLab DDD for 2019 can be seen in Figure F1a-b. Apart from the governmental grant (54 MSEK), additional incomes come from national SciLifeLab funding (1 MSEK), SFO funding from Uppsala University (2 MSEK), and user-fees (6 MSEK) – making a total budget of 63 MSEK/year. Some additional funding from extraordinary initiatives are normally obtained, e.g. SFO funding from Uppsala University for technology developments and national SciLifeLab funding for expensive instrumentation and technology development projects.

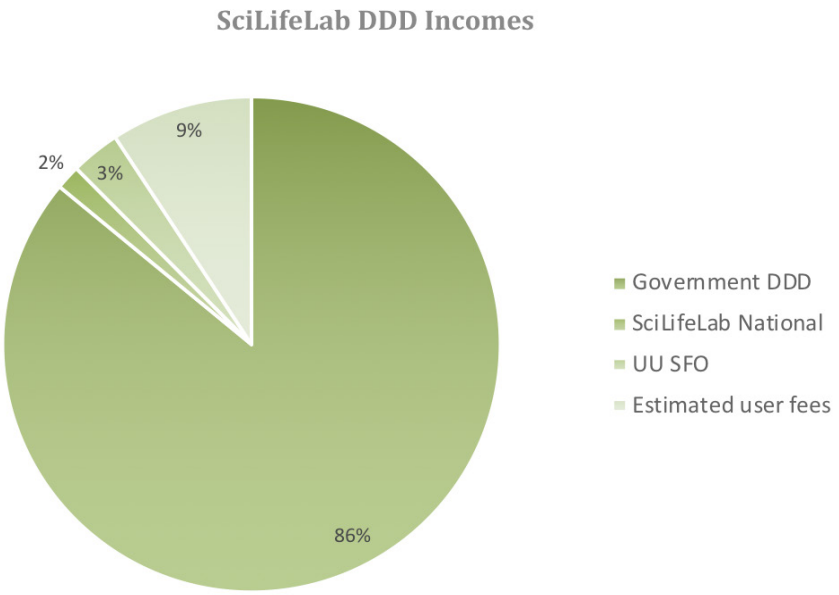


Figure F1a. Budgeted SciLifeLab DDD incomes 2019.

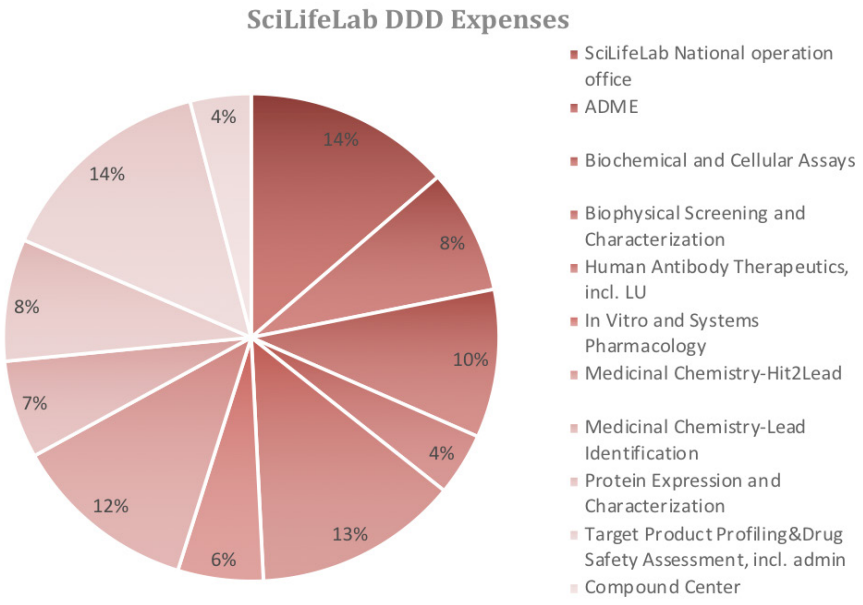


Figure F1b. Budgeted SciLifeLab DDD expenses 2019.

The SciLifeLab DDD operational expenses are also seen in Figure F1. In addition to the 10 facilities that make up SciLifeLab DDD, for 2019, the national SciLifeLab operation fee is 7.5 MSEK (14% of governmental DDD funding) – on top of indirect cost (overhead) to Universities.

From an international perspective, the operational budget of SciLifeLab DDD is reasonable for an academic drug discovery center, and enough to make a global impact through the width of unique capabilities offered by SciLifeLab DDD (points a-d noted above).

Review of Deliverables 2013-2018

Three distinct types of project support are offered by DDD:

1. DDD Programs with the aim of developing a pharmacologically active therapy with potential to progress into development.
2. Technology Development projects with the aim to establish new important drug discovery technologies at SciLifeLab DDD to facilitate Swedish drug discovery research.
3. Commissioned research to make use of spare resources at facilities.

DDD Programs and Technology Development Projects have highest priority. The national DDD steering group evaluate all such projects and decides on the level of support for the next six-month cycle, while commissioned research can be approved by the platform management team every week.

Definition of academic drug discovery success

The definition of success factors for academic drug discovery centers has been reviewed in the literature, see for example: Schultz Kirkegaard, H. and Valentin, F. Academic drug discovery centres: the economic and organisational sustainability of an emerging model, Drug Discovery Today (2014) and Dahlin, J.L. et al. Mitigating risk in academic preclinical drug discovery. Nat. Rev. Drug Discov. (2015).

Success for academic DD centers are: enhanced federal funding and early partnering of programs, eduction of the research community, and, as a stretched goal, programs entering phase 1 clinical trials. Our practical experience supports these conclusions. A large number of projects in the life science area (pharmaceutical project) fail at the interface between governmental funded research and commercialization. There are several reasons for this. Most often, the projects fail to meet industry's high standards of quality and reproducibility of data, and the project are rarely innovative enough to offer true clinical benefits for the patients (i.e. not differentiated from competing solutions). The Swedish government realized this in 2012, when they decided to fund the Drug Discovery & Development Platform at SciLifeLab. Since its inception in 2014, this initiative has developed a project model that delivered clinical trials, international partnerships and led to the creation of Swedish publicly traded companies. Equally important is that most projects have received additional "soft" funding from external sources, such as the Swedish innovation agency´s “Swelife” program and Novo seeds. The investment on SciLifeLab DDD has proven to increase the quality of pharmaceutical projects to a degree that interests global financiers. However, a major challenge remains to increase professionalism in business development.

The SciLifeLab drug discovery model

The SciLifeLab drug discovery model consists of three distinct elements, which focus on required activities in developing a drug discovery program and entrepreneurial skills of the academic scientist based on hands-on training and execution of their skills in their own program.

- **Begin with the goal in mind!**
  Programs proposed to DDD national steering group captures nine different dimensions of ability for drug discovery, namely:
  1. Scientific validity of the therapeutic approach
  2. Medical need and differentiation from standard of care
  3. Safety concerns
  4. The competitive situation
  5. A patent and publication strategy
  6. The feasibility to conduct a phase 2 study with a defined patient population and biomarker availability understood
  7. Competence and ability of the academic research team
  8. Technical feasibility to develop a drug
  9. Entrepreneurial behavior
- **Biannual prioritization!**
  Principal Investigators (PI´s) receive DDD support and coordination through a project leader for six-month periods. The programs are then re-prioritized, by the unbiased national DDD steering group, in competition with new proposals. Lack of key components that adversely affect progression will result in a stopped or delayed project for the next six-month period.
- **Feedback!**
  Regular project reviews provide continuous feedback to the PI, which results in a steep learning curve for the PI in how to become a skilled drug-hunter.

We believe that the SciLifeLab drug discovery model outlined above, paired with innovative ideas from the academic community, funding and an industry quality infrastructure is key for success. A challenge, however, is how to capture and report the increasing capacity and competence of our academic collaborators participating in a DDD program?

The structure, organization and hiring of key personnel to DDD was done in 2013. The first four programs entered the DDD portfolio 2014 and a structured process to review and prioritize programs were in place in late 2015. After entering of projects to the portfolio of SciLifeLab DDD programs, the projects mature according to the phases depicted in Figure F2.

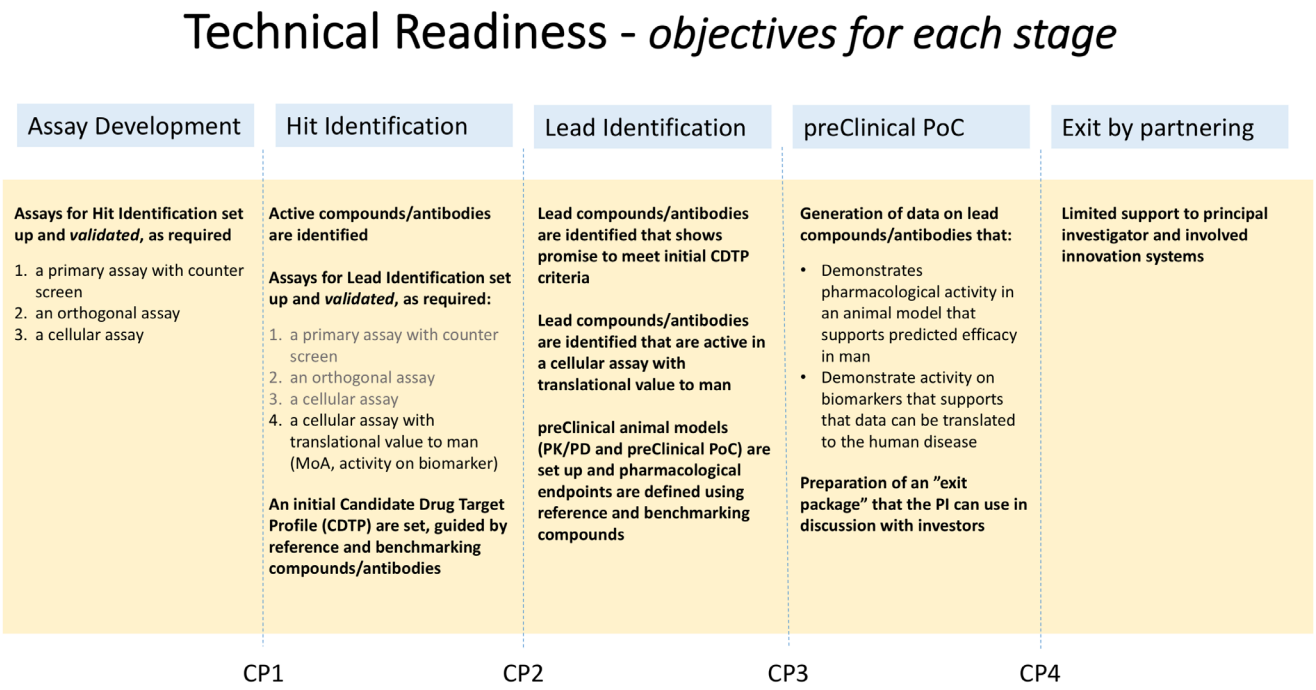


Figure F2. Stages that a SciLifeLab DDD program goes through to identify a pharmacological active compound or antibody. The SciLifeLab DDD leadership team takes the decisions to transit the program over checkpoint (CP) 1 and CP3, while the national SciLifeLab DDD steering group takes the decisions to transit the program over CP2 and CP4.

Data produced at the platform are prepared into reports that are made available to the principal investigator. When the SciLifeLab DDD steering group or the PI decides to stop further activities, the program is either terminated or placed in the last stage of Technical Readiness - "Exit by partnering". A report is prepared that summarize all work at SciLifeLab DDD. This summary report together with all other reports, a copy of raw data stored at the universities and all remaining physical material is handed over to the PI. If the program is placed in the stage "Exit by partnering", the PI will still get support from SciLifeLab DDD to prepare the project in negotiations with investors/potential future partners. We are happy to say that investors/big pharma have been able to reproduce all data from our reports so far.

A focused effort to improve project leader skills and better routines for resourcing allowed us to increase the portfolio size to 17-18 program from 2016 and onwards. As shown in Table F1, the average output of programs leaving DDD ("exits") have been two programs per year since 2016. Two programs have entered clinical phase 1 studies and therefore left DDD and two programs have been licensed to international pharmaceutical industry. Three projects have spun-out to form private companies. These numbers indicate that the SciLifeLab DDD model of drug discovery is functional for the Swedish life science community. We will present examples from ongoing DDD programs at the face-to-face meeting with IAB in March 2019. Note, that the preferred start for a program is when a compound or an antibody is available for further development. Many times, these chemical starting points comes from projects run at the SciLifeLab platform Chemical Biology & Genetic Engineering or from the European Lead Factory. There is a large interest from both global pharmaceutical companies and smaller Swedish SMEs to collaborate with the SciLifeLab DDD as programs. However, we have not prioritized such activities since the ambition and legal possibilities for such industry-academia partnerships are unclear from the principal.

Table F1. Development of the DDD Program portfolio year 2014-2018.

Year	Proposals#	Programs#	Rejections#	Terminations#	Partnering#
2014	47	4	1	0	0
2015	60	10	0	0	1
2016	56	17	0	0	3
2017	26	17	2	3	1
2018	43	18	2	3	2

"Proposals" indicate the number of first meetings with principal investigators for potential programs. "Programs" indicate the number of projects in the portfolio of supported SciLifeLab DDD programs in December that year. Note that the time required to complete a program varies from 6 months to >4 years. A typical program is active under approximately 3-4 years. "Rejections" indicates the number of programs that are terminated before entering the "exit by partnering" stage (see Fig. F2 above) not being partnered, out-licensed or bought by a third party. "Terminations", indicate the number of programs terminated prematurely by the PI or by the SciLifeLab DDD steering group. "Partnering", indicates the number of programs where the ownership of the project has left the principal investigator or that the project has initiated clinical phase 1 studies.

Technology Development

SciLifeLab policies dictate that technology development projects should not take more than 20% of available resources. In 2014-2015, the SciLifeLab phage display libraries SciLifeLab 1 and 2 were constructed. These libraries are fully human and IP free synthetic scFvs libraries that have effectively been used in our DDD programs since then. In 2017, we developed three additional Fab libraries – SciLifeLib 3-5. These libraries were validated in a national call 2018 where they successfully identified new binders to 5/6 selected protein targets. In year 2015, four additional technology development projects were initiated: 1: Refinement of the SciLifeLab compound collection; 2: Review and implementation of new technologies for biophysical studies; 3. Bioanalysis of biologics and; 4: Proteomics for systems pharmacology studies. Responsible facilities for project 1-3 are currently implementing the results from these projects into the facilities. The proteomics approach for systems pharmacology was successful. Unfortunately, DDD lack resources to implement this technology into the facility.

In addition to the projects above, a large number of instrument implementation activities/projects took place 2015-2017, which resulted in unique instrumentation being made available to the Swedish academic community, e.g. supercritical chromatography for separation of enantiomers, advanced LCMS instrumentation for analysis of plasma concentration of biological drugs and metabolites of small-molecule drugs. In 2018, we redefined "Technology development projects" to get more visibility to these activities at the platform – the new strategy and the areas of investments are described in the future strategy section below. The current technology development projects at SciLifeLab DDD 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, 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 take 7% of available resources at DDD. As a note, SciLifeLab policies states that not more than 20% of the platform resources should be spent on technology development.

Furthermore, commencing year 2019, we will be involved in the following SciLifeLab funded programs that has been granted after a peer-review process: Research Community Programs (RCPs) in Biophysical interactions. Technology Developments Programs (TDPs): "BIPOD" led by Dr. Mikael Altun (KI) aiming to develop novel tissue specific Protacs, "Mammalian protein production" led by SciLifeLab fellow Alexey Amunds (SU) aiming to develop medium-sized protein expression capability, and "RIF-Seq: RNA isolation free RNA sequencing" led by Prof. Mats Nilsson (SU). These technology development projects are a good way to establish collaborations both within SciLifeLab and national academia, but also with local and global industry and organizations.

In addition to the intellectual and practical services outlined above, we strive to establish SciLifeLab DDD as the natural portal for Swedish academic drug discovery. This means reaching out to the broader community of life science actors, e.g: University innovation offices/Tech Transfer Office (TTO), translational- and clinical research centers, funding agencies, industry (see below), consultants, students, politicians, etc. In order to unite and cover the interest of so many stakeholders we (sporadically) distribute an external DDD newsletter. Actions to improve the degree of communication has been taken (see future plans below). SciLifeLab DDD also organizes two symposiums every year. Examples from 2018 are: ”Covalent Inhibitors in Drug Discovery” and ”Biomarkers in Drug Discovery”. These symposia are free-of-charge, and have been very popular among academic scientists, health care, industry, and governmental authorities. The symposia serve to create a natural meeting point between industry and academia and are used as networking events, exchange of ideas from large pharma to SMEs, and training for both academic and SME personnel. The biomarker symposia in November 2018 was organized in collaboration with AstraZeneca and the symposia in the Spring 2019 will be done in collaboration with GE Healthcare and their Testa Center for production of biologics. Beginning 2017, we are also organizing Drug Discovery Seminars where invited scientists have the possibility to present their science applied to drug discovery at one of the host universities for SciLifeLab DDD. In 2015, we were actively engaged in leading an externally funded research school in drug discovery and development together with representatives from Uppsala University, Karolinska Institutet, and Lund University. The school was open for PhD students and postdocs from all over Sweden, and in addition to theoretical training they spent 1 month of internship at companies or at DDD. In 2018, we organized a one-week practical course on biophysical methods in drug discovery for PhD students and postdocs.

Innovation system interactions

The innovation environment in Sweden is world unique due to the “Professors privilege law”. SciLifeLab DDD does not offer business development support for the projects, but instead require that the project owners engage their local TTO. These interactions are well functioning, e.g. representative from the host TTO takes part in project meetings and utilize DDD expertise for evaluation of local projects. However, the mandate of the TTO in the Swedish system, with its professor´s privilege, is complicated. The TTO organizations can support the project owner with governmental grants for e.g. IP analysis/filing, business plan preparations, market analysis, etc. However, that money is typically finished when it is time to present the project for investors and do deal-making, and the project owner is then left without support. Such negotiations quickly become very complicated for an individual researcher to run on his/her own. The situation is getting better when a holding company or incubator becomes a partner, but a large number of projects are unfortunately lost in the process after verification and patent costs have already been invested in the project. From our experience, there is still a huge untapped resource of potential drug targets in the academic society that never comes to the attention to the innovation system. We outline strategies to facilitate “output” by facilitating exiting and partnering in the future sections below.

International partnerships and collaborations

The funding of SciLifeLab DDD is aimed to support academic drug discovery at Swedish universities; consequently, no projects from abroad have been supported. Nevertheless, DDD programs are often approached by international companies and venture capital funds for partnering. Business development activities in the SciLifeLab DDD programs are expected to be handled by the principal investigator with support from their TTO. However, in reality DDD personnel has been instrumental in the partnering discussion trough their expertise, network, and time invested.

Since the start, SciLifeLab DDD has allowed Swedish researchers to utilize the infrastructure investment for international collaborations, i.e. by placing externally funded personnel at the infrastructure. The in vitro ADME profiling facility at SciLifeLab DDD participates with in vitro ADME analysis in the IMI program “ENABLE”, which aims to develop new antibacterial agents, and the Human Antibody Therapeutics facility is part of the IMI program “ULTRA-DD”, which develop high-quality affinity reagents for autoimmune targets by selection in the SciLifeLib phage libraries. These examples illustrate that additional collaborative projects can be harbored at the infrastructure, provided external funds are available to cover additional personnel, rent, etc. SciLifeLab DDD can be effectively utilized for coordination of new international multi-center project, e.g. IT and substance management, but the internal engagement has so far been responsive rather than actively scouting to lead such activities.

The SciLifeLab DDD initiative has triggered international interest, and the organization is increasingly approached by international stakeholders for exchange of ideas and best practices. SciLifeLab DDD is part of the international Academic Drug Discovery Consortium (AD2C), and has been invited to co-organize the first World Academic Drug

Discovery Conference together with partners from the US and Saudi Arabia. Other academic initiatives, e.g. in Norway, Finland, and Spain, are turning to SciLifeLab DDD for input on their strategies and plans. Global, i.e. SPARK, and European, i.e. EATRIS, initiatives for translational life-science research would like to see SciLifeLab DDD as partner organization. However, these initiatives require fees for funding in addition to substantial in-kind contribution of time and resources, why they have so far not been prioritized.

Organization

As outlined above, the funding for SciLifeLab DDD represent an "earmarked" part of the general governmental funding to SciLifeLab. This model has facilitated the special objective of SciLifeLab DDD in supplying a model for academic drug discovery that promotes further investments in early programs, while at the same time offering a home in the strong, national, research environment that constitute SciLifeLab. In 2018, new steering documents for SciLifeLab DDD were approved by the SciLifeLab Director Olli Kallioniemi ("SciLifeLab Drug Discovery and Development (DDD) Platform Terms and Conditions for Funding") and by the SciLifeLab DDD platform steering group ("SciLifeLab Drug Discovery and Development (DDD) platform Rules of Procedure") that clearly states responsibilities for key functions within the platform. However, several aspects of SciLifeLab DDD operations are suffering from the fact that DDD as a whole (all facilities included) has had no ability to act as a signing party for agreements. Each SciLifeLab DDD facility is hosted and integrated within departments at one of the five SciLifeLab DDD host universities (KTH, Uppsala University, Stockholm University, Karolinska Institutet, Lunds University). The facilities are therefore part of the department and must follow relevant rules of procedure, delegation of authority and guidance of its host university and department. Starting in 2018, the SciLifeLab DDD host universities now explore the possibility to establish a SciLifeLab DDD office at Uppsala University acting as a contractual entrance point and signing party for all operations at SciLifeLab DDD. The SciLifeLab board and principals for the host universities supported this solution and an agreement to establish this office is to be signed in early 2019.

Cross-Platform Collaboration & External Collaborations

In some reviews, questions have been raised concerning cross-platform/facility interactions and the image of SciLifeLab DDD as an isolated operation within SciLifeLab. It should be emphasized that SciLifeLab DDD operations require intense interactions between the facilities within the platform and the PI team (exemplified in Figure F3). This mode of operation complicates cross-SciLifeLab platform/facility interactions. Nevertheless, good interactions have been established with other facilities at SciLifeLab as "subcontractors" of services to PIs supported by DDD, Figure F4. Examples are, e.g. sequencing/array facilities providing sequence data to the IVSP facility, HDX-MS for epitope mapping provided by Chemical Proteomics, and joint project evaluations and sharing of infrastructure with the Chemical Biology Consortium Sweden (CBCS) facility. We would like to see more efficient use of resources and know-how within the SciLifeLab community. At the same time, SciLifeLab DDD need to stay focused to our prioritized activities (DDD Programs and Technology Development projects). Our spare resources are made available as Service projects and access to instruments.

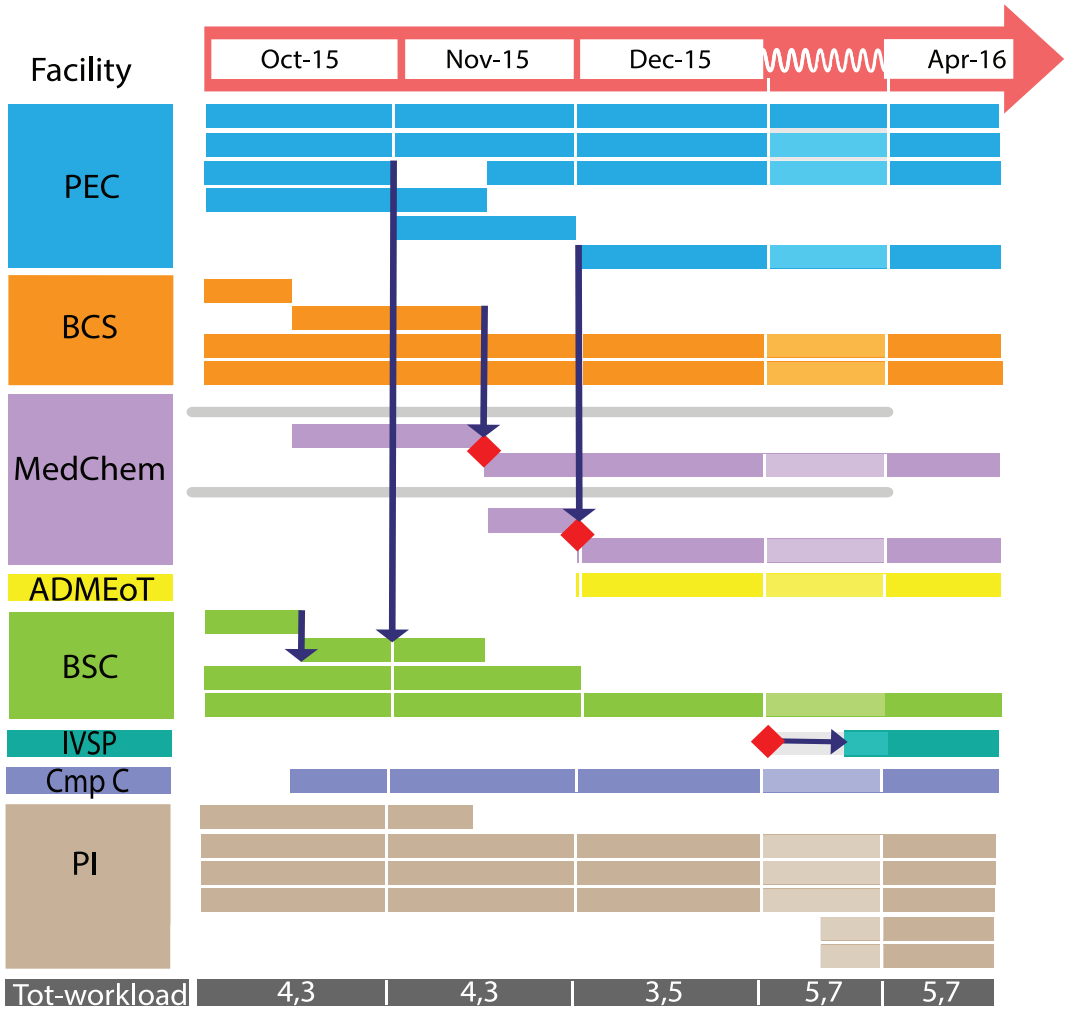


Figure F3. GANTT scheme exemplifying the requirement of project management and intense collaboration between facilities, universities and the principal investigator to progress DDD Programs. Activities under the responsibility of the PI group may also be support from other SciLifeLab facilities, e.g. HDX MS analysis, etc. A similar situation with cross-facility/platform coordination may also apply to Technology Development projects. This depicted GANTT scheme is an anonymized DDD program.

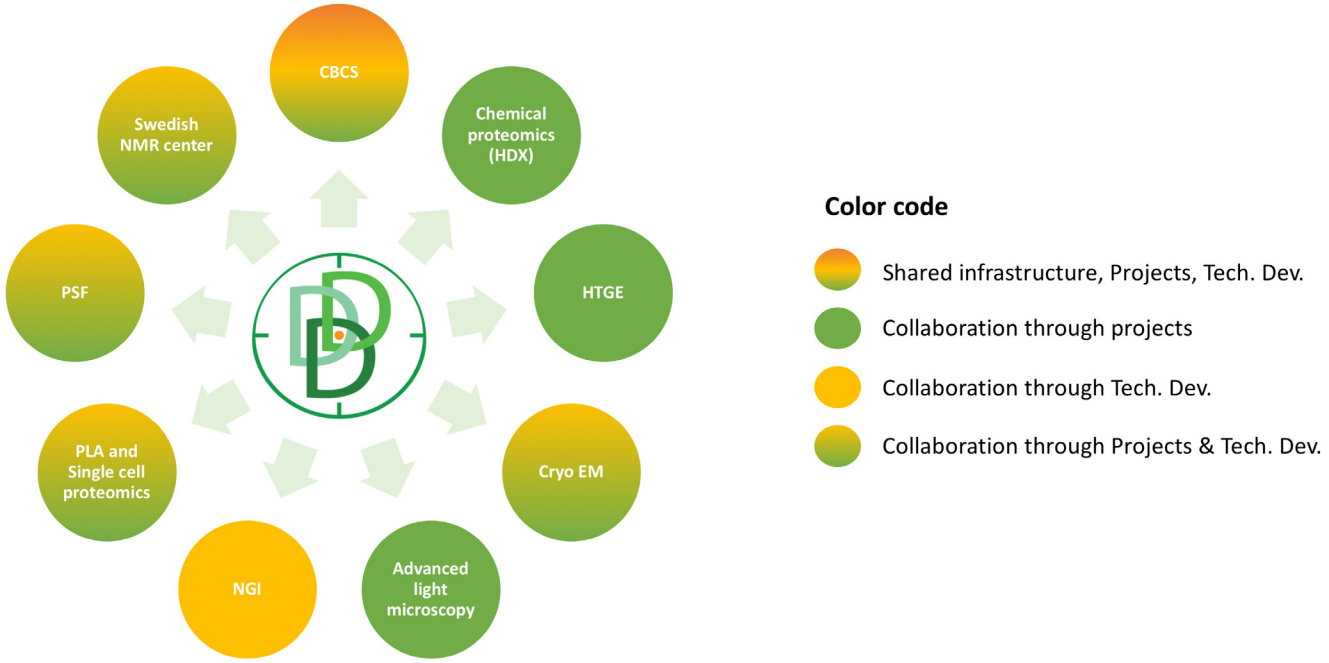


Figure F4. SciLifeLab DDD centric schematic illustration of the SciLifeLab infrastructure echo system. Collaborations with other platforms normally takes place through the project owner, but more recently also through internal technology development projects (TDPs, RCPs, other). Collaborations with SciLifeLab faculty and administration are even more abundant.

Response to Specific Questions Raised by IAB at the 2016 Review

Three specific matters were raised to SciLifeLab DDD in the IAB review 2016.

"In particular, the programmes appeared to be focused on potency, with relatively little focus on drug-like properties of small molecules required for in vivo testing and clinical studies. This means that the Platform may be much less productive than would be the case if other modern approaches were to be taken."

We view this as a misunderstanding of IAB, possibly a mix up between the SciLifeLab DDD and CBCS platforms. One of the distinguishing features with SciLifeLab DDD is actually our in-house competence and resources to perform analysis to assess pharmacokinetic and pharmacodynamics properties of compounds and antibodies. We have a whole facility "ADME" dedicated to these efforts! In addition, we have formed a special group called "The In Vivo design team" led by an experienced pharmacologist and including a discovery toxicologist from the Swedish Toxicology Institute and an expert in PKPD modelling from our ADME facility. The mission for the In Vivo design team is to support the PI in the experimental design of pivotal PK and PKPD studies to be performed in the DDD programs.

"Drug discovery in an academic setting can be very productive and advantage needs to be taken of the critical intellectual mass provided by the SciLifeLab and its community".

Starting in 2019, SciLifeLab DDD will be active partner in several national SciLifeLab programs for technology developments (TDPs and RCPs – see below). SciLifeLab has also acted as a hub which facilitated collaboration in several external grant applications, especially those involving both industrial and academic partners. We agree to that there still are huge untapped resources and competence for drug discovery within SciLifeLab and Swedish life science.

"There should be renewed focus on new classes of therapies, peptides, proteins and nucleic acids that fit well to academic centres and now start to show superior properties. There is considerable activity in this area throughout the world, including in academia, and, therefore, SciLifeLab should develop a distinctive and different perspective so as to create something exceptional rather than replicating the industrial technology of the last century."

In 2016, our portfolio of DDD Programs were divided into small molecules and biologics. We acknowledge that the IAB, because of confidentiality, had no direct insight into our programs. We have therefore decided to introduce a third category of DDD Programs in our portfolio to visualize projects aiming for platform technologies and new modality therapies. The DDD platform supports both vaccination approaches, cell therapies and development of very odd molecules as therapeutics. We can give an overview of these projects to IAB at the face-to-face meeting in March 2019, provided that the IAB members sign a confidentiality statement.

Strategic Future View

In 2004, the former NIH Director Elias Zerhouni minted the phrase Valley of Death to describe why so few of the many academic ideas for therapeutic intervention in disease actually progress all the way to the patient. The Valley of Death still remains and is the key challenge for SciLifeLab DDD to tackle! Our ambition is to develop the SciLifeLab DDD platform towards a 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 SciLifeLab DDD largely represent today into an organization that actively work 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). SciLifeLab DDD 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, SciLifeLab DDD could also support and facilitate studies at specific, highly advanced, in-vivo mice model centers to establish molecular mechanisms. However, most importantly, the SciLifeLab DDD need to stay focused on delivering high quality, drug discovery programs.

As depicted in Figure F5, we have identified four important areas in which strategies need to be developed to accomplish the above ambition.

Deliverables of SciLifeLab DDD programs must maintain the core business for the platform. DDD Programs directly support Swedish academia, builds value by hands on training of scientists, and increased value of potential drugs moving into development. What is the appropriate balance between driving DDD Programs (the core activity of SciLifeLab DDD), driving Technology development and engagement with the Life Science community and international organizations?

SciLifeLab DDD should develop a well-functioning support to other initiatives for translational medicine. Examples of such initiatives are e.g. Wallenberg Center for translational medicine, specialized centers for advanced animal models mimicking human disease, sponsored programs for specific disease areas etc. SciLifeLab DDD should be organized so that such support can be given in the form of e.g. technology development, specific research grant sponsored programs, and capabilities in e.g. design and support of pharmacological studies in animals, identification of suitable bridging biomarkers etc.

SciLifeLab DDD should develop tighter interactions with research funding organizations to reinforce innovation aspects acted on by academic scientists (i.e. input). In parallel, principals should give SciLifeLab DDD a clear remit to support TTOs with drug discovery expertise and wet lab resources. Establishment of public-private partnerships in defined areas is a possibility.

The strategies and main goals depicted in Figure F5 are broken down into the functional areas "DDD Programs", "Technology Development", "Life Science Community Building" and "Organization" and further discussed in the sections below.

If the strategies outlined in Figure F5 are 1) in line with the general strategies of SciLifeLab and host universities; 2) is within the contractual possibilities of the DDD office and; 3) is prioritized by the ScilifeLab DDD national steering group - then additional resources needs to be invested in technical development, administrative functions, business development and internationalization.

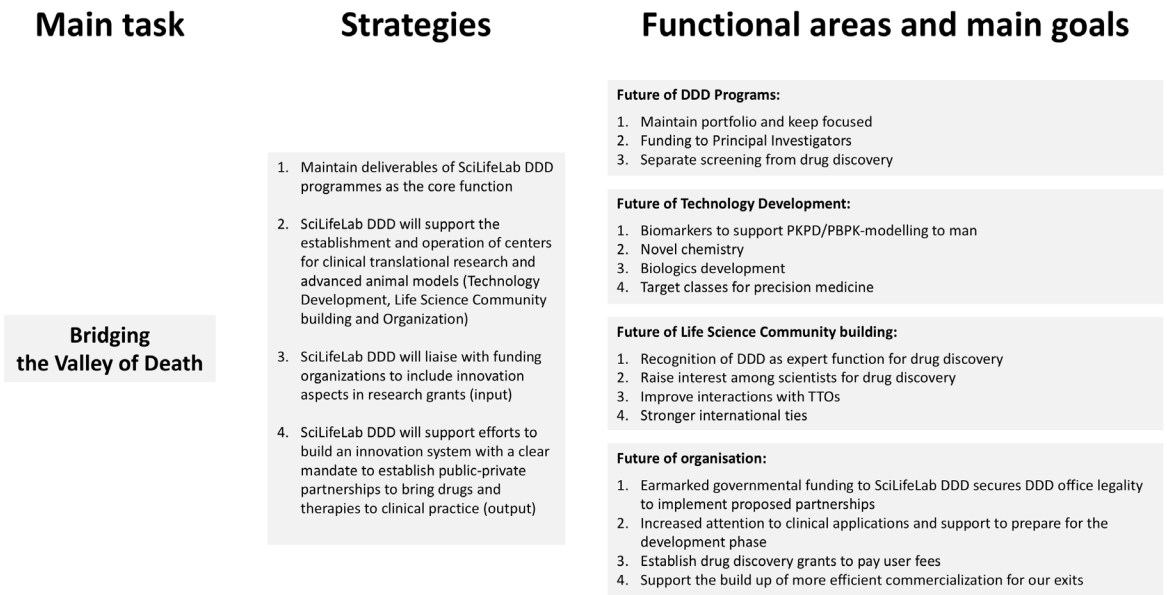


Figure F5. An overview of strategies and goals to help develop SciLifeLab DDD into an active hub for translational drug discovery and development research.

Future of DDD Programs

Key areas to address in the future of SciLifeLab DDD are:

1. Maintain portfolio and keep focused
2. Funding to Principal Investigators
3. Separate screening from drug discovery

Maintaining a rich and attractive portfolio is essential to SciLifeLab DDD and should remain the core focus of SciLifeLab DDD. However, the proportion of academic scientists with an entrepreneurial attitude is low, despite very exciting and groundbreaking research. Hence, a lot of untapped resources and innovation opportunities exists in the academic life science sector in Sweden. A key factor will therefore be to further raise the interest in drug discovery research among Swedish academic scientists and lower the barriers to initiate studies (input issues) by adding incentives to initiate drug discovery efforts. Tight interactions with funding agencies and improvements in Life Science Community Building and Organization is important.

Furthermore, the role of SciLifeLab DDD is to support the translation of exploratory findings coming out from academic science to clinical practice. Although very interesting tools for explorative research can be found by high throughput screening (HTS) of compound libraries, these approaches rarely identify drugs ready for clinical use or the projects may be impossible to develop as a drug discovery program for other reasons. Compound screening and drug discovery are presently distinct facilities/platforms within SciLifeLab. At present, we expect that the separation into different platforms will facilitate the planned development of the Chemical Biology platform into a larger national platform for screening harboring complementary technologies and approaches (e.g. NMR, CRISPR/CAS9 screens, Y2H, technologies available at MAX-4 etc.). At the same time, SciLifeLab DDD can focus on identifying prototype molecules suitable for optimization and progression into preclinical development. Still, SciLifeLab DDD can contribute with advice on how to progress active compounds into drug discovery programs, support with selection technologies, e.g. phage display and DECL, and to confirm the activity of hits by orthogonal assays e.g. biophysical methods like SPR (although available resources could be limiting).

Future of Technology Development

There are still gaps in the SciLifeLab DDD competence and capacity to support DDD Programs. Our definition of a technology development projects is that it should facilitate possibilities to conduct drug discovery projects; involve several facilities to strengthen the platform collaboration offerings; have a potential to attract external funding in competition; and, preferably involve an external partner (possibly in possession of the technology).

For bridging the Valley of Death, we have identified four strategic areas of interest for future technology developments:

1. Biomarkers to support PKPD/PBPK-modelling to man
2. Novel chemistry
3. Biologics development
4. Target classes for precision medicine

The funding situation and the legal framework offered through the DDD office allows collaboration with industry or international partners for technology development projects. We will maintain our interest in building capacity and competence for DECL, Protacs, capabilities for bioanalysis of biologics, and biophysical methods for studying how conformational dynamics of proteins can guide drug discovery. In addition, we will intensify our efforts to identify potential collaboration partners to develop the key areas stated above.

Biomarkers to support PKPD/PBPK-modelling to man

Biomarkers are of increasing value to drug discovery. SciLifeLab DDD does not have the capacity to address biomarker identification and development. Our current resources can give guidance when biomarkers should be used and give

limited support to identify suitable biomarkers. A comprehensive take on biomarkers would require a separate branch of the SciLifeLab DDD platform (although linked, the development of biomarkers differs from development of drugs) and tight interactions with other SciLifeLab platforms, other academic scientists and health care is required. However, we would like to intensify our efforts to identify putative pharmacological biomarkers that bridge between cells, animal models and patients. These biomarkers need to have the same or similar activity in animals and cells in order to allow for accurate PKPD/PBPK predictions at an early stage about efficacy and scaling. In support to our DDD programs, SciLifeLab DDD would like to form cross platform interactions with other facilities/platforms at SciLifeLab, Wallenberg Center for Molecular Medicine and health care to develop a seamless development of biomarkers for all aspects in drug development.

Introduction of technologies to identify novel chemistry for drug discovery

Compared to industry, academic institutions have few options to identify novel starting points for chemistry. Importantly, academic scientists cannot afford to screen large compound collections. We have therefore decided to establish a core competence to build and select binders from DNA Encoded chemical libraries (DECL). The cost to screen large DECLs would be affordable to our academic collaborators with a fair chance to identify novel chemical starting points for drug discovery. To make the DECL technology affordable to academia, we are currently establishing DECL as a core competence for SciLifeLab DDD. The establishment of DECL gives us additional opportunities to engage with external academics, e.g. develop novel water based synthetic chemistry, building blocks, and novel scaffolds; direct integration of machine learning/artificial intelligence to combine chemoinformatics and bioinformatics/structural data to generate 3D-QSAR to guide chemistry and; to develop novel selection and amplification technologies for DNA-tagged compounds on the basis of proximity ligation technologies. Protacs – Proteolysis-targeting chimera, is a novel therapeutic approach to degrade target proteins that relies on selective binding to target protein and an E3 ubiquitin ligase. SciLifeLab DDD is currently exploring this technology and the intention is to apply the technologies above to develop new Protacs and to approach new target classes. This project so far involves the Chemical biology platform at SciLifeLab and the global Structural Genomics Consortium (SGC); AstraZenca is expected to join during the year.

Develop our capabilities to support discovery and development of biologics

Development of biological therapies is a strategic investment in life science from the Swedish government. TestaCenter is a new governmental supported public-private investment at GE healthcare in Uppsala that supports large-scale non-GMP production of biologics for both industrial and academic customers. SciLifeLab DDD is discussing how our competence and capabilities for discovery of biologics can be aligned with TestaCenter to build a facility or incorporate a function to generate production cell lines for biologics, currently a limiting factor for full utilization of the TestaCenter. Note that such a potential facility also could assist with generation of stable cell lines for assay development to serve our academic users.

Increase our capabilities to address specific target classes or medical indications

The emerging era of precision medicine opens for better definition of patient groups and new therapeutic opportunities. However, identified targets often belong to non-traditional classes with a poor track record for drug development. We intend to launch national calls to stimulate joint efforts to address specific targets classes of strategic interest e.g. epigenetic targets or adaptor proteins and challenges to develop therapeutics against these targets. SciLifeLab DDD embrace the concept of new modalities (new chemistry and other modes including cell therapies) as a novel route to approach such targets and patient groups, when possible. This may require additional capabilities, e.g. complement our capabilities to work with ion channels assays, which, in turn, may lead to an increased national footprint of SciLifeLab DDD.

Please note that some of the opportunities outlined above, e.g. biomarker discovery, stable cell-line development with TestaCenter etc., is outside the current remit of SciLifeLab DDD and would require new directions and additional resources from the government.

Future of Life Science Community Building

SciLifeLab DDD is as an academic infrastructure to support academic research in Sweden. Currently, neither the funding situation, nor the legal framework, is clear on how to give full support to industry or internationally. Key areas for improving SciLifeLab DDD as a voice in the Swedish Life Science Community are:

1. Recognition of DDD as expert function for drug discovery
2. Raise interest among scientists for drug discovery
3. Improve interactions with TTOs
4. Stronger international ties

Recognition of DDD as expert function for drug discovery

SciLifeLab DDD has successfully established itself as a network hub for Swedish professionals in the early DDD area and policy and decision makers are increasingly acknowledging this. Acceptance as the national academic expert function for early stage drug discovery is valuable since the national and international recognition of SciLifeLab DDD can help governmental and other agencies to reach the scientific community, help promote collaborations, and set national quality standards for innovation in the drug discovery area, etc.

Raise interest among scientists for drug discovery

Education and training are recognized deliverables from international academic drug discovery centers. As outlined above, SciLifeLab DDD personnel occasionally engages in formal education at their home universities and the platform has offered drug discovery education. A more informal training also takes place through the experience transfer that happens during project discussions and evaluations.

A solid communication strategy is a prerequisite for aspiring to be at the center of Swedish life science community in the drug discovery area. Hitherto, community building has primarily been done by personal visits, newsletters, workshops/symposia and training events. These activities will continue; starting in March 2019 further strengthened by the appointment of a 30% FTE position for external and internal communication. Engagement in formal educational programs, which is the focus of the universities, will continue to be a low priority. Instead, we believe the hands-on training in DDD Programs is the most efficient for us to help bridge the valley of death – the main objective of SciLifeLab DDD – learn by doing!

Improve interactions with TTOs

As outlined above, the professor´s privilege makes the Swedish innovation system special, and the role of the TTOs is poorly defined. From our experience, the exit phase, where programs are being prepared for additional funding or partnering, is the weakest point in the present SciLifeLab DDD model. In this regard, we believe there is potential to improve the innovation system in Sweden.

Although drastic changes to the Swedish innovation system would require political mandate, a realistic step could be to support projects by appointing a person to work with business development at SciLifeLab DDD together with the PIs own TTO function. Advantages with this solution is that the PI has a commercialization expert involved in the program from initiation of drug discovery efforts until take from investors. The commercialization expert will shape the program from start for development and continuously prepare for partnering discussions. As an example, the potential of such engagements is evident through in-kind support from Stockholm business region that has resulted in five invitations to present DDD programs to international companies during 2018.

Stronger international ties

As outlined above, individual Swedish scientists successfully use the SciLifeLab DDD infrastructure to engage in competitive international consortia, e.g. IMI programs, where external funds cover additional personnel, rent, etc. We also recently received a starting grant to establish a strategic partnership with IUPHAR – International union of basic and clinical pharmacology – with the aim to share best-practice Western drug-discovery knowledge with developing countries. Starting in 2018, the Swedish research council now fund Sweden´s participation in EATRIS; which might suggest a more active role of SciLifeLab DDD in EATRIS in the future.

Such activities can be continued, but the question is how we should prioritize international collaborations versus national collaborations? For example, international collaborations could be a necessity to access new technologies. On the other hand, it is not obvious that SciLifeLab DDD should act as a service organization outside of Sweden. Other advantages include additional funding streams, which can help to maintain a critical mass and state-of-the-art infrastructure and international recognition that would promote public-private partnerships to be secured from industry; but the downside is less focus on the current mission to promote the translation of Swedish academic drug discovery ideas towards patient benefit. Our recommendation would be to continue to hold a positive attitude to international collaborations, and to prioritize those that strengthen the capability to deliver vs. the current objectives of promoting Swedish drug discovery programs.

Future of the DDD Organization

Based on the experiences gained through the five initial years of operation we have identified opportunities for improvement. However, most of these opportunities depend on external decisions:

1. Earmarked governmental funding to SciLifeLab DDD secures DDD office legality to implement proposed partnerships
2. Increased attention to clinical applications and to prepare programs for the development phase
3. Establish dedicated funds to pay user fees for PI
4. Support the build-up of more efficient commercialization for our exits

Earmarked governmental funding to SciLifeLab DDD

As described, the creation of a SciLifeLab DDD office as a contractual proxy to sign agreements will have a positive impact on our abilities to serve Swedish academic scientists with DDD programs and to establish Technology development projects with various external parties. However, our abilities to serve industry and international academic scientists will still be limited for DDD programs. Nevertheless, the DDD office will make it possible to access external opportunities and establish partnerships directly with all of SciLifeLab DDD, rather than one individual host university. Earmarked funding to SciLifeLab DDD is essential to retain legality of the DDD office function.

Increased attention to clinical applications and support to prepare for the development phase

The SciLifeLab facility Chemical Biology Consortium Sweden is in the process of applying for separate funding to create the national screening center outlined in the section "Future of DDD programs" above. If granted, this will create a dedicated infrastructure for screening that allows for the full attention of SciLifeLab DDD to prepare our drug discovery programs for the development phase and clinical use. Such a development would require increased funding for operating the drug discovery programs, as well as external partners with a demonstrated commitment to move the program forward.

Establish drug discovery grants to pay user fees

Today, users at the DDD platform only pay approx. 10% of the actual costs as user fees. However, counting expenses for work done at the principal investigator laboratory for the program this becomes a substantial cost over time. The high cost, combined with the poor statistics of success, prohibit many, especially young, academics to venture into drug discovery research. SciLifeLab DDD personnel often help the users to apply for dedicated external funding for their drug discovery program, and a number of programs stall for some time until the funding required for conclusive preclinical proof of concept studies is available. It would therefore be valuable to enable external support with dedicated funds for academic scientists that accepts criteria set up by the funder. For example, a consortia of pharma partners might be interested in sponsoring the user fees of certain programs in exchange for a first right of refusal.

More efficient commercialization for our exits

Financing late preclinical activities is different from academic research grants, and thereby require expertise in business development strategy and access to legal functions. The current SciLifeLab DDD model relies on support from the program owner´s TTO. Unfortunately, this support is usually insufficient – especially in relation to the time invested by the TTO officers. Given the large investment made in the drug discovery programs at SciLifeLab DDD an alternative procedure for commercialization is desirable. One suggested option is the creation of a SciLifeLab linked holding company. However, this solution will not be available in the short term. As outlined above, an immediate and more pragmatic solution could be to hire a business development expert to, in collaboration with University TTO's, support SciLifeLab DDD programs.

Personnel

Finally, we also stress the importance of retaining and developing the personnel at SciLifeLab DDD. This question is of importance for all infrastructures working at the host universities. Life science research is increasingly dependent on infrastructures but the traditional career ladder for scientists may not apply to our staff. Discussion are ongoing at the various universities how to handle this. We believe that technology development projects could be a tool to engage and motivate scientists working at our facilities because data from these projects are, in principle, free to publish. Moreover, the technology development projects are also tools to strengthen cross-platform exchange within SciLifeLab, with health care and industry. However, this is not sufficient to retain highly skilled and experienced personnel. SciLifeLab, universities and the government need to establish a clear policy how to secure top-level expertise at national infrastructures. Here, SciLifeLab DDD turns to centralized efforts at SciLifeLab for driving such efforts.

Appendix G.

Strategy, principles and processes for allocation of space at SciLifeLab at Campus Solna

Contents

Strategy for SciLifeLab Campus Solna

Science for Life Laboratory (SciLifeLab)

KI, KTH, and SU has agreed to establish a joint laboratory placed in the Alfa and Gamma buildings in Solna, referred to as SciLifeLab Campus Solna. SciLifeLab Campus Solna comprise a large and important part of SciLifeLabs overall operations.

The purpose of the joint SciLifeLab Campus Solna

The purpose of the joint laboratory is to be the primary location for SciLifeLab facilities and SciLifeLab Fellows from the host universities in Stockholm. SciLifeLab Campus Solna is the primary and most visible part of the SciLifeLab community, and currently hosts about 60% of the national SciLifeLab infrastructures. The host universities are also locating research groups at SciLifeLab Campus Solna providing synergistic and multidisciplinary opportunities for research initiatives or programs as well as for the national facilities. The research groups may be involved with development of experimental and computational methods as well as new applications that can benefit the facilities or create new research initiatives / programs. The research at SciLifeLab Campus Solna should be oriented towards large-scale and/or technically challenging biological studies that typically are using or developing SciLifeLab facilities. The research environment should produce new scientific, technical and other capabilities that can benefit the academic community, industry and health care as well as the society at large.

Factors for success

Hosting all SciLifeLab fellows as well as a bigger part of the entire infrastructure and many research groups and various collaborations, SciLifeLab Campus Solna is an important part of the identity and brand SciLifeLab as a whole.

Developing SciLifeLab Campus Solna is done through continuous external and international evaluations. Being hosted by Campus Solna thus means that taking part in such evaluations is mandatory. Successful groups will collaborate within SciLifeLab as well as with external partners, and they will contribute to the SciLifeLab community.

Principles and processes for allocation of space at SciLifeLab at Campus Solna

General basics of the principles

SciLifeLab at Campus Solna comprise a large and important part of SciLifeLabs overall operations. Organization and localization issues are central for the ability to meet SciLifeLabs general strategic objectives as well as the goals and profiles of the host universities in Stockholm (KI, KTH and SU).

A dynamic space allocation process is necessary, that takes into consideration factors such as current and future research profiles, synergies between research groups and national infrastructures, new initiatives, new recruitments and research careers, funding decisions etc. These factors are also considered when deciding on groups that will rotate out from SciLifeLab Campus Solna to their host departments/universities.

The following space allocation guidelines and decisions are based upon the operational principles of SciLifeLab as a multi-university collaboration.

Principles for space allocations for the national SciLifeLab infrastructure

National Infrastructure Facilities are evaluated in a 4-year cycle with extensive international review every 4 years, and a lighter midterm checkup in between. The evaluation process, content and budget for different facilities is decided by the Board. The need for space at SciLifeLab Campus Solna will increase and decrease as a consequence of the decisions made. New facilities may enter and old ones may rotate out, merge or cease operations. Localization priorities of facilities must follow the current setup of facilities by the board.

Principles for space allocations for SciLifeLab Fellows

SciLifeLab Fellows appointments are described elsewhere. As a general principle, all new SciLifeLab Fellows in Stockholm should be offered space at Campus Solna. Typically, SciLifeLab Fellows are expected to relocate from SciLifeLab Campus Solna to the host department during the last year of their Fellowship. The Fellows may relocate earlier, after discussions with the fellow and the Head of Department. If the host department would like the Fellow to remain located at SciLifeLab Campus Solna, then this will be considered as a location of a new group.

Principles for space allocations for other research groups

The decisions on localization of research groups at Campus Solna is made case-by-case.

Criteria supporting the move-out or continued localization of a group include:

- overall scientific production
- relevance for the SciLifeLab infrastructure and research programs
- synergies, collaborations and practical contributions to the SciLifeLab community
- the host universities' (Heads of Depts.) motivation why they should remain or move
- strategic future plans for the group/facilities/SciLifeLab community

The research groups should be continuously monitored and will take part in the international evaluations and advisory board meetings of SciLifeLab. The ambition is to allow chosen research groups to stay at least 6 years at a time at SciLifeLab Campus Solna. The preference is to host the whole or main part of the research group at SciLifeLab Campus Solna, but partial presence can in some cases be justified.

Principles for space allocations for other groups including industry, health care and other external partners

These agreements are made case-by-case and with specific agreements for termination.

Decision making for space allocations

All decisions about changes to the lease contracts at SciLifeLab Campus Solna are taken by the Campus Solna Committee (CSC).

The host universities are responsible for keeping an inventory of the groups located at SciLifeLab Campus Solna, and for carrying their own reviews of their groups according to the principles in this document as well as participating in SciLifeLab-wide external reviews.

Campus Solna Manager

The Campus Solna Manager prepares suggested localizations with input from the Campus Solna Committee and the SciLifeLab committees of the host universities and investigates needs and estimated costs for reconstruction. The Campus Solna Manager monitors the current use of space and existing groups and facilities "in real time". If inefficient use is found, the PI of the group or facility will be contacted and asked for the plans for the space. The ambition is to have approximately 4% space vacant at SciLifeLab Campus Solna at any time to be able to rapidly respond to increased needs

of space, although this might not always be possible. The cost for this vacant space will be shared equally by the three universities as described in the steering document. Minor rearrangements can be decided by Campus Solna Manager if all involved parties agree.

Processes for space allocations
The process of initiation of localizations should follow the directives stated below.

For national facilities:
New national facility or phase-down of a facility is decided by the board and the Infrastructure Director is responsible for contacting the host department to initiate a planning process.

In the case of increased/decreased space for an existing facility, the respective SciLifeLab committee for each university is responsible for a formal request to the Campus Solna Committee and the Campus Solna manager.

For SciLifeLab fellows and for research groups:
The ID of the respective host university is responsible for a formal request to the Campus Solna Committee and the Campus Solna manager. This counts for:

- A new SciLifeLab fellow
- A new research group
- Termination of a research group

The SD of the respective host university is responsible for a formal request to the Campus Solna Committee and the Campus Solna manager. This counts for:

- Expansion of a research group (suggested by SD)

The Head of operations is responsible for a formal request to the Campus Solna Committee and the Campus Solna manager. This counts for:

- New industry groups or short-term contracts

Upon decision on termination of a contract, the following notice policies apply:

- Infrastructure facilities: 24 months after decision of phase out
- SciLifeLab fellows and research groups: 12 months (excluding planning time)
- Temporary contracts: according to the contract
- Exceptions are always possible upon mutual agreement.

Appendix H.

SciLifeLab Infrastructure Report

Contents

Infrastructure Organization

Since Jan 1, 2019, the SciLifeLab infrastructure is organized into seven platforms as shown below.

Bioinformatics

- Compute and Storage [U]
- Long-term Support [G, Li, Lu, S, U, Um]
- Support and Infrastructure [G, Li, Lu, S, U, Um]
- Systems Biology [G]

Cellular and Molecular Imaging

- Advanced Light Microscopy [S]
- BioImage Informatics [U]
- Cell Profiling [S]
- Cryo-EM [S, Um]
- Protein Science Facility [S]
- Swedish NMR Centre [G, Um]

Chemical Biology and Genome Engineering

- Chemical Biology Consortium Sweden [S, Um]
- Genome Engineering Zebrafish [U]
- High Throughput Genome Engineering [S]

Diagnostics Development

- Clinical Genomics Gothenburg [G]
- Clinical Genomics Lund [Lu]
- Clinical Genomics Stockholm [S]
- Clinical Genomics Uppsala [U]

Drug Discovery and Development

- ADME (Absorption, Distribution, Metabolism, Excretion) of Therapeutics [U]
- Biochemical and Cellular Assay [S]
- Biophysical Screening and Characterization [U]
- Human Antibody Therapeutics [Lu, S]
- In Vitro and Systems Pharmacology [U]
- Medicinal Chemistry – Hit2Lead [S]
- Medicinal Chemistry – Lead Identification [U]
- Protein Expression and Characterization [S]

G - Gothenburg
Li - Linköping
Lu - Lund
S - Stockholm
U - Uppsala
Um - Umeå

Genomics

- National Genomics Infrastructure [S, U]
- Ancient DNA [U]
- Eukaryotic Single Cell Genomics [S]
- Microbial Single Cell Genomics [U]

Proteomics and Metabolomics

- Autoimmunity Profiling [S]
- Chemical Proteomics and Proteogenomics [S]
- Clinical Biomarkers [U]
- PLA and Single Cell Proteomics [U]
- Plasma Profiling [S]
- Swedish Metabolomics Centre [Um]
- Mass Cytometry [Li, S]

Facility Report 2018

The Facility Report 2018 summarizes basic information, statistics and deliverables for all SciLifeLab infrastructure reporting units. In most cases, reporting unit equals facility, however, Drug Discovery and Development reports on the platform level, and some facilities report on the node level (Cryo-EM, Chemical Proteomics and Proteogenomics, National Genomics Infrastructure and Mass Cytometry).

The Facility Report is primarily based on the annual reporting from the units for 2018 and the SciLifeLab publication database (publications.scilifelab.se). The units are presented platform-wise.

Explanations

Basic information: Facility Directors, Heads of Facilities and FTE resources during 2018.

Resource allocation 2018: Estimated distribution of total FTE resources spent on different user categories.

User Fees 2018: Total amount of user fees, and estimated distribution of costs categories covered by the user fees.

User fees by sector: Distribution of user fee income from different user categories.

Services: A short description of services and technologies provided. For more detailed information about facility services, see www.scilifelab.se/infrastructure.

Users 2018: Distribution of individual users during 2018 based on user affiliation.

Publications: Total number of publications 2016–2018 Publications by category: Service: facility mentioned in acknowledgement; Collaborative: facility member in author's list; Technology Development: facility member as main author.

Publication by Journal Impact Factor: The Journal Impact Factors for 2018 are used for all year's analysis.

Abbreviations

Akademiska sjukhuset	University Hospital, Uppsala
ALF	County Council funding
EPF	The Ehrling-Persson Family Foundation
FTE	Full time equivalent
GU	University of Gothenburg
KAW	Knut and Alice Wallenberg Foundation
KI	Karolinska Institutet
KTH	Royal Institute of Technology (Kungliga tekniska högskolan)
LiU	Linköping University
LU	Lund University
NRM	Naturhistoriska riksmuseet (Swedish Museum of Natural History)
Sahlgrenska	Sahlgrenska University Hospital, Gothenburg
SLL	Stockholms Läns Landsting (Stockholm County Council)
SLU	Swedish University of Agricultural Sciences
SNIC	National center for high-performance computing
SSF	Swedish Foundation for Strategic Research
SU	Stockholm University
UU	Uppsala University
UmU	Umeå University
VR	Vetenskapsrådet (Swedish National Research Council)
VINNOVA	Sweden's Innovation Agency
WABI	Wallenberg Advanced Bioinformatics network (part of the SciLifeLab Bioinformatics network)

Compute and Storage

Bioinformatics platform

Basic information

Facility director: Elisabeth Larsson
Head of facility: Marcus Lundberg
SciLifeLab facility since: 2013
Host university: UU
FTEs: 4.25
FTEs financed by SciLifeLab: 3.3

Funding 2018 (in kSEK)

SciLifeLab: 2800

UU: 800

Total: 3600

Resource allocation 2018

Academia (national): 80%
Academia (international): -
Internal tech. dev.: 20%
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 0

Reagents: -
Instrument: -
Salaries: -
Rent: -
Other: -

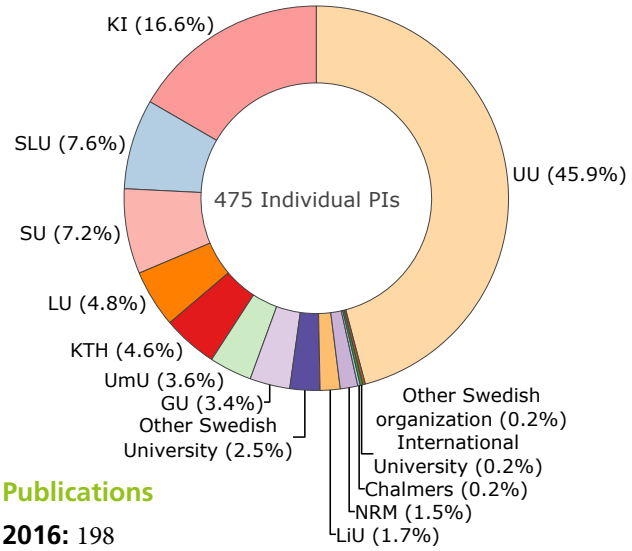
User fees by sector 2018

Academia (national): -
Academia (international): -
Industry: -
Healthcare: -
Other gov. agencies: 100%

Services

High-performance computing and storage resources, maintenance of relevant bioinformatics software and data (e.g. reference genomes), and associated user support. The facility is hosted at Uppsala Multidisciplinary Center for Advanced Computational Science (SNIC-UPPMAX), which is Uppsala University's resource for high-performance computing and related know-how.

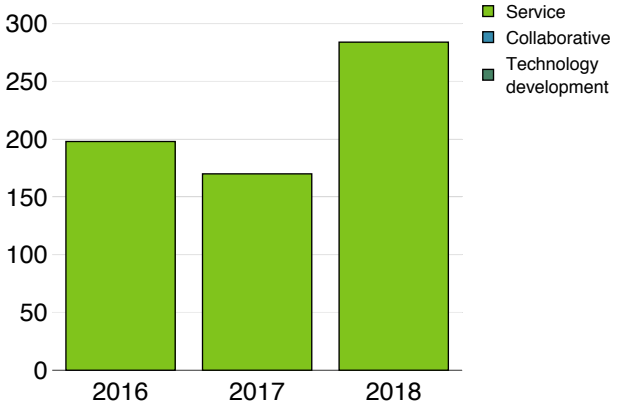
Users 2018



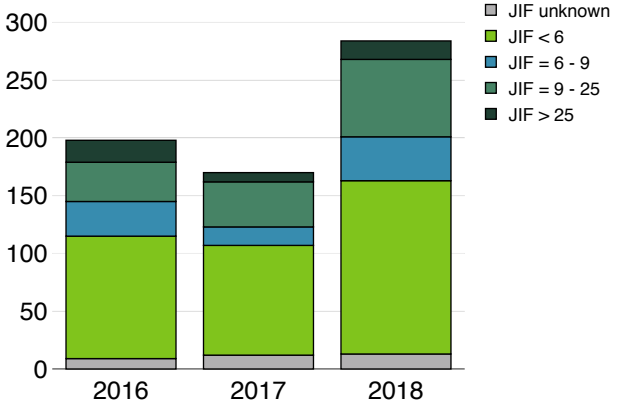
Publications

2016: 198
2017: 170
2018: 284

Publications by category



Publications by Journal Impact Factor



Long-term Support (WABI)

Bioinformatics platform

Basic information

Facility director: Gunnar von Heijne
Head of facility: Pär Engström, Björn Nystedt
SciLifeLab facility since: 2013
Host university: SU, UU, LU, UmU, LiU
FTEs: 20.0
FTEs financed by SciLifeLab: 4.0

Funding 2018 (in kSEK)

SciLifeLab: 4800
KAW: 16000
Universities: 1200
UU: 800

Total: 22800

Resource allocation 2018

Academia (national): 91%
Academia (international): -
Internal tech. dev.: 9%
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 125

Reagents: -
Instrument: -
Salaries: 90%
Rent: 10%
Other: -

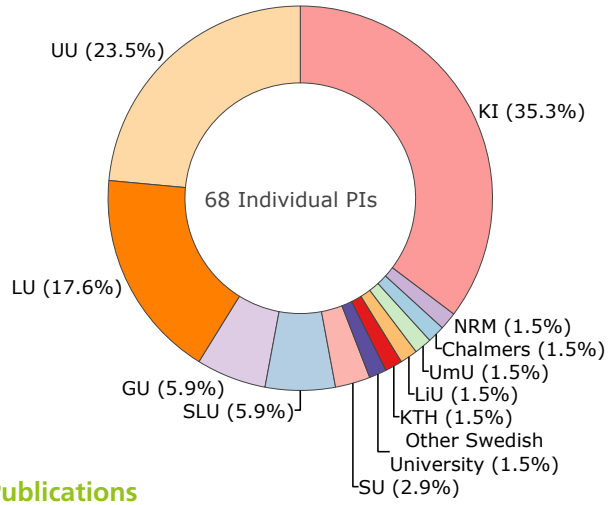
User fees by sector 2018

Academia (national): 100%
Academia (international): -
Industry: -
Healthcare: -
Other gov. agencies: -

Services

• Bioinformatics long-term support to a limited set of scientifically outstanding projects.
• Projects within genomics, transcriptomics, proteomics, epigenetics, metagenomics, metabolomics, and single-cell transcriptomics.
• Tool development
• Bioinformatics teaching at national and international workshops
• Bioinformatics drop-in sessions and consultation meetings

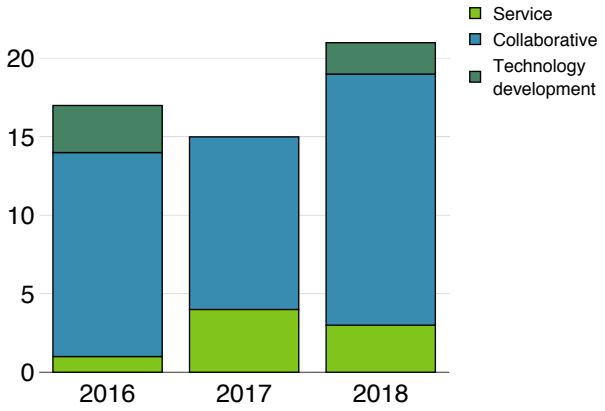
Users 2018



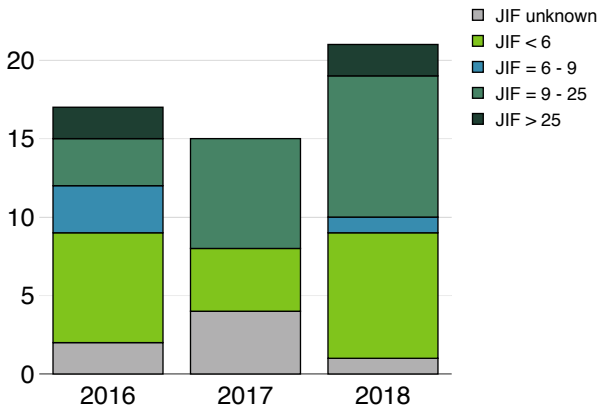
Publications

2016: 17
2017: 15
2018: 21

Publications by category



Publications by Journal Impact Factor



Support and Infrastructure

Bioinformatics platform

Basic information

Facility director: Bengt Persson
Head of facility: Mikael Borg
SciLifeLab facility since: 2013
Host university: Chalmers, GU, LiU, LU, KI, KTH, SLU, SU, UmU, UU
FTEs: 30.0
FTEs financed by SciLifeLab: 7.0

Funding 2018 (in kSEK)

SciLifeLab: 6500
VR: 17000
Elixir: 3000
Phenomenal: 400
Nordforsk: 2000
Universities: 7000

Total: 35900

Resource allocation 2018

Academia (national): 88%
Academia (international): -
Internal tech. dev.: 10%
Industry: 1%
Healthcare: -
Other gov. agencies: 1%

User Fees 2018

Total (kSEK): 3200

Reagents: -
Instrument: -
Salaries: 100%
Rent: -
Other: -

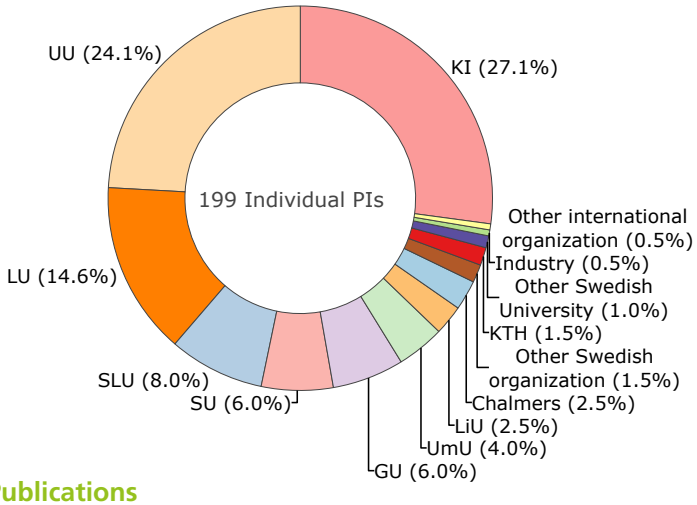
User fees by sector 2018

Academia (national): 98%
Academia (international): -
Industry: 1%
Healthcare: -
Other gov. agencies: 1%

Services

- Bioinformatics drop-in sessions and consultation meetings
- Short- and medium-term support
- Tool development and data publishing
- Mosler secure computing environment
- Proteomics data storage and processing
- Bioinformatics teaching at national and international workshops

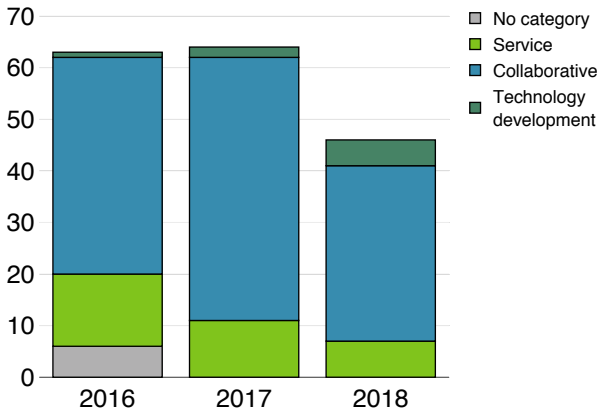
Users 2018



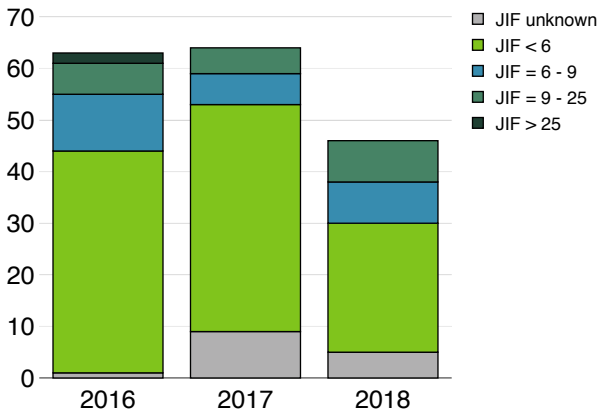
Publications

2016: 63
2017: 64
2018: 46

Publications by category



Publications by Journal Impact Factor



Systems Biology
Bioinformatics platform

Basic information

Facility director: Jens Nielsen
Head of facility: Thomas Svensson
SciLifeLab facility since: 2016
Host university: Chalmers
FTEs: 8.0
FTEs financed by SciLifeLab: 3.0

Funding 2018 (in kSEK)

SciLifeLab: 4000
Chalmers: 1500
KAW: 2000
Total: 7500

Resource allocation 2018

Academia (national): 63%
Academia (international): -
Internal tech. dev.: 27%
Industry: 10%
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 1262
Reagents: -
Instrument: -
Salaries: 100%
Rent: -
Other: -

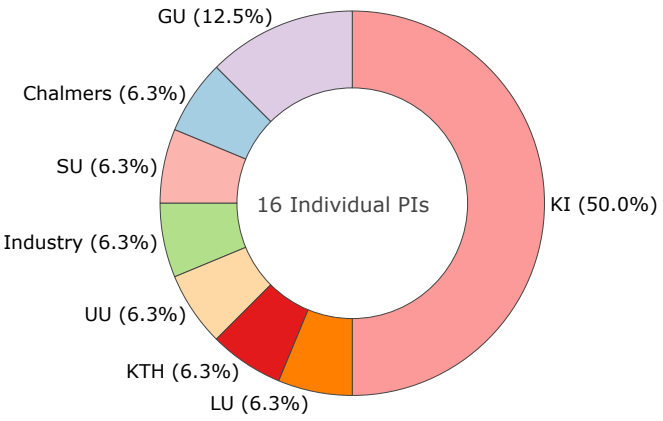
User fees by sector 2018

Academia (national): 83%
Academia (international): -
Industry: 17%
Healthcare: -
Other gov. agencies: -

Services

• Bioinformatics long-term support to a limited set of scientifically outstanding projects
• Tool development
• Focus on systems biology projects
• Bioinformatics teaching at national and international workshops

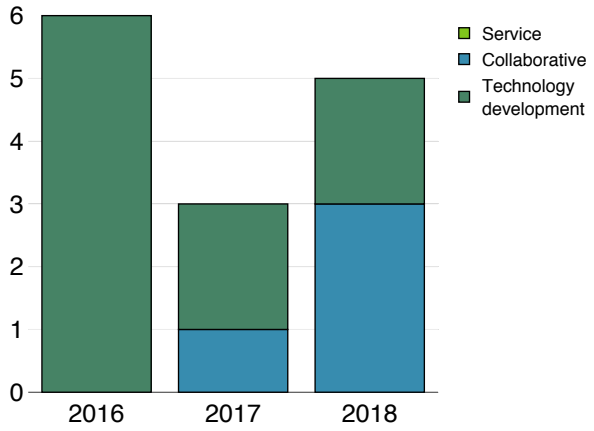
Users 2018



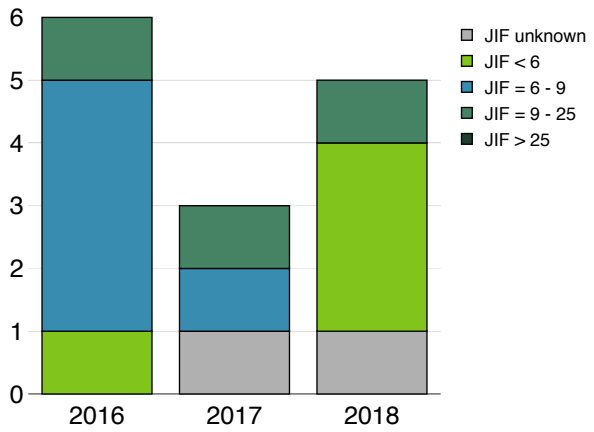
Publications

2016: 6
2017: 3
2018: 5

Publications by category



Publications by Journal Impact Factor



Advanced Light Microscopy (ALM)

Cellular and Molecular Imaging platform

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: 1.5

Funding 2018 (in kSEK)

SciLifeLab: 3400
SSF: 3200
VR: 2200
KTH: 500

Total: 9300

Resource allocation 2018

Academia (national): 60%
Academia (international): 10%
Internal tech. dev.: 20%
Industry: 5%
Healthcare: 5%
Other gov. agencies: -

User Fees 2018

Total (kSEK): 340

Reagents: 100%
Instrument: -
Salaries: -
Rent: -
Other: -

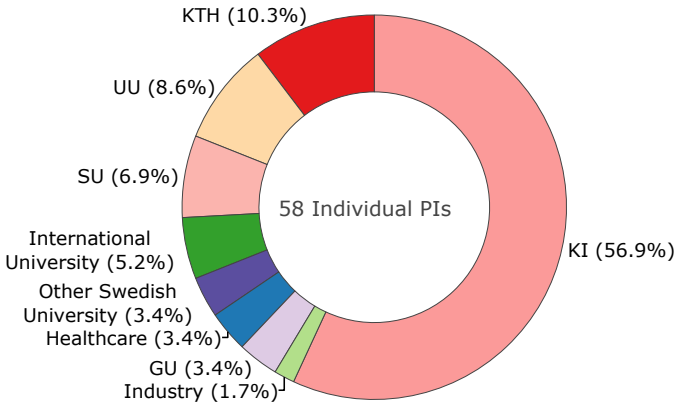
User fees by sector 2018

Academia (national): 100%
Academia (international): -
Industry: -
Healthcare: -
Other gov. agencies: -

Services

• Super-resolution microscopy (SIM, STED, STORM/PALM) – nanoscale cellular imaging of fixed or living samples, and cleared/expanded tissue
• Fluorescence Correlation Spectroscopy - single molecule spectroscopy measurement and analysis to evaluate interaction, aggregation, mobility, dynamics
• Light-sheet microscopy -fast optical sectioning of large volumes of organoids, organisms, cleared/expanded tissues

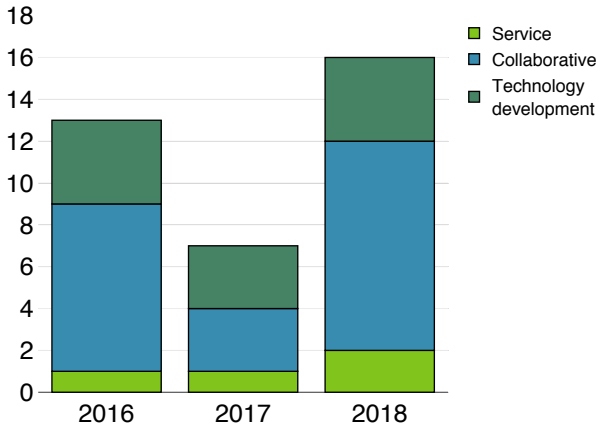
Users 2018



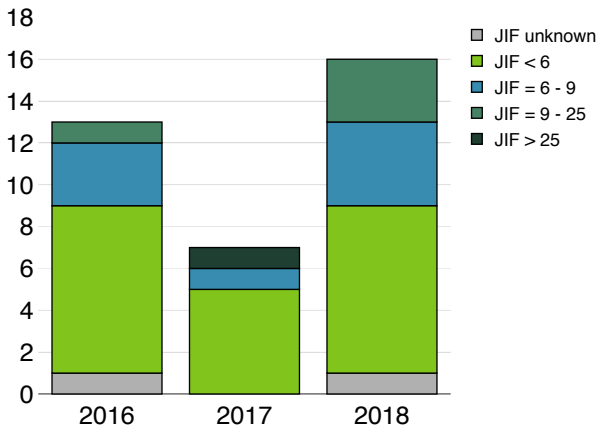
Publications

2016: 13
2017: 7
2018: 16

Publications by category



Publications by Journal Impact Factor



BioImage Informatics

Cellular and Molecular Imaging platform

Basic information

Facility director: Carolina Wählby, Kevin Smith
Head of facility: Petter Ranefall
SciLifeLab facility since: 2016
Host university: UU, KTH
FTEs: 2.0
FTEs financed by SciLifeLab: 1.5

Funding 2018 (in kSEK)

SciLifeLab: 2500

Total: 2500

Resource allocation 2018

Academia (national): 16%
Academia (international): 2%
Internal tech. dev.: 40%
Industry: 22%
Healthcare: -
Other gov. agencies: 20%

User Fees 2018

Total (kSEK): 612

Reagents: -
Instrument: -
Salaries: 100%
Rent: -
Other: -

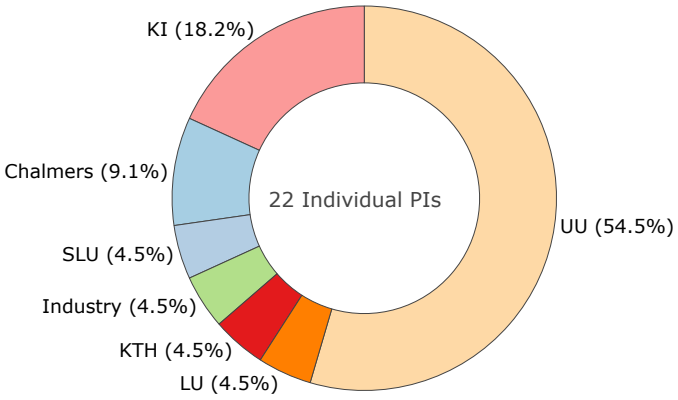
User fees by sector 2018

Academia (national): -
Academia (international): -
Industry: 100%
Healthcare: -
Other gov. agencies: -

Services

- Microscopy imaging and quantitative data analysis.
- Image analysis assay development and image processing algorithm development and software engineering.
- High throughput/large-scale image processing using computing clusters, including data transfer and storage.
- Large-scale data analysis and visualization.

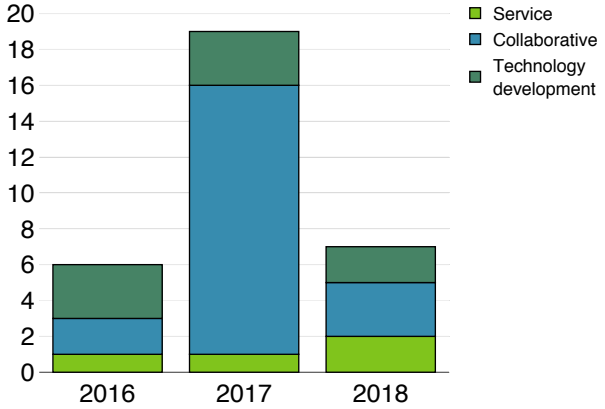
Users 2018



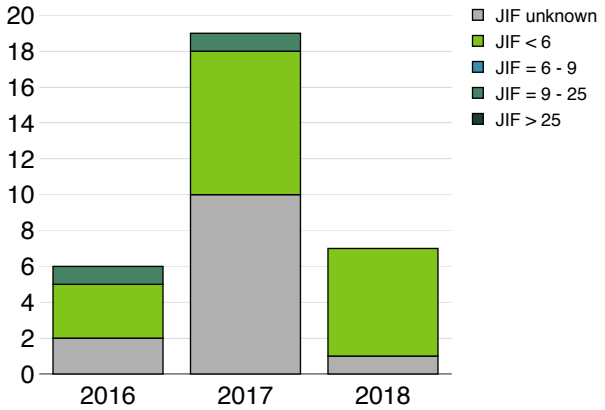
Publications

2016: 6
2017: 19
2018: 7

Publications by category



Publications by Journal Impact Factor *



* Technology development was primarily published in peer-reviewed computer science conferences, which do not provide JIFs.

Cell Profiling

Cellular and Molecular Imaging platform

Basic information

Facility director: Emma Lundberg
Head of facility: Charlotte Stadler
SciLifeLab facility since: 2013
Host university: KTH
FTEs: 4.3
FTEs financed by SciLifeLab: 2.8

Funding 2018 (in kSEK)

SciLifeLab: 3000
VR: 400

Total: 3400

Resource allocation 2018

Academia (national): 40%
Academia (international): 10%
Internal tech. dev.: 30%
Industry: 20%
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 450

Reagents: 50%
Instrument: 25%
Salaries: 25%
Rent: -
Other: -

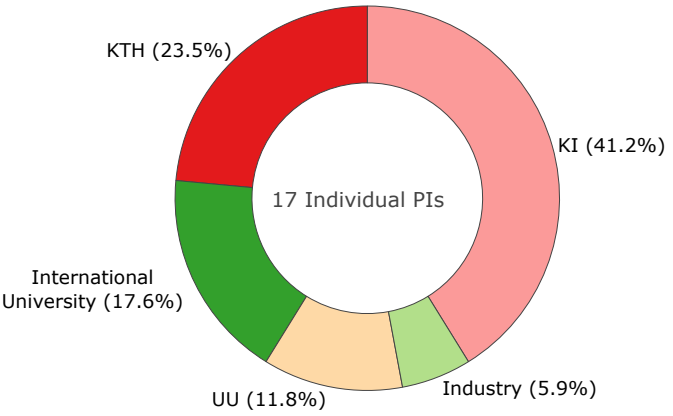
User fees by sector 2018

Academia (national): 50%
Academia (international): -
Industry: 50%
Healthcare: -
Other gov. agencies: -

Services

- Spatial proteomics at single cell resolution
- Automated image analysis.
- Manual image analysis.
- siRNA knockdown.
- Target protein analysis using immunostaining and confocal microscopy. External or HPA antibodies in human or rodent cell lines.

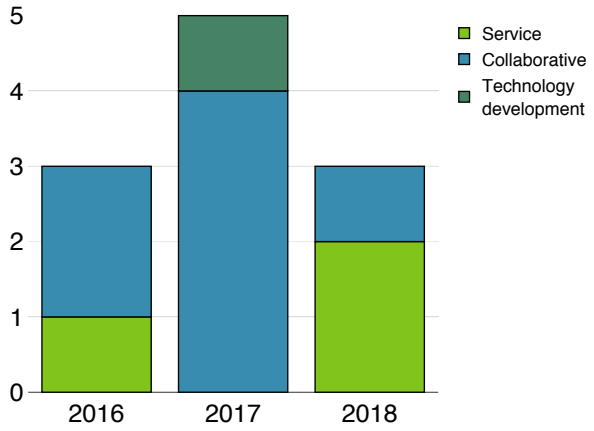
Users 2018



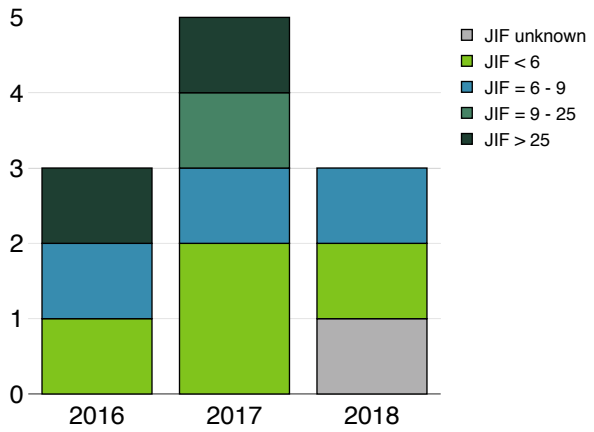
Publications

2016: 3
2017: 5
2018: 3

Publications by category



Publications by Journal Impact Factor



Cryo-EM (SU)

Cellular and Molecular Imaging platform

Basic information

Facility director: Gunnar von Hejine
Head of facility: Marta Carroni
SciLifeLab facility since: 2016
Host university: SU
FTEs: 5.0
FTEs financed by SciLifeLab: 4.0

Funding 2018 (in kSEK)

SciLifeLab: 4500
KAW: 4653
EPF: 3153
SU: 1430

Total: 13736

Resource allocation 2018

Academia (national): 80%
Academia (international): -
Internal tech. dev.: 20%
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 1100

Reagents: 100%
Instrument: -
Salaries: -
Rent: -
Other: -

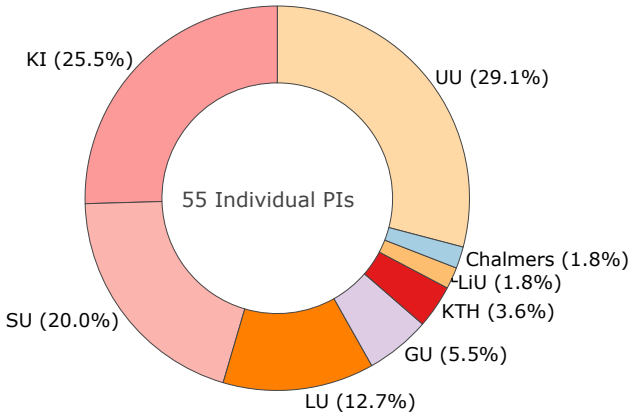
User fees by sector 2018

Academia (national): 100%
Academia (international): -
Industry: -
Healthcare: -
Other gov. agencies: -

Services

• Single-particle Cryo-EM employing a Talos Arctica for sample optimisation and a Titan Krios for high-resolution data collection.

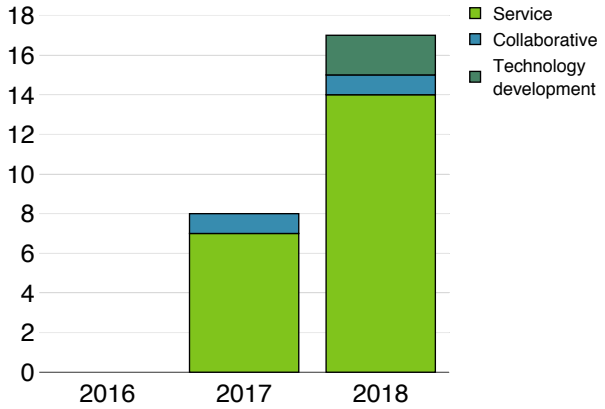
Users 2018



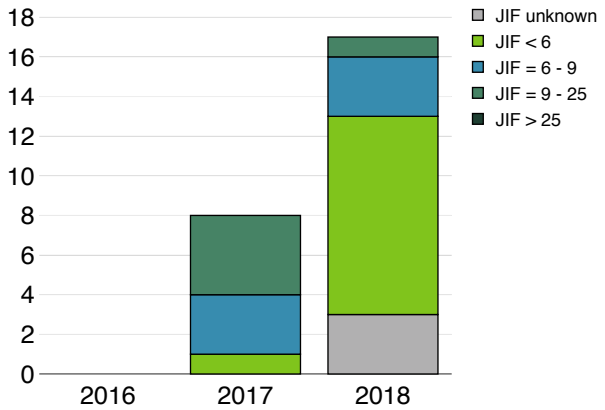
Publications *

2016: 0
2017: 8
2018: 17

Publications by category *



Publications by Journal Impact Factor *



* Total number of publications for the two Cryo-EM nodes

Cryo-EM (UmU)

Cellular and Molecular Imaging platform

Basic information

Facility director: Bernt Eric Uhlin
Head of facility: Linda Sandblad
SciLifeLab facility since: 2016
Host university: UmU
FTEs: 7.8
FTEs financed by SciLifeLab: 4.0

Funding 2018 (in kSEK)

SciLifeLab: 4000
KAW: 1500
UmU: 3000

Total: 8500

Resource allocation 2018

Academia (national): 90%
Academia (international): 10%
Internal tech. dev.: -
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 595

Reagents: 100%
Instrument: -
Salaries: -
Rent: -
Other: -

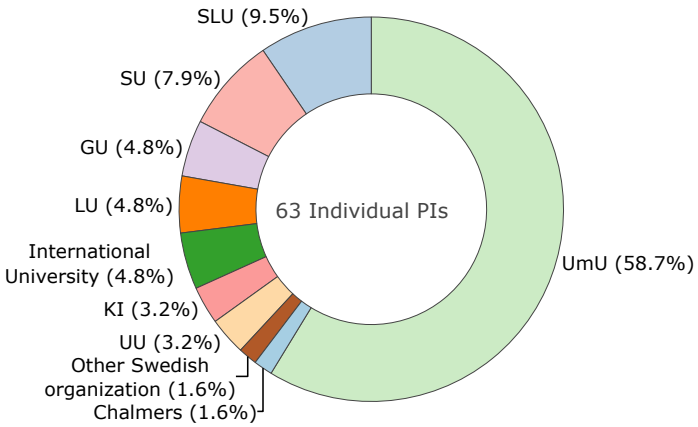
User fees by sector 2018

Academia (national): 90%
Academia (international): 10%
Industry: -
Healthcare: -
Other gov. agencies: -

Services

• Cryo-electron tomography and cryo-EM data collection using Titan Krios 300 kV Cryo-TEM
• Cryo-SEM, SEM Focused Ion Beam (FIB) volume imaging and cryo lamella preparation with Scios SEM
• TEM imaging and sample screening using Talos L120 TEM

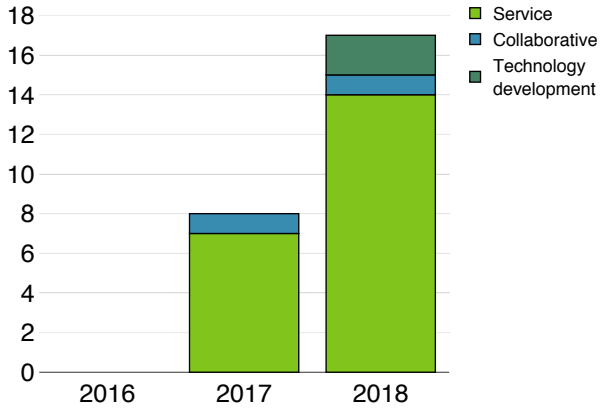
Users 2018



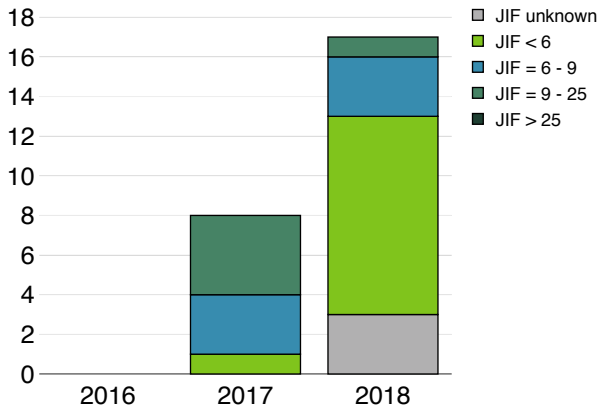
Publications *

2016: 0
2017: 8
2018: 17

Publications by category *



Publications by Journal Impact Factor *



* Total number of publications for the two Cryo-EM nodes

Protein Science Facility

Cellular and Molecular Imaging platform

Basic information

Facility director: Gunter Schneider
Head of facility: Helena Berglund
SciLifeLab facility since: 2013
Host university: KI
FTEs: 4.0
FTEs financed by SciLifeLab: 2.0

Funding 2018 (in kSEK)

SciLifeLab: 1920
KI: 1000
Total: 2920

Resource allocation 2018

Academia (national): 90%
Academia (international): 5%
Internal tech. dev.: -
Industry: 5%
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 1285
Reagents: 60%
Instrument: 35%
Salaries: 5%
Rent: -
Other: -

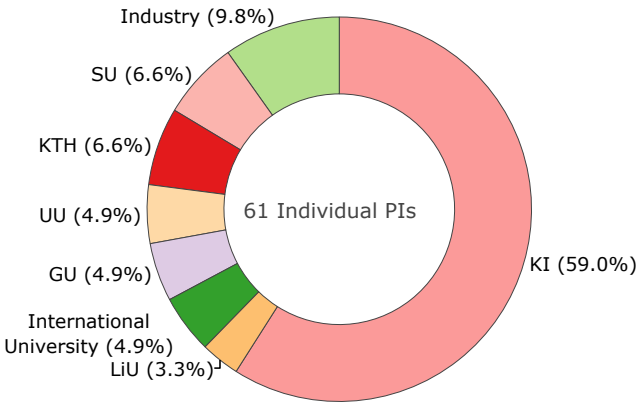
User fees by sector 2018

Academia (national): 87%
Academia (international): 5%
Industry: 8%
Healthcare: -
Other gov. agencies: -

Services

- Multi construct sub-cloning package.
- Production scale cultures.
- Protein purification. Affinity purification utilizing the His-tag followed by a size exclusion chromatography step.
- Small scale expression and solubility screening.
- Tailor made additions. E.g. proteolytic His tag removal, extra purification steps, additional analyses.

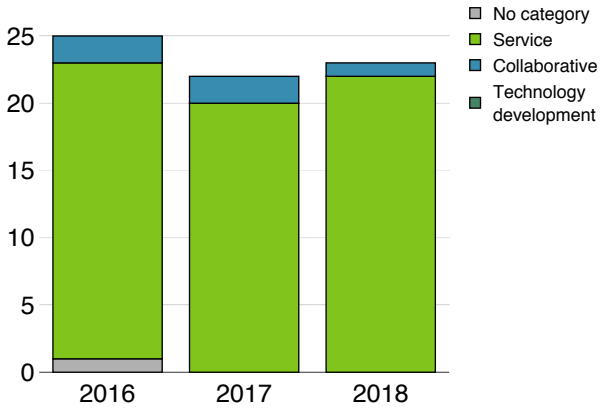
Users 2018



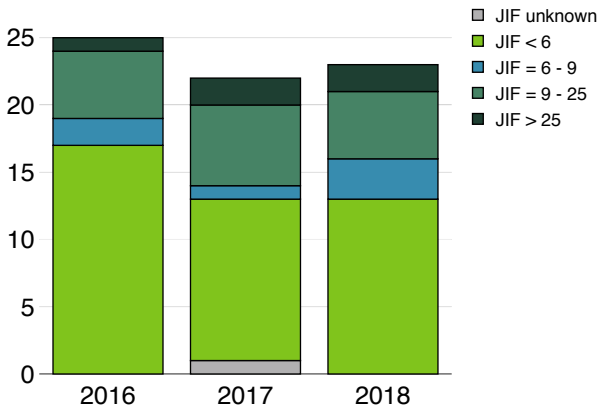
Publications

2016: 25
2017: 22
2018: 23

Publications by category



Publications by Journal Impact Factor



Swedish NMR Centre

Cellular and Molecular Imaging platform

Basic information

Facility director: Göran Karlsson, Gerhard Gröbner
Head of facility: Cecilia Persson, Tobias Sparrman
SciLifeLab facility since: 2016
Host university: GU, UmU
FTEs: 10.2
FTEs financed by SciLifeLab: 3.0

Funding 2018 (in kSEK)

SciLifeLab: 3000
GU: 7400
UmU: 1727
KAW: 7000

Total: 19127

Resource allocation 2018

Academia (national): 60%
Academia (international): 7%
Internal tech. dev.: 15%
Industry: 8%
Healthcare: 8%
Other gov. agencies: 2%

User Fees 2018

Total (kSEK): 1400

Reagents: 20%
Instrument: 70%
Salaries: 10%
Rent: -
Other: -

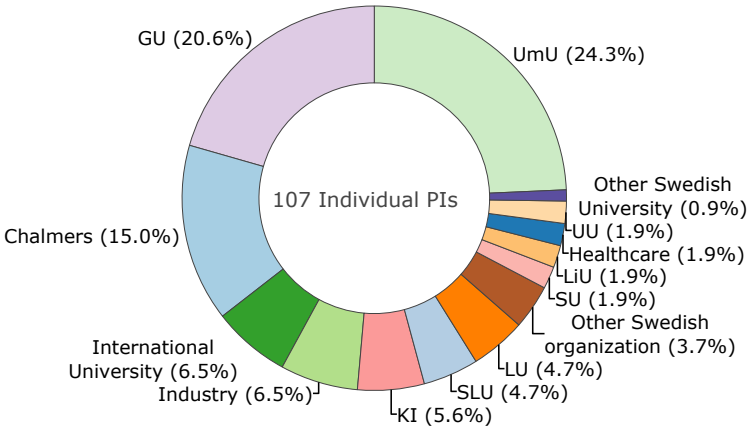
User fees by sector 2018

Academia (national): 75%
Academia (international): 5%
Industry: 14%
Healthcare: 5%
Other gov. agencies: 1%

Services

- Structural biology
- Metabolomics
- Chemical biology and small molecule NMR
- Diffusion, microimaging and MAS NMR

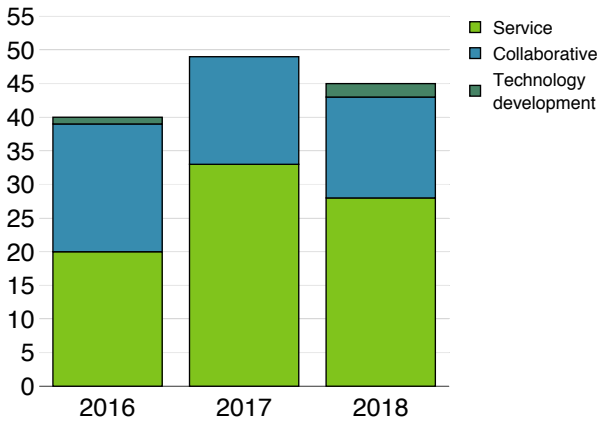
Users 2018



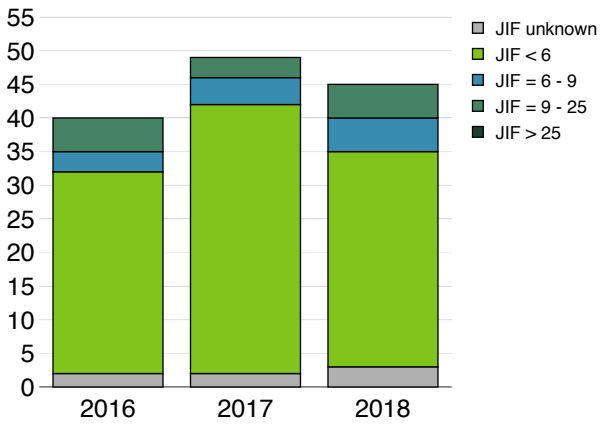
Publications

2016: 40
2017: 49
2018: 45

Publications by category



Publications by Journal Impact Factor



Chemical Biology Consortium Sweden

Chemical Biology and Genome Engineering platform

Basic information

Facility director: Anna-Lena Gustavsson, Erik Chorell
Head of facility: Anna-Lena Gustavsson, Stina Berglund Fick
SciLifeLab facility since: 2013
Host university: KI, UmU
FTEs: 11.0
FTEs financed by SciLifeLab: 5.0

Funding 2018 (in kSEK)

SciLifeLab: 5000
KI: 3000
UmU: 1550

Total: 9550

Resource allocation 2018

Academia (national): 88%
Academia (international): 1%
Internal tech. dev.: 10%
Industry: 1%
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 3400

Reagents: 23%
Instrument: 10%
Salaries: 55%
Rent: 12%
Other: -

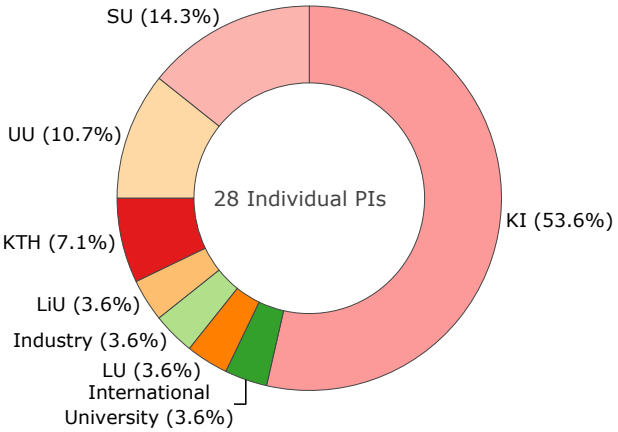
User fees by sector 2018

Academia (national): 98%
Academia (international): 1%
Industry: 1%
Healthcare: -
Other gov. agencies: -

Services

- Assay development
- Biochemical, cell-based and phenotypic high-throughput screening of small-molecule screening libraries
- Chemical proteomics & target identification of small molecule ligands
- Computational chemistry and modelling
- High-throughput imaging technology
- Hit optimization and medicinal chemistry

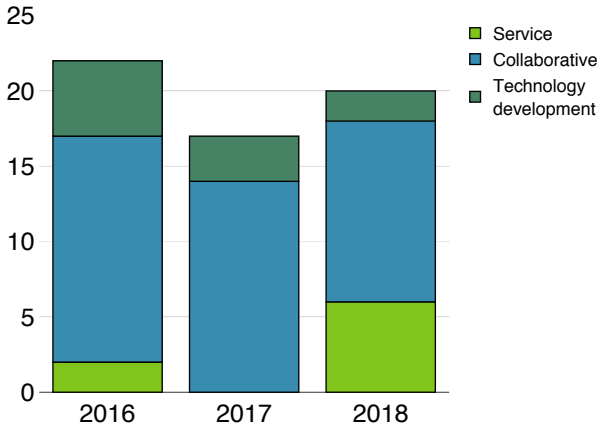
Users 2018



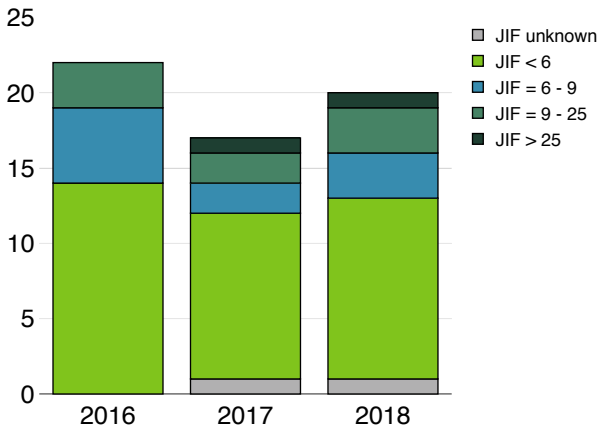
Publications

2016: 22
2017: 17
2018: 20

Publications by category



Publications by Journal Impact Factor



Genome Engineering Zebrafish

Chemical Biology and Genome Engineering platform

Basic information

Facility director: Johan Ledin
Head of facility: Tiffany Klingström, Beata Filipek Gorniok
SciLifeLab facility since: 2016
Host university: UU
FTEs: 6.0
FTEs financed by SciLifeLab: 3.0

Funding 2018 (in kSEK)

SciLifeLab: 2400
UU: 1000
Total: 3400

Resource allocation 2018

Academia (national): 85%
Academia (international): 10%
Internal tech. dev.: 5%
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 1900
Reagents: 20%
Instrument: -
Salaries: 80%
Rent: -
Other: -

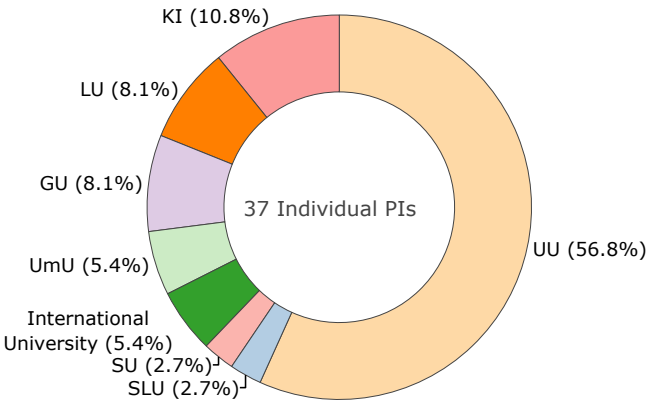
User fees by sector 2018

Academia (national): 95%
Academia (international): 5%
Industry: -
Healthcare: -
Other gov. agencies: -

Services

• CRISPR/Cas9 induced loss of function zebrafish line generation in a selection of readout models
• Development and analysis of CRISPR/Cas9 induced disease models
• Embryo and adult fish production
• Techniques for reverse and forward genetic experiments, visualization of biological processes for extended periods in intact embryos
• Zebrafish caretaking for specific strains

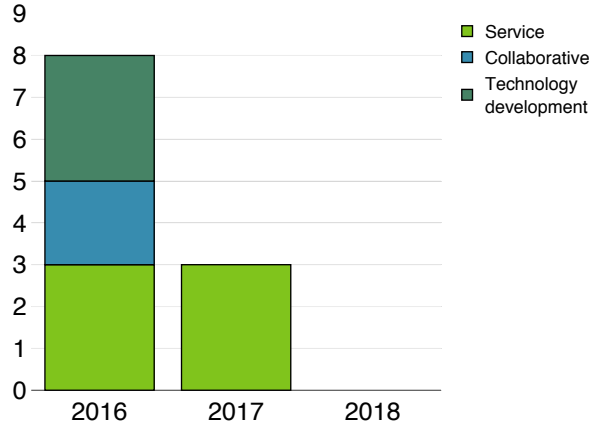
Users 2018



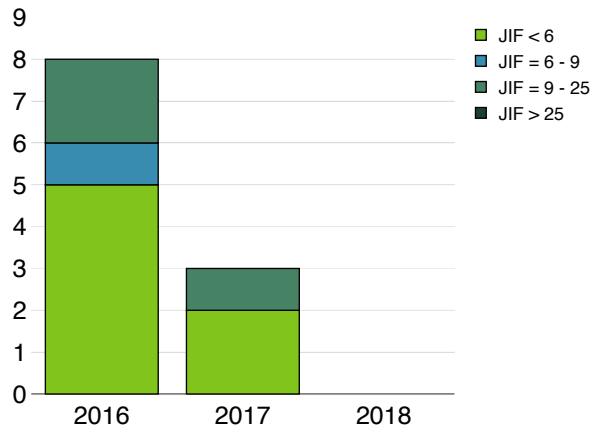
Publications

2016: 8
2017: 3
2018: 0

Publications by category



Publications by Journal Impact Factor



High Throughput Genome Engineering

Chemical Biology and Genome Engineering platform

Basic information

Facility director: Bernhard Schmierer
Head of facility: Bernhard Schmierer
SciLifeLab facility since: 2017
Host university: KI
FTEs: 3.0
FTEs financed by SciLifeLab: 3.0

Funding 2018 (in kSEK)

SciLifeLab: 2800

Total: 2800

Resource allocation 2018

Academia (national): 70%
Academia (international): 10%
Internal tech. dev.: 20%
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 700

Reagents: 50%
Instrument: -
Salaries: 50%
Rent: -
Other: -

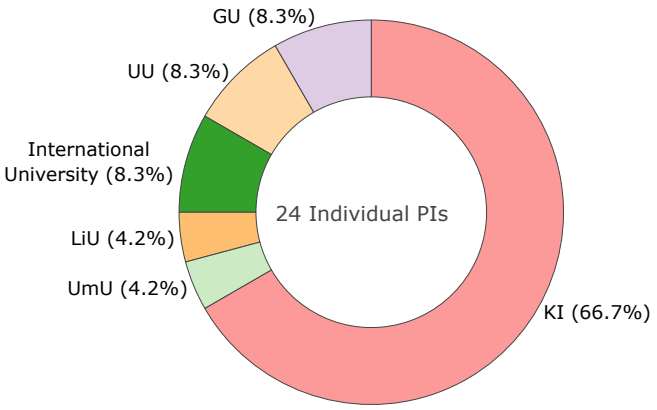
User fees by sector 2018

Academia (national): 73%
Academia (international): 27%
Industry: -
Healthcare: -
Other gov. agencies: -

Services

- Cas9-expressing cell line generation
- High throughput pooled CRISPR screens from screen design to gene hit list
- CRISPRko/CRISPRi/CRISPRa
- Lentiviral CRISPR guide libraries produced and provided
- Custom libraries created according to user specifications
- Library transduction performed
- Next generation sequencing library prepared

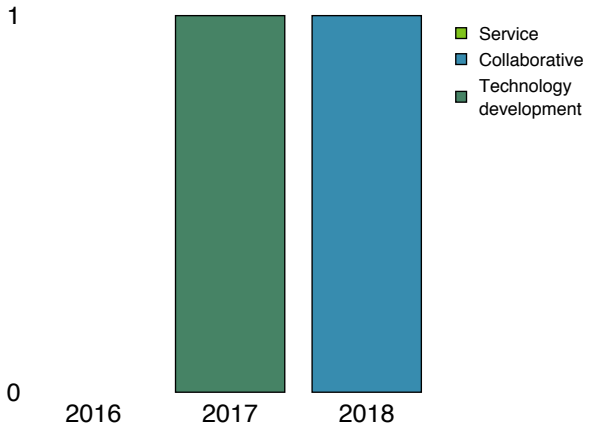
Users 2018



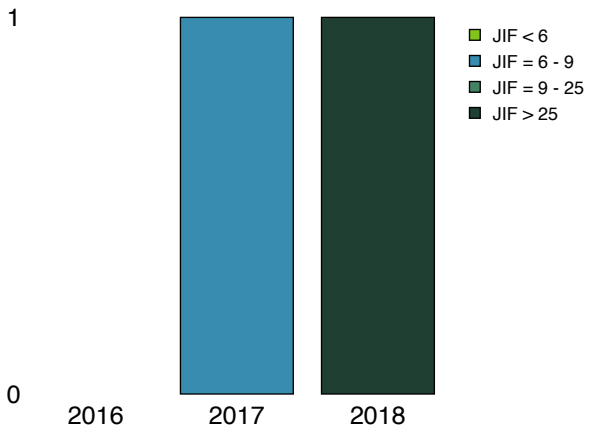
Publications

2016: 0
2017: 1
2018: 1

Publications by category



Publications by Journal Impact Factor



Clinical Genomics Göteborg

Diagnostics Development platform

Basic information

Facility director: Tommy Martinsson
Head of facility: Per Sikora
SciLifeLab facility since: 2016
Host university: GU
FTEs: 5.0
FTEs financed by SciLifeLab: 3.2

Funding 2018 (in kSEK)

SciLifeLab: 2200
GU: 550
Sahlgrenska: 465
Total: 3215

Resource allocation 2018

Academia (national): 25%
Academia (international): -
Internal tech. dev.: 20%
Industry: -
Healthcare: 55%
Other gov. agencies: -

User Fees 2018

Total (kSEK): 753

Reagents: -
Instrument: -
Salaries: -
Rent: -
Other: 100%

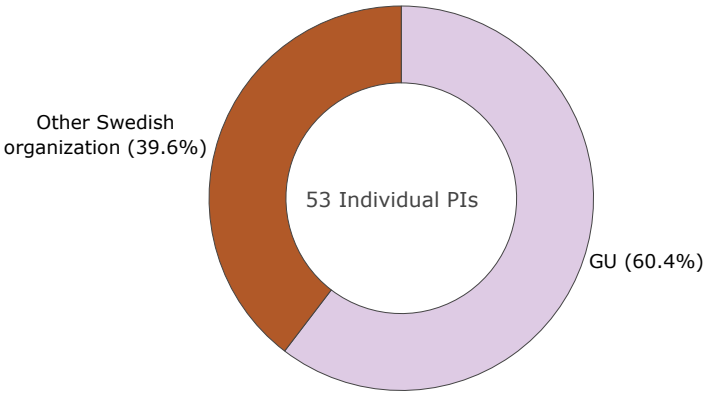
User fees by sector 2018

Academia (national): 20%
Academia (international): -
Industry: -
Healthcare: 80%
Other gov. agencies: -

Services

• Sequencing and bioinformatics support for clinical research and clinical implementation projects with a focus on NGS. Guidance and support on a wide range of NGS applications including WGS for clinical applications. The sequencing facility performs RNA-seq, exome sequencing, panels, metagenomics and bacterial genome sequencing locally, including 10x single-cell, exome and WGS. General consulting and support on cluster hardware and software infrastructure development and storage for NGS applications.

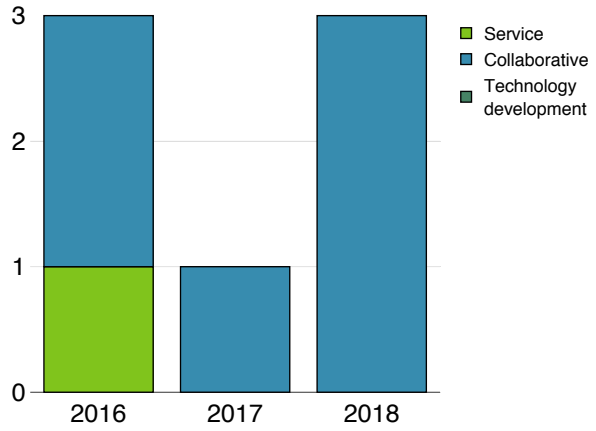
Users 2018



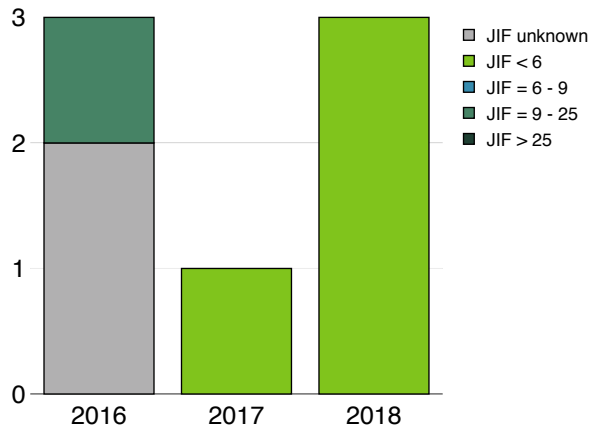
Publications

2016: 3
2017: 1
2018: 3

Publications by category



Publications by Journal Impact Factor



Clinical Genomics Lund

Diagnostics Development platform

Basic information

Facility director: Thoas Fioretos, Åke Borg
Head of facility: Markus Heidenblad, Ingrid Wilson
SciLifeLab facility since: 2016
Host university: LU
FTEs: 7.0
FTEs financed by SciLifeLab: 1.0

Funding 2018 (in kSEK)

SciLifeLab: 2200
ALF: 2000
LU: 2000

Total: 6200

Resource allocation 2018

Academia (national): 70%
Academia (international): -
Internal tech. dev.: 15%
Industry: -
Healthcare: 15%
Other gov. agencies: -

User Fees 2018

Total (kSEK): 4892

Reagents: 80%
Instrument: 15%
Salaries: -
Rent: -
Other: 5%

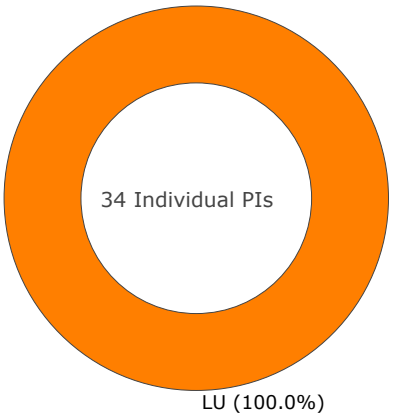
User fees by sector 2018

Academia (national): 100%
Academia (international): -
Industry: -
Healthcare: -
Other gov. agencies: -

Services

• Service in NGS-based technologies for investigators at Lund University and Region Skåne in projects with a strong translational edge or aiming at clinical implementation of new diagnostics assays. National services within specific high-profile areas of the facility.

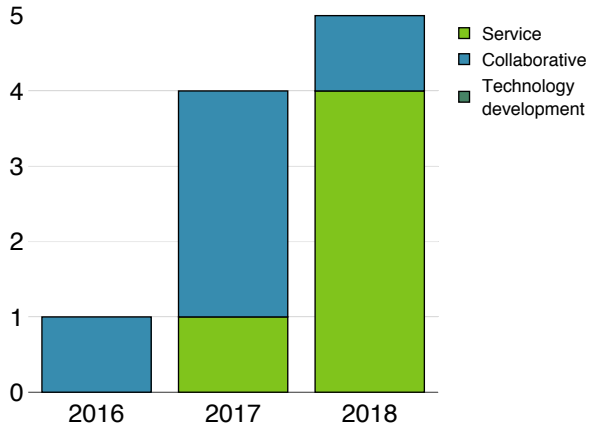
Users 2018



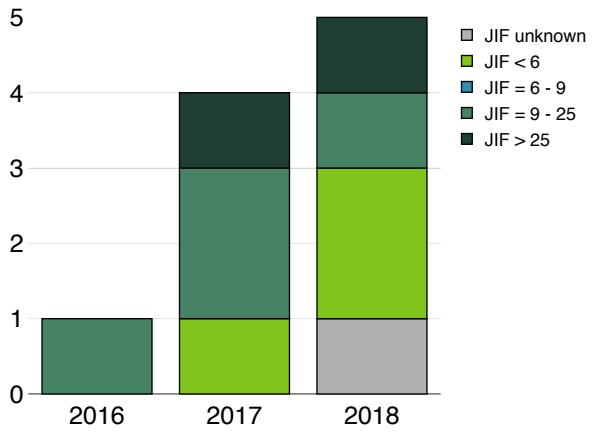
Publications

2016: 1
2017: 4
2018: 5

Publications by category



Publications by Journal Impact Factor



Clinical Genomics Stockholm

Diagnostics Development platform

Basic information

Facility director: Lars Engstrand
Head of facility: Valtteri Wirta
SciLifeLab facility since: 2014
Host university: KI, KTH
FTEs: 19.5
FTEs financed by SciLifeLab: 2.0

Funding 2018 (in kSEK)

SciLifeLab: 5000
KI: 500
SLL: 5000
NFR: 900
Vinnova: 2000

Total: 13400

Resource allocation 2018

Academia (national): 20%
Academia (international): -
Internal tech. dev.: 10%
Industry: -
Healthcare: 70%
Other gov. agencies: -

User Fees 2018

Total (kSEK): 32532

Reagents: 36%
Instrument: 17%
Salaries: 37%
Rent: 7%
Other: 3%

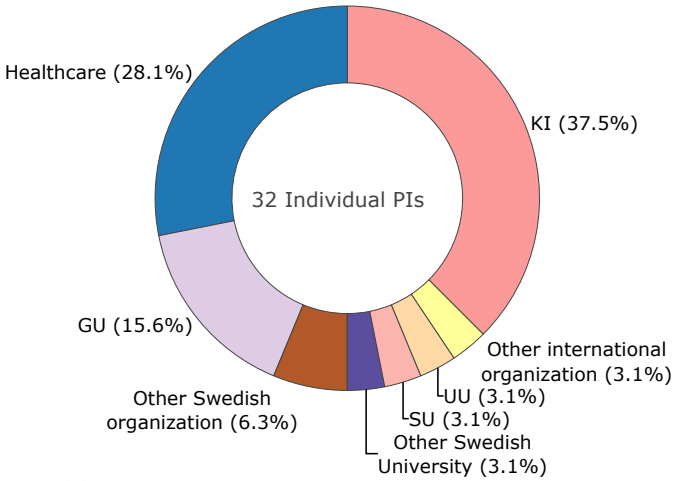
User fees by sector 2018

Academia (national): 14%
Academia (international): -
Industry: -
Healthcare: 85%
Other gov. agencies: 1%

Services

- DNA sequencing.
- Clinical exome and whole-genome sequencing
- Microbial whole-genome sequencing
- Targeted panels using various bait sets (contact for detailed information)
- RNA Seq using both poly A and random priming
- Ready-made libraries (prepared by collaborator)

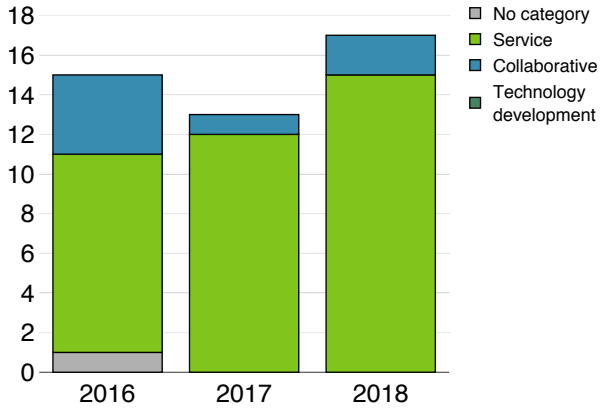
Users 2018



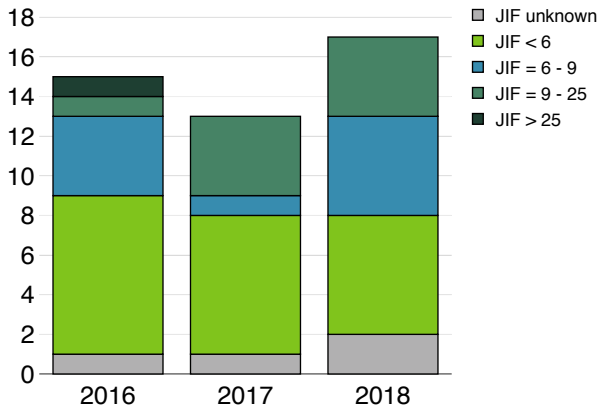
Publications

2016: 15
2017: 13
2018: 17

Publications by category



Publications by Journal Impact Factor



Clinical Genomics Uppsala

Diagnostics Development platform

Basic information

Facility director: Lucia Cavelier
Head of facility: Malin Melin
SciLifeLab facility since: 2014
Host university: UU
FTEs: 10.1
FTEs financed by SciLifeLab: 3.7

Funding 2018 (in kSEK)

SciLifeLab: 2700
ALF: 2000
Akademiska sjukhuset: 3280
Vinnova: 830
Industry: 3220
UU: 400

Total: 12430

Resource allocation 2018

Academia (national): 30%
Academia (international): -
Internal tech. dev.: 20%
Industry: 10%
Healthcare: 40%
Other gov. agencies: -

User Fees 2018

Total (kSEK): 4225

Reagents: 84%
Instrument: 1%
Salaries: 15%
Rent: -
Other: -

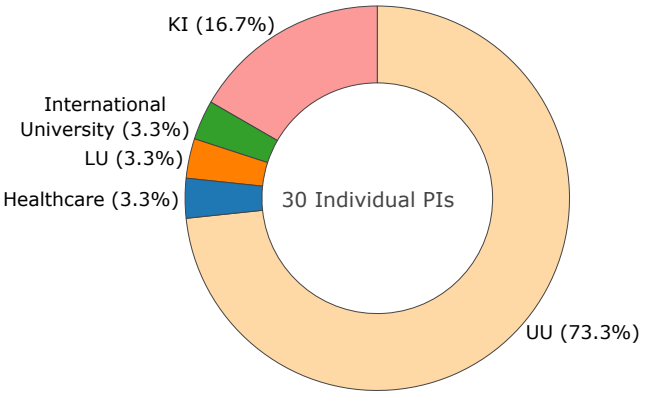
User fees by sector 2018

Academia (national): 24%
Academia (international): -
Industry: 43%
Healthcare: 33%
Other gov. agencies: -

Services

Fully tailored support with translational research projects. Development and clinical implementation of new diagnostic tests.
Examples of applications:
• Exome and gene panel sequencing
• Gene expression and gene fusion analysis with NanoString
• Mutation detection with digital PCR

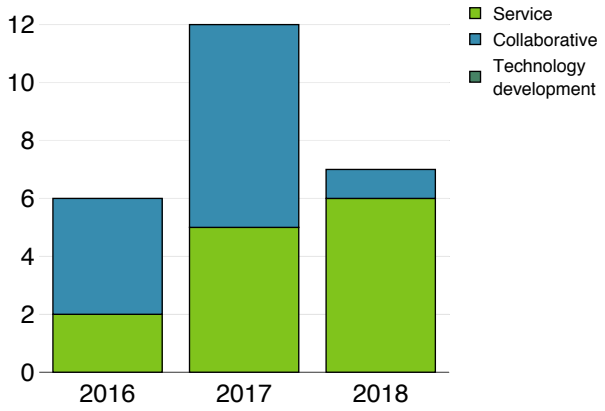
Users 2018



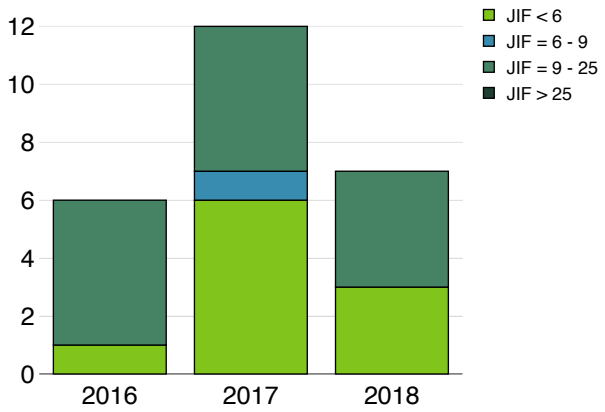
Publications

2016: 6
2017: 12
2018: 7

Publications by category



Publications by Journal Impact Factor



Drug Discovery and Development

Drug Discovery and Development platform

Basic information

Platform director: Per Arvidsson, Kristian Sandberg
SciLifeLab platform since: 2014
Host university: KI, KTH, LU, SU, UU
FTEs: 36.25
FTEs financed by SciLifeLab: 35.0

Funding 2018 (in kSEK)

SciLifeLab: 46154
UU: 3108
Total: 49262

Resource allocation 2018

Academia (national): 92%
Academia (international): -
Internal tech. dev.: 6%
Industry: 2%
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 1682
Reagents: 80%
Instrument: 20%
Salaries: -
Rent: -
Other: -

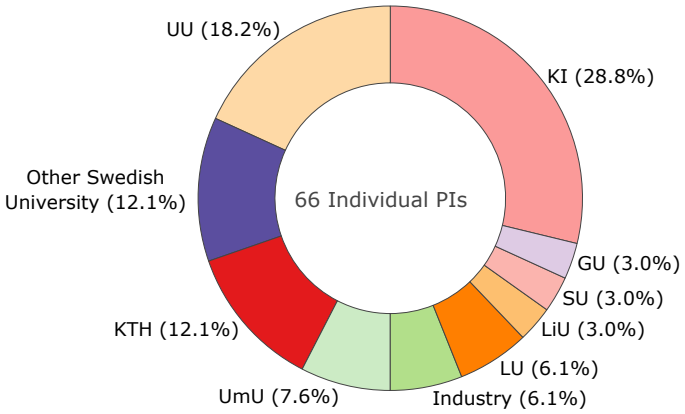
User fees by sector 2018

Academia (national): 88%
Academia (international): -
Industry: 12%
Healthcare: -
Other gov. agencies: -

Services

• Integrated drug discovery efforts to the Swedish academic research community. Industry standard infrastructure, expertise, and strategic support to help progress projects towards a pre-clinical proof-of-concept. The drug leads can be either a small molecule drug or a human antibody therapeutic.

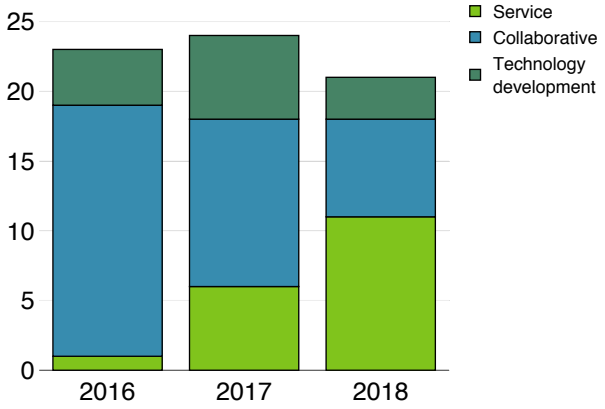
Users 2018



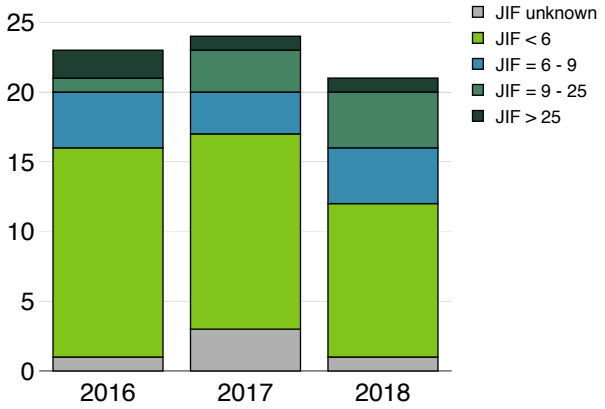
Publications

2016: 23
2017: 24
2018: 21

Publications by category



Publications by Journal Impact Factor



Ancient DNA

Genomics platform

Basic information

Facility director: Mattias Jakobsson, Anders Götherström
Head of facility: Magnus Lundgren
SciLifeLab facility since: 2017
Host university: UU, SU
FTEs: 0.22
FTEs financed by SciLifeLab: 0.22

Funding 2018 (in kSEK)

SciLifeLab: 2000
VR: 57
Wenner-Gren: 100
Total: 2157

Resource allocation 2018

Academia (national): -
Academia (international): -
Internal tech. dev.: 100%
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 0
Reagents: -
Instrument: -
Salaries: -
Rent: -
Other: -

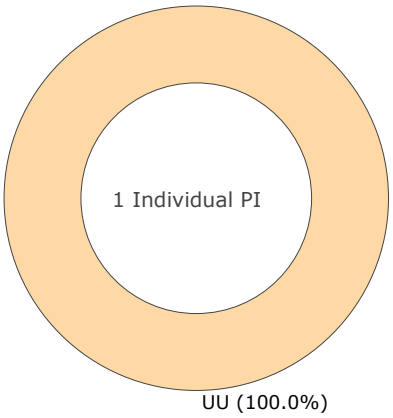
User fees by sector 2018

Academia (national): -
Academia (international): -
Industry: -
Healthcare: -
Other gov. agencies: -

Services

• Identification of samples containing ancient DNA
• Analysis of human remains for ancestry, gender and other traits
• Identification of animal remains

Users 2018



Publications

2016: -
2017: -
2018: -

Eukaryotic Single Cell Genomics

Genomics platform

Basic information

Facility director: Rickard Sandberg
Head of facility: Karolina Wallenborg
SciLifeLab facility since: 2015
Host university: KI
FTEs: 5.15
FTEs financed by SciLifeLab: 5.15

Funding 2018 (in kSEK)

SciLifeLab: 6000
KI: 1000

Total: 7000

Resource allocation 2018

Academia (national): 80%
Academia (international): 10%
Internal tech. dev.: 5%
Industry: 5%
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 5000

Reagents: 70%
Instrument: 2%
Salaries: 8%
Rent: -
Other: 20%

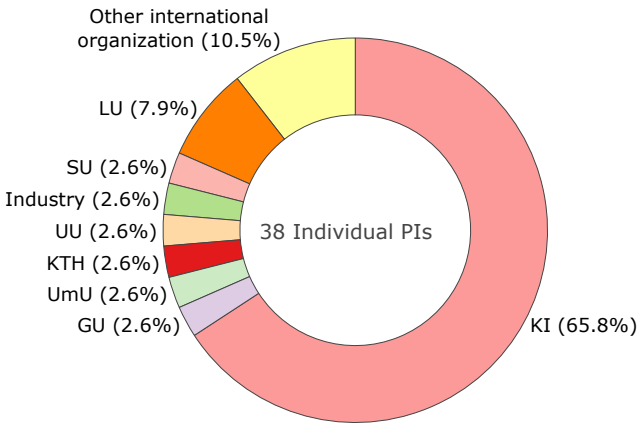
User fees by sector 2018

Academia (national): 85%
Academia (international): 10%
Industry: 5%
Healthcare: -
Other gov. agencies: -

Services

• Study heterogeneity within putatively homogeneous cell populations
• Unbiased discovery of cell types in complex tissues
• Characterizing the cellular and genetic composition of tumors

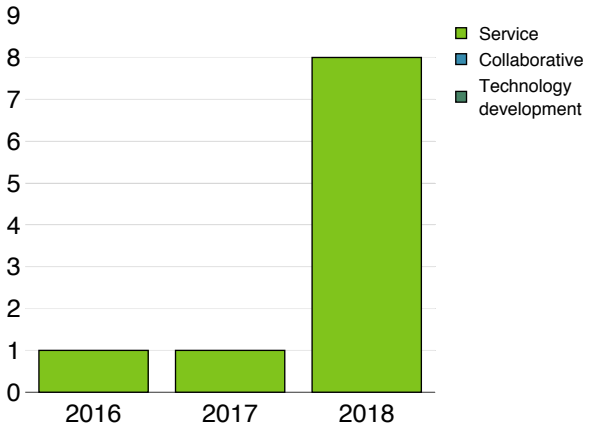
Users 2018



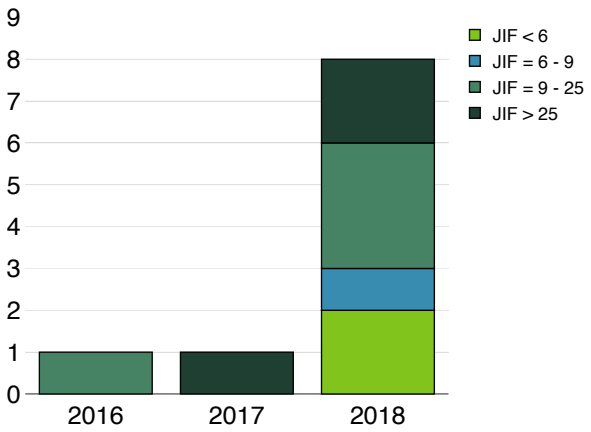
Publications

2016: 1
2017: 1
2018: 8

Publications by category



Publications by Journal Impact Factor



Microbial Single Cell Genomics

Genomics platform

Basic information

Facility director: Stefan Bertilsson
Head of facility: Thijs Ettema
SciLifeLab facility since: 2017
Host university: UU
FTEs: 2.5
FTEs financed by SciLifeLab: 2.5

Funding 2018 (in kSEK)

SciLifeLab: 2200
UU: 1451

Total: 3651

Resource allocation 2018

Academia (national): 60%
Academia (international): 10%
Internal tech. dev.: 30%
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 359

Reagents: 50%
Instrument: 10%
Salaries: 20%
Rent: -
Other: 20%

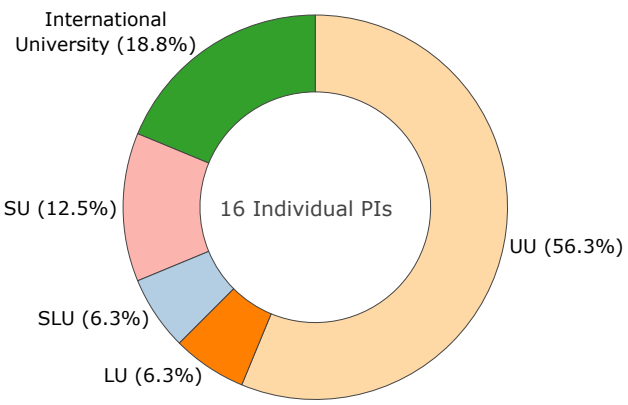
User fees by sector 2018

Academia (national): 78%
Academia (international): 22%
Industry: -
Healthcare: -
Other gov. agencies: -

Services

• Single-cell sorting in microwell plates using fluorescence-assisted cell sorting (FACS) or the C1 Single-Cell Auto Prep system
• Lysis and whole-genome amplification (WGA) of individual cells using multiple-strand displacement amplification (MDA)
• PCR screening of amplified single cell genomes for marker genes (e.g. microbial 16S rRNA, protein-coding genes)
• Advising in the design of single-cell experiments, whole-genome sequencing, genome assembly and bioinformatics support

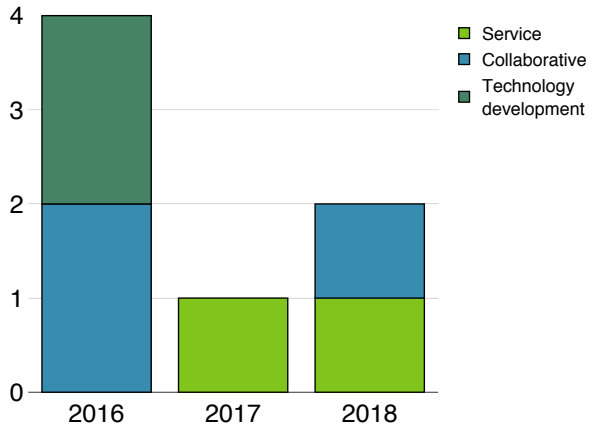
Users 2018



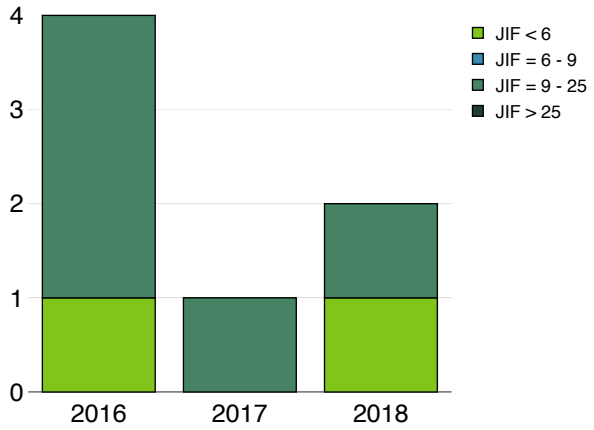
Publications

2016: 4
2017: 1
2018: 2

Publications by category



Publications by Journal Impact Factor



NGI Stockholm

Genomics platform

Basic information

Facility director: Joakim Lundeberg
Head of facility: Ellen Sherwood, Philip Ewels
SciLifeLab facility since: 2013
Host university: KI, KTH, SU
FTEs: 25.5
FTEs financed by SciLifeLab: 16.5

Funding 2018 (in kSEK)

SciLifeLab: 22900
VR: 9400
KAW: 10069
Total: 42369

Resource allocation 2018

Academia (national): 85%
Academia (international): 2%
Internal tech. dev.: 10%
Industry: 2%
Healthcare: 2%
Other gov. agencies: -

User Fees 2018

Total (kSEK): 35000
Reagents: 83%
Instrument: 13%
Salaries: 2%
Rent: 1%
Other: 1%

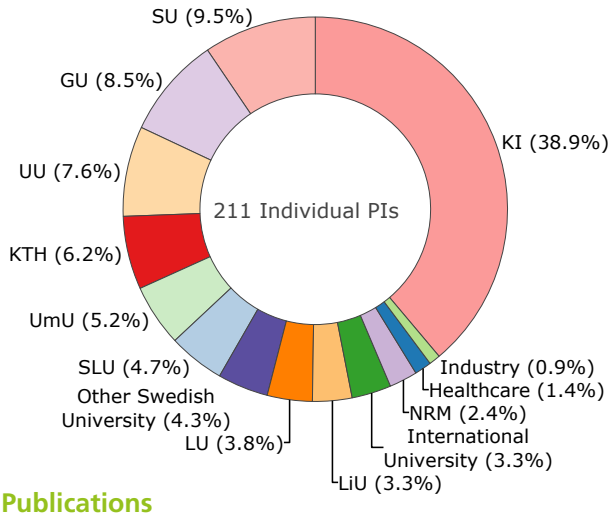
User fees by sector 2018

Academia (national): 95%
Academia (international): 2%
Industry: 1%
Healthcare: 2%
Other gov. agencies: -

Services

• DNA and RNA sequencing of user provided samples
• Establishing novel sequencing applications addressing the needs of users
• Outreach activities including provide guidelines and support for sample collections, study design and protocol selection

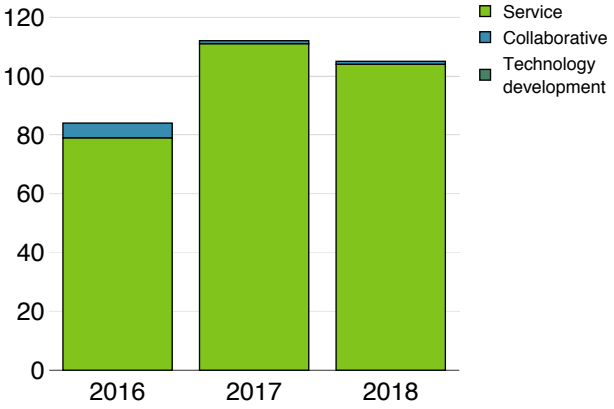
Users 2018



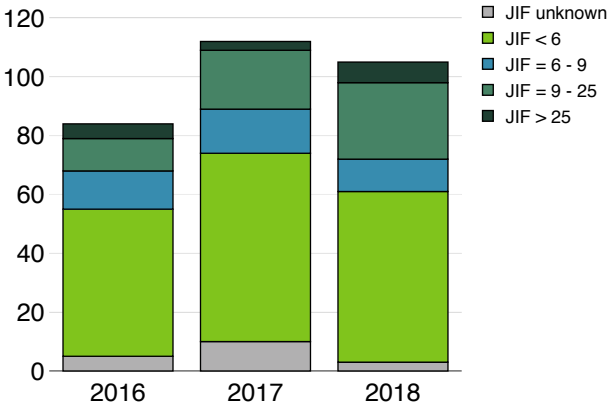
Publications

2016: 84
2017: 112
2018: 105

Publications by category



Publications by Journal Impact Factor



NGI Uppsala SNP&SEQ

Genomics platform

Basic information

Facility director: Ann-Christine Syvänen
Head of facility: Ulrika Liljedahl, Tomas Axelsson
SciLifeLab facility since: 2013
Host university: UU
FTEs: 34.0
FTEs financed by SciLifeLab: 23.0

Funding 2018 (in kSEK)

SciLifeLab: 12900
UU: 3450
VR: 5835
KAW: 11400

Total: 33585

Resource allocation 2018

Academia (national): 89%
Academia (international): 6%
Internal tech. dev.: 3%
Industry: -
Healthcare: -
Other gov. agencies: 2%

User Fees 2018

Total (kSEK): 52000

Reagents: 77%
Instrument: 15%
Salaries: 2%
Rent: 6%
Other: -

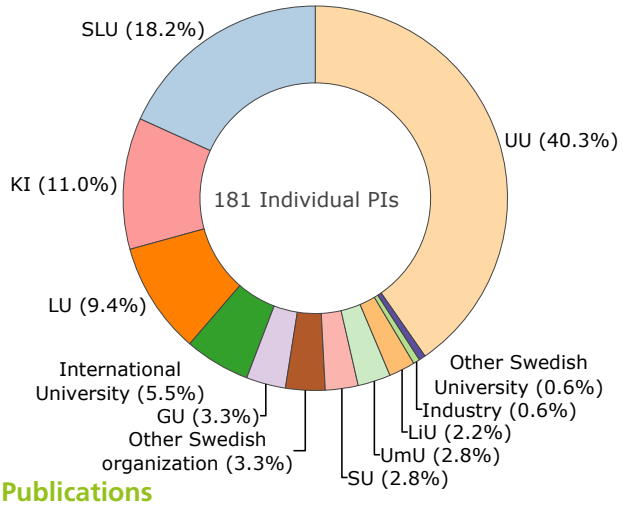
User fees by sector 2018

Academia (national): 95%
Academia (international): 3%
Industry: -
Healthcare: 1%
Other gov. agencies: 1%

Services

• Semi automated SNP genotyping based on primer extension technology with fluorescence or mass detection, or by sequencing by synthesis in an accredited laboratory
• Whole genome sequencing (WGS), de-novo sequencing, targeted genomic sequencing, transcriptome sequencing (RNA), sequencing of chromatin immunoprecipitated DNA (ChIP seq), and bisulfite sequencing for DNA methylation analysis.

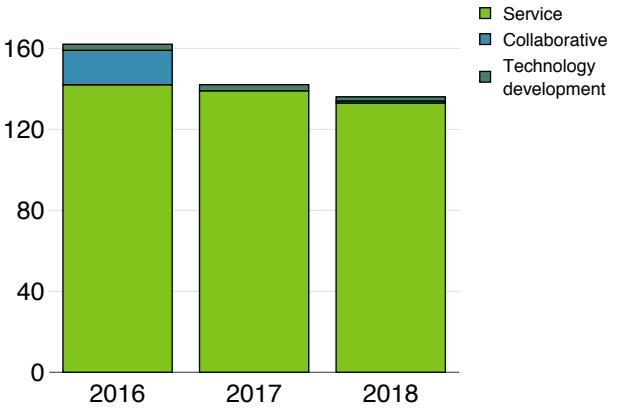
Users 2018



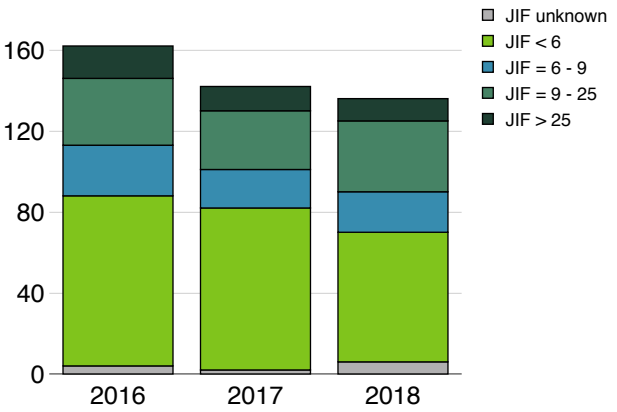
Publications

2016: 162
2017: 142
2018: 136

Publications by category



Publications by Journal Impact Factor



NGI Uppsala UGC

Genomics platform

Basic information

Facility director: Ulf Gyllensten
Head of facility: Inger Lindström
SciLifeLab facility since: 2013
Host university: UU
FTEs: 12.0
FTEs financed by SciLifeLab: 9.0

Funding 2018 (in kSEK)

SciLifeLab: 8700
UU: 1000
VR: 3600
Vinnova: 700

Total: 14000

Resource allocation 2018

Academia (national): 83%
Academia (international): 5%
Internal tech. dev.: 10%
Industry: -
Healthcare: 2%
Other gov. agencies: -

User Fees 2018

Total (kSEK): 8200

Reagents: 65%
Instrument: 27%
Salaries: 5%
Rent: -
Other: 3%

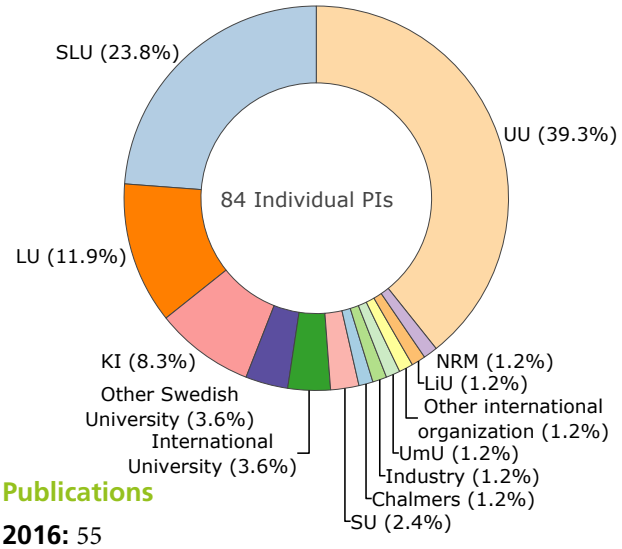
User fees by sector 2018

Academia (national): 93%
Academia (international): 5%
Industry: -
Healthcare: 2%
Other gov. agencies: -

Services

• Genomic analysis by tailor made NGS projects on Pacific Biosciences and Ion systems.
• Genotyping and Sanger sequencing services for multiple applications, such as human cell line authentication.
• Capillary Electrophoresis based services including Sanger sequencing, fragment analysis, and genotyping.

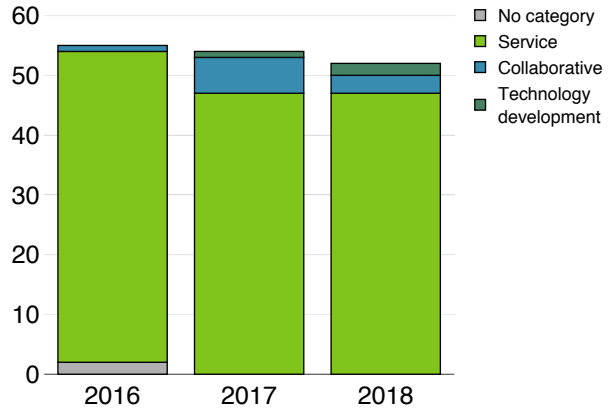
Users 2018



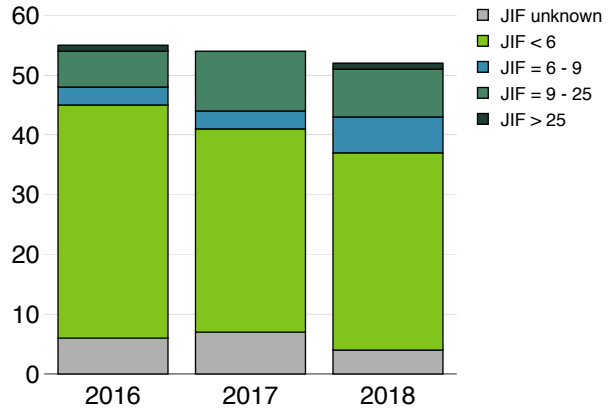
Publications

2016: 55
2017: 54
2018: 52

Publications by category



Publications by Journal Impact Factor



Autoimmunity Profiling

Proteomics and Metabolomics platform

Basic information

Facility director: Peter Nilsson
Head of facility: Ronald Sjöberg
SciLifeLab facility since: 2013
Host university: KTH
FTEs: 3.0
FTEs financed by SciLifeLab: 3.0

Funding 2018 (in kSEK)

SciLifeLab: 2400

Total: 2400

Resource allocation 2018

Academia (national): 60%
Academia (international): 20%
Internal tech. dev.: 15%
Industry: 5%
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 450

Reagents: 40%
Instrument: 60%
Salaries: -
Rent: -
Other: -

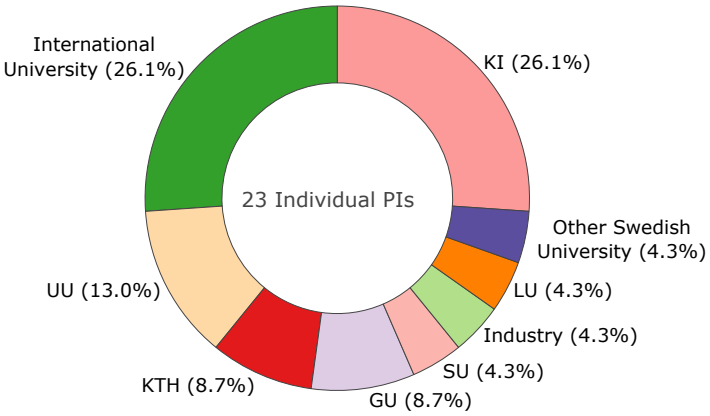
User fees by sector 2018

Academia (national): 38%
Academia (international): 12%
Industry: 50%
Healthcare: -
Other gov. agencies: -

Services

- Autoantibody profiling
- Epitope mapping
- Antibody validation
- Infrastructure for commercial protein arrays

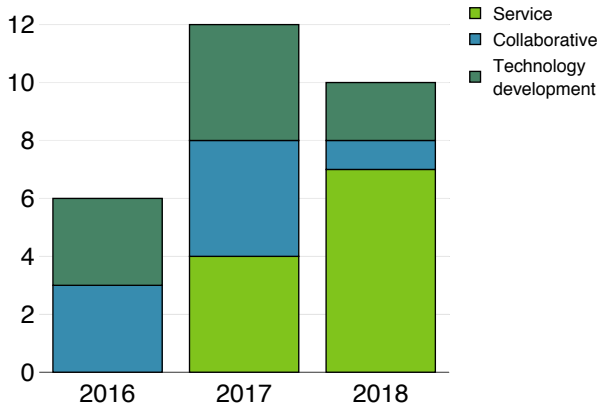
Users 2018



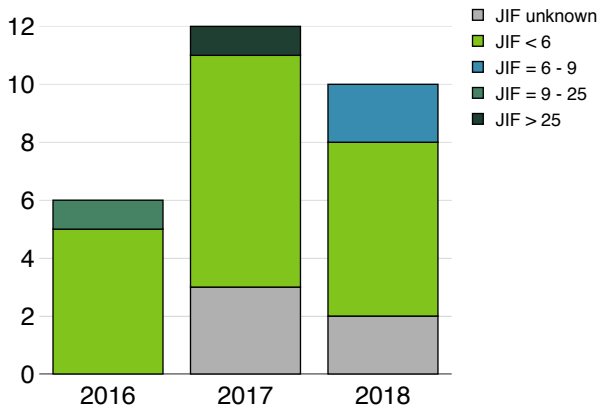
Publications

2016: 6
2017: 12
2018: 10

Publications by category



Publications by Journal Impact Factor



Chemical Proteomics and Proteogenomics (MBB)

Proteomics and Metabolomics platform

Basic information

Facility director: Roman Zubarev
Head of facility: Massimiliano Gaetani
SciLifeLab facility since: 2017
Host university: KI
FTEs: 1.83
FTEs financed by SciLifeLab: 0.0

Funding 2018 (in kSEK)

SciLifeLab: 1600
VR: 2280
KI: 1900

Total: 5780

Resource allocation 2018

Academia (national): 40%
Academia (international): 5%
Internal tech. dev.: 50%
Industry: 5%
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 747

Reagents: 21%
Instrument: 34%
Salaries: 19%
Rent: 15%
Other: 11%

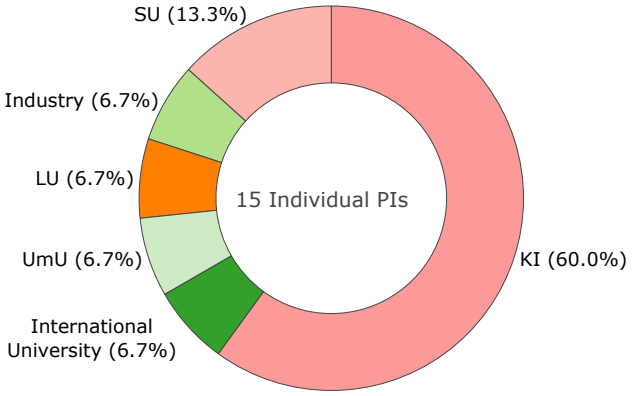
User fees by sector 2018

Academia (national): 63%
Academia (international): 6%
Industry: 31%
Healthcare: -
Other gov. agencies: -

Services

• Affinity capture using click chemistry based probes followed by MS analysis.
• Kinetic profiling post compound exposure
• Proteome-wide mapping of changes in thermal stability of proteins after chemical perturbation.
• Identification of key proteins and mechanism of action identification
• Key protein characterization by top-down proteomics
• Interaction interface elucidation by hydrogen-deuterium exchange MS

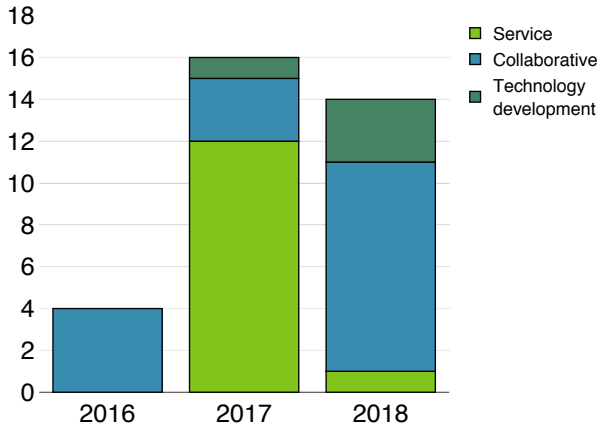
Users 2018



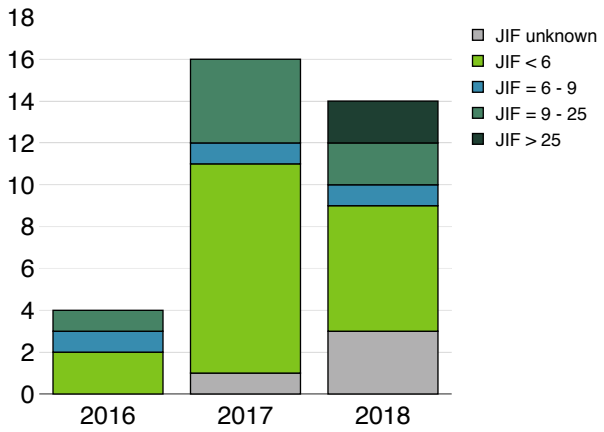
Publications *

2016: 4
2017: 16
2018: 14

Publications by category *



Publications by Journal Impact Factor *



* Total number of publications for the two CPP nodes

Chemical Proteomics and Proteogenomics (OnkPat)

Proteomics and Metabolomics platform

Basic information

Facility director: Janne Lehtiö
Head of facility: Maria Pernemalm
SciLifeLab facility since: 2017
Host university: KI
FTEs: 6.5
FTEs financed by SciLifeLab: 1.2

Funding 2018 (in kSEK)

SciLifeLab: 2400
VR: 2730
KI: 1900

Total: 7030

Resource allocation 2018

Academia (national): 79%
Academia (international): 5%
Internal tech. dev.: 15%
Industry: -
Healthcare: 1%
Other gov. agencies: -

User Fees 2018

Total (kSEK): 2807

Reagents: 12%
Instrument: 30%
Salaries: 43%
Rent: 10%
Other: 5%

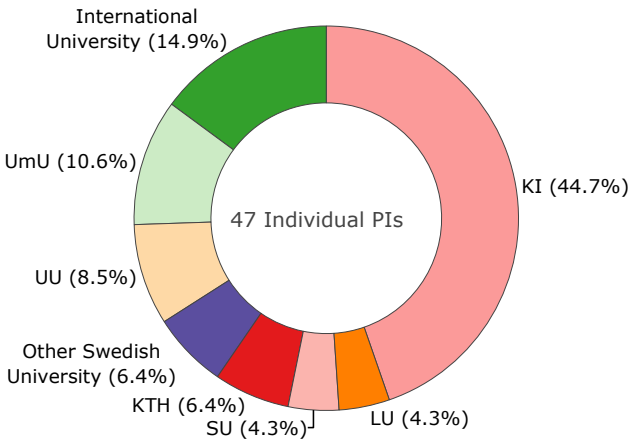
User fees by sector 2018

Academia (national): 91%
Academia (international): 8%
Industry: -
Healthcare: 1%
Other gov. agencies: -

Services

• Unbiased proteogenomics in any species with a sequenced genome.
• Personalized proteomics. Individual sequence based search database generation for variant analysis at the protein level coupled with in-depth quantitative proteome analysis.
• Disease state/Variant proteomics. Database supplemented with all known SNPs and disease causing genetic alterations.
• XenoProteomics. Database supplemented with peptides from disease causing pathogens.

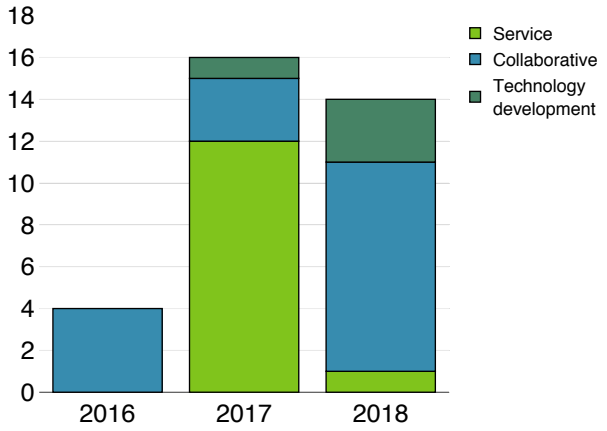
Users 2018



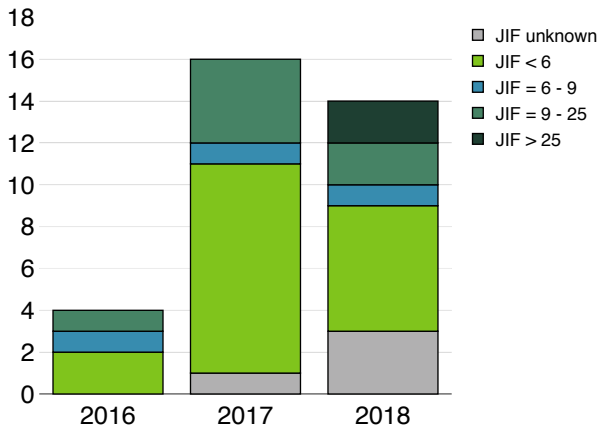
Publications *

2016: 4
2017: 16
2018: 14

Publications by category *



Publications by Journal Impact Factor *



* Total number of publications for the two CPP nodes

Mass Cytometry (KI)

Proteomics and Metabolomics platform

Basic information

Facility director: Petter Brodin
Head of facility: Lakshmikanth Tadepally
SciLifeLab facility since: 2015
Host university: KI
FTEs: 3.5
FTEs financed by SciLifeLab: 2.5

Funding 2018 (in kSEK)

SciLifeLab: 4000

Total: 4000

Resource allocation 2018

Academia (national): 80%
Academia (international): -
Internal tech. dev.: 20%
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 1930

Reagents: 50%
Instrument: 30%
Salaries: -
Rent: 20%
Other: -

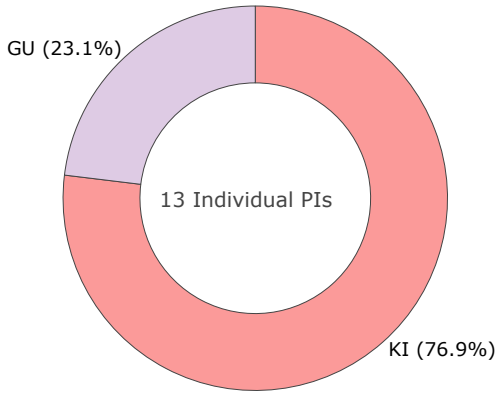
User fees by sector 2018

Academia (national): 100%
Academia (international): -
Industry: -
Healthcare: -
Other gov. agencies: -

Services

• Single-cell functional analysis based on intracellular cytokine/chemokine production.
• Single-cell phenotypic analysis by mass cytometry (CyTOF).
• Single-cell phospho-proteomic analysis of intracellular signalling pathways upon drug treatment or stimulation.

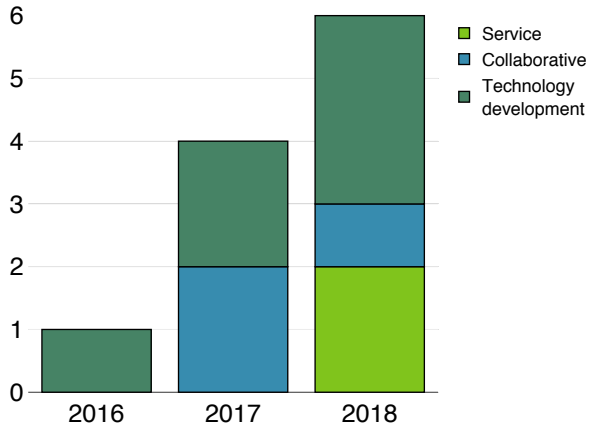
Users 2018



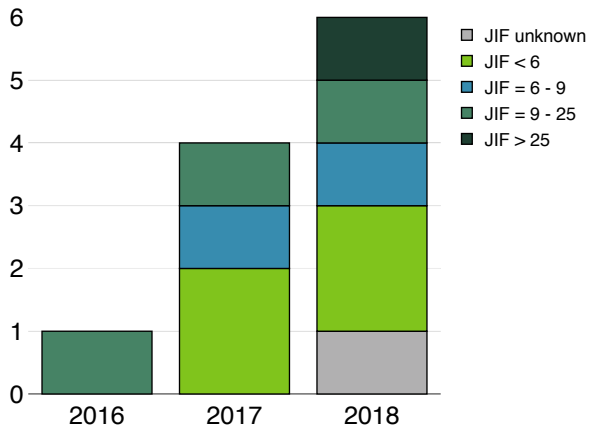
Publications *

2016: 1
2017: 4
2018: 6

Publications by category *



Publications by Journal Impact Factor *



* Total number of publications for the two Mass Cytometry nodes

Mass Cytometry (LiU)

Proteomics and Metabolomics platform

Basic information

Facility director: Jan-Ingvar Jönsson
Head of facility: Jörgen Adolfsson
SciLifeLab facility since: 2015
Host university: LiU
FTEs: 2.6
FTEs financed by SciLifeLab: 1.5

Funding 2018 (in kSEK)

SciLifeLab: 2000
LiU: 800

Total: 2800

Resource allocation 2018

Academia (national): 100%
Academia (international): -
Internal tech. dev.: -
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 208

Reagents: 100%
Instrument: -
Salaries: -
Rent: -
Other: -

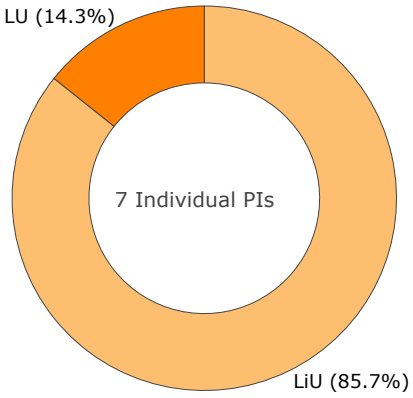
User fees by sector 2018

Academia (national): 100%
Academia (international): -
Industry: -
Healthcare: -
Other gov. agencies: -

Services

• Single-cell functional analysis based on intracellular cytokine/chemokine production.
• Single-cell phenotypic analysis by mass cytometry (CyTOF).
• Single-cell phospho-proteomic analysis of intracellular signalling pathways upon drug treatment or stimulation.

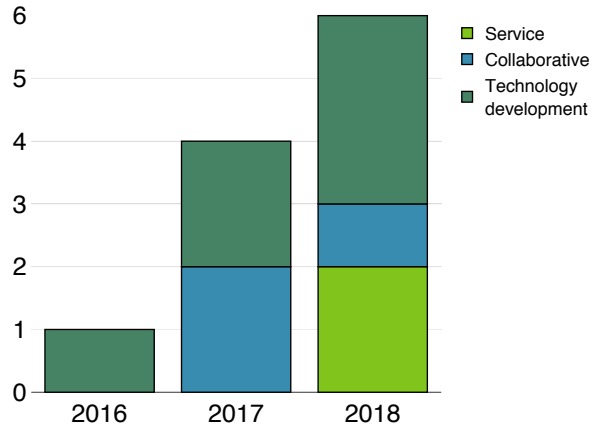
Users 2018



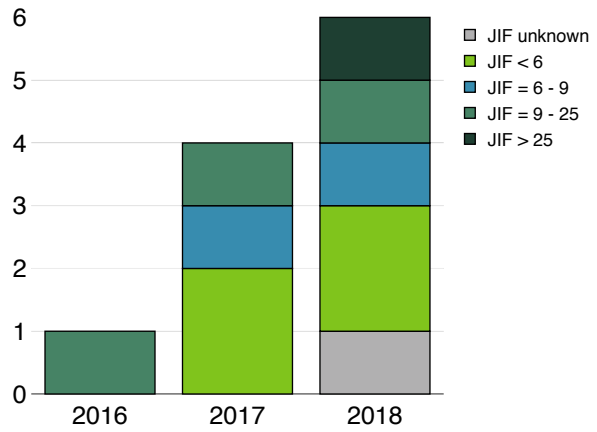
Publications *

2016: 1
2017: 4
2018: 6

Publications by category *



Publications by Journal Impact Factor *



* Total number of publications for the two Mass Cytometry nodes

PLA Proteomics*

Proteomics platform

* Merged with Single Cell Proteomics from Jan 1, 2019

Basic information

Facility director: Masood Kamali-Moghaddam, Ulf Landegren
Head of facility: Masood Kamali-Moghaddam
SciLifeLab facility since: 2013
Host university: UU
FTEs: 2.25
FTEs financed by SciLifeLab: 2.25

Funding 2018 (in kSEK)

SciLifeLab: 2800

Total: 2800

Resource allocation 2018

Academia (national): 70%
Academia (international): 10%
Internal tech. dev.: 19%
Industry: 1%
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 80

Reagents: 100%
Instrument: -
Salaries: -
Rent: -
Other: -

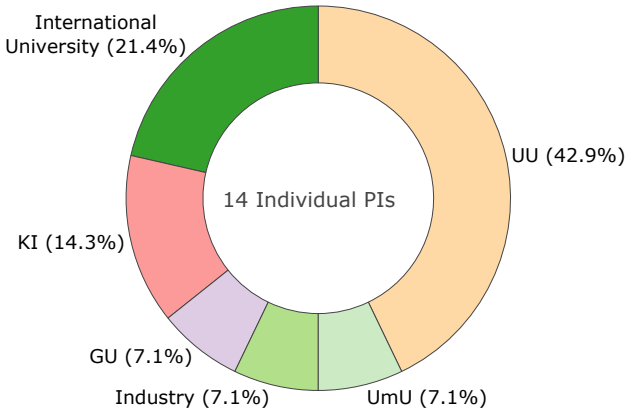
User fees by sector 2018

Academia (national): 99%
Academia (international): -
Industry: 1%
Healthcare: -
Other gov. agencies: -

Services

• Validation, optimization and assay development using client-selected antibodies
• In situ PLA. In situ PLA is applied for detecting proteins and their interactions and post-translational modifications using either client-selected antibodies or previously validated antibodies from a continuously updated list

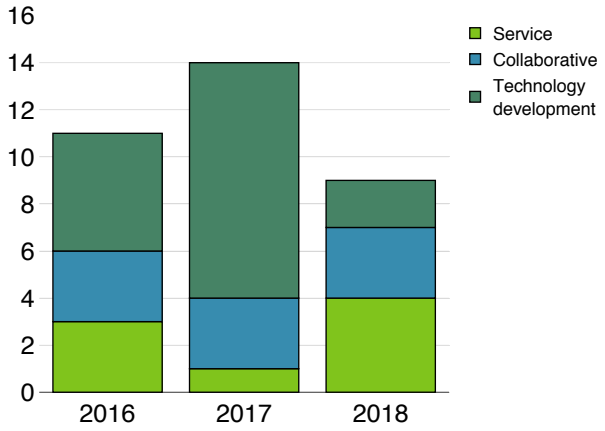
Users 2018



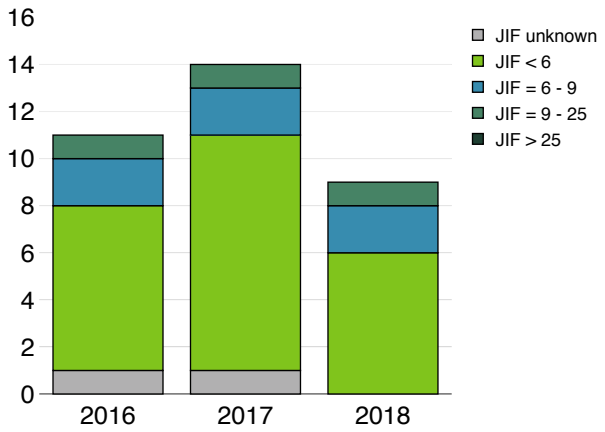
Publications

2016: 11
2017: 14
2018: 9

Publications by category



Publications by Journal Impact Factor



Plasma Profiling

Proteomics platform

Basic information

Facility director: Jochen Schwenk
Head of facility: Philippa Pettingill
SciLifeLab facility since: 2013
Host university: KTH
FTEs: 5.0
FTEs financed by SciLifeLab: 3.0

Funding 2018 (in kSEK)

SciLifeLab: 3200

Total: 3200

Resource allocation 2018

Academia (national): 80%
Academia (international): 5%
Internal tech. dev.: 15%
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 745

Reagents: 80%
Instrument: 15%
Salaries: -
Rent: -
Other: 5%

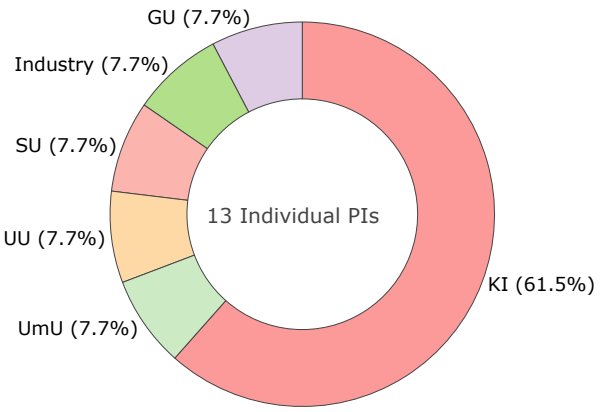
User fees by sector 2018

Academia (national): 80%
Academia (international): -
Industry: 20%
Healthcare: -
Other gov. agencies: -

Services

- Exploratory protein profiling of body fluids (Luminex-based)
- Protein analysis by multiplexed immunoassays
- Development of novel sandwich immunoassays (Luminex-based)
- Development of alternative immunoassays concepts (Luminex-based)
- Consulting on protein analysis using immunoassays

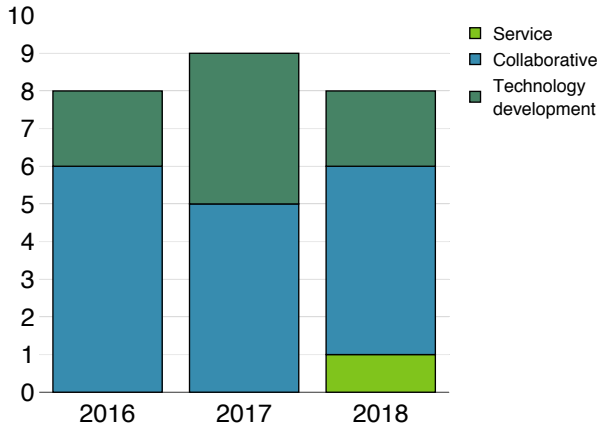
Users 2018



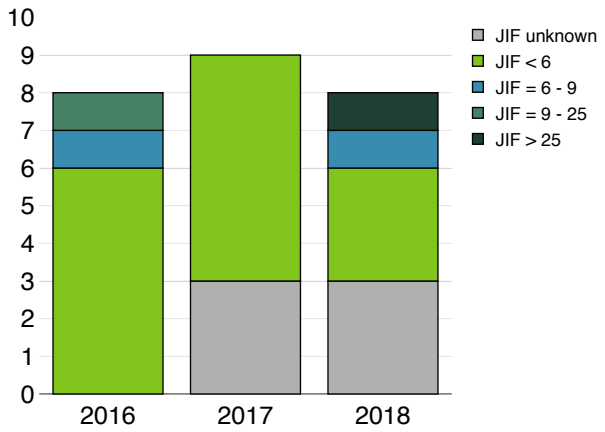
Publications

2016: 8
2017: 9
2018: 8

Publications by category



Publications by Journal Impact Factor



Single Cell Proteomics*

Proteomics and Metabolomics platform

* Merged with PLA Proteomics from Jan 1, 2019

Basic information

Facility director: Ulf Landegren
Head of facility: Maria Hammond
SciLifeLab facility since: 2017
Host university: UU
FTEs: 1.4
FTEs financed by SciLifeLab: 1.4

Funding 2018 (in kSEK)

SciLifeLab: 1000
UU: 400
Total: 1400

Resource allocation 2018

Academia (national): 60%
Academia (international): -
Internal tech. dev.: 40%
Industry: -
Healthcare: -
Other gov. agencies: -

User Fees 2018

Total (kSEK): 150
Reagents: 70%
Instrument: -
Salaries: 10%
Rent: -
Other: 20%

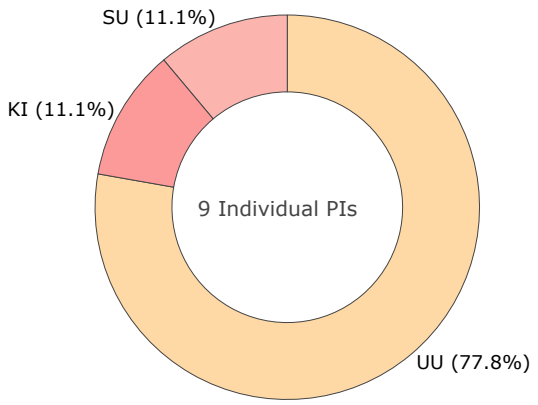
User fees by sector 2018

Academia (national): 100%
Academia (international): -
Industry: -
Healthcare: -
Other gov. agencies: -

Services

• Conjugation of oligonucleotides to antibodies for custom single-binder or proximity-based protein assays
• 92-plex protein detection in single or a few human cells using proximity extension assays (PEA; Olink Proteomics)
• Targeted protein analysis, alone or combined with targeted RNA analysis
• High throughput qPCR via the Fluidigm BioMark HD system

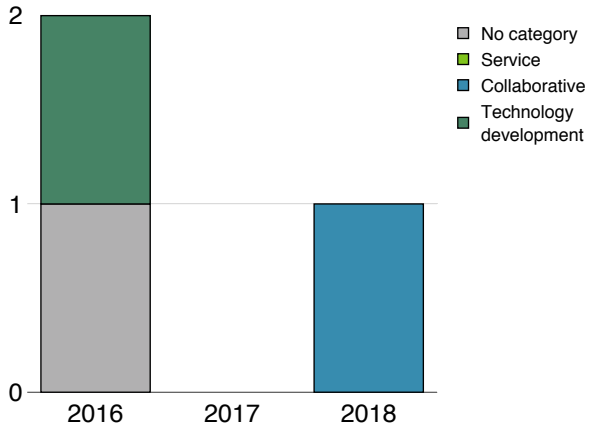
Users 2018



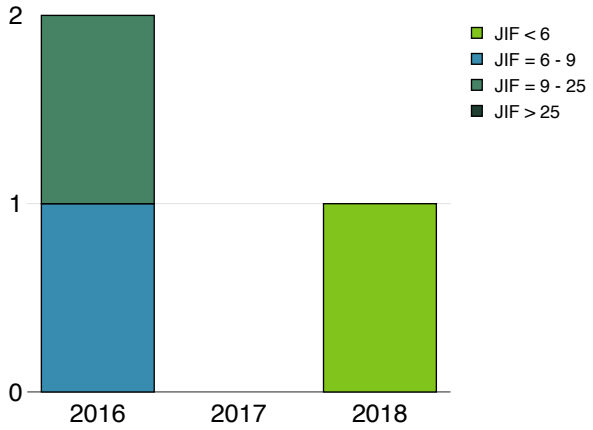
Publications

2016: 2
2017: 0
2018: 1

Publications by category



Publications by Journal Impact Factor



Swedish Metabolomics Centre

Proteomics and Metabolomics platform

Basic information

Facility director: Thomas Moritz, Anders Nordström
Head of facility: Annika Johansson
SciLifeLab facility since: 2017
Host university: SLU Umeå, UU
FTEs: 7.0
FTEs financed by SciLifeLab: 1.5

Funding 2018 (in kSEK)

SciLifeLab: 3000
KAW: 7000
SLU: 1000
UmU: 1000
Chalmers: 350

Total: 12350

Resource allocation 2018

Academia (national): 75%
Academia (international): 2%
Internal tech. dev.: 20%
Industry: 2%
Healthcare: 1%
Other gov. agencies: -

User Fees 2018

Total (kSEK): 4000

Reagents: 50%
Instrument: 30%
Salaries: 10%
Rent: 8%
Other: 2%

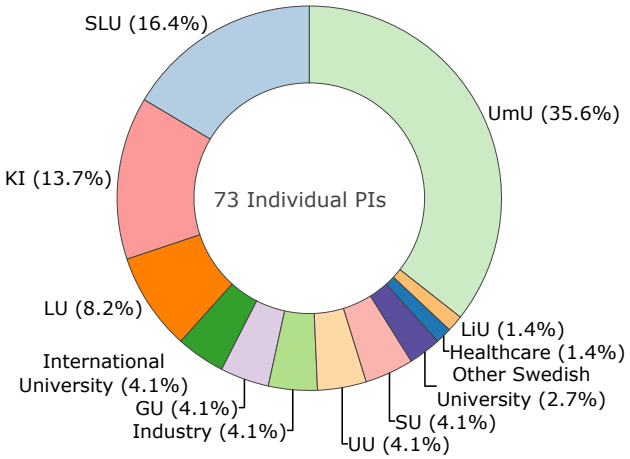
User fees by sector 2018

Academia (national): 90%
Academia (international): 4%
Industry: 5%
Healthcare: 1%
Other gov. agencies: -

Services

- Untargeted metabolite profiling (metabolomics)
- Targeted metabolite profiling
- Targeted lipid profiling
- Study design and method development
- Basic statistics
- Open lab access services

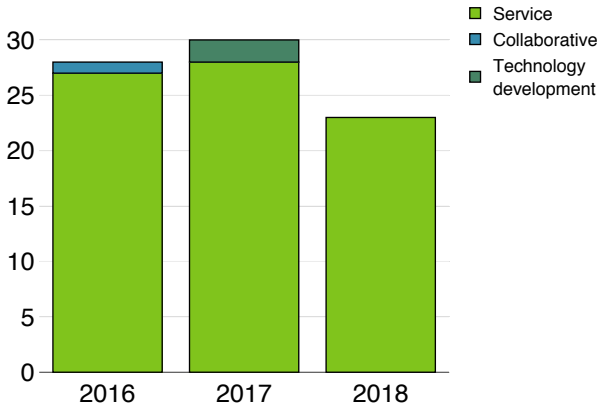
Users 2018



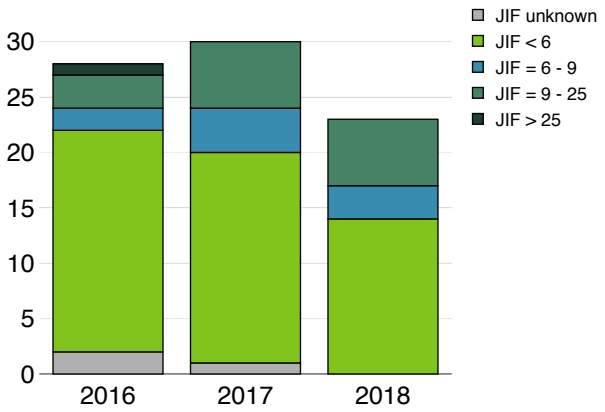
Publications

2016: 28
2017: 30
2018: 23

Publications by category



Publications by Journal Impact Factor



Terms and Conditions for Funding

This is a draft version of the Terms and Conditions for Funding document that will be included as an Appendix to the 2019 Facility Agreements to be signed by corresponding Facility Director, Head of Facility, the Head of Host University Department, the SciLifeLab Director and the SciLifeLab Head of Operations. Note that separate versions of this document will be prepared for Drug Discovery and Development, Bioinformatics Platform, and the National Genomics Infrastructure, since the governance of these units slightly differ from the current default SciLifeLab facility governance policies. However, the majority of the content is generic.

SciLifeLab

SciLifeLab Research Infrastructure Platforms and Facilities

Terms and Conditions for Funding

Introduction

SciLifeLab (Science for Life Laboratory) is a national center for life science research in the field of molecular biosciences. The mission includes offering researchers from all across Sweden access to advanced technical analyses of samples, support for data analysis and specialist expertise in molecular biosciences. SciLifeLab is regulated by a special governmental ordinance (förordningen (2013:118) om Nationellt centrum för livsvetenskaplig forskning) and university directives (regleringsbrev) to KTH and UU. In addition, there are a number of agreements and steering documents that describe the agreements among the host universities on how to manage SciLifeLab (see www.scilifelab.se).

SciLifeLab operates the national infrastructure with funding from the National SciLifeLab budget. Facilities are organized into technology platforms, which are further divided into facilities. Facilities and platforms have been approved by the SciLifeLab Board based on international evaluations and national discussions carried out every four years. The infrastructure is available to all Swedish researchers. The national research infrastructure is organized, financed, managed and developed with a long-term view to promote high quality interdisciplinary research in Sweden within and between academic institutions, industry and healthcare.

This governance and policy document aims to clarify the conditions and expectations linked to the appointment of facilities and platforms as part of the national SciLifeLab infrastructure, the criteria for services provided, funding issues, organizational structure, and other operational principles.

General

Each facility is hosted by and integrated with one or several departments within one or several universities. The facilities are part of the department operations and must follow applicable rules of procedure, delegation of authority and guidance of its host-university and department.

National SciLifeLab funding that the Board approves is provided to the specific host department(s) and host universities of the facility. The Head of the host department will agree in writing to the terms and conditions of the SciLifeLab funding, including the financial, HR, legal and reporting requirements.

SciLifeLab follows the directives of the host universities, for example that all employees and students must be treated with respect and be given the opportunity to work and study on equal terms regardless of sex, transgender identity or expression, ethnicity, religion or other belief, disability, sexual orientation, age or social background. Equal opportunities are a quality issue for the organization and a justice issue for the individual as regulated in the Higher Education Act (SFS 1992:1434), Discrimination Act (SFS 2008:567).

This *Terms and Conditions for Funding* document applies by default to all SciLifeLab facilities and platforms. Exceptions may be described as an appendix or as a completely separate version of this document.

Criteria for Funding of SciLifeLab Facilities

Nominations as national SciLifeLab facilities and funding decisions are made by the SciLifeLab Board, based on recommendations from the Director and the Management Group. The decisions will be based on international evaluations, internal discussions in the Management Group, as well as discussions with host university representatives and the National SciLifeLab Committee (NSC). Below are the most important criteria for the assessments. A SciLifeLab facility 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**.
- Serve **multiple research groups** in high-quality research projects **across the nation**.
- **Function in** a high-quality research environment supporting continuous development of the facility services
- 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.
- Provide complementary and **synergistic opportunities** within and across SciLifeLab platforms.
- Participate in **national coordination** of similar facilities at other universities in Sweden (when applicable)
- Promote **translational implementation** of research findings into healthcare, industry and society (when applicable)

Evaluation and Decisions on Facility Funding

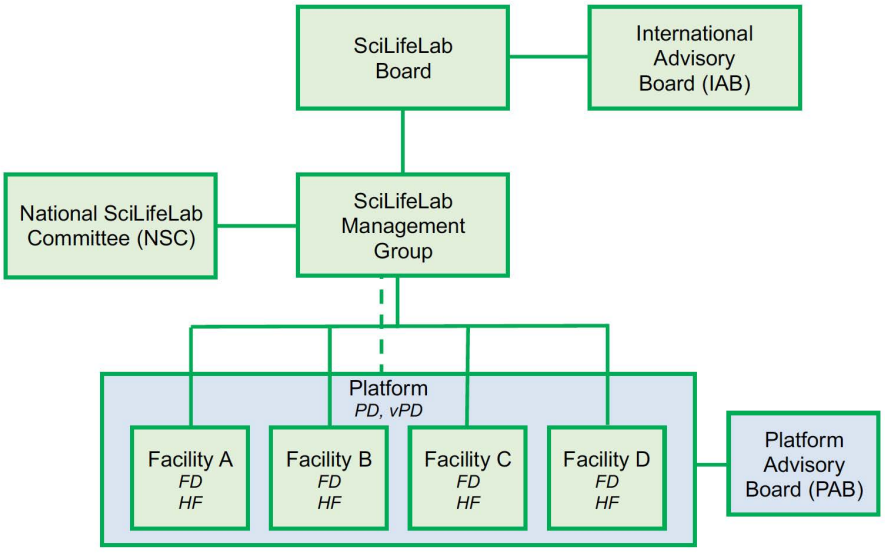
SciLifeLab platforms and facilities are evaluated by international panels every four years (2016, 2020, 2024 and so on) complemented by strategic discussions with representatives from the host universities and the National SciLifeLab Committee (NSC). Based on the outcome of the evaluations and discussions, the SciLifeLab Board decides on the organization of platforms and funding of the facilities for the next two + two years. A midterm check-up of facilities will be performed halfway through the four-year funding period to ensure that conditions, expectations and suggestions given to facilities have been acted upon. Based on this important check-up, the SciLifeLab Management Group and the Board will decide upon the continued funding for another 2-year period. This may involve adjusting the funding or undertaking other changes to facilities or platforms.

Phasing out of Facility Funding

If the SciLifeLab Board decides to phase out funding of a facility, funding is first decreased to 80% level compared to the previous funding year for 18 months after the decision. The facility should provide service during the entire phase out funding period and deliveries should be reported for the first year of the period. Once the SciLifeLab funding ends (after the 18-months period), the SciLifeLab brand/name cannot be used in association with the facility. Facilities may also be merged with other facilities or reorganized across platforms. In exceptional circumstances, such as gross negligence of good infrastructure practice or proven scientific misconduct, funding may be withdrawn immediately based upon a board decision (see below).

Governance

The default organisation of the SciLifeLab infrastructure is outlined in the figure below (special terms and conditions may apply for some platforms).



Facility Director and Head of Facility. Each facility is managed by a Facility Director (FD) and a Head of Facility (HF). Facilities may have operations at several departments and can have more than one FD and/or HF.

The FD is responsible for the scientific leadership and the strategic development of the facility, and is usually responsible for management of the facility personnel. The FD should always be accessible for communication with the Platform Director and the SciLifeLab Management Group (MG). The FD is appointed by the SciLifeLab Director on a two + two year basis in conjunction with the funding decision. For facilities with several sources of funding, the FD should be jointly appointed by the SciLifeLab Director and other significant external funding bodies. The FD reports to the SciLifeLab Infrastructure Director.

The HF is appointed by and reports to the FD, and is responsible for the everyday operations at the facility, including project management and allocation of facility resources. The HF is directly responsible for ensuring good communication with the users, and is also responsible for communication with the SciLifeLab administration and Operations Office. The FD and the HF can be the same person. Replacement of FD must always be approved by the SciLifeLab Director, and replacement of HF must always be reported to the Infrastructure Coordinator at the SciLifeLab Operations Office.

The FD and HF are responsible for the high-quality and reproducible data production and high level of scientific know-how within the service area. The FD and HD need to agree on who is responsible for:

- Coordination of project applications
- Communication with potential and existing users
- Project prioritization models
- Operational plans
- Training and competence development of staff
- Build-up of economy structure according to instructions from Operations Office (OO)
- Budget
- User fee models for academic users and for full cost models
- Annual report preparation
- Outreach
- User workshops and courses
- Communication
- Technology development
- Data management and user guidance together with Data Center on open access, FAIR and GDPR requirements
- Maintenance of the SciLifeLab facility webpage, including list of services

Platform Director and Vice Platform Director. Based on research area and services provided, SciLifeLab facilities are organised into platforms that are managed by a Platform Director (PD) and when applicable, a Vice Platform Director (vPD). The responsibilities of the PDs (and vPDs) include to lead the work in the Platform Management Group (see below), and to assemble feedback reports and material on platform level requested for evaluations by the International Advisory Board (IAB). The PD should be able to represent the entire platform at SciLifeLab meetings, in communication with the MG and the Board, as well as in external communication and outreach. The Facility Directors within a platform (see below), nominate PD and vPD candidates among themselves to the MG, which in turn selects candidates to be approved by the SciLifeLab Board. The PD position(s) for a platform may also be publicly announced by Board decision. The PD is responsible for communication with the Platform Advisory Board (see below) on strategic and operational issues on a regular basis. The PD is appointed by the SciLifeLab board on a two + two year basis. Replacement of PD must be approved by the SciLifeLab Board. SciLifeLab Director may nominate a temporary PD or vPD until the next board meeting.

Platform Management Group. The PD (and vPD), FDs and/or HFs, and additional staff according to the choice of PD, constitute the management of the platform. The Platform Management Group should meet on a regular basis and has the overall responsibility for the strategic and scientific development of the platform.

Platform/Facility Advisory Board. Each platform should appoint a Platform Advisory Board to advise on long-term scientific development and strategic issues on the platform level. The Platform Advisory Board should include 3–5 national and/or international experts with competences relevant for the platform research fields, and should be selected to cover the range of technologies provided by the platform. When appropriate, advisory

boards can be appointed on the facility level instead (Facility Advisory Board). Additional authority can be given to the Advisory Board after approval by the SciLifeLab Director.

Project Prioritization. In order to ensure unbiased user access to facility services on equal terms regardless of the user´s affiliation, facilities should develop, document and apply appropriate and transparent models for project prioritization. Facilities can appoint a Project Prioritization Committee (PPC) responsible for the prioritizing of project proposals. The PPC can also be the advisory group. Project prioritization should primarily be based on scientific impact and technical feasibility. The PPC should ensure that services are provided on equal terms to academic users. In addition, all facilities should be prepared to allocate up to 15% of the services to healthcare, industry, governmental agencies and international users. In facilities dedicated to diagnostic development and health care services, these percentages can be higher. Facilities are also encouraged to make sure that project prioritization considers favourably young principal investigators, SciLifeLab fellows, NMMP fellows, recipients of ERC grants and other major national or international young investigator grants. Data handling and data management plan should also be considered, ideally in collaboration with the SciLifeLab Data Centre and the Bioinformatics platform (see below).

Platform/Facility Steering Groups/Boards (when applicable). For platforms/facilities receiving funding from other bodies (e.g. the Swedish Research Council (VR)), the funder typically expects the appointment of a Steering Group/Board. Such Steering Groups/Boards cannot (unless otherwise agreed with the SciLIfeLab Board) assume responsibility for the steering of SciLifeLab-funding.

Platform/Facility Steering Groups/Boards (when applicable). For platforms/facilities receiving significant funding from other bodies (e.g. the Swedish Research Council (VR)), and have appointed Steering Groups/Boards related to external funding, the Steering Groups/Boards cannot (unless otherwise agreed) assume responsibility for the SciLifeLab-funded activities.

Additional Facility Funding

An expectation for a successful and sustainable SciLifeLab facility is that it continues to receive funding from its host university(ies), other participating universities or other funding agencies. The facilities and platforms should always contact the SciLifeLab Management Group well in advance before applying for external infrastructure funding, particularly from VR. This is mandatory if the SciLifeLab funding will be used as counter funding in the application, since the funding period for the VR grant may exceed the current funding commitment of SciLifeLab.

User Fees

SciLifeLab facilities should charge user fees according to pre-defined and documented cost models. Facilities are responsible for the preparation and implementation of cost models, including a full cost model in accordance to Ekonomistyrningsverket's guidelines "Sätt rätt pris" (www.esv.se/publicerat/publikationer/2014/satt-ratt-pris). Cost models should specify what is covered by the user fees and should be aligned with common practice at the facility host university.

Service and Users

The facilities should provide high quality services to users who are engaged in research projects of high scientific impact. The service should be such that the users can pursue projects without being an expert in the facility technology. Facilities should define criteria for prioritizing projects primarily based on scientific impact, technical feasibility and other facility-specific criteria. The service should be accessible on equal terms to all Swedish academic users including the MG, Board, NSC, and SciLifeLab committee members, Facility/ Platform Directors and SciLifeLab Faculty and Fellows. Service should also be accessible to researchers within the private sector, healthcare and governmental agencies. Part of the facility capacity may also be used for service to international users. The users carry the responsibility for any necessary legal or ethical considerations regarding analyses and material (e.g. ethical permits, Nagoya protocol, GDPR etc), and the facility should make sure the user has understood this responsibility.

Facilities are encouraged to actively identify opportunities to participate in large-scale research projects that address grand societal challenges within life science related areas. This includes active participation in the SciLifeLab Research Community Projects as well as interactions with SciLifeLab and NMMP fellows, ERC grant recipients and other promising young PIs.

Technology Development

Up to 20% of SciLifeLab funding provided to a facility can be used to develop, implement and adapt new or improved services, methods and technologies. These efforts should not entail resource building or *bona fide* research projects. Method and technology development may involve collaboration with national and international academia, industry, health care and governmental agencies, with young PIs to be considered favourably in research collaborations. SciLifeLab and host universities will in addition support technology development through Technology Development Project (TDP) grants.

Quality control

SciLifeLab facilities should implement quality control processes to ensure that services are delivered in accordance with the high quality standards SciLifeLab users have the right to expect. Adherence to good laboratory practices is expected, including documentation of standard operating procedures, use of electronic lab notebooks (ELN or equivalent systems), electronic sample and data workflow systems (LIMS or equivalent) , project planning systems (ProjectPlace or similar), and electronic systems for communication with users (Data Centre's Order Portal, for example). Facilities should consult the SciLifeLab Data Centre for guidance on systems to use, and to communicate any needs regarding IT systems and data management tools.

Data Management and Sharing

SciLifeLab facilities should guide users with the analysis, storage, availability and accessibility of the data produced by the facility. Supported projects must be assigned a unique identifier and facilities should collect the appropriate project information to enable tracking and reporting. Facilities will be required to submit such data to a central database to facilitate cross platform services, at the time when SciLifeLab will provide the infrastructure platform for this.

In accordance with increasing demands from funders and scientific journals, we recommend that projects that include data management of any type set up a Data Management Plan (DMP). For example, Vetenskapsrådet has announced that from 2019, all supported projects will be required to have DMPs. We recommend that facilities ensure users set up a plan that estimates at least existing and requested resources to deal with data analysis and management, including computing, storage, archiving, security, and accessibility. Templates and guidelines for DMPs can be provided by the SciLifeLab Data Centre. In the near future, DMPs will be required for all SciLifeLab supported projects.

Facilities are required to inform supported projects about the obligations:

a) to acknowledge SciLifeLab support in publications, using the unique identifier assigned at the start of the project, and
b) to report back to SciLifeLab when data has been used in a publication and where the data has been deposited.

SciLifeLab supported projects should adhere to the principles of open science, including open access to both publications and data to the greatest extent possible, given ethical, legal and intellectual property considerations. The facilities must ensure that sensitive and confidential information (e.g. from health care-related projects) is handled in accordance with current laws, regulations and host university practices, including GDPR directives.

The SciLifeLab Data Centre will provide support to the facilities to address requirements and recommendations in this section.

Courses and Training

The facilities should provide courses and training related to technologies, analyses and application of the technologies and data generated by the facility. Courses and training should be offered to national academic user communities. Preferably, courses and training should also be offered to users within healthcare, governmental agencies, industry as well as international user according to rules and regulations for “uppdragsutbildning”. Costs for courses and training are usually covered by facility budgets or through participant fees (if applicable).

Communication and Branding

The facility should actively communicate to potential users regarding opportunities for existing and new services at the facility, both through own initiatives and by participating in events organized centrally at the SciLIfeLab level. New possibilities and important research results produced using service provided by the facility should actively be communicated to the research community and to the society.

SciLifeLab facilities should keep their web-site up to date and be active towards SciLifeLab communiocations office in terms of how communication and web traffic can be improved. With SciLIfeLab web site being continuously developed, the facilities should participate in making the web site as attractive as possible and well branded.

All SciLifeLab facilities and platforms should be primarily branded under the SciLifeLab name. The VR- and KAW-funded network names can be used as secondary, but not alone. VR networks that only partially overlap with SciLIfeLab facilities and platforms are suggested to negotiate branding with the SciLifeLab management (contact infrastructure coordinator).

All members of the SciLifeLab community should follow the SciLifeLab’s communication handbook guidelines (www.scilifelab.se/staff/documents-and-templates). In order for SciLifeLab’s brand to be clear, strong and recognizable, it is important that it is handled consistently and purposefully. The handbook is available as a tool for this and differentiates SciLifeLab from other organizations.

National and International Networking/Strategic Collaborations

SciLifeLab platforms and facilities should, whenever applicable, have a national role in developing and maintaining infrastructure networks in their specific service area. The platforms and facilities will be in contact with local core facilities across the country.

SciLifeLab platforms and facilities should participate in international networks, including relevant EU networks and infrastructures (e.g. European Strategy Forum on Research Infrastructures (ESFRI), European Molecular Biology Laboratory (EMBL), and European Bioinformatics Institute (EMBL-EBI) and other global partners to sustain a cutting-edge, internationally competitive development.

Reporting

SciLifeLab facilities must report to the MG annually and upon request. The yearly report normally includes project deliveries, number of users and their national distribution, quality and efficacy metrics for data production, publications, financial report and budget for the coming year. The financial report should contain complete financial information for the facility including national funds, funds for drug discovery and development, Strategic Research Area (SFO)-funding, VR, KAW and additional funding and user fees. This information should be extracted from the host university’s financial systems every third month by the responsible economist at the department and/or university and delivered to KTH in a predefined format. Reported deliverables will be used in the annual reports to the Ministry of Education and Research, as well as in other web-based or printed material that describes SciLifeLab activities.

For the major evaluation of the infrastructure every fourth year, more detailed evaluation material and future plans will be requested. This will include general descriptions of facility/platform (e.g. instruments, staff, service etc.), SWOT analysis, benchmarking and operational plans (incl. four-year budget).

Facilities with phased-out funding from SciLifeLab or under reorganization should report during their first year of phasing out.

Agreements

Facility Agreements. All SciLifeLab facilities are organized under a department (or sometimes several departments) at a Swedish university. To clarify funding conditions and the responsibilities of the department and SciLifeLab respectively, SciLifeLab will provide an agreement to be signed by the Head of Department, the FD, HF, the SciLifeLab Director, and the SciLifeLab Head of Operations. The agreements only needs to be signed with departments receiving direct national funding from SciLifeLab. The departments should ensure that the personal research funding of the scientists operating the facilities is kept separate from the national infrastructure funding. Thus, facility funding cannot be used to support the research funding of the PD, FD and HD or other staff members. Conversely, research funding of the of the PD, FD and HD should not be applied to back up salaries if the facility is subject to phase-down or loses other infrastructure funding.

User Agreements. SciLifeLab facilities should prepare and employ User Agreements. The agreements should specify the conditions, responsibilities for each party, estimated fees, and timelines. In User Agreements, facilities must include writing to collect consent to process personal data in accordance with GDPR, and optionally consent to share limited project information with other SciLifeLab facilities for the purpose of planning project specific services. User agreements should be prepared in consultancy of the legal department of the facility´s host university.

Other agreements. Agreements that concern national VR-funded infrastructure platforms that substantially overlap with SciLifeLab funded facilities/platforms, need to be discussed with the Infrastructure Director and the Management Group to clarify mandate and responsibility of potential steering groups. Unless otherwise agreed, the SciLifeLab Management and Board are fully responsible for strategic decisions of the facility.

Principles for Publications

When SciLifeLab facility staff members make significant intellectual contributions to research, the persons involved should be included as co-authors in accordance with the Vancouver principles. For all other publications that are the result of the use of routine facility services, the SciLifeLab facility should be included in the acknowledgment section of the paper. The facilities should actively encourage users to undertake such acknowledgements.

Freedom to operate and non-competition

SciLifeLab expects that the facility can provide the services to its users without interfering with commercial interests and with companies providing similar services. Freedom to operate and non-competition are particularly critical when providing full-cost services to industry and health care.

Conflicts of Interest

Facility personnel, FD and HD should avoid personal conflicts of interest e.g. involving companies providing equipment, reagents or services in the facility operations. Facility scientists can be engaged in external activities according to permissions from the host university. These may include spin-off companies arising out from SciLifeLab facilities, which should be carefully structured not to act in a competitive manner. Facility staff must disclose to the SciLifeLab Head of Operations any such potential conflicts of interest.

Scientific and Infrastructure Misconduct

If there is a suspicion of scientific misconduct either by SciLifeLab users or by the platform/facility executives/personnel, the suspicion should be disclosed according to the practices of the host universities involved. The PD and the SciLifeLab Infrastructure Director should also be notified and MG should be made aware of each such case. The host universities are in charge of investigating whether there is evidence of scientific misconduct as well as potential consequences, and should keep the SciLifeLab well informed of the progress of the investigation. In exceptional documented cases of misconduct, facility funding may be discontinued based on a board decision without an 18 month grace period.

Updates and Changes

SciLifeLab reserves the right to change and make additions to this document at any time, and such changes or modifications shall be effective after being communicated to the platforms, facilities and host departments.

Appendix I.

SciLifeLab bibliometric analysis

Contents

Bibliometric analysis of SciLifeLab scientific output

For the second year running, SciLifeLab has contracted the Centre for Science and Technology Studies, CWTS, at Leiden University for a bibliometric analysis of our scientific publishing since 2010. Their analysis uses advanced field-normalized bibliometric indicators and follows the principles stated in the Leiden Manifesto (Hicks et al., 2015), an influential statement presenting best practice guidelines for the proper use of numerical indicators in research evaluations. It is important to note that, the field-normalized impact indicators were not calculated for 2017 and 2018 publications due short and incomplete citations window. Nevertheless, SciLifeLab values the rigorous analytic approach and that fact that, the scientific production was analyzed by an external party. This appendix is a summary of the bibliometric statistics and findings from the CWTS report.

SciLifeLab publications

Two types of publications are considered as scientific output facilitated by SciLifeLab: publications co-authored by SciLifeLab affiliated researchers (referred to as "affiliated publications" in the following text), and publications that are the result of the utilization of infrastructure ("facility publications").

The category SciLifelab affiliated publications was mined by CWTS from Web of Science through searching the "affiliation" field for "Sci Life Lab*"; "SciLifeLab*"; "Science for Life Laboratory"; "Scilife lab*" and "SciLife Ctr". The 3860 publications from 2010-2018 collected this way can be searched and browsed through a specific instance of the publications database run by the Data Centre.[1]

The second category, facility publications, were self-reported by facilities into the publications database [2] and categorized as "service" – published results from a project that has received facility support; "technology development" – technology development work published by facility staff; and "collaborative" – publications resulting from collaborative projects involving both facility staff and external researchers.

The key conclusion of the CWTS report was "We find that the research impact of SciLifeLab and its Facilities is well above world average. Its citation performance remained high and relatively stable over the years. The output of the SciLifeLab and its Facilities are also increasing over time. These findings clearly support their statement of being a national hub in their field as well as an internationally leading research institution".

As SciLifeLab vision is to be a national hub for molecular life sciences, we believe the bibliometric analysis conducted by CWTS shows that we are on the right way. We believe continual assessment of scientific output and decision making based on deep data analytics will be very important for SciLifeLab in years to come, and will increasingly use bibliometric data sources and tools to assess scientific impact as a result of our operations. This will include scientific publications but also data publishing or other types of impact such as patents, grants, policy documents or news reporting. In particular we will put emphasis on openness of published findings and data.

[1] https://publications-affiliated.scilifelab.se
[2] https://publications.scilifelab.se

Methods

Bibliometric indicators calculated by CWTS (Table I1) were based on an in-house version of the Web of Science online database, the CI system. The CWTS regularly updates its CI system with citation data provided by Clarivate Analytics. The CI system database version used for calculating the indicators presented in the report contains up-to-date data provided by Clarivate Analytics until and including week 39 of 2018.

The scientific impact of these publications was analyzed using advanced bibliometrics methods and following the principles stated in the Leiden Manifesto (Hicks et al., 2015). In brief, indicators centered on publication output, were considered using a full counting approach, while citation impact indicators were fractionalized. Moreover, field-normalized impact indicators were calculated based on citations received excluding self-citations, while citation scores were normalized with respect to the 4,113 micro-fields classification, which is the most detailed publication-based classification created by CWTS. It is important to note that due to the short citations window, publications from 2017 and 2018 are only included in the statistics on total number of publications per year and sub-category, and not in the calculations of field-normalized impact indicators such as MNCS and PP top 10%.

Table I1. The CWTS analysis considered 11 main bibliometric indicators.

Indicator	Dimension	Method	Definition
P	Output	Full	Total number of publications.
P'	Output	Fractional	Publication weight.
MCS	Impact	Full	The average number of citations.
TCS	Overall	Full	Total number of citations.
MNCS	Impact	Fractional	The average normalized citation score.
MNJS	Journal Impact	Fractional	The average normalized citation score of journals.
PP (top 10%)	Impact	Fractional	The proportion of publications in the top 10%.
P (top 10%)	Impact	Fractional	The number of publications in the top 10%.
Internal coverage	Output	Full	Proxy of work being covered by the WoS.
PP (uncited)	Overall	Fractional	The proportion of publications not cited by WoS papers.
PP (self-citations)	Overall	Fractional	The proportion of self-citations.

Results

Affiliated researcher publications

In this section, we first present the bibliometric analysis of SciLifeLab affiliated researcher publications from 2010-2018.

Publication output

In 2010-2018, SciLifeLab's most frequent types of scholarly output were research articles, meeting abstracts, and reviews, with 84.6%, 5.96%, and 5.73% share of the total output, respectively (Figure I1). Other important scholarly documents produced by SciLifeLab were editorials (2.02%), and letters (1.17%), and various types of output, each accounting for less that 1% of the output volume. The number of both articles and reviews grew steadily from 2010-2017 and, we expect a significant increase also for 2018 when these numbers are available (the data for 2018 include publications only until week 39, 2018) (Figure I2).

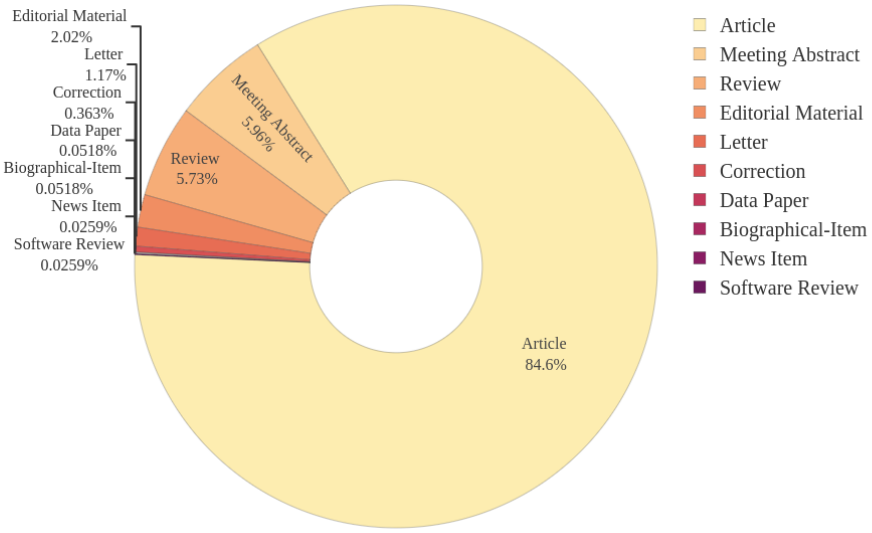


Figure I1. SciLifeLab output by document type (2010-2018)

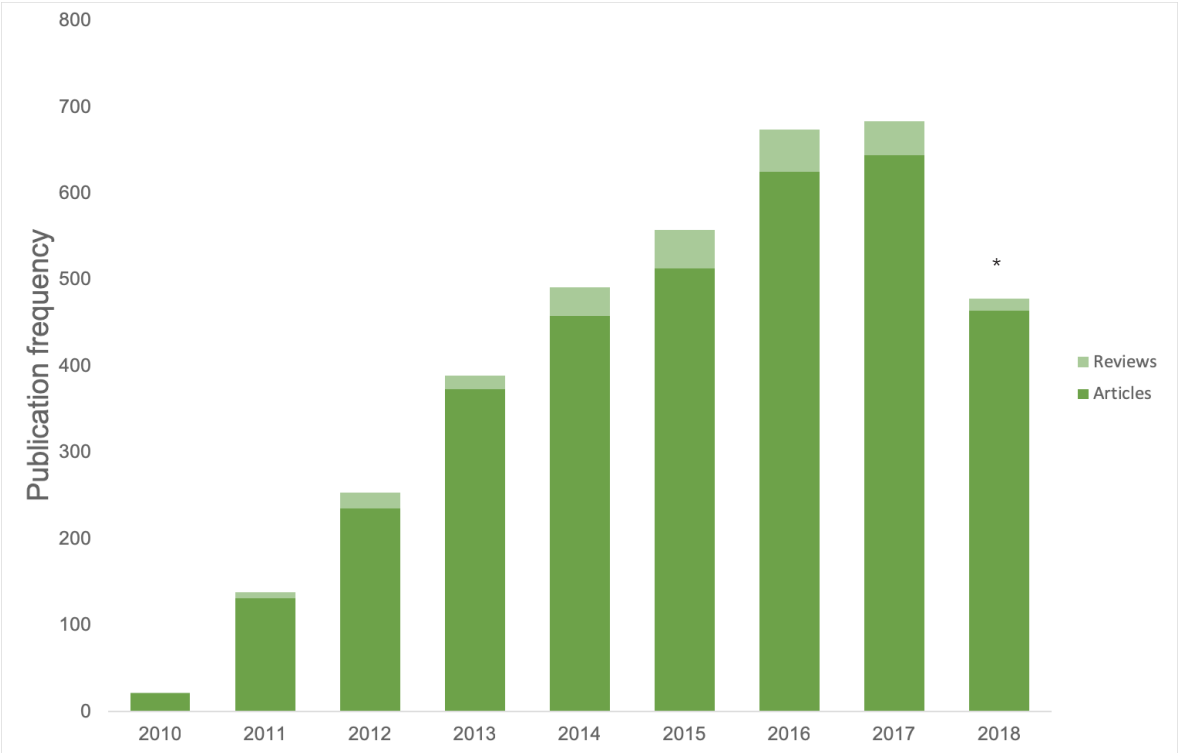


Figure I2. SciLifeLab affiliated publications - Annual number of publications categorized as articles and reviews (2010-2018). * number of publications untill week 39, 2018.

Scientific impact and time trends

SciLifeLab performance indicators and time trends are shown in Table 2. In brief, the overall indicator of output (P) shows that a total of 2,524 distinct Web of Science indexed publications have been produced by SciLifeLab affiliated researchers. This output has been cited 45,783 times, excluding self-citations, which on average is 18.14 citations per publication. The overall MNCS value for SciLifeLab (2010-2011) is 1.56, which means that SciLifeLab's publications receive 56% more citations than the average publication in the same field and year. MNCS>1.20 is considered high. These publications appear in journals with an average field-normalized citation impact of 1.48, which is also high. In terms of the PP (top 10%) indicator, 17% of the output by the SciLifeLab are among the upper 10% of frequently cited publications worldwide. In other words, the SciLifeLab has 1.7 times more top publications than expected by the top 10% threshold. The proportion of uncited publications is low, with only 7% of the total number of publications remaining uncited. Furthermore, 20% of all citations of SciLifeLab publications are self-citations, which is not considered high. In conclusion, the fact that SciLifeLab's PP (top 10%), MNCS, and MNJS indicator scores present consistently high scores that are well above the world average over the years confirms SciLifeLab's high scientific impact.

Table I2. SciLifeLab performance indicators (2010-2016). Recent years 2017-2018 are not included due to short and incomplete citation window. Source: CI system database, CWTS at Leiden University.

Year	P	P '	MCS	TCS	MNCS	MNJS	P(top 10%)	PP(top 10%)	PP(uncited)	PP(self cits)
2010-2016	2524	967.61	18.14	45783	1.56	1.48	166.41	17%	7%	20%
Time trends										
2010	22	8.69	37.77	831	1.89	1.65	3.42	39%	3%	16%
2011	138	53.56	26.57	3667	1.37	1.45	9.20	17%	4%	17%
2012	253	114.70	22.99	5817	1.74	1.62	17.43	15%	5%	16%
2013	389	156.30	23.58	9173	1.58	1.47	30.03	19%	4%	16%
2014	491	186.68	22.24	10922	1.50	1.36	30.02	16%	4%	17%
2015	557	209.51	17.86	9948	1.64	1.53	37.12	18%	5%	17%
2016	674	238.17	8.05	5425	1.47	1.46	39.19	16%	14%	18%

Facility reported publications

In this section, we look at the output and impact, based on the same indicators presented in the previous section, for the publications reported by SciLifeLab facilities as resulting from their operations.

Publication output

In the period 2010-2018, the most important scholarly outputs of Facilities were research articles, reviews, and letters, with 95%, 2.33%, and 1.37% share of the total output, respectively (Figure I3).

While the number of articles grew steadily between 2010 and 2016, the number of reviews has remained relatively low through the years (Figure I4). In 2017 there was a slight decline in articles, and in 2018 there has been a sudden decline in both articles and reviews.

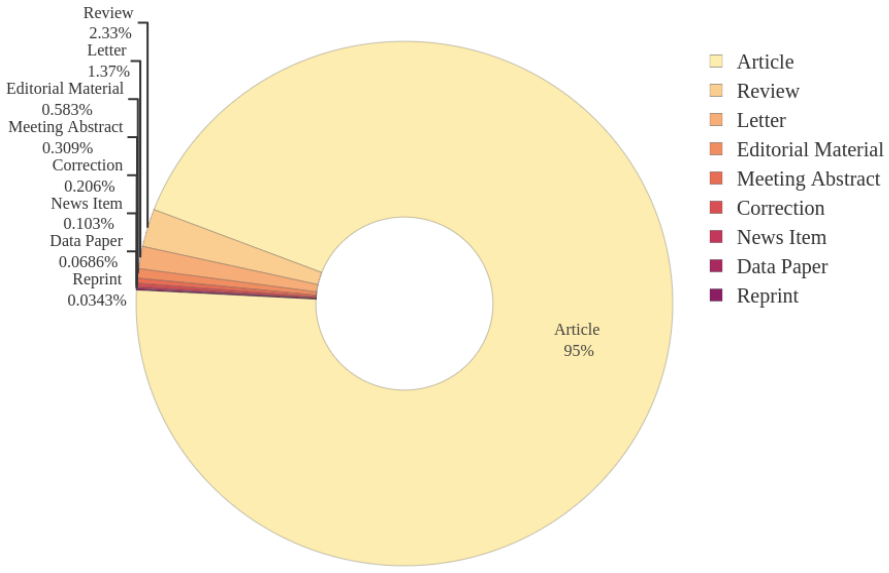


Figure I3. Facility reported output by publication type (2010-2018)

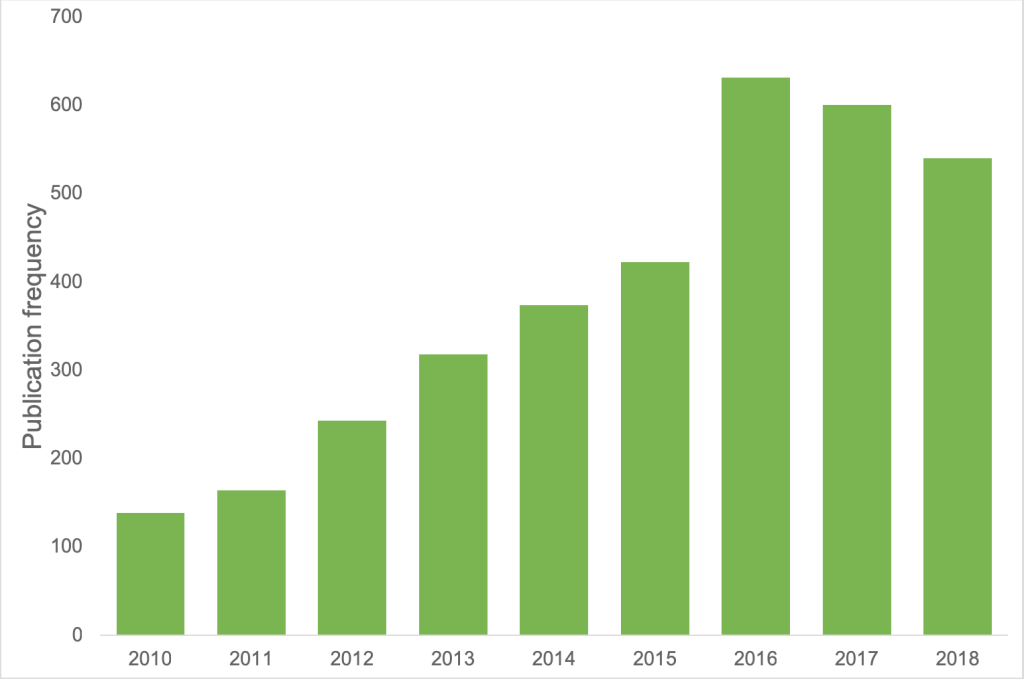


Figure I4. Annual publication output resulting from utilization of SciLifeLab infrastructure. Publication frequency reported by facilities in the SciLifeLab website (https://publications.scilifelab.se). Those publications derive from the usage of SciLifeLab research infrastructure, including service, collaborative projects and technology development projects.

Scientific impact and time trends

Performance indicators and time trends for facility reported publications are shown in Table I3. Altogether, the three field-normalized citation impact indicators combined indicate that publications derived from the operation of SciLifeLab's infrastructure generally have a high impact.

Table I3. Facilities performance indicators (2010-2016). Source: CI system database, CWTS at Leiden University.

Year	P	P '	MCS	TCS	MNCS	MNJS	P(top 10%)	PP(top 10%)	PP(uncited)	PP(self cits)
2010-2016	2158	848.93	17.19	37102	1.39	1.44	137.19	16%	7%	25%
Time trends										
2010	130	57.20	23.39	3041	1.35	1.57	9.66	17%	5%	22%
2011	161	60.36	21.08	3394	1.38	1.50	12.73	21%	5%	23%
2012	234	98.82	18.48	4325	1.44	1.45	15.96	16%	6%	21%
2013	296	124.95	22.28	6594	1.38	1.54	21.38	17%	5%	19%
2014	358	149.99	20.25	7250	1.27	1.27	21.87	15%	5%	22%
2015	400	148.05	20.48	8190	1.57	1.60	22.55	15%	5%	18%
2016	579	209.55	7.44	4308	1.34	1.35	33.04	16%	13%	23%

SciLifeLab Research Profile analysis

To visualize the whole spectrum of research fields covered by the publications of SciLifeLab as well as the corresponding impact in those fields, the research profile analysis was performed by CWTS. CWTS calculated a breakdown of output and impact into fields of science as defined by the Web of Science Journal Subject Categories ("JSCs"). The JSCs have the advantage to refer to broad disciplinary areas with descriptive relevance. For each JSC, impact will be mainly given by the Mean Normalized Citation Impact indicator (MNCS) which is calculated and displayed using a much more sophisticated structure. The top 20 research fields for the SciLifeLab are listed in Table I4.

Table I4. List of the top 20 scientific areas to which SciLifeLab has contributed publications.

Rank	SciLifeLab Research areas	MNCS	P (publication frequency)
1	Mathematical & computational biology	4,98	44
2	Multidisciplinary sciences	3,10	292
3	Computer science, interdisciplinary applications	2,91	12
4	Ecology	2,83	27
5	Biochemical research methods	2,51	167
6	Biotechnology & applied microbiology	2,45	132
7	Reproductive biology	2,21	9
8	Evolutionary biology	2,08	42
9	Biochemistry & molecular biology	1,76	302
10	Biology	1,67	21
11	Microbiology	1,66	47
12	Chemistry, analytical	1,61	36
13	Environmental sciences	1,52	14
14	Chemistry, multidisciplinary	1,46	55
15	Genetics & heredity	1,44	247
16	Biophysics	1,42	43
17	Pharmacology & pharmacy	1,32	44
18	Cell biology	1,30	129
19	Oncology	1,21	118
20	Immunology	1,15	45

Collaboration Network Analysis

The collaboration network of SciLifeLab was performed focusing on organizations that have co-authored at least twenty publications with SciLifeLab between 2012 and 2016, which is in total 78 collaborators. This collaboration network gives a general overview of the structure of scientific collaboration as well as the impact of the publications produced among SciLifeLab and partners. Organizations that are components of another organization have been merged with parent organizations. In most cases, these are hospitals, institutes, or research programs within a university and, therefore, do not appear in the network analysis. The top international collaborators are listed in Table I5 while the national collaborators are in Table I6.

Table I5. The Top 20 SciLifeLab International Collaborators

Rank	Institute, country	MNCS	P (publication frequency)
1	Wellcome Trust Sanger Institute, UK	11,76	64
2	University of Oxford, UK	6,53	101
3	Stanford University, USA	6,35	52
4	University of North Carolina, Chapel Hill, USA	6,14	39
5	Helmholtz Center Munich, D	6,03	36
6	Imperial College London, UK	4,91	43
7	Massachusetts General Hospital, USA	4,67	43
8	University of Helsinki, FIN	4,64	110
9	University of Edinburgh, UK	4,03	41
10	King's College London, UK	4	38
11	Massachusetts Institute of Technology, USA	3,26	107
12	University of Tartu, FIN	3,23	48
13	University of Copenhagen, DK	3,18	61
14	Harvard University, USA	2,87	134
15	National Institutes of Health, USA	2,85	52
16	University of Cambridge, UK	2,79	52
17	National Institute of Health and Welfare, FIN	2,77	43
18	Folkhälsan Research Centre, FIN	2,43	58
19	University College London, UK	2,26	45
20	Erasmus University Rotterdam, NL	2,11	47

Table I6. List of National collaborators of SciLifeLab affiliated researchers

Rank	Institute, country	MNCS	P (publication frequency)
1	Chalmers University of Technology	2,27	38
2	Stockholm University	1,8	132
3	Uppsala University	1,61	469
4	Linköping University	1,58	53
5	University of Gothenburg	1,53	67
6	Swedish University of Agricultural Sciences	1,5	75
7	Umeå University	1,49	58
8	Karolinska Institute	1,4	470
9	KTH Royal Institute of Technology	1,38	113
10	Lund University	1,27	133
11	Dalarna University College	0,92	25

Reference:

Hicks, D., Wouters, P., Waltman, L., de Rijcke, S., & Rafols, I. (2015) Bibliometrics: The Leiden Manifesto for research metrics. Nature. 23;520(7548):429-31. doi: 10.1038/520429a.

Appendix J.

SciLifeLab Research Community Programs (RCPs)

Contents

Biology of Molecular Interactions

Abstract

Coordinating PI: Alexey Amunts

Co-coordinating PI: Ilaria Testa

Number of participating PI's at start: 8

Affiliation of key participants: Stockholm University; KTH Royal Institute of Technology; Gothenburg University; Karolinska Institute; Lund University; Umeå University; Uppsala University

Contact: molecular.interactions@scilifelab.se; Twitter account: @SciLifeLab_BMI

The program for Molecular Interactions is established to account for the complex dynamics of the cellular phenomena and to explore a therapeutic potential of studied macromolecules. The program brings together 23 research groups complemented by molecular biology orientated facilities including cryo-EM, super-resolution imaging, protein production, proteomics and drug discovery that set up to provide the needed research infrastructure. To further develop technological innovations and support translational opportunities, the program bridges partnerships with the MAX IV laboratory and leading pharma companies AstraZeneca and Sobi. Taken together this provides a promising environment for conducting fundamentally important research and training.

Background

Aims

The proposed research community will establish a collaborative research aiming to investigate structure and dynamics of molecular interactions. The program combines disciplines spanning from chemical biology to clinical proteomics and is formed around 4 SciLifeLab facilities, 23 research groups across Sweden, MAX IV laboratory and pharma companies AstraZeneca and Sobi. The collaborative approach will remove barriers between groups and ensure that the infrastructure is accessible, so that everyone including students may get trained on the sophisticated and unique equipment. This will allow tackling questions that out of reach for any single research group.

The program will function first as a platform for formulating focus areas. This will be assisted by weekly seminars, conferences and an annual meeting. This way we aim to identify new opportunities for particularly challenging projects that would benefit from a multi-disciplinary approach. Then, the proposed projects will be formulated into dedicated funding applications highlighting the leverage from the synergy between the research groups and infrastructures.

In addition, the research community aims to start co-development of new cross-infrastructure techniques and instrumentation with a potential of providing a national resource in the future, beyond current state of the art. This will be promoted through shared workshops.

Finally, the established network aims to create a pool of highly skilled researchers by providing top students and postdocs with attractive opportunities to develop in academy and industry, which will further contribute to the international competitiveness.

Short summary

The research program will account for the complex dynamics of the biological phenomena and explore the therapeutic potential of the studied macromolecules. It is formed around four existing facilities (Cryo-EM, Mass spectrometry, Mass cytometry, Drug discovery), complemented by know-how academic and industrial partners across Sweden.

Description of program

Living cells function due to dynamic interactions between and within macromolecular complexes, which are yet to be fully understood in the terms of composition, atomic structure and kinetics. The program will focus on the complex structures and dynamics underlying the function of macromolecular complexes. Structural studies will be a key component of this effort, and computational biology combined with mass spectrometry techniques will be important to interpret the vast amounts of data produced and to propose further targets. Since understanding fundamental biological processes on the molecular level has implication for human disease, an effort exploring new therapeutics is integrated into the program.

The program will kick off through a series of research presentations and scientific discussions, where focus areas will be identified and new collaborative projects will be formulated. These projects will also include development of new methods, and will be advanced through intra-program workshops. Shared recruitment calls will assist in forming a pool of highly skilled researchers for the program, and the practical implementation will be assisted by scientists exchange.

The program is based on the existing infrastructures, expert groups in structural studies across Sweden; young PIs and

SciLifeLab fellows represent ~1/3 of the research groups in the proposed community. In addition, MAX IV laboratory, AstraZeneca and Sobi are involved as external collaborators to share expertise. We expect the community to operate as an entity, with scientific bonding across university borders and facilities with the aim of providing a breeding ground for new concepts. While the central hub of the activity will be at SciLifeLab, the connectivity between participating groups from different parts of Sweden will be developed through a dedicated funding for internships of students and postdocs.

The profile of the program will be communicated through the SciLifeLab webpages. In addition, the research agenda will be further promoted by participating Universities, the MAX IV laboratory and social media channels implementing visual aids for visualization.

How SciLifeLab infrastructure is critical to the RCP, and how the RCP is critical to the infrastructure

The research program relies on four existing SciLifeLab infrastructures, with mammalian protein production to be established:

1. Cryo-EM
2. Mass spectrometry
3. Mammalian protein production (to be established)
4. Mass cytometry
5. Drug discovery

The macromolecules will be characterized by structural biology (Cryo-EM, NMR, X-ray crystallography) and mass spectrometry. The latter can inform structural techniques by providing definition of subunit stoichiometry and help identify densities in maps. This will also be used to define and study different conformational states of protein-protein and proteinnucleic acid complexes as well as post-translational modifications. To improve the mass spectrometry-aided structural characterization, we will implement chemical crosslinking protocols to reveal neighboring subunits. Furthermore, native mass spectrometry (Landreh) will be applied to tackle intact complex assemblies and ligand interactions to identify new therapeutic targets that could be then subjected for a detailed molecular analysis.

X-tay crystallography (Achour, Drew, Hällberg, Jovine, Selmer) will provide atomicresolution information on individual subunits and their interaction to inform cryo-EM map fitting, whereas NMR (Petzold) will provide complementary information, such as weak interaction information with atomic resolution, details on molecular dynamics and information from within living cells. To follow the kinetics of these assemblies, nextgeneration time resolved techniques will be developed (collaboration with MAX IV, Neutze) and combined with molecular dynamics simulation (Carlsson, Delemotte). Single-molecule studies (Deindl) will complement the functional analysis, while in situ structural biology will be carried out by cryo-electron tomography (Carlson, Höög, Sandblad) to bridge highresolution studies on isolated components with cellular biology.

The establishment of a mammalian protein production facility will allow large scale biosafety level 2 preparations and development of tailored methods for dealing with multicomponent complexes and membrane proteins (collaboration with AstraZeneca, Sobi, structural biologists). The newly developed technology of introducing unnatural amino acids in recombinant proteins (Elsässer) will be implemented for protein engineering such as crosslinking of molecular assemblies, fluorescent labeling, and protein-small molecule conjugation. To ensure high quality production, the mass cytometry facility will be instrumental for evaluation of cells for expression. Finally, the drug discovery facility will apply their expertise to investigate any therapeutic potential of the studied macromolecules.

No. of universities participating: 7 (GU, KI, KTH, LU, SU, UMU, UU)

No. of other organizations participating: 3 (MAX IV, AZ, Sobi)

RCP Budget

Types of costs (in kSEK)	Year 1	Year 2	Year 3
Part-time coordinator	250	250	250
Meetings (seminar, workshops)	515	515	515
Events (annual meeting)	650	650	650
Data analysis and data sharing	100	100	100
Training and scientists exchange	120	120	120
Visual aids for science communication	270	270	270
Other (recruitment)	90	90	90
Overhead costs			
Totalt	1995	1995	1995

The Human Protein Atlas

Abstract

Coordinating PI: Mathias Uhlén

Co-coordinating PI: Cecilia Lindskog

Number of participating PI's at start: 9

Affiliation of key participants: KTH Royal Institute of Technology, Uppsala University; Chalmers University of Technology; Karolinska Institute; Lund University

Contact: mathias.uhlen@scilifelab.se

The Human Protein Atlas (HPA) program is an effort to map all human proteins in cells, tissues and organs using integration of various omics technologies, including antibody-based imaging, mass spectrometry-based proteomics, transcriptomics and systems biology. All the data in the knowledge resource is open access to allow free exploration of the human proteome (1). HPA is part of various international initiatives (2) and it involves SciLifeLab groups at KTH, KI, SU, Uppsala University, Lund University and Chalmers. The program has contributed to several thousands of publications in the field of human biology and disease and was recently selected by the organization ELIXIR as a core database of fundamental importance for the life science community. The Protein Atlas consists of three separate parts, each focusing on a particular aspect of the genome-wide analysis of the human proteins; the Tissue Atlas (3), the Cell Atlas (4) and the Pathology Atlas (5). [1]

Background

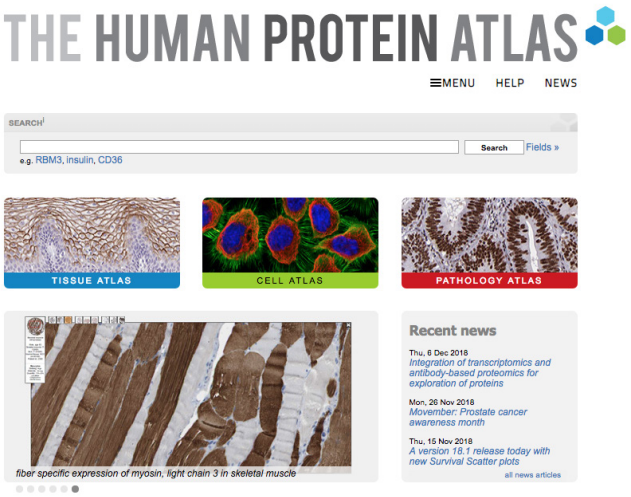
Summary

This proposal is for the Human Protein Atlas (HPA) to become a Research Community Program (RCP) at the Science for Life Laboratory. We propose a multi-disciplinary program involving 15 principal investigators from six major Swedish universities, including eight SciLifeLab national infrastructure facilities. The main objective is to continue the creation of an open access data resource (Human Protein Atlas - www.proteinatlas.org) already including three distinct parts (Tissue, Cell and Pathology Atlas), but to add during the next three years a Metabolic Atlas, a Blood Atlas and a Brain Atlas. We expect close to 100 researchers to be involved in the program through the 15 principal investigators and the results will be available as open access database resource. The funding will mainly come from the non-profit Knut and Alice Wallenberg (KAW) Foundation and the European infrastructure program ELIXIR. If approved, a RCP coordinator will be funded 50 % responsible for communication both within the SciLifeLab community as well as outside. The coordinator will also be responsible for at least one RCP-organized workshop every year and to build up educational course materials.

Background

The HPA is an international program started in 2003 with the aim to map all human proteins in cells, tissues and organs using integration of various omics technologies, including antibody-based imaging, mass spectrometry-based proteomics, transcriptomics and systems biology. The main funding to the HPA consortium is provided by the non-profit KAW Foundation (Stockholm, Sweden), and the mapping has been focused on cells and tissues of human origin. All the data in the knowledge resource (Figure 1) is open access to allow scientists both in academia and industry free access to the exploration of the human proteome. The HPA program has contributed to several thousands of publications in the field of human biology and disease and was recently (July, 2017) selected by the organization ELIXIR as a database core resource due to its fundamental importance for a wider life science research community.

The version 18 (launched December, 2017) consists of three separate parts, each focusing on a particular aspect of the genome-wide analysis of the human proteins: the Tissue



[1] 1. Uhlen et al (2010). Towards a knowledge-based human protein atlas. Nature biotechnology. 28, 1248.
2. Uhlen et al (2016). A proposal for validation of antibodies. Nature Methods. 13: 823-7
3. Uhlen et al (2015). Tissue-based map of the human proteome. Science 347: 1260419
4. Thul et al (2017). A subcellular map of the human proteome. Science 356 (6340): eaal3321.
5. Uhlen et al (2017). A pathology atlas of the human cancer transcriptome. Science 357 (6352)

Atlas showing the distribution of the proteins across all major tissues and organs in the human body, the Cell Atlas showing the subcellular localization of proteins in single cells, and finally the new Pathology Atlas showing the impact of protein levels on survival of patients with cancer. The Tissue Atlas described by Uhlen et al. (2015) contains information regarding the expression profiles of human genes both on the mRNA and protein level. The protein expression data are derived from antibody-based protein profiling using immunohistochemistry. Altogether protein profiling in 76 different cell types, corresponding to 44 normal human tissues together with the underlying images of immunohistochemically stained normal tissues are available as high-resolution in the Tissue Atlas. The Cell Atlas described by Thul et al. (2017) provides high-resolution insights into the spatial distribution of proteins within cells. The protein expression data are derived from antibody-based profiling using immunofluorescence confocal microscopy. A panel of 56 cell lines, selected to represent various cell populations in different organs of the human body, forms the basis of the Cell Atlas. In this cell line panel, the mRNA expression of all human genes has been characterized using deep RNA-sequencing. The subcellular distribution of proteins is investigated in a subset of the cell lines, and classified into 32 different organelles and fine cellular structures. The Pathology Atlas described by Uhlen et al. (2017) is based on the analysis of 17 main cancer types, including glioma, using data from 8,000 patients. In addition, a new concept for showing patient survival data is introduced, called Survival Scatter plots. The Pathology Atlas includes more than 400,000 such plots as well as 5 million pathology-based images generated by the HPA consortium.

Objectives for the next three years

The objective for the next five years is to take advantage of the SciLifeLab infrastructure to create a more comprehensive Protein Atlas using expertise from the different facilities present at SciLifeLab. The focus will be to allow more integration of the data created by involving the systems biology groups at SciLifeLab (Nielsen, Mardinoglu), focus on the human, mouse and pig brain in collaboration with Stanford University (Prof Deiserroth) and to create a resource of the proteins and the cells in human blood, involving many of the SciLifeLab facilities, including CyTOF (Brodin), plasma profiling (Schwenk) and protein arrays (Nilsson). In addition, we will continue to work on the existing Cell and Tissue Atlas in collaboration with facilities at SciLifeLab, such as cell profiling (Lundberg), Tissue profiling (Lindskog) and Clinical genomics (Engstrand). Funding is secured to 2020 from the Knut and Alice Wallenberg Foundation.

Involvement of the SciLifeLab infrastructures

As outlined above, many of the national facilities will be involved in this work. A short summary of this can be seen in Table J1.

Table J1. Involvement of SciLifeLab facilities in proposed RCP

SciLifeLab facility	Responsible	Short description
Cell profiling	Emma Lundberg (KTH)	Subcellular localization (Cell Atlas)
Tissue profiling	Cecilia Lindeskog (UU)	Tissue distribution (Tissue Atlas)
CyTOF	Petter Brodin (KI)	Immune-cell analysis (Blood Atlas)
Clinical genomics	Lars Engstrand (KI)	Transcriptomics (Blood and Brain Atlas)
Systems biology	Jens Nielsen (Chalmers)	Integration of data (Metabolic Atlas)
Plasma profiling	Jochen Schwenk (KTH)	Protein analysis (Blood Atlas)
Protein arrays	Peter Nilsson (KTH)	Protein analysis (Blood Atlas)
Tissue profiling	Jan Mulder (KI)	Brain imaging (Brain Atlas

Table J2. Additional research groups involved in proposed RCP

Research group	University	Short description
Mathias Uhlén	KTH	Program Director
Fredrik Ponten	UU	Responsible biobank handling
Tomas Hökfelt	KTH	Brain mapping
Adil Mardinoglu	KTH	Network analysis and systems biology
Björn Forsström	KTH	Targeted proteomics (mass spectrometry)
Sophia Hober	KTH	Protein science and secretome project
Hanna Tegel	KTH	Secretome project and antibody generation
Åsa Sievertzon	KTH	Bioinformatics
Kalle von Feilitzen	KTH	Data warehouse and LIMS
Karin Jirström	Lund	Cancer and pathology mapping

In addition to these facilities, a network of additional research groups will be involved in this program. A short summary of some of these research groups (and co-applicants on the proposal) is shown in Table J2.

Building of resources and open access policy

As part of the HPA effort, we have generated more than 50,000 polyclonal antibodies towards various recombinant human 100-150 amino acid Protein Epitope Signature Tag (PrEST) protein fragments. Each antibody has been affinity purified using the recombinant protein fragment as capture ligand, to ensure that all antibodies in the pool bind to epitopes present on the target protein. The generation of these antibodies has involved more than 300 person years and resulted in approximately 20,000 validated antibodies that have been used to characterize human proteins in cells, tissues and organs. The validation has involved protein micro arrays, Western blots, immunohistochemistry and cellbased immunofluorescence. Moreover, we have created routines to export string-data in TSV or XML format and APIs for data extraction.

Training, education and coordination (internal and external)

If approved, a RCP coordinator will be funded 50% to be responsible for communication, both within the SciLifeLab community as well as outside. The coordinator will also be responsible for at least one RCP-organized workshop every year and to begin build up educational material based on the data from the resource.

Strategic impact

The Human Protein Atlas provides information of a major part of the protein-coding genes in humans and is widely used by both academic and industrial groups around the world. Researchers from more than 200 countries have visited the database and at present, the resource has more than 100,000 unique visitors every month. The HPA was in July 2017 selected as a Core Data Resource by the European infrastructure program ELIXIR due to its "fundamental importance to the wider life-science community and the long-term preservation of biological data". The program outlined in this RCP proposal will allow the resource to be even more valuable for life science researcher to the benefit of the SciLifeLab community as well as external researcher in Sweden and abroad.

Funding and budget

The budget to the program includes funding from the KAW Foundation to the Wallenberg Center for Protein Research (WCPR) of 40 MSEK annually and funding from the Vetenskapsrådet for our collaboration with ELIXIR (2 MSEK annually). Funding is currently secured until 2020, but follow-up applications will be prepared. Faculty funding to the various principal investigators will amount to approximately 10 MSEK annually for research related to this program. In addition, six of the SciLifeLab facilities involved in the program will have funding from SciLifeLab beyond 2018, while two will be terminated, but these two will instead focus on the participation in this RCP, with external funding.

If the RCP program is approved, a budget of 1 MSEK will be dedicated to coordination, training and education. A 50% RCP coordinator will be designated and at least one workshop will be organized annually funded by this coordination budget. In addition, we will start building up educational material based on the resource created at SciLifeLab.

Large-scale clinical genomics and complex diseases

Abstract

Coordinating PI: Richard Rosenquist Brandell

Co-coordinating PI: Patrick F. Sullivan; Sarah Bergen; Paul Franks; Maria Gomez

Number of participating PI's at start: 11

Affiliation of key participants: Karolinska Institute; Gothenburg University; Karolinska University Hospital; KTH Royal Institute of Technology; Linköping University; Lund University; Lund University Hospital; Umeå University Hospital; Uppsala University; Uppsala University Hospital; Örebro University; Örebro University Hospital

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In this SciLifeLab Research Community Program, we will bring together researchers from all over Sweden working on large-scale genomics as a way to understand the causes of complex genetic diseases (e.g. cardiovascular, metabolic, neurological, autoimmune, allergic and psychiatric diseases) as well as to help improve treatment. Our primary goal is to connect the community to take the next step for complex diseases in precision medicine. This is a joint program between the Genomic Medicine Sweden (GMS) initiative and the Genomic Aggregation Project in Sweden (GAPS). These initiatives have worked separately up to this point, but there are clear advantages to combining efforts. The goal of GMS is to develop new infrastructures within Swedish healthcare enabling clinical implementation of genomic medicine for individualized diagnosis and treatment, i.e. precision medicine. Ultimately, GMS will improve healthcare, strengthen Swedish research, and provide a foundation for innovation and collaboration with the private sector. We will build upon the infrastructures already existing within SciLifeLab for high-throughput sequencing (NGI/Clinical Genomics) and bioinformatics (NBIS). In the past 3 years, GAPS has brought together research groups from across Sweden who study the genetic basis of common diseases. We have aggregated existing genomic data from over 100,000 Swedes and have deep connections to groups doing similar work across Europe but especially in the Nordic countries. The primary focus of GMS is rare diseases, cancer, and infectious diseases. Together with GAPS and the Swedish community working on complex diseases, the next step for GMS will be to extend the scope and also include complex diseases, with the objective to bring precision medicine to the clinic.

Background

Aims

The overall scientific aim of the Large-scale clinical genomics and complex diseases program is to bring the community working on complex diseases together with the clinical genomics community to share experiences and increase knowledge in order to implement a complex disease strategy into the next phase of Genomic Medicine Sweden (GMS). The specific goal of this project is to define pilot cases within complex diseases where genomics could be introduced to pave the way for precision medicine above and beyond the initial diseases being studied by GMS (i.e., rare diseases and cancer).

Short summary

This joint program between the Genomic Medicine Sweden (GMS) initiative and the Genomic Aggregation Project in Sweden (GAPS) will bring together scientific and clinical expertise in Sweden in the area of complex diseases. The goal is to identify examples of complex diseases of high-relevance to the Swedish population where genomics and other "omics" technologies could be introduced in the clinical setting to identify at risk groups for intensive preventive interventions, patient stratification for optimization of treatment, prompting adverse events, and monitoring.

Description of program

It is hard to conceive any area of contemporary medicine where precision medicine lacks relevance. Genomics has already improved our understanding of the genetic basis of diseases such as cancer and rare disorders and has markedly improved individual risk assessment, treament and follow-up.

The national Diagnostic Development (DD) platform within SciLifeLab launched the Genomic Medicine Sweden (GMS) initiative in June 2017. In collaboration with Swedish healthcare, we are currently developing a new type of infrastructure at the national level. The ultimate aim of GMS is to integrate findings from next-generation sequencing into individual patient electronic healthcare records and registries enabling personalized management and care, and to provide a unique

resource for population-based, cross-disciplinary research projects within the field of precision medicine. The primary focus of GMS has been on rare diseases, cancer and infectious diseases/microbiology. Pioneering pilot projects have been performed within the DD platform in close collaboration between the platform and healthcare, resulting in customized, quality-assured tools for data analysis and data sharing, with multidisciplinary teams enabling translation into individual clinical action in selected disease areas. As proof-of-concept, more than 10,000 patient samples have been processed using the DD platform for clinical diagnostics of inherited diseases and cancer, often resulting in an immediate impact on clinical decision-making and patient care. Clinical whole-genome sequencing performed at Karolinska University Hospital is offered to patients with rare diseases and so far, more than 3,000 patients' samples have been analyzed. The ambition is now to leverage these pilots into a national effort analysing up to 45,000 patient samples annually.

The Genomic Aggregation Project in Sweden (GAPS) consortium began in April 2016. GAPS has thus far formed a network of 35 research groups and recruited cohorts across Sweden with existing SNP- array genotypes (N>180,000 participants). GAPS focuses on complex diseases, conditions of great importance to the public health with unequivocal heritability but whose inheritance patterns are complex (i.e., do not conform to basic Mendelian assumptions). Although GAPS has been running in parallel with GMS, the two organisations have been in continuing discussions for more than 2-years about joint initiatives.

Cohorts in GAPS include case control studies focused on cardiovascular, metabolic, neurological, autoimmune, allergic, and psychiatric diseases as well as multiple cohort studies unselected for a particular disease. [1]

In addition, GAPS has attracted international interest, given the outstanding possibilities afforded by Swedish electronic medical records. The GAPS SAB includes Daniel MacArthur (Broad/Harvard), Gonçalo Abecasis (University of Michigan/Regeneron), and Jeff Barrett (Sanger Institute/Genomics PLC). While many consortia aggregate studies of specific diseases, GAPS has adopted a powerful approach of gathering all genetically informed studies regardless of phenotype. This strategy holds many advantages. The Swedish National Register data in combination with genetically informed samples at large scale allow unprecedented, high powered analyses across a broad range of phenotypes. GAPS capitalizes on uniquely Swedish strengths, and brings together researchers within Sweden across many fields.

The purpose of this effort is to make complex diseases part of the GMS coordinated implementation of genomics/omics in clinical settings. This is logical, and avoids needless duplications. By joining forces, GMS and GAPS will gather the community of scientists working on complex diseases in order to take the next step for this disease group to bring precision medicine to the clinic. Our goal is to identify pilot diseases for which precision medicine using "omics" technologies are maturing for introduction into healthcare. Through its design with nation-wide population-based genomic and other "omic" studies, coupled with clinical diagnostic and outcome data, this program will also provide a setting to perform cutting-edge research and innovation.

GMS-GAPS RCP scientific interaction activities

We are organizing the first joint GMS and GAPS meeting on November 26th. At this meeting, the specific nature of the collaboration will be discussed. The form of GMS-GAPS activities will also be determined.

How the SciLifeLab infrastructure is critical to the RCP, and how the RCP is critical to the infrastructure

Both for GMS and GAPS the SciLifeLab infrastructure is crucial and heavily integrated into the workflows. Considering the very rapid development of high-throughput technologies, it will be particularly important to ensure that cutting-edge genomic techniques and bioinformatics are available. Here, the SciLifeLab infrastructure will play an important role as a provider of new techniques, instruments and expertise. This RCP program would further strengthen our already close collaboration with NGI and NBIS, which recently published the SweGen whole-genome data resource[2]; however, we also foresee more active

[1] Bergen SE, Sullivan PF. National-scale precision medicine for psychiatric disorders in Sweden. Am J Med Genet Part B. 2017;1–5.

[2] Ameur A, Dahlberg J, Olason P, Vezzi F, Karlsson R, Martin M, Viklund J, Kähäri AK, Lundin P, Che H, Thutkawkorapin J, Eisfeldt J, Lampa S, Dahlberg M, Hagberg J, Jareborg N, Liljedahl U, Jonasson I, Johansson Å, Feuk L, Lundeberg J, Syvänen AC, Lundin S, Nilsson D, Nystedt B, Magnusson PK, Gyllensten U. SweGen: a whole-genome data resource of genetic variability in a cross-section of the Swedish population. Eur J Hum Genet. 2017 Nov;25(11):1253-1260.

interaction with the Single-Cell Biology, Proteomics and Metabolomics, and Drug Discovery and Development platforms.

There is ongoing work between the SciLifeLab Data Centre and GMS and GAPS. As an example, GAPS investigators and SciLifeLab Centre are planning a Swedish allele frequency database and imputation reference. This combined initiative will facilitate the SciLifeLab Data Centre objective of maximizing the scientific impact of SciLifeLab generated data by working together with the Data Centre infrastructure and by performing centralized quality control, analysis, and training.

The GMS initiative has the potential to significantly improve diagnostics, risk prediction and clinical outcome, and for the first time on a large scale, provide individualized therapy and follow-up in Sweden based on genomic high-throughput measurements. The effort will unite all six healthcare regions through a common ethical, legal, technical and analytical infrastructure. Data analysis/interpretation, storage and sharing modules will constitute a new type of national resource. A combination of healthcare records, national registers, and sequence data will provide academia with a world-unique resource for biomedical research. The initiative will open up new opportunities for partnerships to develop new types of diagnostics tools and for innovative biomarker-based clinical trials to be performed, ultimately resulting in more effective therapies. For the society at large, this initiative will help ensure that genomic medicine is implemented in a coordinated manner on a national scale, providing all patients equal access to this new opportunity.

All these aspects are in line with the mission of SciLifeLab to be a national center that combines frontline technical expertise with advanced knowledge of translational medicine and molecular bioscience. An RCP grant supporting the GMS and GAPS will in turn provide a new framework for SciLifeLab to demonstrate its societal impact as a key national infrastructure developing new high-throughput technologies and applications.

RCP budget

The budget includes two project coordinators (40/40 %; the remaining will be financed through our Vinnova grant and other funding sources) who will coordinate the national activities within GMS- GAPS-SciLifeLab, and partial costs for meetings/events, exchanges between sites, travel costs and data coordination.

Types of costs (in kSEK)	Year 1	Year 2	Year 3
Part-time coordinator	505	505	505
Meetings	150	150	150
Events	0	0	0
Data analysis and data sharing	100	100	100
Training and scientists exchange	125	125	125
Travel costs	100	100	100
Other (please specify)	0	0	0
Overhead costs	220	220	220
Totalt	1200	1200	1200

The Human Developmental Cell Atlas

Abstract

Coordinating PI: Joakim Lundeberg

Co-coordinating PI: Emma Lundberg

Number of participating PI's at start: 5

Affiliation of key participants: KTH Royal Institute of Technology; Karolinska Institutet; Stockholm University; Uppsala University

Contact: joakim.lundeberg@scilifelab.se

The RCP project is organized around Human Developmental Cell Atlas initiative, located and managed at SciLifeLab. The Human Developmental Cell Atlas procures human fetal samples and process them according to the highest ethical and technical standards; performs single cell RNA-seq and spatial analyses on these samples; performs computational analyses to discover cell types, model their activity, build the 3D atlas, and store and disseminate the data; ensure that all ethical, experimental and computational procedures are aligned and integrated with the international Human Cell Atlas. In particular this RCP focus' on assembling expertise at Swedish Universities for analysis and annotation of developmental tissue from brain, lung and heart. The consortium aims to accelerate research into human biology and disease, and strengthen Swedish science by building on our very strong position in single-cell genomics, proteomics and infrastructures.

Background

Aims

We propose to establish Swedish consortium focused around the *creation a Human Developmental Cell Atlas:* a comprehensive molecular atlas of human prenatal development.

Short summary

The project will focus on assembling expertise for analysis of developmental tissue from brain, lung and heart. The consortium will *accelerate research* into human biology and disease, and *strengthen Swedish science* by building on our very strong position in single-cell genomics, proteomics and infrastructures.

Description of program

Background

The cell is a fundamental unit of life, yet we know surprisingly little about them. Specific types of cells exist in every organ, and serve specialized functions defined by the specific genes and proteins active in each cell type. However, no comprehensive map of human cell types or their distribution exists. There are about 300 known cell types in the human body, but recent studies estimate the true number to be 10-fold higher.

In London, October 2016, a collaborative community of world-leading scientists met and agreed to take on the massive challenge and build a Human Cell Atlas (https://www.humancellatlas.org); a collection of spatiotemporal maps that will describe and define the cellular basis of health and disease. In scope and level of ambition, the Human Cell Atlas (HCA) has been compared to the Human Genome Project. When completed, the atlas will give us a unique molecular ID card for each cell type (e.g. gene expression signature), and a three-dimensional map of how cell types assemble together to form tissues. The molecular signatures will allow us to model cells and the mechanism for their specific function, thus provide insight into how variations and deviations contribute to health and disease. It will allow us to identify exactly where and when disease-associated genes are active in our body and analyze the regulatory mechanisms that create organs and tissues.

Very recently, new tools such as *single-cell genomics* have put these lofty goals within reach. It is an ambitious but achievable project, that requires a community of biologists, clinicians, technologists, physicists, computational scientists, software engineers, and mathematicians.

Swedish leadership

Sweden has been a clear leader in single-cell technology in recent years, with strong international impact. The main annual meeting for single-cell genomics is co-organized by Swedish scientists (Linnarsson, Sandberg), and Swedish scientists have developed key technologies leading to substantial biological discoveries (see references). A large number of local scientists have benefited from these technologies and infrastructure, establishing a strong Swedish track record particularly in developmental biology and neuroscience.

Focus area

Human prenatal development is a key challenge for the Human Cell Atlas, where Sweden has a unique ability to contribute. First, research on the human embryo is relatively uncontroversial here, and we have established robust and ethical protocols for routine sampling of tissues. Second, Sweden has strong and well-established research in developmental biology, particularly in the nervous system. Third, approximately 3 000 human proteins have yet not been spatially localized in human tissue by the Human Protein Atlas initiative most likely due to that developmental tissue has not yet been included or investigated.

Current status

We have recently received, in international competition, initial support to perform a pilot project on human prenatal development as part of the philanthropic Chen Zuckerberg Initiative. The granted project, although not fully funded, aims to create an atlas of the developing human embryo, focusing on the first two trimesters, which span the most important events of embryogenesis: formation of the nervous system and peripheral organs, birth of most cell types, and the first steps of maturations of cells into their adult forms. The ambition for the developmental atlas is to have four key components: (1) a catalog of all developmental cell types based on gene activity (using single-cell RNA-seq and spatial transcriptomics technology) (2) focused spatial analysis of a panel of proteins and transcripts to validate biomarkers of tissue development (using in situ sequencing and proteomics technology) (3) a three-dimensional map of the location of cell types in tissues and organs; and (4) a common coordinate framework, ensuring the data can be browsed and searched in multiple dimensions, and that prior and future datasets can be aligned using the atlas as scaffold.

RCP application

In this application we aim to seek support for a scientific coordinator to expand and explore the massive amount of data that is generated within the Human Developmental Cell Atlas (HDCA). All data will be generated at SciLifeLab using existing platforms and pilot core facilities. Raw data will be uploaded to the HCA data coordination platform. A Swedish HDCA web portal (associated with SciLifeLab) will be developed for project and data presentation.

For wider dissemination we will take advantage of the research community (RCP) to identify analysis and visualization tools adapted for scientific exploration of HDCA output:

- Defining a user-friendly interface and its functionality.
- Defining a set of analytical tools for data exploration (pathways, regulome, RNA velocity etc)
- Defining functionality of 3D visualization
- Downloading of processed data.
- Presentation of tutorials and SOPs for experimental workflows.

In addition, the RCP aim to engage a larger scientific community beyond the already included list of PIs, having expertise in heart, lung and brain, from both developmental point of view as well as disease. We will promote an organ centric view of the project by inviting experts within each biological field to contribute and be part of the HDCA project by:

- Being involved in experimental designs (taking into developmental phase, replication, disease models into consideration)
- Exploring the data for scientific advancements
- Assisting in annotation of results to be presented on the webportal

Furthermore, the RCP will continuously update the web portal as new data is generated and as the community requests new types of analytical tools. To maximise the impact, the RCP will also focus on creating the network and ensure that the computational resource will facilitate discovery and exploration in the broadest sense.

We will bring attention to the RCP by:

- Public releases and announcement of new datasets provided at the web portal
- Being part of outreach activities held by SciLifeLab and/or its platforms at Swedish Universities
- Provide thematic webinars/lectures/tutorials on the topics such as: HDCA, experimental tools, analytical tools etc.
- Connecting groups of organ developmental expertise into HDCA project

Significance

Human disorders of development, including malformations of the heart and brain, metabolic disorders, neurological disease and defects caused by toxins and infection, are leading causes of human suffering. Neurodevelopmental disorders such as autism, schizophrenia, epilepsy, intellectual disability and cerebral palsy can be particularly devastating. The Human Developmental Cell Atlas together with RCP community will accelerate research to prevent, diagnose and treat such disorders, in several ways:

- *Serve as a reference map for disease genes to help locate the tissue, cell type and time when disease genes are active.* This will help convert genetic clues into functionally testable mechanistic hypotheses, leveraging the huge investments already made into genome-wide association studies (GWAS).
- *Define markers and signatures* that allow well-defined cell types to be isolated and manipulated, e.g. using antibodies and cell sorting. Identifying the relevant cells is the first key step in understanding the mechanism of disease and develop tools for early diagnosis.
- *Identifying potential drug toxicity* by revealing where and when a specific drug target is active. For example, a drug target in the adult liver might also be active in the developing retina and cause childhood blindness. Such risks

will be easily identifiable in the Atlas.

- *Provide a direct view of human biology in vivo.* Much of our current knowledge about human biology is derived from in vitro studies and model organisms. The Human Developmental Cell Atlas will reveal human development at high resolution, without the distortions of cell culture or rodent models. Indeed, many of human developmental diseases that are linked to metabolic dysfunction can directly take advantage of the findings and could provide new treatment options.
- *Revitalize a massive body of legacy data.* Large-scale efforts over the past years have collected vast bodies of data in both healthy and diseased humans, but at the tissue level. Advanced computational methods exists that can deconvolute such data into their cell type constituents, thus greatly increasing the value of existing datasets.

In sum, a *Human Developmental Cell Atlas would be transformative and the RCP community would secure the value of the data being generated.* Every aspect of life science research relies on knowing cell types and their molecular properties. A coherent, integrated Developmental Cell Atlas would transform research into developmental disorders by (1) revealing the biology of human development at its most fundamental level, and (2) generating experimental data, computational methods and technological infrastructure to accelerate research from basic biology to the clinic. Finally, a strong Swedish presence in the international Human Cell Atlas initiative using a RCP as stepping stone will ensure that we are positioned to reap the rewards of this large and exciting endeavor.

Management

The approach is cross-disciplinary, and the applicant together with associated PIs have expertise ranging from engineering, basic biomedical research, computation and clinical medicine and will form the initial core group. The RCP project will have a flat type of organization where participants will meet to plan topical network activities in heart, lung and/or brain with the goal to expand the RCP group with additional members in respective field. Another important task within the RCP group is discuss data sharing and access of data. Project meetings and scientific exchange will be held regularly and will foster a new generation of scientists, promoting gender equality in science.

Budget

We propose to a 75% coordinator that is responsible for networking, scientific exchange and data coordination, access and visualization.

How the SciLifeLab infrastructure is critical to the RCP, and how the RCP is critical to the infrastructure

The RCP project will be organized around the ongoing Human Developmental Cell Atlas initiative, located and managed at SciLifeLab. The Human Developmental Cell Atlas procures human fetal samples and process them according to the highest ethical and technical standards; performs single-cell RNA-seq and spatial analyses on these samples; performs computational analyses to discover cell types, model their activity, build the 3D atlas, and store and disseminate the data; ensure that all ethical, experimental and computational procedures are aligned and integrated with the international Human Cell Atlas.

Several technical platforms are used for the RCP and the Human Developmental Cell Atlas project. The Eukaryotic Single-Cell Genomics platform (PIs Linnarsson, Sandberg) has state-of-the-art instrumentation to prepare material for single cell analysis including droplet and valve microfluidics, microwell arrays and robotics. The facility was used to analyze nearly a million single cells during 2017. Two additional pilot facilities focusing on in situ technologies have recently started, Spatial Transcriptomics facility (PI Lundeberg) and In situ sequencing (PI Nilsson). The National Genomics Infrastructure platform (PIs Lundeberg, Syvänen, Gyllensten) is one of Europe's largest genome centers (>70 FTEs). This ISO certified platform is responsible for data generation. SciLifeLab also host the Human Protein Atlas platform for high-throughput spatial proteomics with access to antibodies for all human proteins, and the High-content microscopy facility (PI Lundberg) performing large-scale spatial proteomics analysis using this antibody resoure.

RCP budget

Types of costs (in kSEK)	Year 1	Year 2	Year 3
Part-time coordinator	570	570	570
Meetings	100	100	100
Events			
Data analysis and data sharing	50	50	50
Training and scientists exchange	50	50	50
Travel costs	25	25	25
Other	0	0	0
Overhead costs	250	250	250
Totalt	1045	1045	1045

Aquatic Microbiome Research Initiative

Abstract

Coordinating PI: Stefan Bertilsson

Co-coordinating PI: Rachel A Foster

Number of participating PI's at start: 6

Affiliation of key participants: Uppsala University; Stockholm University; Chalmers University of Technology; Gothenburg University; KTH Royal Institute of Technology; Linnaeus University; Swedish University of Agricultural Sciences; Umeå University

Contact: Stebe@ebc.uu.se

Aquatic Microbiome Research Initiative (AMRI) bring together Swedish researchers and technology competence centers in a collaborative effort to advance our understanding of one of the earth's largest biomes: the aquatic microbial world. Activities within AMRI are focused on the following broader themes, each led by a coordinator: microbial biogeography across and within aquatic biomes (Jarone Pinhassi), functional diversity (Anders Andersson), microbial interactions and evolution (Rachel A Foster) and microbes as ecosystem engineers (Stefan Bertilsson). Planned AMRI activities include an annual 'All Hands' meeting, quarterly workshops on specific technologies and topics such as single cell analyses, advanced isotope analyses and imaging, enviornmental genomics and metabolomics. We will also enable short-term student/postdoc research exchanges, promote the initiation of collaborative joint pilot experiments, and build platforms for shared data analysis, protocols and best practices. The long-term goal is to coordinate research on the organization and functioning of microbial landscapes and provide an active network for expanding Swedish research beyond regions or local laboratories. AMRI is an open platform and new researchers are encouraged to contact coordinators and/or AMRI project assistant, Caroline Littlefield Karlsson (caroline.littlefieldkarlsson@lnu.se), for more information. [1]

Background

Aims

The overarching goal of the Aquatic Microbiome Research Initiative-Research Community Program (AMRI-RCP) is to engage leading Swedish researchers with backgrounds in microbial ecology, evolution and geochemistry, *in a collaborative effort to advance our understanding of aquatic microorganisms and their functional role in the environment*. This multi- and interdisciplinary RCP will be a novel and unique forum to address the major and pressing challenges in microbial ecology and water resource management. It is broadly recognized that access to clean water and productive waters to sustain aquaculture and fisheries, is a major challenge for the past, contemporary and future societies. Still, our understanding of the key factors and mechanisms/processes controlling the chemical and biological status of natural water resources is incomplete. For instance, the role of microorganisms in improving and/or compromising the chemical status of waters, in mediating cycling of bioactive elements and ecological and evolutionary mechanisms that enable microorganisms to spread and adapt to a changing environment are yet to be fully elucidated.

In light of recent advances in the field of aquatic microbial research and the combined expertise within the RCP, we now have an unprecedented opportunity to bridge this knowledge gap by more extensively engaging with SciLifeLab infrastructures in large-scale collaborative environmental genomics and other state of the art bio-molecular analyses. Only very recently have such methods been put to use for cultivation-independent reconstruction and large scale analyses of metabolic properties, biogeochemical functions and overall emerging traits of complex communities and ecosystems. Within AMRI, we will take on this challenge. By coordinating and coupling national leaders in this rapidly developing research area with complementary experts in isotope tracer methodology and measurements, geochemistry and metabolic ecosystem modelling, we will form a national and international platform for advances in microbial ecosystem science. This research will also augment and revitalise aquatic resource management to take microorganisms into full consideration in evaluating ecosystem services and environmental quality assessment.

Short summary

Water connects biomes and their resident microbiota. Aquatic microorganisms contribute to emerging properties of ecosystems, and in this RCP we will explore genome-enabled characteristics of entire microbial communities and combine

[1] Bunse, C. and J. Pinhassi (2017). Marine bacterioplankton seasonal succession dynamics. Trends in Microbiology. 25(6):464-505
Hugerth et al (2015). Metagenome-assembled genomes uncover a global brackish microbiome. Genome Biology 16:e279
Smith et al (2017). Microbial formation of labile organic carbon in Antarctic glacial environments. Nature Geoscience.10(5): 356-359
Bravo et al (2017). Molecular composition of organic matter controls methylmercury formation in boreal lakes. Nature Communications. 8:e14255

this with isotope tracers, geochemistry and metabolic models to fully appreciate their biology and role in the biosphere.

Description of program

AMRI activities will be organized in four working groups, each with a coordinator, research questions, and actions but at the same time each of these groups will engage the majority of the RCP partners. A steering group consisting of the work-group leaders and a part time RCP coordinator will oversee the broader strategic coordination and governance of the RCP while the project leaders (PI Bertilsson and coPI Foster) will be responsible for the administrative interactions with the SciLifeLab operations office and management. A team of 28 collaborating PIs have come together from diverse areas within aquatic microbiology (e.g. biogeochemistry, modelling, evolution, cell biology, bioinformatics). The participants come from a multitude of organisations, career stages and scientific backgrounds and form a strategic team well positioned to address the challenges in aquatic microbiome research and water resource management. Several of the PIs are already engaged in SciLifeLab as faculty, fellows or platform staff, but part of our RCP mission is also to connect additional Swedish researchers and infrastructure with this SciLifeLab, and this is reflected in the composition of the team. Additional groups are expected to join the RCP during the course of the project and new working groups may also be developed with new/additional coordinators and questions. Each of the four working groups will focus on a unique set of challenges/questions:

1. *Microbial biogeography across and within aquatic biomes* (Lead: Jarone Pinhassi) How is microbial diversity structured across environmental gradients and how do communities respond to changes in externally defined environmental conditions? What is the imprint of the past (i.e. priority effects)? How active are microbial populations and what are the roles of microbial seed banks and dormancy in shaping biogeographical patterns?
2. *Functional diversity* (Lead: Anders Andersson) How are ecological and metabolic functions structured across time and space in aquatic microbiomes? How does community assembly and genetically encoded diversity in metabolisms and ecological functions contribute to actual biogeochemical processes and in regulating biogeochemical cycling of carbon, nitrogen, phosphorus, sulphur and other bioactive elements? How can diversity in metabolic processes be implemented in biogeochemical models?
3. *Microbial interactions and evolution* (Lead: Rachel Foster) What are the functional and evolutionary implications of prevailing interactions over shorter and longer timescales? What characterizes interactions between closely related and more distant populations or even across different domains of life? How active are individual microbes and microbial populations? What metabolites are exchanged between microbes? What enables microorganisms to cross biome boundaries and colonize new environments?
4. *Microbial impacts on ecosystems* (Lead: Stefan Bertilsson) Microorganisms respond to differences in environmental properties, but in what ways and to what extent do their metabolic capacity and growth also change the nature, stability and other emergent properties of aquatic ecosystems? New species with entirely new traits may invade systems once certain thresholds are surpassed and this may push entire ecosystems in unexpected directions. How can we account for this in aquatic resource management and possibly explore it for knowledge-based ecosystem management?

Within the RCP we will organise several joint activities focused around thematic actions:

- We will develop, establish and share best practices in linking community-level genome, transcriptome, proteome and metabolome data to ecosystem-level processes of environmental and natural resource concern.
- Collaborative opportunities between PIs within the RCP will promote comparative cross-ecosystem studies that will enable us to move beyond studies restricted to individual ecosystems or biomes and make it possible to extrapolate to entire landscapes or global scale. This will maximize impact and promote biological insight.
- By collaborating broadly and openly and by combining and linking existing project resources and funding with complamentary analytical expertise and instrumentation within the RCP in joint pilot experiments, we will shed new light on cryptic processes or organisms in aquatic biomes and open up new areas for future research proposals, strategic initiatives and research infrastructure capacity building.
- AMRI will take strategic initiatives in relevant international networks and organisations and be a contact point for national and international collaborations and joint proposals. The PIs all have extensive international collaboration evidenced by publications and CVs, and these links and connections will be explored more broad networking opportunities within AMRI. Additionally the RCP will organise mini-symposia and courses within the SciLifeLab context and also interact and collaborate

with SciLifeLab platforms with regards to novel tools, techniques and services particularly relevant to the RCP. For example, students and postdoctoral researchers will be encouraged to participate in short-term research rotations; a means to access expertise outside his/her department/laboratory and fostering of collaborations amongst AMRI partners.

- The RCP will interact with relevant SciLifeLab facilities and provide input about services and opportunities. Representatives for NGI, Single Cell Biology, Metabolomics and NBIS are engaged in the RCP and we will also form a link to other relevant Swedish infrastructures such as the Gothenburg Imaging Mass Spectrometry Facility (Go:IMS), the SLU Stable Isotope Laboratory, the VR funded Swedish Infrastructure for Ecosystem Science (Lead by Bertilsson) and Biodiversity informatics infrastructures such as NBIS, Swedish Lifewatch and Biodiversity Atlas Sweden (also VR funded).

How the SciLifeLab infrastructure is critical to the RCP, and how the RCP is critical to the infrastructure

Aquatic Microbial Ecology is at the forefront of high impact science and is a fast growing and exciting field. Advances in technology, e.g. single cell, sequencing platforms, microscopy, and computational sciences, is currently strong in Sweden, and many Swedish researchers are at the forefront of their respective research topic. With more coordination and extensive collaboration enabled by the RCP, we will use resources and expertise in optimal ways, open new areas of research, push methodology, and in this way maintain international leadership. The mechanistic insights with regards observation and identifying aquatic microbial function and interactions critically depend on infrastructure and services provided by NGI, Advanced Light Microscopy, Single-Cell Biology, Proteomics, Metabolomics and Bioinformatics. Access to/collaboration with these infrastructures gives us a competitive edge compared to international peers and competing initiatives. We are already major users of some of these infrastructures, but with coordination, training and further development of tools and best practices, we will be able to do so more efficiently. The RCP and the PIs taking part in the initiative can also promote and contribute to development and adoption of novel methods and practices that can be adopted by the platforms and SciLifeLab. The RCP will also promote the use of large-scale biomolecular methods in environmental science and serve as an example for more broadly engaging SciLifeLab as a partner in ongoing and planned efforts to monitor and manage the environment and our natural resources. Finally, we have partnered with the National Center for Imaging Mass Spectrometry (NCIMS) and with state of the art instrumentation to visualise and measure microbial activities and interactions.

RCP budget

Types of costs (in kSEK)	Year 1	Year 2	Year 3
Part-time coordinator (20 %)	145	145	145
Meetings	100	100	100
Events	100	100	100
Data analysis and data sharing	80	80	80
Training and scientists exchange	200	200	200
Travel costs	56	57	56
Outreach	10	10	10
Overhead costs (44.6 %)	308	309	308
Totalt	999	1001	999

Phenotypic Drug Discovery in Human Disease

Abstract

Coordinating PI: Oscar Fernández-Capetillo

Co-coordinating PI: Karin Forsberg Nilsson

Number of participating PI's at start: 8

Affiliation of key participants: Lund University; Uppsala University; Gothenburg University; Karolinska Institute; KTH Royal Institute of Technology

Contact: oscar.fernandez-capetillo@ki.se

The low success rate of drug approvals despite the ongoing enormous technological developments calls for an urgent improvement of the drug discovery workflow. Disease-relevant models, phenotypic screening and target ID technologies, are three key aspects in this process. However, several challenges such as access to biological starting points, difficult assay development, or the high cost of target ID, often hamper the forward development of efficient drug discovery. To address these challenges, and to impact precision medicine in a collaborative and efficient manner, we have initiated the the Phenotypic Drug Discovery in Human Disease RCP. Through annual meetings, workshops and lab exchange programs, we will engage research groups and facilities in areas comprising (i) disease-relevant models, (ii) assay design and development of phenotypic screens, and (iii) chemical proteomics technologies and alternative target ID methods, to ultimately improve the state-of-the-art drug development workflow and increase the number of drugs successfully approved.

Background

Aim

The goals of this RCP are to agglomerate and bring together all the parts (research groups and facilities) involved in the development of disease-relevant models for drug discovery and target identification workflow, that is: A) biological starting points, B) phenotypic screens and C) target ID, in order to provide:

1. An excellent platform for sharing expertise and solving challenges
2. Networking
3. Create collaborations
4. A niche for collaborative development of: disease-relevant models, robust phenotypic assays and robust target identification methodologies
5. An excellent scientific critical mass for potential joint funding

Short summary

Low success rate of drug approvals despite the ongoing enormous technological developments, calls for an urgent improvement in the drug discovery workflow. Disease-relevant models that can be applied to precision medicine, phenotypic screening and target ID technologies, are three key aspects in this workflow. This RCP will engage expertise research groups and facilities to collaboratively solve drug discovery workflow challenges.

Description of program

Despite enormous technological developments, the success rate for approved new drugs has not significantly, and accordingly, improved in the last decades in spite of some occasional peaks. Poor Research and Development efficiency due to the lack of efficacy in Phase II and III clinical trials (failure rates of 40-70% between 2008 and 2015), and an estimated success rate from Phase I to approval of only 10%, has led to a stalling in drug discovery and development (Shih HP et al., Nat Rev Drug Discov, 2018). Therefore, a large effort has been devoted to developing alternative strategies for drug discovery (Eder J et al., Nat Rev Drug Discov, 2014; Jones LH and Bunnage ME, Nat Rev Drug Discov, 2017; Moffat JG et al., Nat Rev Drug Discov, 2014; Schneider G, Nat Rev Drug Discov, 2018). In particular, the development of disease-relevant cell assays including patient- derived primary cells for precision medicine, complex cellular co-cultures, as well as organoids, which are emerging as novel and more physiologically significant models, and are expected to improve the R&D efficiency in drug discovery and development, both in basic research phases as well as screening campaigns (Horvath P et al., Nat Rev Drug Discov, 2016; Jabs J et al., Mol Syst Biol, 2017).

Used to discover 37% of the first-in-class drugs and 18% of follower drugs approved by the FDA between 1999 and 2008 (Swinney DC and Anthony J, Nat Rev Drug Discov, 2011), cell-based phenotypic screens, have become a key standard in drug discovery. In this context, as well as in later validation and development stages, disease-relevant cellular models are of immense importance (Dugger SA et al., Nat Rev Drug Discov, 2017; Moffat JG et al., Nat Rev Drug Discov, 2017). Phenotypic screens are used for repurposing of known drugs, predictive toxicity, and also to identify new and uncharacterized molecules with unknown molecular target and associated mode of action (MoA). This challenge has triggered the development of new crucial technologies focused on target identification (Fellmann C et al., Nat Rev Drug Discov, 2017; Schenone M et al., Nat Chem Biol, 2013).

Drug discovery is a highly multidisciplinary field, in this perspective, the development of relevant cellular and patient-derived models, state of the art phenotypic screening and the follow-up target deconvolution, pose great tools, but are also highly challenging, often hampering the forward development of the drug discovery workflow, e.g. (A) Biological starting points: Initial accessibility, collection and further culturing of patient material, development of relevant cellular models, generation and development of 3D organoids; (B) Assay design and development: Assay robustness, access to infrastructures, image and data analysis, image and data storage; (C) Chemical proteomics technologies and alternative target ID methods: High costs, lack of reference compounds, data processing.

To address these challenges in a collaborative and efficient manner, the proposed RCP – *Phenotypic Drug Discovery in Human Disease* – will focus on gathering expertise from: (A) Biological starting points: hospitals and research groups working with disease- relevant models (such as patient-derived material, organoids and cellular models), to explore and share best practices, challenges and current approaches, for the use of these biological starting points in phenotypic screens and drug discovery; (B) Assay design and development: research groups and facilities specialized in genetic and chemical screens, with expertise in chemical libraries, as well as in the development of robust complex assays, and their adaptation to phenotypic high throughput screens; and (C) Chemical proteomics technologies and alternative target ID methods: expert research groups and infrastructure services focused on developing reliable target identification protocols. See Figure J1.

The participant research groups and facilities in Figure J1, have devoted their efforts to each of these expertise areas, becoming highly specialised, developing cutting-edge technologies and leading their fields. In addition, academic institutions have successfully implemented a key facility-based infrastructure enabling those groups lacking a specific technology, and providing expertise. However, the development of disease models, protocols and new technologies, often take place in a scattered manner, resulting in time-consuming problem-solving and delays in project development. Thus, the goal of this RCP is to agglomerate and bring together all the parts involved in this drug discovery workflow, in order to provide the perfect platform for sharing expertise, networking, create collaborations, and additionally, offer an excellent scientific critical mass for potential joint funding.

All groups and facilities in this RCP (see figure 1) from universities across Sweden (Karolinska Institutet, Uppsala University, KTH Royal Institute of Technology, Umeå University, Lund University, Gothenburg University and Astra Zeneca), have confirmed their commitment and participation in this RCP. It is worth mentioning that among the participants there are already large ongoing projects from which this RCP will benefit, that is:

- Michael Sundström (Scientific Director of European Initiatives at the Structural Genomics Consortium): The vast and diverse drug discovery projects within the SGC, together with its large network of research groups and universities, makes it a great participant in this RCP, immediately interconnecting both networks.
- Brinton Seashore-Ludlow and Päivi Östling (Kallion-

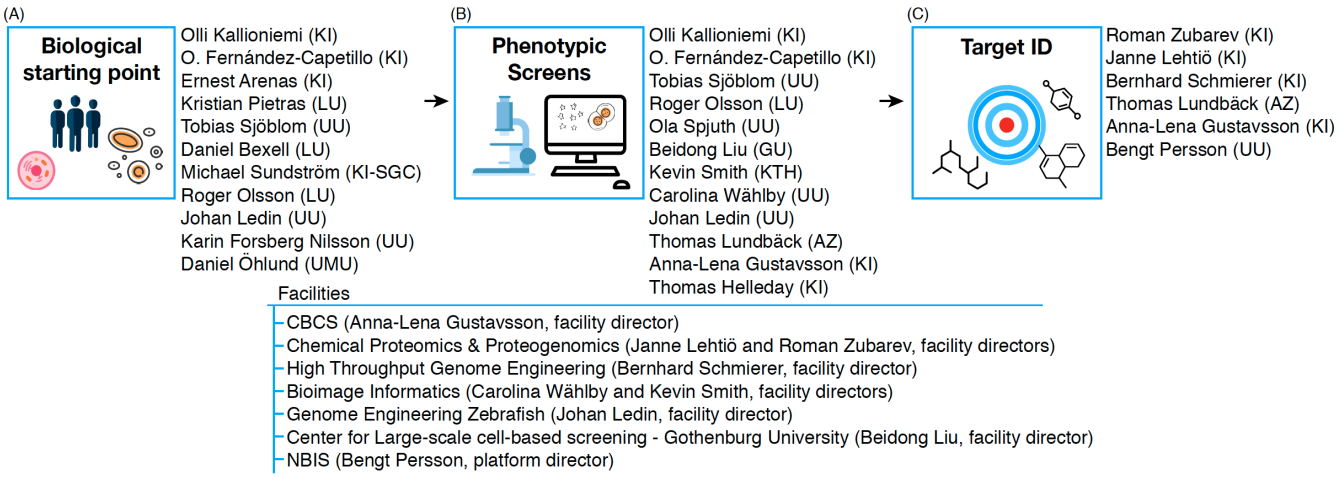

Figure J1. The participant research groups and facilities, and their expertise areas.

iemi's group): The Kallioniemi's group has embarked in a large project funded by Vinnova, with its main focus on developing a nano- scale precision medicine platform to be implemented in both precision diagnostics, treatment, and drug discovery efforts. Key to its success is the generation of relevant cell models, which will be profiled on their systems medicine platform.

- CBCS (Anna-Lena Gustavsson) and Astra Zeneca (Thomas Lundbäck): An open innovation partnership was recently created between CBCS and AZ, making AZ's characterised compound libraries accessible to research groups through their open innovation platform.

This RCP will provide an engaging networking platform to encourage cutting-edge research collaborations in the form of:

- *Annual meetings:* in which the involved groups and facilities will share their latest research and progress, representing a great opportunity to meet peers in person.
- *Workshops in relevant aspects of the drug discovery workflow such as:*
  (i) development of challenging disease-relevant models: establishing patient material in the lab, co-culturing techniques, organoid formation techniques.
  ii) high-throughput technologies: liquid handling, phenotypic screens, high content imaging, image and data analysis, chemical libraries.
  (iii) technologies for target ID: chemoproteomics, chemical biology, gene editing.
- *Lab exchange programs*: promotion of lab members exchange among research groups and facilities to learn key techniques on-site.
- *PDD in Human Disease on-line space:* an on-line space (the final format is to be determined) with exclusive content to the RCP participants will serve to share information about meetings and workshops, as well as a window for publications and collaborations emerging from the RCP participants.

This RCP represents a great opportunity to collaboratively improve the current status of the disease- relevant drug discovery workflow. It would not only help research groups heavily specialised in certain aspects of this field, but also facilities nation-wide as they would thrive with potential new projects. Certainly, bringing together the excellence in science and expertise currently scattered in this field will further benefit the development of new and better technologies, disease models, more efficient screening approaches and more reliable and robust target identification methods; overall aiming at improving the rate of potential new uses for old drugs, as well as novel treatments for a plethora of diseases currently lacking a cure.

How the SciLifeLab infrastructure is critical to the RCP, and how the RCP is critical to the infrastructure

The excellent infrastructure constellation currently available at SciLifeLab represents a critical ground for this RCP. Many of the participant groups, despite developing their own technologies, lack key components for their projects such as automated high-throughput liquid handling, high-throughput imaging, compound libraries (expertise and handling), image analysis expertise, access to the state-of- the-art technologies for target identification and cutting-edge bioinformatics systems development.

Therefore, the participant research groups in this RCP would immediately benefit from the also participant facilities listed above. Similarly, the aforementioned facilities would immediately benefit from projects emerging from the research groups. This synergy is crucial for the success of this RCP as ideas and projects coming from the participant research groups need the national facilities for their success, and at the same time, the facilities and platforms would increase the portfolio of projects nationwide.

RCP budget

Types of costs (in kSEK)	Year 1	Year 2	Year 3
Part-time coordinator	150 000	150 000	150 000
Meetings	150 000	150 000	150 000
Events	180 000	180 000	180 000
Data analysis and data sharing	90 000	90 000	90 000
Training and scientists exchange	100 000	100 000	100 000
Travel costs	150 000	150 000	150 00
Other	0	0	0
Overhead costs	168 674	168 674	168 674
Totalt	988 674	988 674	988 674

Swedish Tumor Microenvironment (STorM) Program

Abstract

Coordinating PI: Kristian Pietras

Co-coordinating PI: Anna Dimberg

Number of participating PI's at start: 5

Affiliation of key participants: Lund University; Uppsala University; Karolinska Institute; KTH Royal Institute of Technology; Linköping University Hospital; Stockholm University; Norrlands University Hospital

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Cancer arises as a consequence of a series of genetic alterations in any of the more than 200 specialized cell types of our body. Through these genetic changes, cancer cells may evade the strict control of cell division and form a tumor. Recent studies highlight the importance of communication between cancer cells and their surrounding tissue (the tumor microenvironment) to enable a tumor to develop into a clinically manifested disease. Various cell types in the tumor microenvironment provide a range of factors that promote the initiation of cancer, fuel the growth of malignant cells, facilitate the spread of the disease and make tumors resistant to treatment. The Swedish Tumor Microenvironment (STorM) network leverages the power of thirty internationally leading research groups in the field spanning across the entire country. The overarching aim of the program is to identify novel communication pathways within the tumor microenvironment that can be exploited as cancer drug targets and biomarkers. The program will foster cross-disciplinary studies which optimally combines experimental studies in cell and animal models, correlative analyses of clinical samples, and cutting-edge technology.

Background

Aim

1. To juxtapose basic research, clinical science and cutting-edge technology development to spur breakthrough research into the mechanisms of metastatic dissemination of cancer
2. To create a cross-disciplinary training ground of the highest international standard for the next generation cancer researchers
3. To support the application-based development of existing technology platforms at SciLifeLab and inspire inclusion of novel platforms into the SciLifeLab infrastructure.

Short summary

The overall goal of the STorM program is to identify novel paracrine signaling pathways that can be exploited as cancer drug targets and biomarkers. The program will foster cross-disciplinary studies which optimally combines *experimental studies* in cell and animal models, *correlative analyses* of clinical samples, and cutting-edge *technology*.

Description of program

Background and rationale for the program

Cancer accounts for more than 1.2 million yearly deaths in the EU, and the worldwide death toll amounts to 7.6 million. With the projected increase of the elderly population in the EU by 77% between 2010-2050, the incidence of cancer is expected to rise steadily. Our knowledge of cancer has exploded ever since the discovery of oncogenes during the 1970's. We now understand the basis for the disease at the molecular level and novel targeted drugs have been developed. Despite this positive development, the death rate of cancer has not decreased accordingly during the same time period. *Thus, the need for new and effective cancer therapies is imperative.*

The traditional tumor cell-centric cancer view largely disregards the context in which malignant cells subsist in primary tumors or in metastases. However, cancer progression involves co-evolution of the surrounding microenvironment to an activated state involving paracrine communication. This creates a dynamic signaling circuitry of paracrine interaction between specific cellular subsets, promoting cancer initiation and progression through manners also including evasion of immune surveillance. *Hence, future cancer studies must consider the concept of tumors as multi-cellular entities.*

Studies of the tumor microenvironment continuously uncover new cell types. Indeed, subsets of tumor cell types are being defined by differential marker expression and associated with distinct functions, e.g. effects on cancer cell proliferation, differentiation and drug sensitivity, and suppression of immune surveillance. The increasing awareness of the importance of the cellular organization in tumor phenotypes emphasize the need *to study tumors with higher spatial resolution applying cutting-edge and novel methods for high content in situ tissue profiling.* Three SciLifeLab facilities are well positioned to contribute to this goal, through existing and novel technologies; *Eukaryotic Single Cell Genomics* (represented by co-founder Rickard Sandberg), *Cell and Tissue Profiling* (represented by facility director Emma Lundberg) and *BioImage Informatics*

(represented by facility director Carolina Wählby). The proposed program will also rely heavily on *research which integrates analyses of developmental processes, cancer model studies and materials from well-annotated patient cohorts.*

Research topics and defining technologies

The overall goal of the project is to identify novel paracrine signaling pathways that can be exploited as cancer drug targets and biomarkers. Studies will take advantage of the ability of the RCP to perform cross-disciplinary studies which optimally combines experimental and descriptive studies in cell and animal models, correlative analyses of clinical samples, and cutting-edge technology.

In this effort, we propose to harness the power of *developmental biology* to identify paracrine signaling pathways involving distinct cell types that impact either on the growth of epithelial cells or control the activity of the immune system. Recognizing that 90 % of cancer deaths are the result of disseminated disease, a specific focus will be placed on understanding *the cellular and molecular circuitry of metastatic lesions in experimental, as well as patient tumors.* A defining methodological feature of the program will be the emphasis on *high-content in situ profiling of paracrine signaling.*

Composition of the Program

The *Swedish Tumor Microenvironment (STorM) Program* brings together research groups of the highest international standard and complementary expertise in *basic science* and *translational science* with laboratories developing c*utting-edge technologies* related to high resolution and multiplexed *in situ* visualization of gene expression or protein localization.

The program is truly cross-disciplinary and includes expertise in tumor biology (KP, AÖ, RSJ, DÖ, AL, GJ, CM, AP, JN, TS), vascular biology, immunology and developmental biology (UE, CR, CB, MK, LCW, TM, MK, MP, ED, IA, AD), and surgery, oncology and pathology (AB, FP, JS, PS, JB). The STorM Program moreover includes expertise in single cell large-scale genomic analyses (RS), high resolution *in situ* aof gene expression (MN) and protein localization (EL), and digital image analyses (CW). *Taken together, the STorM program is thus optimally designed to discover new paracrine regulatory pathways, to be exploited as biomarkers and/or anti-cancer drug targets, through studies inherently integrated with technology development. The ultimate aim of the program is to strive for clinical implementation, capitalizing from the significant participation of clinical scientists in the program.*

The STorM Program is built on a core of research groups with successful and long-standing collaborations. The final composition of the STorM Program benefits from the inclusion of additional research groups and a strong integration with methodology-based SciLifeLab groups. *It is expected that there will be significant synergistic effects through this format where the biomedical, clinical and technology-based research groups will support each other.* The composition of the consortium also reflects active considerations regarding balanced geographic and career age distribution.

Program activities

The STorM Program will improve interactions between research groups involved in cutting-edge basic, clinical and technology research with implications for studies on the tumor microenvironment at a national level. This will be achieved by implementing the following program activities:

1. A yearly convention for all STorM Program team members, including research presentations by PhD-students and postdocs, poster sessions, and dedicated networking activities. Moreover, the meeting will include benchmarking of the Swedish research landscape within the field by invitation of internationally prominent keynote speakers. In particular, an emphasis will be placed on clinical science in order to inspire and foster new initiatives aiming for implementation of research findings for patient benefit. Another important focus for these meetings will be technology development, exposure of collaborations with non-STorM Program SciLifeLab facilities and potential initiatives towards development and implementation of novel technologies needed within the program. Apart from highlighting the SciLifeLab facilities included as full members of the STorM Program, invitations will be extended broadly to SciLifeLab facilities to participate at the yearly convention.
2. To train the next generation of cancer scientists, and to improve the exchange between participating laboratories, the STorM Program involves financial support for travel and education to enable short-term visits between team members and participation in PhD-level courses. Emphasis will be given on exchange between groups involved in different categories of research (i.e. basic science, translational science or technology development). A set of novel cross-disciplinary PhD courses will be developed.
3. Full administrative support to initiatives for applications to secure external funding for collaborative projects between the STorM program team members. Dedicated activities at the yearly retreat will be held to identify projects with high potential.

How the SciLifeLab infrastructure is critical to the RCP, and how the RCP is critical to the infrastructure

Contributions of SciLifeLab facilities to the STorM RCP

It is well recognized that present cell profiling of developmental processes and cancer is hampered by the lack of better defined cellular subsets and associated markers. Single cell RNA Seq, as provided by the *Eukaryotic Single Cell Genomics* facility, is emerging as a powerful tool for discovery of novel molecularly defined cellular subsets and recent studies from program team members (KP, AÖ, CB, CR) in productive collaborations with the facility show surprising heterogeneity even in seemingly homogenous population of cells. The identification and functional characterization of these cells in human material will be important to better understand progression of the disease.

In situ mapping of complex paracrine cell signaling requires high-content analyses using multiple specific and sensitive antibodies/probes. For this purpose, the expertise and experience of the *Cell and Tissue Profiling* facility will be critical. Emerging methodologies, such as the CODEX (Co-Detection by IndEXing) method for co-stainings with up to 50 antibodies or the SciLifeLab-derived method of multiplexed RNA in situ analyses (co-applicant MN) will also be instrumental in this context.

Interpretation and full realization of the potential of original data from multiplexed high content in situ tissue profiling will require expertise in digital image analyses. Similarly, conversion of the information into quantifiable "metrics" of biomarker potential will also be dependent on bio-image analyses. The expertise of the *BioImage Informatics* facility will thus be critical for the project, both during exploratory phases and more applied biomarker studies. Rapid developments in the fields of tissue image-analyses, including deep-learning strategies, will be critical in these efforts.

Apart from the included SciLifeLab facilities, it is envisaged that other emerging and/or existing platforms, such as *Single Cell Proteomics, Mass Cytometry, and Clinical Biomarkers,* will be important for the implementation of the SToRM Program. As stated above, active measures will be taken to include such platforms in the program activities, e.g. at the yearly meeting and through exchange programs.

Contributions of the STorM RCP to development of SciLifeLab facilities

Technology development will be a specific focus area at each yearly network meeting, to enable and stimulate inclusion of new platforms in the program and provide direct user feedback. Interactions between the *Eukaryotic Single Cell Genomics* platform and the user community in the single-cell genomics field is of the utmost importance and the RCP will provide a natural platform for discussions that will be very useful for the future development of the facility. The *Cell and Tissue Profiling facility* will benefit from the RCP through the closeness to the other single cell facilities. This RCP would enable a more rapid development of robust methods for integration of single-cell sequencing data and in situ data with spatial protein data, which would be of benefit for future users of the facility. The *BioImage Informatics Facility* continuously develops new tools for extracting information from large-scale image-based research. By participating in the STorM RCP, enough momentum will be gained to motivate improvements in method usability and subsequent bioinformatics. Efforts to apply AI and deep learning will benefit from access to clinically well- annotated material, subjected to multimodal profiling. All these developments depend on close collaborations with a broad spectrum of researchers, and a facility such as the BioImage Informatics facility relies on this type of development for delivery of high-impact technologies and long-term survival.

RCP budget

Types of costs (in kSEK)	Year 1	Year 2	Year 3
Part-time coordinator (40 %)	348,000	354,960	362,059
Meetings	300,000	300,000	300,000
Training and scientists exchange	100,000	100,000	100,00
Development of PhD-level courses	75,000	75,000	75,000
Overhead costs (21,5 %)	176,945	178,441	179,968
Totalt	999,945	1,008,401	1,017,027

Appendix K.

SciLifeLab Fellows

Contents

PM. SciLifeLab Fellows program

With the new rules regarding ”Assistant Professor” (SFS 2017:844 *Förordning om ändring i högskoleförordningen* (1993:100)) the guidelines for the SciLifeLab Fellows program (Appendix 5, Board protocol #2) are being updated. The new guidelines apply for all Assistant Professor positions (four to six years) announced at the host universities after April 1, 2018 within the SciLifeLab Fellows program.

Background

To further strengthen the environment at SciLifeLab, the four host universities recruit a number of young research leaders to SciLifeLab (so called SciLifeLab Fellows), within the framework of the so-called Strategic research funding, here called SFO-funding. These positions are appointed in international competition and provided with advantageous economical support. Contributions from the SFO-budget cease after a specific period of time (six years), after which the Fellow – if offered a permanent position after evaluation – will continue to work at his/her home department (Uppsala) or move from SciLifeLab Campus Solna to his/her home department (Stockholm). The aim is that the promoted Associate Professor will continue to be active in SciLifeLab’s scientific community.

Criteria for recruitment (SciLifeLab Fellows)

- Minimum scope and time for financing:
The position is financed with in total 3 MSEK/year for 4 years + 2 MSEK/year for 2 years for the 6-year Assistant Professor. For the 4-year Assistant Professor the position is funded with in total 3 MSEK/year for 4 years followed by 2 MSEK/year for 2 years upon promotion to Associate Professor. The position is financed from each university´s SFO-budget or other faculty funding. The funds can be used for salary, premises costs, instruments or other costs for research within the field of employment, as well as departmental and university overhead.

- Recruitment process:
The position is established as an Assistant Professorship (biträdande lektorat) spanning four to six years. The appointment is administered by each university according to standard procedures. The position should be in a research area that is in line with SciLifeLab’s profile and with the research interests of the host department. In the assessment of scientific excellence, it is recommended that particular emphasis be placed on the candidate's ability to use and develop new techniques within molecular biosciences / molecular medicine for the study of fundamental and applied topics in health and environment.

The Scientific Director of respective host university should have insight and preferably take part in the recruitment process. When candidates are interviewed, the department/university should invite the SciLifeLab Scientific Director to attend part of the program.

In connection to finalizing the contract for employment between the host department and the recruited SciLifeLab Fellow, an agreement should be signed between the department and SciLifeLab that clarifies each party’s (financial) commitment for the Fellow. The agreement is established between the SciLifeLab Head of Operations (KI, KTH, SU) or the Vice-head of Operations (UU) and the Head of Department.

- Coordinated recruitment of SciLifeLab Fellows:
All recruitments should, when possible, be advertised jointly in international media coordinated by SciLifeLab. To optimize coordination of joint advertising and research areas the time plan below should be followed.

Y1 January	Integration Director initiates discussions about new SciLifeLab Fellow recruitments at each university
Y1 March	Coordination between departments (and universities)
Y1 May	Discussion and consensus in MG+ID
Y1 June	Decision on research area for recruitment within each university-SciLifeLab committee
Y1 Sept-Oct	Announcement of positions at the universities and joint advertising coordinated by SciLifeLab
Y2	Start of new SciLifeLab Fellow

- Localization of SciLifelab Fellow:
The SciLifeLab Fellow is employed at a department at KTH, KI, SU or UU. The positions are physically located to SciLifeLab in Stockholm (Campus Solna) or to a department associated to SciLifeLab in Uppsala.

Campus Solna
The SciLifeLab Fellow is located at Campus Solna for six years. After six years the Fellow will relocate to the home department, unless the Head of Department/host university identifies strong arguments motivating the SciLifeLab Fellow to remain at Campus Solna (e.g. if the research is dependent on specialized equipment). If the host university wishes that the SciLifeLab Fellow should continue to be located at Campus Solna after the six-year period, an application should be made from the host university to the Campus Solna Committee. This should include a motivation for the continued location at Campus Solna, and clarify in what way this SciLifeLab Fellow is important for SciLifeLab´s operations.

- Career support:
The employing department and SciLifeLab should together assure that the SciLifeLab Fellow receives a suitable introduction to his/her university and to SciLifeLab. The Head of Department at the employing department provides for that the SciLifeLab Fellow will receive the career support, including teaching hours, to meet the promotion criteria.

The Head of Department at the employing department is responsible for securing that, apart from the Head of Department, a departmental contact person should be assigned to each SciLifeLab Fellow. The name of the contact person should be notified to the Scientific Director. The Scientific Director has the responsibility to be the contact person for SciLifeLab Fellows from his/her university. The contact person at the department and the Scientific Director should facilitate the establishment and integration of the SciLifeLab Fellow at the department and at SciLifeLab.

SciLifeLab Fellows

Adil Mardinoglu

KTH Royal Institute of Technology

Recruited from: Chalmers University of Technology, Sweden

Starting date: 2015

Extension date:

Possible conversion to a permanent position: Assistant professor 2018

Research interests

Mardinoglu lab at SciLifeLab develop Genome-scale metabolic models (GEMs) for human cells/tissues and employ these comprehensive models in the analysis of the omics data obtained from subjects with complex diseases including obesity, Non-alcoholic fatty liver disease (NAFLD), Type 2 diabetes (T2D) and certain types of cancer (e.g. Hepatocellular Carcinoma) This is an exciting area of biomedical research, driven by the increase of common metabolic disorders as well as recent discoveries of metabolic reprogramming in cancer.

Group members

- Cheng Zhang, Postdoc
- Rui Benfeitas, Postdoc
- Battisti Umberto Maria, Postdoc
- Chunxia Gao, Postdoc
- Woonghee Kim, Postdoc
- Leticia Monjas, Postdoc
- Xiangyu Li, Postdoc
- Muhammad Arif, PhD student
- Alen Lovric, MSc

List of key publications as SciLifeLab Fellow

Mardinoglu, A., Wu, H., Björnson, E., Zhang, C., Hakkarainen, A., Rasanen, S. M., . . . Boren, J. (2018). *An Integrated Understanding of the Rapid Metabolic Benefits of a Carbohydrate-Restricted Diet on Hepatic Steatosis in Humans. Cell Metabolism,* 27(3), 559-571.e5

Mardinoglu, A., Uhlen, M. & Boren, J. (2018). *Broad Views of Non-alcoholic Fatty Liver Disease.* CELL SYSTEMS, 6(1), 7-9

Lovric, A., Graner, M., Bjornson, E., Arif, M., Benfeitas, R., Nyman, K., . . . Boren, J. (2018). *Characterization of different fat depots in NAFLD using inflammation-associated proteome, lipidome and metabolome.* Scientific Reports, 8, Article ID 14200.

M. Uhlén, C. Zhang, S. Lee, E. Sjöstedt, L. Fagerberg, G. Bidkhori, R. Benfeitas, M. Arif, Z. Liu, F. Edfors, K. Sanli, K. von Feilitzen, P. Oksvold, E. Lundberg, S. Hober, P. Nilsson, J. Mattsson, J. M. Schwenk, H. Brunnström, B. Glimelius, T. Sjöblom, P. Edqvist, D. Djureinovic, P. Micke, C. Lindskog, A. Mardinoglu, F. Ponten. *A pathology atlas of the human cancer transcriptome.* 2017. Science

S. Lee, C. Zhang, Z. Liu, M. Klevstig, B. Mukhopadhyay, M. Bergentall, R. Cinar, M. Ståhlman, N. Sikanic, J. K. Park, S. Deshmukh, A. M. Harzandi, T. Kuijpers, M. Grøtli, S. J. Elsässer, B. D. Piening, M. Snyder, U. Smith, J. Nielsen, F. Bäckhed, G. Kunos, M. Uhlen, J. Boren, A. Mardinoglu, *Network analyses identify liver-specific targets for treating liver diseases.* 2017. Molecular Systems Biology, 13:938

Alexey Amunts

Stockholm University

Recruited from: MRC-LMB, Cambridge, UK

Starting date: 2015

Extension date:

Possible conversion to permanent position: September 2019

Research interests

Our research group investigates the fundamental question of how proteins are synthesized, folded and assembled into functional multicomponent membrane complexes that drive the cellular energy production.

Living cells ultimately depend on the conversion of energy derived from foodstuff and light into the chemical form of energy. This crucial bioenergetic step is performed in the membrane systems of mitochondria and chloroplasts. Each one of these organelle types has developed dedicated ribosomes that have diverged from the cytoplasmic counterparts. While mitoribosomes synthesize proteins involved in the oxidative phosphorylation, chlororibosomes produce components driving the pohotosynthetic reactions through pigment-protein units. To dissect the mechanism and dynamics of translation, membrane insertion and bioenergetics in organelles, we use cryo-EM.

Our group determined cryo-EM structures of the human mitoribosome with mRNA, tRNAs and translation activators in 8 different functional states, as well as its assembly intermediates. It revealed unique mechanisms of mRNA binding, tRNA translocation and assembly regulation. We also determined structures of the chlororibosome with translation factors that revealed divarication of the exit tunnel and experimental evidence for convergent evolution of ribosomes from chloroplasts and mitochondria.

These studies showed that protein synthesis machineries in organelles have adopted intricate compositions and unique tasks, adding incredible complexity to the records. The achieved understanding of the architecture of these specialized systems provides now a framework to study even more sophisticated questions regarding the assembly and evolution mechanisms of the critical bioenergetic membranes that fuel life.

Group members

- Shintaro Aibara, Postdoc
- Juni Andréll, Researcher
- Yuzuru Itoh, Postdoc
- Rasmus Kock Flygaard, Postdoc
- Alexander Muhleip, Postdoc
- Linnea Axelsson, Student
- Annemarie Perez Boerema, Student
- Vivek Singh, Student
- Victor Tobiasson, Student

Funding sources

- 2017-2021 Swedish Foundation for Strategic Research future leaders grant, €1.2M
- 2017-2022 Ragnar Söderberg Foundation fellowship in medicine, €0.8M
- 2017-2020 Swedish Research Council starting grant, €0.4M
- 2017-2019 Scilifelab computation development pilot for cryo-EM, €0.3M
- 2018-2024 Cancer Society Junior Investigator Award, €0.6M
- 2019-2021 SciLifeLab equipment upgrade for cryo-EM, €0.2M
- 2019-2021 SciLifeLab TDP, €0.25M
- 2019-2024 Wallenberg Foundation project grant, €3.1M
- 2019-2024 ERC starting grant

List of key publications as SciLifeLab Fellow

Petrov A., Wood E., Bernier C., Norris A., Brown A. and Amunts A. (2018). *Structural patching fosters divergence of mitochondrial ribosomes.* Molecular Biology and Evolution in press.

Perez Boerema A., Aibara S., Paul B., Tobiasson V., Kimanius D., Forsberg B. O., Wallden K., Lindahl E. and Amunts A. (2018). *Structure of the chloroplast ribosome with chl-RRF and hibernation-promoting factor.* Nature Plants 4, 212-217.

Singh V. and Amunts A. (2018). Application of cryo-EM for visualization of mitoribosomes. Methods in Molecular Biology in press.

Aibara S., Andrell J., Singh V. and Amunts A. (2018). *Rapid isolation of the mitoribosome from HEK cells.* Journal of visualized experiments 140.

Perez Boerema A., Aibara S., Paul B., Tobiasson V., Kimanius D., Forsberg B. O., Wallden K., Lindahl E. and Amunts A. (2018). *Structure of the chloroplast ribosome with chl-RRF and hibernation-promoting factor.* Nature Plants 4, 212-217.

Claudia Kutter

Karolinska Institutet
Recruited from: CRUK Cambridge, UK
Starting date: 16 February 2016
Extension date: 16 February 2020
Possible conversion to a permanent position: NA

Research interests

Over 200 highly specialized cells with diverse morphologies and functionalities exist in the human body, yet virtually every cell in the body contains the same genetic information. To exert cell-specific functions high fidelity mechanisms evolved to restrict the synthesis and processing of discrete sets of regulatory RNA molecules. Abnormal cell behavior as seen in many fatal human diseases, such as cancer, is often the consequence of aberrant transcripts formation.

Research in our group focuses on identifiying and characterizing the regulatory interdependencies of protein-coding and noncoding RNAs (long noncoding, transfer and small RNAs) transcriptome-wide in mammalian somatic tissues and in the germline. Our goal is to gain mechanistic insights into the transcriptional and post-transcriptional regulation and processing of RNAs during organ development, cell differentiation and disease progression.

We are particularly interested in:

- revealing the origin, evolution and disease association of ncRNAs
- deciphering the molecular mechanism underpinning regulation by ncRNAs and
- explaining ncRNA functions.

We are an integrated team of experimental and computational scientists. Our approaches include:

- applying and developing high-throughput RNA sequencing methodologies and epigenetic profiling coupled to powerful computational analysis,
- detailed biochemical assays and complementing screening methodologies and
- phenotypic characterization using CRISPR/Cas genome editing tools in cell lines and tissues.

Group members

- Laura Catharina Hinte (Master student)
- Siddharth Tomar (Research assistant)
- Dr Mikaela Behm (Postdoctoral researcher)
- Dr Jonas Søndergaard (Senior research specialist)
- Keyi Gang (PhD student)
- Ionut Atanasoai (PhD student)
- Christian Sommerauer (Erasmus student, 6 months, finish in 2018)
- Christina Savva (Intern student, finish in 2018)
- Sharmistaa Kumar (Intern student, finish in 2018)
- Siddharth Tomar (Master student, finish in 2018)
- Dr Jente Ottenburghs (Postdoctoral researcher, finish in 2018)
- Dr Jonas Søndergaard (Postdoctoral researcher, finish in 2018)

Funding sources

- KI KID funding 2018-00947 (co-applicant)
- KI KID funding 2018-00904
- VR international postdoctoral grant 2017-06173
- Chinese Research Council
- Ruth & Richard Julin foundation 2018-00328
- KI KID funding 2016-00189
- Wallenberg academy fellow KAW 2016.0174
- SciLifeLab fellow research program
- Ruth & Richard Julin foundation 2017-00358
- SciLifeLab summer fellow support

Conference:

- Wenner Gren ESh2018-0019; SciLifeLab (co-applicant); Vetenskapradet 2018-06577; Wenner Gren ESh2018-0014 (co-applicant); Vetenskapradet 2018-00767 (co-applicant); EMBO w18/54 (co-applicant); Marcus Wallenberg foundation; SciLifeLab; Wenner Gren ESh2017-0017 (co-applicant); Vetenskapradet 2017-06253 (co-applicant)

Equipment:

- SciLifeLab, Sweden (joint application)

Travel & Poster awards

- Karolinska Institute 2018-02821; Several poster/presentation prices

List of key publications as SciLifeLab Fellow

†correspoding authorship

Kutter C.†, Jern P. and Suh A. *"Bridging gaps in transposable element research with single molecules and single cells"* Mobile DNA (2018), 9:34

Ernst C., Odom D.T. and Kutter C†. *"The emergence of piRNAs against transposon invasion to preserve mammalian genome integrity"* Nature Communications (2017) 8(1), 1411

Ernst C., Pike J., Aitken S.J., Long H.K., Eling N., Stojic L., Connor F., Rayner T.F., Lukk M., Klose R.J., Kutter C. and Odom D.T. *"Successful transmission and transcriptional deployment of a human chromosome via mouse male meiosis"* eLife (2016) 5:e20235

Rudolph K.L.M., Schmitt B.M., Viller D., White R.J., Marioni J.C.†, Kutter C.† and Odom D.T.† *"Codon-driven translational efficiency is stable across diverse mammalian cell states"*. PLoS Genetics (2016) 12 (5), e1006024

Daniel Globisch

Uppsala University

Recruited from: The Scripps Research Institute, USA

Starting date: September 2015

Extension date: April 2018 (year 5 and 6 with SciLifeLabs help)

Possible conversion to a permanent position: None. I am the only fellow that have been hired on a non-tenure track position (Swedish: Forskarassistent), which was not obvious when accepting the position.

Research interests

The Globisch lab is an international research group with focus on the development of new Chemical Biology-based methodologies to improve the analysis of small molecule metabolites in biological samples. These new methodologies are aimed at enhancing the scope of metabolomics-based research. In our multidisciplinary research we work at the interface of Chemistry and Biology with a combination of Organic Chemistry, Chemical Biology techniques, Biochemistry, mass spectrometric analysis of metabolites, and metabolomics. The discovery of specific early-stage biomarkers, new drug targets and the development of new therapeutic interventions are crucial for disease prevention and management towards personalized medicine.

Biomarker Discovery is a challenging and multidisciplinary task. We develop new tools for mass spectrometric analysis and are focussed on elucidating microbiota metabolism in the human host. We investigate any human sample type, e.g. fecal, urine, and plasma samples from pancreatic cancer patients.

Group members

- Daniel Globisch, Associate Professor
- Mário Correia, PhD student
- Caroline Ballet, postdoctoral researcher
- Louis Conway, postdoctoral researcher
- Abhishek Jain, postdoctoral researcher
- Weifeng Lin, Master's student
- Mia Elfström, internship student
- Clara Hild, Erasmus+ exchange student
- Samantha Sasse, Erasmus+ exchange student
- Spyke Schumacher, internship student

Funding

- SciLifeLab Starting Grant
- Vetenskapsrådet (Swedish Research Council)
- Carl Tryggers Foundation
- Grant for a postdoctoral fellow from SciLifeLab (UU)

List of key publications as SciLifeLab Fellow

N. Garg+, L. P. Conway+, C. Ballet, M. S. P. Correia, F. K. S. Olsson, M. Vujasinovic, J.-M. Löhr, D. Globisch* Angew. Chem. Int. Ed. 2018, 57, 13805 –13809. *"Chemoselective Probe Harboring a Unique Bioorthogonal Cleavage Site for Investigation of Gut Microbiota Metabolism"*

C. Ballet+, M. S. P. Correia+, L. P. Conway, T. L. Locher, L. C. Lehmann, N. Garg, M. Vujasinovic, S. Deindl, J.-M. Löhr, D. Globisch* Chem. Sci. 2018, 9, 6233–6239. *"New enzymatic and mass spectrometric methodology for the selective investigation of gut microbiota-derived metabolites"*. Featured in the 2018 Chemical Science HOT Article Collection

N. Garg, A. Hansson, H. K. Knych, S. D. Stanley, M. Thevis, U. Bondesson, M. Hedeland, D. Globisch* Org. Biomol. Chem. 2018, 16, 698-702. *"Structural elucidation of major selective androgen receptor modulator (SARM) metabolites for doping control"*.

Erika Comasco

Uppsala University

Recruited from: Uppsala University

Starting date: December 2017

Extension date:

Possible conversion to a permanent position:

Research interests

Focusing on psychoneurobiology, activities of the group include:

- Research on the molecular underpinnings of gonadal hormones´influence on women's behaviour and mental health; by employing genetic, endocrine, pharmacological, neurophysiological and neuroimaging measures, we aim to characterize diagnosis- and treatment-related biomarkers of sex-specific disorders.
- Research on the effects of early-life stress and alcohol exposure on brain and behaviour; (epi)gene-environment interactions are investigated in rodents as well as human population-based samples, with special focus on adolescence, to identify biomarkers of vulnerability to alcohol use and misuse.

Group members

- Erika Comasco, Associate professor
- Manon Dubol, postdoc
- Julia Breedh, PhD student
- Maria Vrettou, PhD student

Funding sources

- SciLifeLab,
- Swedish Society of Medicine,
- Alcohol Research Council of the Swedish Alcohol Retailing Monopoly,
- European Union,
- Swedish Research Council

List of key publications as SciLifeLab Fellow

Evidence for a Link Between Fkbp5/FKBP5, Early Life Social Relations and Alcohol Drinking in Young Adult Rats and Humans. Nylander I, Todkar A, Granholm L, Vrettou M, Bendre M, Boon W, Andershed H, Tuvblad C, Nilsson KW, Comasco E. Molecular Neurobiology. 2017 Oct;54(8):6225-6234.

Fabien Burki

Uppsala University

Recruited from: University of British Columbia

Starting date: 01 March 2016

Extension date: submitting application for promotion to Associate Professor

Possible conversion to a permanent position: 2020 (this has been planned internally in my department)

Research interests

We aim to integrate the poorly studied protists (i.e. microbial eukaryotes) in global evolutionary models. Protists have dominated eukaryotic life since the origin of complex cellular structures, but very few species are in culture and so they have mostly remained enigmatic. As a result, we only have a very partial view of the broad eukaryotic diversity, which prevents us to derive an accurate picture of the origin and evolution of the cells that ultimately resulted in the diversity we can observe today. In my group, we explore the microbial dark matter to bridge gaps in our understanding of the deep eukaryote evolution. Our main questions relate to some of the most transformative lifestyle transitions in the evolution of complex life, such as the origin and spread of plastids or transition to parasitism. All of these lifestyle transitions have occurred repeatedly across the tree, but because we are missing key evolutionary lineages our understanding is patchy.

We use a combination of novel culture-independent genomics, transcriptomics, environmental DNA (eDNA) approaches but also more traditional protistology to identify unknown or orphan groups that represent missing evolutionary links. We attack the problem of partial sampling from two highly complementary angles: 1) phylogenomics, a gene-rich but taxon-limited method that allows to reconstruct the deep nodes in the tree of eukaryotes; 2) long-amplicon metabarcoding, a gene-poor but taxon-rich new method we are developing to phylogenetically and taxonomically resolve eDNA samples. Together, we hope that these approaches will produce a much more accurate representation of eukaryote evolution so that we can better reconstruct the history of life and the ancestral characteristics of the major eukaryotic groups.

Group members

- Fabien Burki (PI)
- Mahwash Jamy (PhD student)
- Anders Alfjorden (PhD student)
- Vasily Zlatogursky (postdoc)
- Ioana Brännström (postdoc)

Funding

- SciLifeLab Postdoc fellowship
- VR research project grant
- FORMAS Future research leaders
- Carl Tryggers Stiftelse
- Wenner-Gren Stiftelse
- Uppsala University Start-up

List of key publications as SciLifeLab Fellow

Bass D, Ward GM, Burki F. 2019. *Ascetosporea.* Curr. Biol. In press

Whelan S, Irisarri I, Burki F. 2018. *PREQUAL: detecting non-homologous characters in sets of unaligned homologous sequences.* Bioinformatics. 34(22):3929-3930.

Strassert JFH, Jamy M, Mylnikov AP, Tikhonenkov DV, Burki F. 2018. *New phylogenomic analysis of the enigmatic phylum Telonemia further resolves the eukaryote tree of life.* bioRxiv.

Janouškovec J, Tikhonenkov DV, Burki F, Howe AT, Rohwer FL, Mylnikov AP, Keeling PJ. 2017. *A new Lineage of Eukaryotes Illuminates Eraly Mitochondrial Genome Reduction.* Curr. Biol. 27(23):3717-3724.

Burki F. 2017. *The Convoluted Evolution of Eukaryotes with Complex Plastids.* Advances in Botanical Research. 84:1-30.

Ilaria Testa

KTH Royal Institute of Technology

Recruited from: Max Planck Institute for Biophysical Chemistry, Germany

Starting date: April 2015

Extension date: 4 years full funding + 4 years extension with less funding (KTH fellow)

Possible conversion to a permanent position: Since November 1st 2018 I'm tenure at KTH, Applied Physics

Research interests

My research group works at the interface of physics, chemistry and neuroscience on the development and application of cutting-edge imaging technology.

Fluorescence microscopes, and especially their confocal and two-photon variants, are unique in their ability to observe directly morphological changes and molecular reactions in living cells. However, they are limited in resolution by the diffraction barrier (about 200-300 nm). This limitation is overcome with great success by the field of super-resolution microscopy.

In our lab we develop novel paradigms and concepts based on super-resolution light microscopy or fluorescence nanoscopy suitable for live cell imaging with the overarching goal of addressing contemporary challenges in biophysics and molecular biology. We continuously push the spatial and temporal resolution of novel nanoscopes with the use of new molecular switchers combined to custom designed illumination schemes. This way, our technology allows the precise identification of populations of biomolecules depending on their localization, abundance and dynamics inside their native environment with a spatial accuracy far beyond the diffraction limit of light (30-70 nm).

A special effort is dedicated to investigate the localization and function of neuronal proteins, especially in synapses, where trafficking organelles and protein complexes due to the crowding call for high resolution imaging in space and time.

Group members

- Ilaria Testa, Associate Professor (Physics, Microscopy)
- Giovanna Coceano, Postdoc (Biotechnology)
- Francesca Pennacchietti, Postdoc (Biophysics)
- Elham Jalalvand, Postdoc (Neuroscience)
- Lea Rems, Shared-Postdoc (Computational Neuroscience)
- Jonatan Alvelid, PhD student (Engineering Physics)
- Andreas Boden, PhD student (Biomedical Engineering)
- Martina Damenti, PhD student (Neuroscience)
- Xavier Casas Moreno, PhD student (Optics-Image processing)

Funding sources

- ERC starting grant MoNaLISA (2015-2020)
- SFO SciLife basic funding (2015-2019 + 4 years)
- VR starting grant (2017-2021)
- SSF future group leader grant (2017-2022)
- GGS prize 2016

List of key publications as SciLifeLab Fellow

Luciano A. Masullo*, Andreas Bodén*, Francesca Pennacchietti*, Giovanna Coceano, Michael Ratz and Ilaria Testa. *Enhanced photon collection enables four dimensional fluorescence nanoscopy of living systems.* NATURE COMMUNICATIONS. 2018

Cáceres Bojanala, Kelley L, Dreier J, Manzi J, Di Federico F, Chi Q, Risler T, Testa I, Sherwood DR, Plastino J. *Forces drive basement membrane invasion in Caenorhabditis elegans.* PNAS. 2018

Francesca Pennacchietti*, Ekaterina O. Serebrovskaya*, Aline R. Faro*, Irina I. Shemyakina*, Nina G. Bozhanova, Alexey A. Kotlobay, Nadya G. Gurskaya, Andreas BodŽn, Jes Dreier, Dmitry M. Chudakov, Konstantin A. Lukyanov, Vladislav V. Verkhusha, Alexander S. Mishin and Ilaria Testa. *Fast reversibly photoswitching red fluorescent proteins for live-cell RESOLFT nanoscopy.* NATURE METHODS. 2018

Katharina N Richter, ..., Giovanna Coceano, ..., Ilaria Testa et al. *Glyoxal as an alternative fixative to formaldehyde in immunostaining and super-resolution microscopy.* EMBO JOURNAL. 2017

Emmanuel Terriac, Giovanna Coceano, Zahra Mavajian, Tijmen A. G. Hageman, Andreas F. Christ, Ilaria Testa, Franziska Lautenschläger and Annica K. B. *Gad Vimentin Levels and Serine 71 Phosphorylation in the Control of Cell-Matrix Adhesions, Migration Speed, and Shape of Transformed Human Fibroblasts.* CELLS. 2017

Jens Carlsson

Uppsala University

Recruited from: Stockholm University

Starting date: 2015-06-30

Extension date: 2019-07-01

Possible conversion to a permanent position: Application for promotion submitted in Dec 2018

Research interests

The goal of my research group is to improve atomic-level understanding of protein-ligand interactions using computer models. We mainly focus our efforts on G protein-coupled receptors (GPCRs), which are involved in essential physiological processes and the targets of numerous therapeutic drugs. Using physics-based models, we model on how small molecules interact with GPCRs and thereby modulate their function with the goal to develop novel strategies for drug development.

The aims of my ongoing research are to design GPCR ligands with tailored signaling and selectivity profiles as well as to demonstrate that structure-based virtual screening can identify modulators of challenging drug targets and novel (allosteric) binding sites. To accomplish these goals, we develop strategies for structure-based virtual screening using a combination of cheminformatics, structure prediction, molecular docking, and molecular dynamics simulations. All our projects are driven by predictions based on computer models, which are evaluated experimentally in our own laboratory or in collaboration with international research groups.

Our projects are funded by grants from the European and Swedish research councils. We are part of the Dept. of Cell and Molecular Biology and SciLifeLab at Uppsala university.

Group members

- Jens Carlsson, PI
- Mariama Jaiteh (Phd student)
- Pierre Matricon (Phd student)
- Stefanie Kampen (Phd student)
- Andreas Luttens (Phd student)
- Axel Rudling (PhD completed)
- Anirudh Ranganathan (PhD completed)
- Jon Kapla (Postdoc)
- Nicolas Panel (Postdoc)
- Flavio Ballante (Postdoc)
- Duy Duc Vo (Postdoc)
- Wilber Romeo-Fernandez (Postdoc)
- Alexey Zeifman (Postdoc now at RBV capital, Russia)
- David Rodriguez (Postdoc now at Lundbeck, Denmark)

Funding

- Swedish research council (starting grant and project grant)
- European research council (starting grant)
- Swedish foundation for strategic research
- Science for life laboratory (SciLifeLab fellows)
- Åke Wiberg foundation
- Göran Gustafsson foundation

List of key publications as SciLifeLab Fellow

Kennedy J.A., Ballante F., Johansson J.R., Milligan G., Linda Sundström L., Nordqvist A, and Carlsson J. (2018) *Structural characterization of agonist binding to protease-activated receptor 2 through mutagenesis and computational modelling.* ACS Pharmacol Transl Sci 1, 119-133.

Jaiteh M., Zeifman A., Saarinen M., Svenningsson P., Brea J.M., Loza M.I., and Carlsson J. (2018) *Docking screens for dual inhibitors of disparate drug targets for Parkinson's disease.* J Med Chem 61, 5269-5278.

Rudling A., Gustafsson R., Almlöf I., Homan E., Scobie M., Warpman Berglund U., Helleday T., Stenmark P., and Carlsson J. (2017) F*ragment-based discovery and optimization of enzyme inhibitors by docking of commercial chemical space.* J Med Chem 60, 8160-8169.

Petersen J., Wright S.C., Rodríguez D., Matricon P., Lahav N., Vromen A., Friedler A., Strömqvist J., Wennmalm S., Carlsson J., and Schulte G. (2017) Agonist-induced dimer dissociation as a macromolecular step in G protein-coupled receptor signaling. Nat Comm 8, 226.

Matricon P., Ranganathan A., Warnick E., Gao Z.G., Rudling A., Lambertucci C., Marucci G., Ezzati A., Jaiteh M., Dal Ben D., Jacobson K.A., and Carlsson J. (2017) F*ragment optimization for GPCRs by molecular dynamics free energy calculations: Probing druggable subpockets of the A2A adenosine receptor binding site.* Sci Rep 7, 6398.

Kristina Jonas

Stockholm University

Recruited from recruited from: LOEWE-Zentrum für Synthetische Mikrobiologie, Germany

Starting date: 2016

Extension date: currently on maternal leave

Possible conversion to a permanent position: NA

Research interests

Our lab investigates the mechanisms by which bacteria control their own growth and reproduction. In particular, we want to understand how bacteria dynamically adjust their growth rate and mode of proliferation in response to fluctuating external conditions, for example changes in nutrient availability or at the onset of environmental stress, to ensure their survival. To this end, we study the regulatory circuits governing bacterial cell cycle progression and how these circuits cross-talk with stress response pathways to allow the integration of environmental information into the cell cycle. For our studies, we use a multi-disciplinary approach combining classical genetics, cell biology and biochemistry with modern live-cell imaging and high-throughput techniques. As our primary model organism we utilize the fresh water bacterium Caulobacter crescentus, which divides asymmetrically and has well-defined cell cycle phases. In addition, we do some of our work in Escherichia coli and Salmonella enterica to study how the C. crescentus cell cycle circuit relates to the one of other bacteria, and to investigate how precise regulation of cell cycle progression contributes to bacterial persistence and pathogenesis.

Group members

- David Leslie, PhD student
- Kristina Heinrich, PhD student
- Frederic Schramm, PhD student
- Kristen Schroeder, PhD student

List of key publications as SciLifeLab Fellow

Schramm F.D., Schroeder K., Alvelid J., Testa I. and Jonas K. *Growth-driven displacement of protein aggregates along the cell length ensures partitioning to both daughter cells in Caulobacter crescentus.* 2018. bioRxiv (pre-print)

Felletti M., Omnus D.J. and Jonas K. *Regulation of the replication initiator DnaA in Caulobacter crescentus.* 2018. Biochimica et Biophysica Acta (BBA) Gene Regulatory Mechanisms

Schramm F.D., Heinrich K., Thüring M., Bernhardt J. and Jonas K. *An essential regulatory function of the DnaK chaperone dictates the decision between proliferation and maintenance in Caulobacter crescentus.* 2017. PLOS GENETICS

Liu, J; Francis, LI; Jonas, K; Laub, MT; Chien, P. *ClpAP is an auxiliary protease for DnaA degradation in Caulobacter crescentus.* 2017. MOLECULAR MICROBIOLOGY

Lucie Delemotte

KTH Royal Institute of Technology

Recruited from: recruited from EPFL, Lausanne, Switzerland

Starting date: 15 Feb 2016

Extension date: SFO funding until 2023

Possible conversion to a permanent position: Applying for associate professor Jan 2019, position opened by SCI school. Docent title awarded by KTH Nov 2018.

Research interests

The cellular membrane acts as a barrier to isolate the cell's inside from the outside world. To communicate with its environment, the cell uses membrane proteins that facilitate the transport and permeation of otherwise impermeant species. Dysfunction of these proteins lead to diseases such as epilepsy, heart arrhythmias or paralysis. These proteins are also privileged drug targets since they are accessible from the outside of the cell.

Recent developments in structural biology have provided us with static structures of these exquisite molecular machines, yielding the first insights into how these proteins may perform their function. We provide further insight into their function and regulation by their environment by using molecular dynamics simulations, which we run-on high-performance computers afforded by the Swedish National Infrastructure for Computing. This allows not only to understand the complex interplay between the ion channel and its environment, particularly components of the cell membrane but also to delve into the details of how these molecular machines harness energy and perform their role at the atomistic level.

We collaborate with groups all over the world to tackle questions of biomedical relevance in a collaborative fashion. For example, we investigate the fundamental aspects of heart channel activation with electrophysiologists from the University of Wisconsin, Madison; we understand and design novel drugs to treat epilepsy with researchers from the University of Linköping or else, we gain access to the molecular level details of G-Protein coupled receptor activation with computational chemists from the University of Uppsala.

Group members

- Lucie Delemotte (PI, Assistant Professor)
- Marina Kasimova (Postdoc)
- Lea Rems (Researcher)
- Oliver Fleetwood (PhD student)
- Annie Westerlund (PhD student)
- Sarah McComas (PhD student)
- Immanuel Sanka, (Ms)
- Panagiotis Apostolakis, (Ms)
- Alma Andersson, (Ms)
- Christin Friberg, (Bs)
- Xueqing Wang, (Ms)

Funding

- SFO Start-up
- Gustafsson prize for technical physics
- VR starting grant
- KTH postdoc grant
- Swedish National Infrastructure for Computing (CPU time)
- Pittsburgh Supercomputing Center (PSC) (CPU time)

List of key publications as SciLifeLab Fellow

MA Kasimova, E Lindahl, L Delemotte *"Determining the molecular basis of voltage sensitivity in membrane proteins"* The Journal of general physiology, 2018, 150 (10), 1444-1458

AM Westerlund, L Delemotte *"Effect of Ca2+ on the promiscuous target-protein binding of calmodulin"* PLoS computational biology, 2018, 14 (4), e1006072

AI Fernández-Mariño, TJ Harpole, K Oelstrom, L Delemotte, B Chanda *"Gating interaction maps reveal a noncanonical electromechanical coupling mode in the Shaker K+ channel"* Nature structural & molecular biology, 2018, 25 (4), 320

TJ Harpole, L Delemotte *"Conformational landscapes of membrane proteins delineated by enhanced sampling molecular dynamics simulations"* Biochimica et Biophysica Acta (BBA)-Biomembranes, 2018, 1860 (4), 909-926

AM Westerlund, TJ Harpole, C Blau, L Delemotte *"Inference of Calmodulin's Ca2+-Dependent Free Energy Landscapes via Gaussian Mixture Model Validation"* Journal of chemical theory and computation, 2017, 14 (1), 63-71

Magda Bienko

Karolinska Institute

Recruited from: Massachusetts Institute of Technology, USA

Starting date: 2015-01-01

Extension date: 2019-12-31

Possible conversion to a permanent position: On November 9th I was awarded a Senior Researcher funding as a 2-year extension of my current position. However, to be able to receive these funds I need to be hired on a permanent position, for which I am currently applying

Research interests

Our research group focuses on understanding the fundamental principles that govern how the three-dimensional architecture of the human genome is established and maintained. To this end, we apply single-molecule DNA and RNA fluorescence in situ hybridization (FISH) techniques to visualize the position and structure of DNA loci and chromosomes, together with the expression of selected genes, at high resolution in thousands of individual cells. In parallel, we develop new methods based on next-generation sequencing, that allow us to measure the radial position of DNA loci genome-wide. We combine state-of-the-art cell culture techniques with genetic and chemical manipulation of genome structure and function, and then apply our methods to probe for structural and functional changes that occur genome-wide or at selected loci.

In the past four years, we have established a powerful platform—iFISH—that enables us to produce hundreds of oligonucleotide probes for DNA and RNA FISH at affordable cost, in a short time. We are now using iFISH to label all human chromosomes with DNA FISH probes evenly spaced every one megabase (Mb), and then build an atlas of chromosome structures and arrangements in different cell types and tissues. In parallel, we have developed a method for Genomic loci Positioning by Sequencing—GPSeq—that allows us to measure, genome-wide, the radial position that a DNA locus occupies in the nucleus, with respect to the nuclear periphery/center. We are now applying GPSeq to find out whether different cell types harbor different radial genome configurations, as well as to learn how chromosomal territories form and arrange themselves in the nucleus, at the end of each mitosis.

Group members

- Magda Bienko, PhD, Principal Investigator
- Silvano Garnerone, senior scientist
- Lei Xu, senior scientist
- Federico Agostini, postdoc
- Joaquin Custodio, postdoc
- Erik Wernersson, postdoc
- Eleni Gelali, PhD student
- Gabriele Girelli, PhD student
- Tomasz Kallas, PhD student
- Ana Mota, PhD student

Funding

- Science for Life Laboratory
- Karolinska Institute
- Human Frontier Science Program (HFSP)
- European Research Council (ERC)
- Swedish Research Council (VR)
- Ragnar Söderberg Foundation

List of key publications as SciLifeLab Fellow

CUTseq enables integrated imaging and multi-region sequencing of individual tissue sections. Xiaolu Zhang, Silvano Garnerone, Marcin Nicoś, Caterina Marchio, Michele Simonetti, Tiziana Venesio, Anna Sapino, Johan Hartman, Magda Bienko*, Nicola Crosetto*.in review for Nature Communications

iFISH is a free resource for large-scale parallelized design and production of DNA FISH probes. Eleni Gelali, Xinge Li, Gabriele Girelli, Masahiro Matsumoto, Erik Wernersson, Joaquin Custodio, Ana Mota, Maud Schweitzer, Katalin Ferenc, John P. Schell, Fredrik Lanner, Nicola Crosetto*, Magda Bienko*. in revision for Nature Communications

RollFISH achieves robust quantification of single-molecule RNA biomarkers in paraffin-embedded tumor tissue samples. Wu C, Simonetti M, Rossell C, Mignardi M, Mirzazadeh R, Annaratone L, Marchiò C, Sapino A, Bienko M, Crosetto N, Nilsson M. Commun Biol. 2018 Nov 28

An Application-Directed, Versatile DNA FISH Platform for Research and Diagnostics. Gelali E, Custodio J, Girelli G, Wernersson E, Crosetto N, Bienko M. Methods Mol Biol. 2018

Genome-Wide Profiling of DNA Double-Strand Breaks by the BLESS and BLISS Methods. Mirzazadeh R, Kallas T, Bienko M, Crosetto N. Methods Mol Biol. 2018

Marc Friedländer

Stockholm University

Recruited from: Centre for Genomic Regulation (CRG), Spain

Starting date: July 2014

Extension date:

Possible conversion to a permanent position: In August 2018 I was promoted to tenured associate professor at my host department at Stockholm University.

Research interests

The Friedländer group applies state-of-the-art computational and genomic methods to address fundamental questions in RNA biology. The focus is on quantitatively describing and functionally characterizing mammalian transcriptomes, and methods include next-generation sequencing of single and pooled cells, as well as development of source code and custom wet-lab protocols.

Of particular interest to us are microRNAs: 22 nucleotide RNAs that can regulate the expression of protein-coding genes. Since they confer regulation on the majority of human genes, it is not surprising that microRNAs are involved in numerous biological processes, including cardiovascular, immunological, neurodegenerative, and psychiatric diseases and cancer. Even though miRNAs have been systematically studied for more than ten years, fundamental questions regarding their biogenesis and function remain unanswered.

We study microRNA function by profiling these regulators and their gene targets in the single cells where the interactions between them occur. From the measurements we infer copy-per-cell numbers for the transcripts, and we develop mathematical models to describe the kinetics of regulation. For this purpose, we apply single-cell sequencing methods and single-molecule FISH. To study microRNA biogenesis, we have developed a method to measure processing of thousands of RNA structures simultaneously in mammalian cells.

Among our collaborators are Rory Johnson (University of Bern), Claudia Kutter, Vicent Pelechano, Rickard Sandberg, Magda Bienko, Nicola Crosetto (KI) and the SciLifeLab Eukaryotic Single Cell Genomics facility. Our research is funded by SFO, by Vetenskapsrådet and an ERC starting grant.

Group members

- Marc Friedländer (group leader)
- Inna Biryukova (wet-lab manager)
- Bastian Fromm (senior scientist)
- Morteza Aslanzadeh (PhD student)
- Wenjing Kang (PhD student)
- Vaishnovi Sekar (PhD student)
- Marcel Tarbier (PhD student)

Funding

- SFO Start-up
- Gustafsson prize for technical physics
- VR starting grant
- KTH postdoc grant
- Swedish National Infrastructure for Computing (CPU time)
- Pittsburgh Supercomputing Center (PSC) (CPU time)

List of key publications as SciLifeLab Fellow

Kang W; Eldfjell Y; Fromm B; Estivill X; Biryukova I; Friedländer MR†, 2018. *miRTrace reveals the organismal origins of microRNA sequencing data.* Genome Biology 19(1):213

Bonath F; Domingo-Prim J; Tarbier M; Friedländer MR†; Visa N†, 2018. *Next-generation sequencing reveals two populations of damage-induced small RNAs at endogenous DNA double-strand breaks.* Nucleic Acids Research.

Kang W; Bang-Berthelsen CH; Holm A; Houben AJ; Müller AH; Thymann T; Pociot F; Estivill X; Friedländer MR†, 2017. *Survey of 800+ data sets from human tissue and body fluid reveals xenomiRs are likely artifacts.* RNA 23(4):433-445

Mikael Sellin

Uppsala University

Recruited from: ETH Zürich, Institute of Microbiology, Switzerland

Starting date: 2016-12-01 Associate Senior Lecturer (Tenure Track)

Extension date:

Possible conversion to a permanent position: Evaluation for extension: by 2020-11-31

Research interests

Gut infections constitute a leading cause of morbidity worldwide. Pathogenic enterobacteria, e.g. Salmonella, Escherichia, and Shigella species, account for more than half a billion disease cases each year. These bacteria can bind to and/or invade the epithelium of the intestinal mucosa, thereby eliciting gut inflammation. Antibiotic treatment has proven inefficient at clearing gut bacterial infections and may in some cases even increase bacterial shedding from an infected individual. Moreover, the heavy use of antibiotics in healthcare and agriculture has led to fast spread of resistance mechanisms among clinical isolates. Hence, there are both curiosity-driven and societal incentives to better understand the mechanisms driving gut bacterial disease.

Bacterium - host cell interplay has traditionally been studied in simplified cell culture settings. Such experiments have uncovered a wealth of potential biochemical interactions between microbe and host cell. However, to understand the underpinnings of a "real" gut infection, additional approaches are needed that more faithfully recapitulate the properties of the intact gut mucosa. The Sellin lab employs state-of-the-art organoid culture, combined with bacterial genetics and high-resolution live imaging, to study the mechanisms driving gut bacterial disease. We focus on clinically relevant enterobacteria, particularly Salmonella and Shigella species. The ambition is that our work will uncover the physiologically relevant mechanisms used by these pathogens to invade the intestinal mucosa and trigger gut inflammation.

Group members

- Maria Letizia Di Martino – Researcher
- Jens Eriksson – Researcher
- Pilar Samperio Ventayol – Post-doctoral fellow
- Stefan Fattinger – PhD student
- Viktor Ek – PhD student
- Petra Geiser – PhD student
- Eva Skovajsova – Project assistant
- Labolina Spång – MSc student

Funding

- SciLifeLab
- Swedish Research Council
- Swedish Foundation for Strategical Research
- Knut och Alice Wallenberg Foundation
- Malin och Lennart Philipson Foundation
- Carl Trygger Foundation

List of key publications as SciLifeLab Fellow

Westermann AJ, Venturini E, Sellin ME, Förstner KU, Hardt WD, Vogel J. T*he Major RNA-Binding Protein ProQ Impacts Virulence Gene Expression in Salmonella enterica Serovar Typhimurium.* MBio. 2019 Jan 2;10(1). pii: e02504-18.

Sellin ME, Müller AA, Hardt WD. *Consequences of Epithelial Inflammasome Activation by Bacterial Pathogens.* J Mol Biol. 2018 Jan 19;430(2):193-206.

Moor K, Diard M, Sellin ME, Felmy B, Wotzka SY, Toska A, Bakkeren E, Arnoldini M, Bansept F, Co AD, Völler T, Minola A, Fernandez-Rodriguez B, Agatic G, Barbieri S, Piccoli L, Casiraghi C, Corti D, Lanzavecchia A, Regoes RR, Loverdo C, Stocker R, Brumley DR, Hardt WD, Slack E. *High-avidity IgA protects the intestine by enchaining growing bacteria.* Nature. 2017 Apr 27;544(7651):498-502.

Diard M, Bakkeren E, Cornuault JK, Moor K, Hausmann A, Sellin ME, Loverdo C, Aertsen A, Ackermann M, De Paepe M, Slack E, Hardt WD. *Inflammation boosts bacteriophage transfer between Salmonella spp.* Science. 2017 Mar 17;355(6330)

Dolowschiak T, Mueller AA, Pisan LJ, Feigelman R, Felmy B, Sellin ME, Namineni S, Nguyen BD, Wotzka SY, Heikenwalder M, von Mering C, Mueller C, Hardt WD. *IFN-γ Hinders Recovery from Mucosal Inflammation during Antibiotic Therapy for Salmonella Gut Infection.* Cell Host Microbe. 2016 Aug 10;20(2):238-49.

Olof Eriksson

Uppsala University

Recruited from: Uppsala University

Starting date: 2018-08-01

Extension date: N/A'

Possible conversion to a permanent position: 2022

Research interests

I'm applying state-of-the-art molecular imaging techniques, e.g. Positron Emission Tomography (PET), for advancement of our understanding and management of different pathologies, in particular metabolic disease and cancer.

My current main research interests are:

- non-invasive imaging methodologies for assessment of beta cell-mass in diabetes,
- imaging markers for activated T-cells, for use in immuno-oncology and in the many diseases where inflammation is an important feature,
- assisting drug development, by design of novel imaging based endpoints (e.g. in vivo mode of action, drug biodistribution),
- translational research, i.e. bringing radiopharmaceuticals from design and radiolabeling, via preclinical evaluation, to clinical proof-of-concept.

Group members

- Olof Eriksson, Assistant Professor
- Recruitments PhDs and postdocs ongoing (December 2018)

Funding

- SciLifeLab,
- Göran Gustafssons stiftelse,
- JDRF,
- EFSD,
- Diabetesfonden,
- Barndiabetesfonden,
- ExoDiab,
- Diabetes Wellness etc.

List of key publications as SciLifeLab Fellow

Just started as SciLifeLab Fellow

Oskar Karlsson

Stockholm University

Recruited from: Uppsala University

Starting date: 2018-05-01 on a tenure track position

Extension date:

Possible conversion to a permanent position: possible promotion after four years.

Research interests

Increasing societal dependence on manmade chemicals and lack of knowledge about their potential adverse effects is a major threat to wildlife and human health. Evidence show that exposure to air pollution or the over 100,000 chemicals that contaminate our environment are main risk factors for many chronic diseases. Understanding what environmental contaminants we are exposed to, their properties and the interactions with biological systems are therefore essential.

There has been a rapidly increasing interest in whether environmental factors modulate the establishment and maintenance of epigenetic modifications, and thereby affect gene expression and phenotype in humans and wildlife. We aim to combine experimental model systems, omics tools and molecular epidemiological research to study Gene-Environment interactions and epigenetic basis of disease. In particular, our research focuses on developmental origins of health and disease with an emphasis on the exposome and underlying molecular mechanisms. The projects concern the effects of environmental exposures such as endocrine disrupting chemicals, flame retardants, pesticides, metals, particulate air pollution, temperature changes, as well as drugs, psycho-social stressors and ethnical disparities. Ongoing efforts include studies of paternal epigenetic inheritance.

Group members

- Paula Pierozan, Postdoc
- Daiane Cattani, Postdoc
- Liselott Källsten, PhD student
- Eleftheria Theodoropoulou, PhD student
- Radwa Almamoun, PhD student

Funding

- Formas, A non-toxic environment, 12 MSEK, 2019-2022
- Formas, A non-toxic environment, 12 MSEK, 2019-2022 (Co-PI)
- VR, Sustainability and resilience, 5.6 MSEK, 2019-2021
- ERC Starting Grant, 15 MSEK, 2018-2022
- SciLifeLab Fellow Start-up Package, ACES, Stockholm University
- VR, Starting Grant, 3.1 MSEK, 2018-2021
- Formas, Future Research Leaders, 3 MSEK, 2018-2020
- Formas, Mobility Starting Grant, 3.42 MSEK, 2013-2017

List of key publications as SciLifeLab Fellow

Just started as SciLifeLab Fellow

Paul Hudson

KTH Royal Institute of Technology
Recruited from: U.C Berkeley, US
Starting date: June 2014
Extension date: May 2018
Possible conversion to a permanent position: Became lector May 2018

Research interests

We are pursuing applied and fundamental research into the metabolism of autotrophic (CO2-fixing) bacteria. Most of our expertise is on photosynthetic cyanobacteria though we are also exploring lithoautotrophic, H2-consuming bacteria. We aim to engineer new strains that can efficiently convert CO2 to chemicals, in particular biofuels. This often involves significant modifications to the native metabolism. One area of research is to quantify the energy investments of the autotrophic cell under different conditions, such as its metabolome, proteome, and translatome. A second arm is to use this information to guide metabolic engineering. For example, we can design and insert new metabolic pathways to biofuel that are better matched with the host metabolism. Our lab uses genome-scale modeling, systems biology, CRISPR/Cas-based gene regulation, and adaptive evolution.

Group members

- Paul Hudson (Associate Professor, PI)
- Lun Yao (Postdoc)
- Michael Jahn (Postdoc)
- Ivana Cengic (Graduate student)
- Kiyan Shabestary (Graduate student)
- Markus Janasch (Graduate student)
- Johannes Asplund-Samuelsson (Graduate student)
- Jan Karlsen (Graduate student)
- Johann Bauerfeind (Visiting researcher)

Funding

- Vetenskapsrådet
- Sweden Research Council Formas
- Swedish Council for Strategic Research SSF
- European Union H2020
- Science for Life Laboratory

List of key publications as SciLifeLab Fellow

Jahn M, Vialas V, Karlsen J, Maddalo G, Edfors F, Forsström B, Uhlen M, Käll L, Hudson EP*. *Growth of Cyanobacteria Is Constrained by the Abundance of Light and Carbon Assimilation Proteins* (2018). Cell Reports 25. P478-486.

Karlsen J+, Asplund-Samuelsson J+, Thomas Q, Jahn M, Hudson EP*. *Ribosome Profiling of Synechocystis Reveals Altered Ribosome Allocation at Carbon Starvation* (2018). mSystems 3. P1-12

Asplund-Samuelsson J, Janasch, M, Hudson EP*. *Thermodynamic analysis of computed pathways integrated into the metabolic networks of E. coli and Synechocystis reveals contrasting expansion potential* (2018). Metabolic Engineering 45 223-236

Yao L, Cengic I, Anfelt J, Hudson EP*. *Multiple gene repression in cyanobacteria using CRISPRi.* (2015) ACS Synthetic Biology 5, 207−212

Anfelt J, Kaczmarzyk D, Shabestary K, Renberg B, Rockberg R, Nielsen J, Uhlen M, Hudson EP*. *Genetic and nutrient modulation of acetyl-CoA levels in Synechocystis for n-butanol production.* (2015) Microbial Cell Factories 14 (1) 1-12

Sebastian Deindl

Uppsala University

Recruited from: Harvard University, USA

Starting date: October 2014

Extension date: Promotion to Associate Professor: December 2017

Possible conversion to a permanent position: October 2018

Research interests

Molecular machines are proteins or protein complexes that convert stored or supplied chemical energy into conformational changes to carry out molecular or cellular work. How do the molecular structures and dynamics of protein machines together enable their function? Research efforts in the Deindl laboratory are aimed at addressing this question using a combination of single-molecule fluorescence imaging approaches, structural techniques (primarily X-ray crystallography), biochemistry and computer simulations.

Knowledge of the static architecture of molecular machines alone may not satisfactorily explain how they work. Molecular machines are dynamic in nature and their conformational variability, i.e. the time-dependent fluctuations in their structures, are inherent to their mechanisms and functions.

Single-molecule fluorescence imaging

In order to investigate this dynamic nature, we explore single-molecule fluorescence imaging approaches to directly visualize molecular machines in real time. Their complex dynamics can be difficult to capture in classical bulk experiments since ensemble averaging can obscure the presence of multiple kinetic pathways or transient states. Investigations at the single-molecule level, however, can allow us to directly observe these processes and to correlate structural dynamics with function.

We hope to combine real-time dynamic information from these single-molecule experiments with biochemical and structural data in order to create movies of molecular machines that provide a quantitative and mechanistic understanding of how they work.

Group members

- Sebastian Deindl, Associate Professor (tenured)
- Josefin Ågren, Research Project Student
- Luka Bačić PhD Student
- Klaus Brackmann, Research Engineer
- Oscar Bromström, Research Project Student
- Oan Ho, Postdoctoral Researcher
- Laura Lehmann, PhD Student
- Guanzhong Mao, Postdoctoral Researcher
- Emil Marklund, PhD Student (co-supervisor; main supervisor: Johan Elf)
- Anton Sabantsev, Postdoctoral Researcher
- Martha Schattenhofer, Project Coordinator
- Alan Shaw, Postdoctoral Researcher
- Brad Van Oosten, Postdoctoral Researcher

Funding

- EMBO Young Investigator Award
- ERC starting grant
- SciLifeLab
- Wallenberg Academy Fellows
- Knut and Alice Wallenberg Foundation
- Swedish Research Council

List of key publications as SciLifeLab Fellow

Marklund*, Amselem*, Kipper, Zheng, Johansson, Deindl**, Elf**. *Direct observation of rotation-coupled protein diffusion along DNA on the microsecond timescale* bioRxiv 2018. Under review

Sabantsev, Levendosky, Zhuang, Bowman**, Deindl** *Direct observation of coordinated DNA movements on the nucleosome during chromatin remodeling.* Under review

Ballet, Correia, Conway, Locher, Lehmann, Garg, Vujasinovic, Deindl, Löhr, Globisch. *New enzymatic and mass spectrometric methodology for the selective investigation of gut microbiota-derived metabolites.* Chemical Science 2018

K. Kipper, N. Eremina, E. Marklund, S. Tubasum, G. Mao, L. C. Lehmann, J. Elf, and S. Deindl. *Structure-guided approach to site-specific fluorophore labeling of the lac repressor LacI.* PLoS One 2018

Lehmann, Hewitt, Aibara, Leitner, Marklund, Maslen, Maturi, Chen, van der Spoel, Skehel, Moustakas, Boulton**, Deindl** *Mechanistic Insights into Autoinhibition of the Oncogenic Chromatin Remodeler ALC1* Molecular Cell 68 (2017)

Simon Elsässer

Karolinska Institute

Recruited from: University of Cambridge, UK

Starting date: 2015

Extension date: 2018

Possible conversion to a permanent position: None

Research interests

Proteins perform a myriad of functions in every living cell. Traditional biochemical approaches for elucidating molecular mechanism rely on a reductionist's approach of simplifying complex systems into biochemically tractable problems. However, some of the most intriguing problems of biology, for example how the eukaryotic genome is packaged in the nucleus in such way that the relevant information for any given cell state can be made available 'on demand', can ultimately only be answered in the context of the full complexity of the living cell. We are exploring solutions to answer my biochemical questions in the context of the living cell. Methodology that would allow such strategy would need to provide a means for: 1) selectively addressing(i.e. manipulate and/or observe) a specific protein of interest in the context of the entire protein complement. 2) precisely synchronizing the biochemical process to be studied within an entire population of cells, so that meaningful biochemical and 'omics' readouts can be made from the cell population. Synthetic building blocks in form of non-canonical amino acids(ncAAs), introduced into the protein of interest, provide such means for performing biochemistry in the living cell. My laboratory currently focuses on a number of areas:

- Development of mammalian ncAA technology for studying proteins in situ, as well as for protein engineering
- Quantitative ChIP-Seq for studying dynamic evolution of chromatin states (also using ncAA technology) in the context of pluripotency and lineage commitment
- The small proteome (peptidome) of mammalian cells, in particular in the context of pluripotency and lineage commitment
- Elucidating the role of unusual DNA structures such as G4 quadruplexes, DNA/RNA hybrids and ssDNA through development of genome-wide profiling methods

Group members

- Angelo Salazar (PhD Student)
- Anna-Maria Katsori (Postdoc)
- Banushree Kumar (PhD Student)
- Birthe Meineke (Postdoc)
- Carmen Navarro (Postdoc)
- Dörte Schlesinger (PhD Student)
- Jing Lyu (PhD Student)
- Johannes Heimgartner (Master Student)
- Jurgen Eirich (Postdoc)
- Lorenzo Lafranchi (Postdoc)
- Philip Yung (Postdoc)
- Rozina Caridha (Lab Manager)
- Rui Shao (PhD Student)

Funding

- ERC
- Ragnar Söderbergs Foundation
- Ming Wai Lau Center
- Wallenberg Foundation Project Grant
- Cancerfonden
- Vetenskapsrådet
- Åke Wibergs Stiftelse
- STINT
- Clas Groschinskys Minnesfond

List of key publications as SciLifeLab Fellow

Meineke B, Heimgärtner J, Lafranchi L, Elsässer SJ, *"Methanomethylophilus alvus Mx1201 provides basis for mutual orthogonal pyrrolysyl tRNA/aminoacyl-tRNA synthetase pairs in mammalian cells"*, ACS Chemical Biology (2018)

Elsässer SJ, *"Generation of stable amber suppression cell lines"*, Methods in Molecular Biology (2018)

Yung PYK, Elsässer SJ, "Evolution and molecular mechanisms of epigenetic chromatin states", Current Opinion in Chemical Biology (2017)

Elsässer SJ, Ernst RJ, Walker OS, Chin JW, *"Genetic code expansion in stable cell lines enables encoded chromatin modification"*, Nature Methods (2016)

Elsässer SJ, Noh KM, Diaz N, Allis CD, Banaszynski LA, *"Histone H3.3 is required for endogenous retroviral element silencing and genome stability"*, Nature (2015)

Tanja Slotte

Stockholm University

Recruited from: Uppsala University

Starting date: April 14th, 2014

Extension date: Docent in Ecological Genomics December 15th, 2016

Possible conversion to a permanent position: Promoted to Associate Professor (permanent position) on October 29th, 2018

Research interests

Understanding the forces that shape genetic variation is a long-standing aim in evolutionary biology. Due to the rapid recent improvements in sequencing technologies, the availability of data on genomic variation has greatly increased. However, understanding how natural selection shapes genomic variation still remains challenging and requires sophisticated analytical approaches.

In our research, we investigate how variation in recombination rates affects genetic variation and natural selection. We test theoretical predictions by utilizing natural variation in plant mating systems, which modulates effective recombination rates. We also utilize variation in recombination rates across genomes, for instance by studying the evolution of supergenes, genomic regions of reduced recombination which control complex adaptive polymorphisms. Our work generally involves analyses of large-scale sequencing data sets from plant systems (e.g. Arabidopsis relatives, and the classic Linum system studied already by Darwin).

Using population genomic analyses, we have shown that mating system variation can have a major impact on genetic variation and natural selection. We have further identified a role for cis-regulatory changes in rapid floral adaptation to a new mating system in the crucifer genus Capsella. Currently, we are studying the evolution at a classic supergene, the distyly S-locus. These studies are of broad general importance for our understanding of how natural selection shapes genomic patterns of variation and how complex adaptations can evolve.

Group members

- Juanita Gutierrez, PhD student
- Robert Horvath, PhD student
- Jörg Bachmann, PhD student
- P. William Hughes, Postdoctoral fellow
- Marco Fracassetti, Postdoctoral fellow
- Benjamin Laenen, Researcher
- Aurélie Désamoré, Research engineer

Funding

- European Research Council (ERC)
- Swedish Research Council
- SciLifeLab National Biodiversity Projects

List of key publications as SciLifeLab Fellow

Laenen B, Tedder A, Nowak MD, Toräng P, Wunder J, Wötzel S, Steige KA, Kourmpetis Y, Odong T, Drouzas AD, Bink M, Ågren J, Coupland G and Slotte T. 2018. *Demography and mating system shape the genome-wide impact of purifying selection in Arabis alpina.* Proceedings of the National Academy of Sciences of the USA 115:816-821.

Lafon-Placette C, Hatorangan MR, Steige KA, Cornille A, Lascoux M, Slotte T, Köhler C. 2018. *Paternally expressed imprinted genes associate with hybridization barriers in Capsella.* Nature Plants 4:352-357.

Steige KA, Laenen B, Reimegård J, Scofield DG, Slotte T. 2017. *Genomic analysis reveals major determinants of cis-regulatory variation in Capsella grandiflora.* Proceedings of the National Academy of Sciences of the USA 114:1087-1092. *Equal contributions

Horvath R, Slotte T. 2017. *The role of small RNA-based epigenetic silencing for purifying selection on transposable elements in Capsella grandiflora.* Genome Biology and Evolution 9: 2911-2920

Steige KA, Reimegård J, Koenig D, Scofield DG, Slotte T. 2015. *Cis-regulatory changes associated with a recent mating system shift and floral adaptation in Capsella.* Molecular Biology and Evolution 32:2501-2514

Vicent Pelechano

Karolinska Institute

Recruited from: EMBL, Heidelberg, Germany

Starting date: Feb 2016

Extension date: Should be decided during 2019

Possible conversion to a permanent position: Not applicable at KI. Position depends always on your own funding.

Research interests

Genomics of gene expression

One of the biggest challenges in biology is to understand how apparently identical cells respond differently to the same stimulus. We are especially interested in understanding how the intrinsic complexity of gene expression contributes to non-genetic cellular adaptation. To deliver an integrated view of the mechanisms driving the appearance of divergent cellular phenotypes, as well as to refine our knowledge of the basic process of gene expression, we study: the epigenetic status, transcript isoform usage and post-transcriptional mRNA regulation.

In addition to our interest in the fundamental dissection of gene expression, our lab actively develops novel sequencing technologies. We have developed a diversity of approaches to study gene expression, chromatin organization and to improve clinical analysis. We investigate the complexity of overlapping human transcript isoforms simultaneously sequencing both the 5' and 3' ends of each RNA molecule (TIF-Seq). Our lab has also shown how the existence of widespread co-translational mRNA degradation allows studying ribosome dynamics by sequencing mRNA degradation intermediates (5P-Seq). By combining experimental and computational biology, we aim to decrease the gap between research fields and contribute to a better mechanistically understanding of the gene expression process.

Group members

- Alisa Alekseenko, PhD student
- Bingnan Li, Postdoc
- Donal Barrett, Research Technician
- Eva Brinkman, Postdoc
- Jingwen Wang, Postdoc
- Lilit Nersisyan, Postdoc
- Ryan Hull, Postdoc
- Sueli Marques, Senior Lab Manager
- Susanne Huch, Postdoc
- Xiushan Yin, Visiting Professor
- Yerma Pareja Sanchez, PhD student
- Yujie Zhang, PhD student

Funding

- VR starting grant
- Wallenberg Academy Fellow (KAW Foundation)
- Ragnar Sörderberg Foundation (Swedish Foundation´s Stating Grant)
- Karolinska Institutet (SciLifeLab Fellow and KI Funds)

National Fellows

Sari Peura

Swedish University of Agricultural Sciences

Recruited from: Uppsala University

Starting date: 1 Jan 2017

Extension date:

Possible conversion to a permanent position: Docent title awarded by SLU September 2018

Research interests

Carbon is the most abundant element in all organisms and carbon cycle is one of the determining factors for the life on earth. In the boreal and arctic regions, lakes and ponds play a major role in the carbon cycle, especially as emitters of GHGs, especially CO2 and CH4. I am studying the organisms and mechanism that produce and consume these gases, as well as remobilize carbon from long-term storage, especially permafrost. I am studying these from the perspective of climate change and how the alterations in environmental conditions may impact the carbon cycle and the involved organisms. I am addressing this topic by combining molecular methods with biogeochemical and process analyses to get a holistic picture of the interactions between organisms, processes and the environment.

Group members

- Sari Peura (PI)
- Anushree Sanyal (Postdoc)
- Mariana Kluge (PhD Student)
- Gaëtan Martin (PhD Student)

Funding

- FORMAS Future Research Leaders
- SciLifeLab National Biodiversity grant

List of key publications as SciLifeLab Fellow

S Peura, M Buck, SL Aalto, SE Morales, H Nykänen, A Eiler. 2018. *Novel autotrophic organisms contribute significantly to the internal carbon cycling potential of a boreal lake.* mBio 9:e00916-18.

C Wurzbacher, RH Nilsson, M Rautio, S Peura. 2017. *Poorly known microbial taxa dominate the microbiome of permafrost thaw ponds.* The ISME journal 11:1938 1941.

Aleksej Zelezniak

Chalmers University, Gothenburg

Recruited from: the Francis Crick Institute, UK

Starting date: May 2017

Extension date:

Possible conversion to a permanent position: the current faculty model at Chalmers considers promotion to tenure

Research interests

Metabolism is a primordial biological system responsible for interconversion of environmental chemicals to energy and cellular building blocks in all living species. Whenever organisms are genetically affected or facing new environment they do need to adapt their metabolism to satisfy their individual growth demands. At the same time, in natural environments, organisms never exist in isolation but rather constantly interacting with other species. Ranging from local competition for the same resources up to emergent global social interactions, metabolism shapes individual species behavior and provides a common communication platform of all living entities. At Zelezniak lab we are interested in studying how genetic, environmental factors affect operation and regulation of cellular metabolic networks. At the single species level, we want to understand how complex phenotypes emerge from the underlying molecular levels organized via central biological dogma. At the multicellular level, we want to understand what is the role of metabolism in the cell-to-cell interactions, in particular, its role in the co-existence of microbial species. Answering these questions will allow us not only to design organisms with desired metabolic properties for biotechnology purposes but also engineer synthetic microbial communities with specific health benefits.

We are combining best practices of data science with machine learning and metabolic modeling to develop novel technologies for getting insights about biological mechanisms directly from molecular data. Furthermore, together with our collaborators, we are actively involved in developing mass spectrometry technology to enable fast, robust, precise and inexpensive proteome acquisitions from any biological sample. At the same time, we are actively interested in expanding the scope of our computational methods applications with the goal to gain mechanistic insights about the following biological processes: the role of metabolic interactions in shaping healthy gut microbiome, designing stable microbial communities for bioremediation and other biotechnological applications, transcription and translation control.

Group members

- Jan Zrimec (Postdoc)
- FIlip Buric (PhD student)
- Sara Jonason (MS student)
- Francisco Zorrilla (MS student)

Funding

- Scilifelab Starting package
- Chalmers Area of Advance support for BigData research projects (running costs + research engineers)
- Swedish National Infrastructure for computing
- 2017 Innovation-2-translation grant from Francis Crick institute, London (running costs) 2018 Innovation-2-translation grant from Francis Crick institute, London (running costs)

List of key publications as SciLifeLab Fellow

Zelezniak A, Vowinckel J, Capuano F, Messner CR, Demichev V, Polowsky N, Muelleder M, Kamrad S, Klaus B, Keller M, Ralser M *Machine learning predicts the yeast metabolome from quantitative proteome of kinase knockouts.* Cell Systems, 7, 1-17, 2018

Vowinckel J*, Zelezniak A*, Bruderer R, Mülleder M, Reiter L, Ralser M *Cost-effective generation of precise label-free quantitative proteomes in high-throughput by microLC and data-independent acquisition.* Scientific reports 8 (1), 4346, 2018

Campbell K, Herrera-Dominguez L, Correia-Melo C, Zelezniak A, Ralser M *Biochemical principles enabling metabolic cooperativity and phenotypic heterogeneity at the single cell level.* Current Opinion in Systems Biology, 1, 2017

Haas R, Zelezniak A, Iacovacci J, Kamrad, Townsend SJ, Ralser M *Designing and interpreting 'multi-omic' experiments that may change our understanding of biology* Current Opinion in Systems Biology 6, 37-45, 2017

Alam MP, Olin-Sandoval V, Stincone A, Keller MA, Zelezniak A, Luisi BF, Ralser M *The self-inhibitory nature of metabolic networks and its alleviation through compartmentalization.* Nature communications, Vol(8), 16018, 2017

Comments about being a SciLifeLab Fellow

Uppsala University SciLifeLab Fellows

What has worked well as SciLifeLab fellow?

The Fellow program has been very supportive in many areas (career development, financial), with for example the organization of a leadership in science training (this was very good, and should be made available to every new recruit early on), the availability of funds to organize events at a minimal application burden, or workshops for trainees (e.g. presentation skills). The startup funding was generous and instrumental in getting quickly a group size with a critical mass. The fact that the money can be carry over is also essential, because it allows to get accustomed to the Swedish system whilst lowering the risks of spending big amounts unwisely.

"The funding has been fantastic and made it possible to explore many new ideas!

The interactions with the other fellows have also been very valuable for me. For example, I was given the opportunity to organize several symposia funded by SciLifeLab. This has contributed to collaborations and has created an environment where PhD students interact with each other at SciLifeLab. Being at SciLifeLab has also stimulated me to interact with some of the platforms. I have ongoing collaborations with the Chemical Biology Consortium (CBCS), Uppsala Drug Optimization and Pharmaceutical Profiling Platform (UDOP), and the national bioinformatics infrastructure (NBIS)."

- "Flexible startup funding for fellows that has allowed us to focus on research rather than on forms and budgeting.
- Good and friendly support from SciLifeLab fellows program administrative staff.
- Excellent opportunities to network with elite scientists."

"SciLifeLab has provided me with an exceptional framework to advance my research as well as with stimulating opportunities to develop as a researcher. The constellation of techniques and know-how available at SciLifeLab is allowing me to move forward my projects by conducting state-of-the-art research. Ad-hoc events, such as the annual meeting of the National Molecular Medicine Fellows Program, broadened my scientific network and stimulated my development as a young research leader."

- The generous startup funding provided by SciLifeLab has been incremental to start my independent laboratory. This startup package is very unusual for European universities and represents a unique opportunity to be internationally competitive and to work on high-risk/high-gain projects that require more time to develop.
- Furthermore, SciLifeLab has always been very supportive and many scientific contacts for successful collaborations have been established through the SciLifeLab network.
- Organized meetings for SciLifeLab Fellows have strengthened our interaction and provided information on the Swedish scientific landscape. The organization and co-payment for the EMBO leadership course at Uppsala University was one of the best investments in us fellows.

What could have been done differently to make your work succeed better as a SciLifelab fellow?

"I think that the first generation of Fellows suffered from the lack of clarity resulting from the new type of academic positions that most of us were appointed to. It would have been beneficial to have such a fundamental document as the "SciLifeLab Fellows program" available from the start. Along the same line, the dual system (appointed to a department but receiving money from SciLifeLab) has also been difficult to navigate. When I need to prioritize, it is still unclear whether my department or SciLifeLab should come first (although since my department will ultimately promote me, I am more incline to devote more time there but it feels unnatural). An example is teaching: I feel that I am teaching more than I should given the fellowship, but at the same time I need to build my portfolio for my promotion. So it is unclear how research will be valued against eg research (which is why I moved here in the first place, for research). On another note, one suggestion to help international recruits would be to give them a more precise idea of the cost of things in Sweden; I found that it took me too long to know what I could and could not afford with the SLL start-up (eg PhD students, postdocs)."

"I think that SciLifeLab could have contributed to negotiating with the department regarding the conditions for the fellow to make sure that there was a future after four years. I think many fellows, including me, were a bit naive and thought that if we were successful as scientist, we would be tenured. This was not the case. Instead, several us did not get tenure-track positions and/or we have felt that there were no plans for integration of our groups at the department.

I think that SciLifeLab could have contributed more to educating the fellows regarding the administrative part of becoming a group leader (e.g. recruitment, economy, etc). This is a relatively small investment, but could have a large impact on success of a new research group. SciLifeLab could work more on promoting collaborations with the fellows and the SciLifeLab platforms. The meetings (retreats) we had together with the other fellows could have been better organized with more invited speakers and clearer themes."

- "Lower administrative barriers to start using SciLifeLab facilities.
- Clearer plan for the prolongation period of the fellows program (year 5-6) already at the outset."

"Support to research based on the use of infrastructures not yet linked to SciLifeLab would be greatly appreciated and likely beneficial to long-term strategies aiming to extend the SciLifeLab portfolio of services."

KTH SciLifeLab Fellows

What has worked well as SciLifeLab fellow?

"The fellow's program has been beneficial, with leadership training, funding to organize retreat etc… The startup funding associated with the position has been instrumental in setting up the group and getting a headstart."

What could have been done differently to make your work succeed better as a SciLifelab fellow?

"Much time was spent in simply understanding the dual system (belonging to specific universities and to scilifelab), setting up the system with SDs has improved the situation greatly and should have been done earlier.

I still don't feel much a sense of community outside the fellows and the people in my division. Bringing back the PI lunches has been excellent to try foster that more.

Having more local admin support would have helped too.

Most of the issues have been resolved now, so it is only that I would have benefitted from that happening earlier."

What has worked well as SciLifeLab fellow?

- "Alignment with other SciLifeLab fellows (e.g. weekly joint group meetings and journal club with the groups of Vicent Pelechano and Marc Friedlander as well as Simon Elsasser (journal club only))
- Co-supervision of students (e.g. I am a co-supervisor of PhD students in Vicent Pelechano and Simon Elsasser's group and Vicent Pelechano is the co-supervisor of one of my PhD student)
- Collaboration with Cecilia Williams (SciLifeLab, KTH, KI)
- Shared equipment between research groups on y4, in part obtained by SFO-funded equipment grant
- Board member of "Science for Life Seminar Series"
- Hosting researchers from abroad within the "Science for Life Seminar Series" (Michael Wilson (Sickkids, Toronto), Elizabeth Murchison (Uni Cambridge), Ian Mills (Uni Belfast), Anders Lund (BRIC Copenhagen), Markus Landthaler (MPI-MG))
- Hosting of journal editors at SciLifeLab (Anne Faerch Nielsen (EMBO J), Tjago Faial (Nature Genetics))
- SciLifeLab financial support for conference organization (2018 EMBO meeting RNA: Structure meets Function, 2019 EpiChrom symposium)
- Joint advertisement of positions in Science Magazine
- Featuring of my group's research efforts in Science Magazine
- SciLifeLab IT infrastructure, HR and other administrator
- Branding of SciLifeLab amongst Sweden-based researchers
- International work environment and availability of courses for personal development (presentation skills) which is attractive to local and foreign researchers
- Annual meetings with SciLifeLab fellows and research staff
- SciLifeLab PI lunches"

"I have enjoyed very much interactions with other SciLifeLab Fellows. It is a very dynamic and competent group of junior group leaders.

I have also been pleased with collaborative opportunities here at SciLifeLab. I have been collaborating with groups of Simon Elsaesser, Marc Friedlander, Mats Nilsson and Joakim Lundeberg. Finally, I have benefitted from the service of the Super-resolution microscopy facility."

- "The generous startup package was extremely helpful to hit the ground running and produce preliminary data that was crucial for later successful grant applications
- Integration into the already established Division of Chemical Biology and Translational Medicine from KI at SciLifeLab was very helpful to avoid having to buy all basic lab equipment, such as centrifuges, incubators, gel docs, microscopes (Basic equipment provided from SciLifeLab was limited to a TC hood, fridges and freezers)
- We bought a common NextSeq 500 with other fellows and supported to 50% by SFO funding, which is a crucial tool for our research. Note that SFO funding has only been used once for a common equipment call.
- Community amongst the fellows is very good. Good regular exchange, active collaborations and working instrument sharing.
- After slow start, I have found collaborators in-house (e.g. being part of a Technology Development Project "Mammalian Protein Production)."

What could have been done differently to make your work succeed better as a SciLifelab fellow?

- "Availability as well as strategic alignment of lab and office space from the start. – No lab and office space was available when I started and when I got the lab space it took over a year to install benches and shelves despite constant nagging. A major problem is still that our group is next to a number of facilities who have no interest in scientific interactions as they have national service but no research duties. Perhaps also more local administrative support would be helpful.
- Inaccessibility of equipment. – Usually research groups are willing to share the equipment but facilities do not contribute to this. Equipment is expensive for a small research group. It is useful to have the equipment grant (provided by SFO not SciLifeLab). Access to idle machines in the facilities should be encouraged. Research groups should be brought into close proximity (ideally on the same floor) and facilities should get relocated.
- Lack of SciLifeLab research interactions/collaborations. – Largely because the facilities have no interest in working with researchers. Too few research groups (and no incentive to collaborate) with who one can interact beyond the fellows. Perhaps the annual meetings and PI lunches will improve this situation. Strategic funding for a joint research position could also lead to more interactions.
- Branding of research activities at SciLifeLab. – Many Sweden-based researchers (and funding agencies) assume that my group provides service but does not perform research.

- Limited mentorship or scientific support. – Due to high turnover and reoccurring reorganization of administrative and supporting staff, it is unclear who is responsible for what at SciLifeLab. Mentor/contact person would be useful. Perhaps the SDs will take over this task eventually if they reside in this position for longer."

"I have been rather dissatisfied with the use of facilities and overall access to instrumentation. In my view, this institute has not yet been set up properly to run as a research center and I am still confused why research groups have been invited to join SciLifeLab."

- "Not very good integration into SciLifeLab community from the start, particularly because Magda and me got between the lines of various internal power plays between KI and KTH management at the time. Much better now.
- Lab space allocation was a mess, only solved after 1 year. As many groups expanded on my floor, we are now very tight with space again with no reasonable option to expand.
- Integration into in-house method development did not work. E.g. Method development by SciLifeLab fellows is largely in parallel to work in the Genomics Facility and Single Cell Genomics with little exchange. I was not invited to join internal events by the Genomics Facility.
- Platforms for getting to know the colleagues in the same building were very scares in the beginning. Recently, a PI lunch seminar series has been restarted which helps a lot to establish contacts with other PIs in the building.
- Access to equipment owned by national facilities (liquid handling, qPCR, sonicators, automated microscopy, sequencers, mass spectrometers) is either impossible or very restrictive, despite the fact that many large expensive equipment is not in constant use by the facilities. Where access is possible, basic user training is very difficult to organize and at the disgression of the facility.
- Senior faculty at SciLifeLab don't act as mentors for SciLifeLab fellows. I feel mentoring is crucial at the early independent career stage.
- the junior labs are not well integrated in ongoing bigger research projects. Participation in SciLifeLab flagship projects could help adding to the fellows' publication record."

Stockholm University SciLifeLab Fellows

What has worked well as SciLifeLab fellow?

"I like the concept that research groups from different scientific fields and three Universities are working in the same building. Have recently received three larger grants that all have been benefitting on interaction and collaboration with Jonathan Martin, another SciLifeLab researcher. It should be noted that he also belongs to my department at SU. However, hoping to have similar projects with other SciLifeLab researchers in the future."

"This position has offered a fantastic opportunity to establish my own independent group, and the SFO funding has made it possible to pursue more challenging questions than might have otherwise been possible. Working in the same place as many bioinformaticians and genomicists has made it easier to plan projects. I especially want to highlight the bioinformatics and genomics platforms, which have been very helpful both with advice on project design and with implementing non-standard methods. "

"I find that being part of the Fellowship community has greatly facilitated my research. In particular, I work closely with some of the other Fellows, for instance having shared group meetings and journal clubs. In general, SciLifeLab is a stimulating environment, where there are many possibilities for collaborations and sharing of ideas."

"It has attracted young talents"

What could have been done differently to make your work succeed better as a SciLifelab fellow?

"Think that SciLifeLab has structural and management issues that should be solved. I started in May, and the decision that I would establish my group at SciLifeLab/SU was taken many months before that, but do still not have full access to lab space. Loosing so much time is of course problematic when you are a young researcher with a four-year position. I hope that most things will be ok in January.

In general, I am happy with my situation at SciLifeLab and looking forward to build new strong collaborations. However, as an organization SciLifeLab could gain a lot by improving the management structure, with clear allocation of responsibility and improved communication."

"I and my group would have benefited from easier access to longer-term collaborations with SciLifeLab bioinformaticians (e.g. at NBIS). We know from experience that they are highly skilled and can substantially improve the quality of genomic analyses, as we previously had WABI long-term bioinformatics support. Perhaps SciLifeLab could allocate some funding that SciLifeLab fellows could apply for, to cover long-term support by/collaborations with NBIS bioinformaticians? "

"I find that some of facilities here at the Stockholm site could contribute more to the local research environment, in terms of actively collaborating and sharing access to equipment – if they do not contribute to the critical mass here, there is no reason why they should take up precious space at SciLifeLab.

I would like to see SciLifeLab develop more in the direction of an independent entity, but this does not seem realistic under the current government mandate, and with the Universities unwilling to give more autonomy to SciLifeLab."

"Support research in the terms of communal equipment, auxiliary services (autoclave, cell culture, technical support to deal with equipment break down). Have a large welcoming canteen on the top floor open until late so that people from different labs would meet for lunch/tea and discuss science; the current building design is not welcoming, and G-2 lunchroom is not functioning as a meeting place for exchange, its empty most of the time."

Chalmers University of Technology SciLifeLab Fellows

What has worked well as SciLifeLab fellow?

"Annual retreat works well, it is a good opportunity to meet other fellows share experiences in Swedish academia."

What could have been done differently to make your work succeed better as a SciLifelab fellow?

"I understand that most of fellows are around Stockholm area and all the issues are related to local organizational issues. Perhaps retreat could be more scientific, maybe also two days, could have been organized as a symposium of Sci-Lifelab research spectrum."

Swedish University of Agricultural Sciences, SLU SciLifeLab Fellows

What has worked well as SciLifeLab fellow?

"The startup funding from SciLifeLab has facilitated me to start building my own research group and follow the research line that I have been building towards since my PhD work.""

What could have been done differently to make your work succeed better as a SciLifelab fellow?

"As a national fellow I am a bit outside the core activities and feel that there are things happening I am not aware of. Also, the continuation after the 4 years (the additional 2 years funded by host university and SciLifeLab jointly) are not clear which is creating extra stress."

Notes


SciLifeLab

Karolinska Institutet
KTH
VETENSKAP OCH KONST
Stockholms universitet
UPPSALA UNIVERSITET