

Webinar on:

Calls for new project support from the chemical
biology unit and drug discovery & development
platform @ SciLifeLab

Anna-Lena Gustavsson CBCS
Per Arvidsson DDDp

Agenda:

- 10.00-10.20 Intro and CBCS call for projects, Anna-Lena
- 10.20-10.35 DDD and call for projects, Per
- 10.35 Q&A

SciLifeLab a government-funded national infrastructure



Max-IV

Next-generation synchrotron



ESS

European Spallation Source



SciLifeLab

Molecular Life Sciences

Institution for the **advancement of molecular biosciences** in Sweden.

Started in 2010 by Karolinska Institutet, KTH Royal Institute of Technology, Stockholm University and Uppsala University.

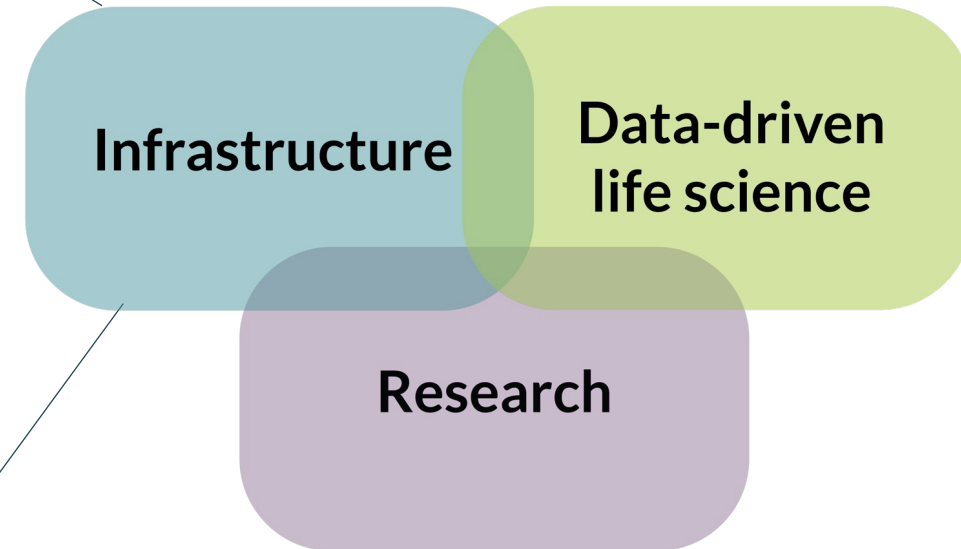
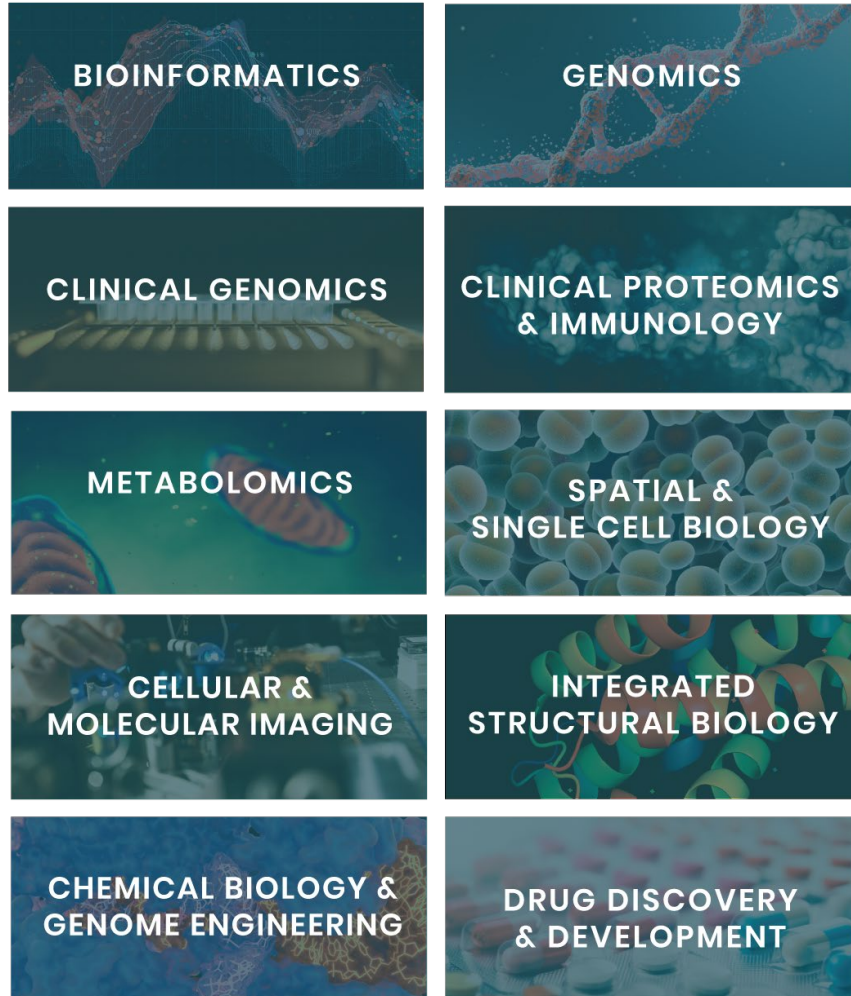
Today, activities at **all major Swedish universities**.



Infrastructure Platforms @ Scilifelab



Platforms





*SRC & SciLifeLab funded National Infrastructure for
Chemical Biology at six universities
Anna-Lena Gustavsson*

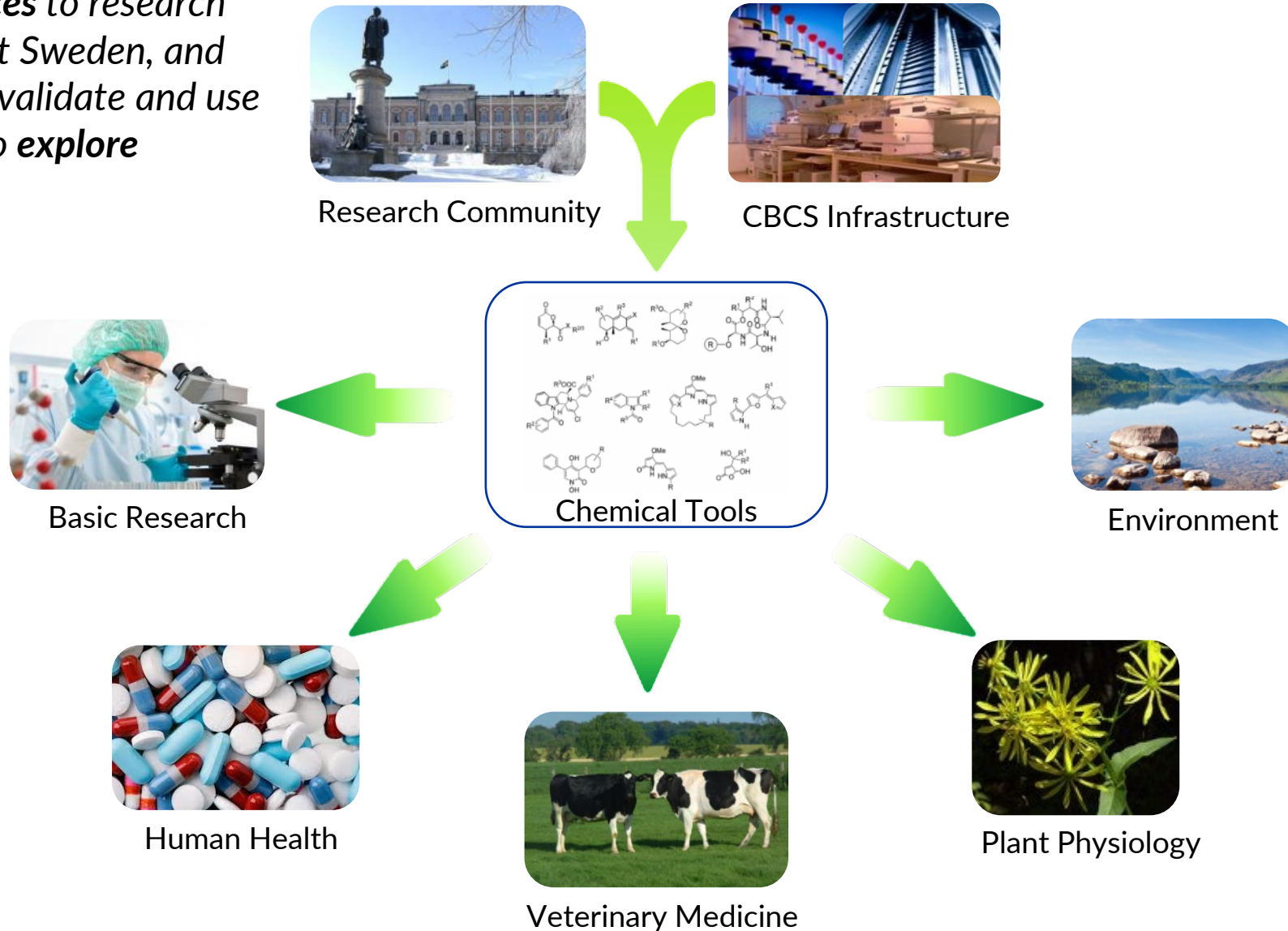


integrates high-capacity screening platforms throughout Europe



The CBCS Mission

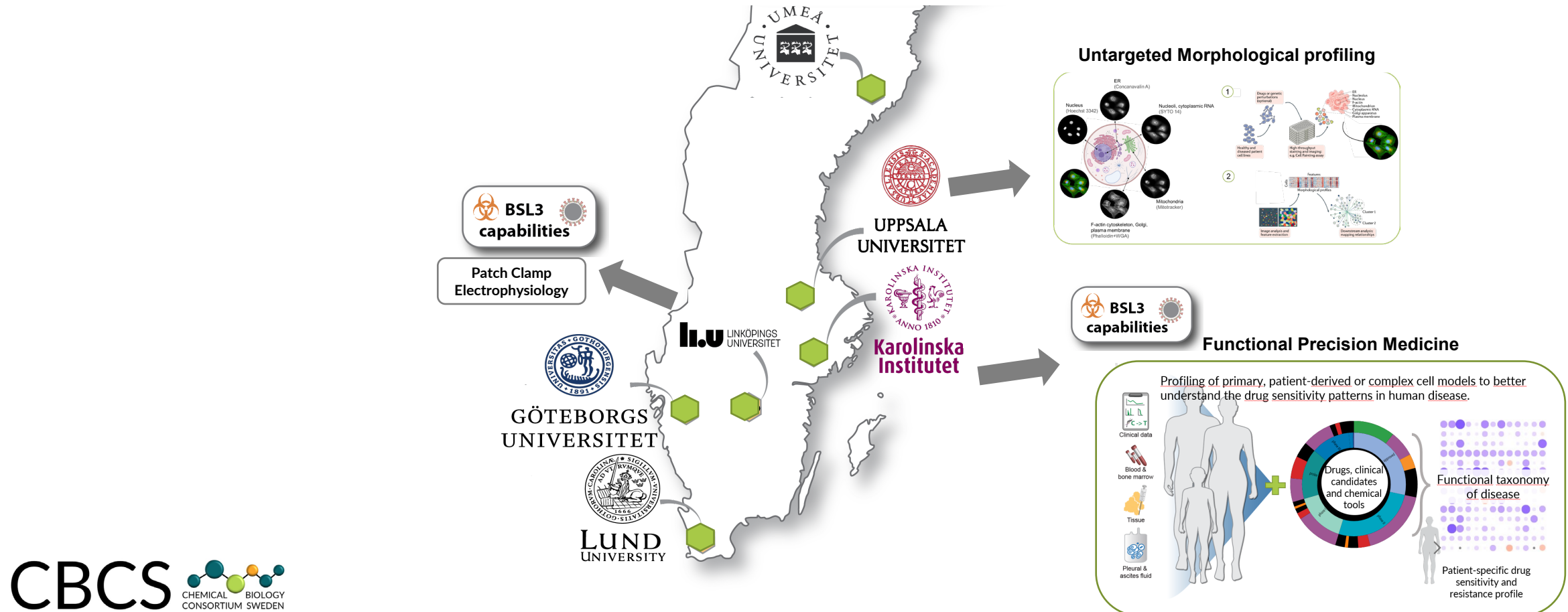
*“to provide **services** to research groups throughout Sweden, and together identify, validate and use **small molecules** to **explore biology**.”*



CBCS - a distributed infrastructure



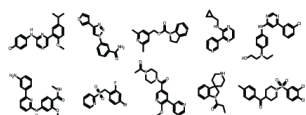
- ~25 FTEs- mixture of chemists and biologist
- In operation at KI and Umu for more than a decade.



CBCS Research Services

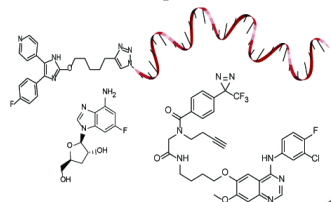


High-quality chemical libraries



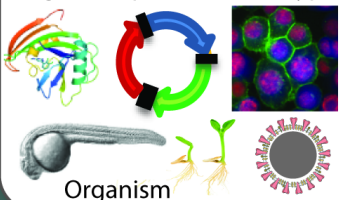
~ 350,000 compounds,
chemically diverse to
chemogenomics libraries

Enabling chemistry & quality assurance of hit compounds

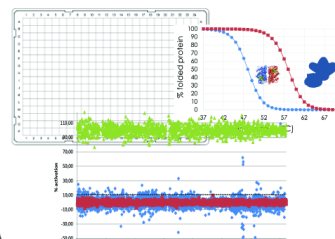


Industry-standard Assay development

Target Reporter Phenotypic



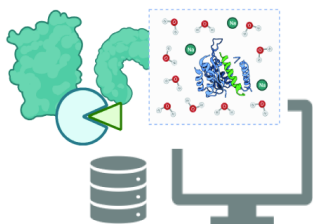
Small molecule screening



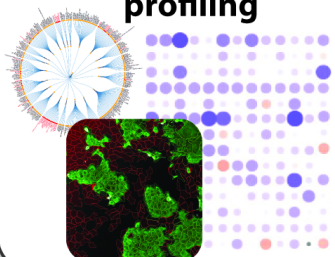
Chemical Biology Services



Virtual Screening & Chemoinformatics



Disease & compound profiling



**High-quality data &
knowledge fueling
biological discovery
& innovation**

Understanding of fundamental
biological processes

Contribution to basic science

High impact publications

Drug Discovery & Development



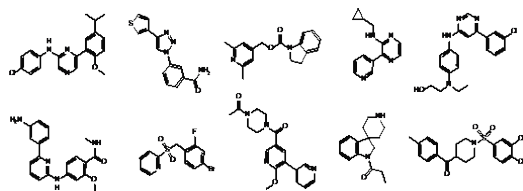
Pharmaceutical industries

Innovation offices at universities

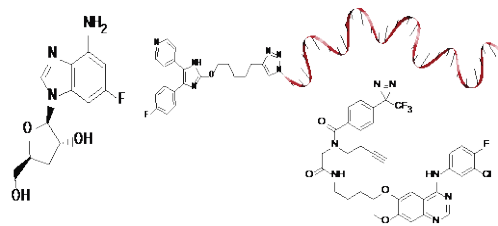
Incubation system for start-ups

The Compound Collection

High-quality
chemical libraries

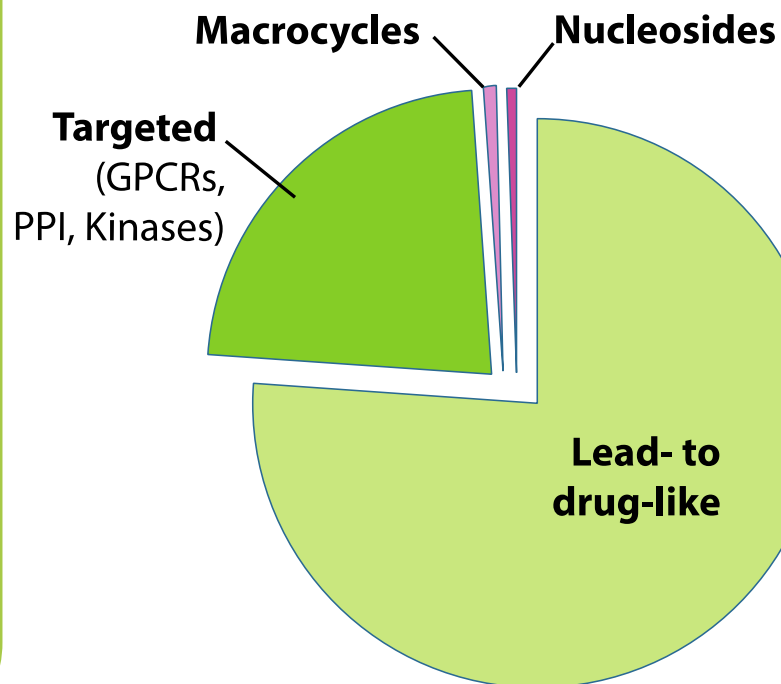


~350 000 compounds

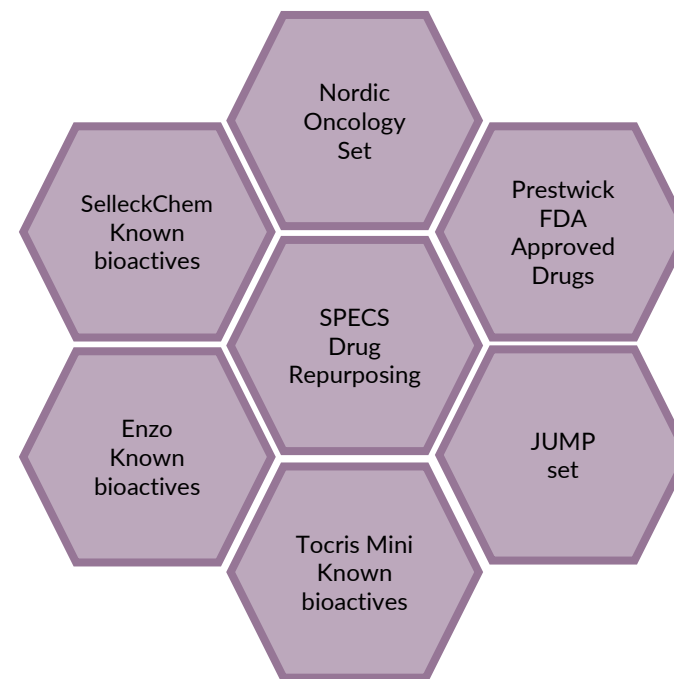


Enabling chemistry for
follow-up and validation

Primary Screening set
37k small molecules



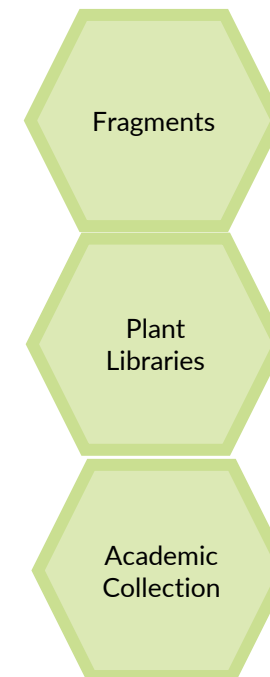
Annotated compounds
Drugs & Tools



AstraZeneca

Phenotypic Screening Collection
14 000 compounds covering 1700 targets

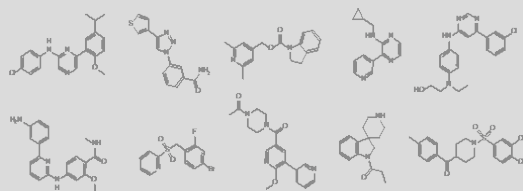

**Specialized
Libraries**



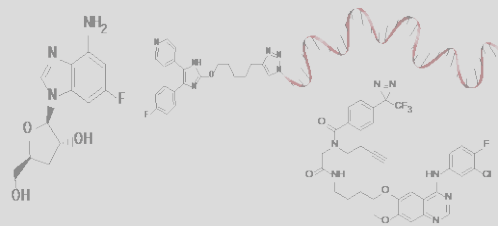
The Compound Collection



High-quality
chemical libraries



~350 000 compounds



Enabling chemistry for
follow-up and validation

Primary Screening set
37k small molecules

Macrocycles Nucleosides

eu:openscreen

Access 100 000 diverse set of compounds

Lead-to
drug-like

Annotated compounds
Drugs & Tools

Nordic
Oncology
Set

Prestwick
FDA
Approved
Drugs

SPECS
Drug
Repurposing

Enzo
Known
bioactives

JUMP
set

Tocris Mini
Known
bioactives

AstraZeneca 

Phenotypic Screening Collection
14 000 compounds covering 1700 targets

Specialized
Libraries

Fragments

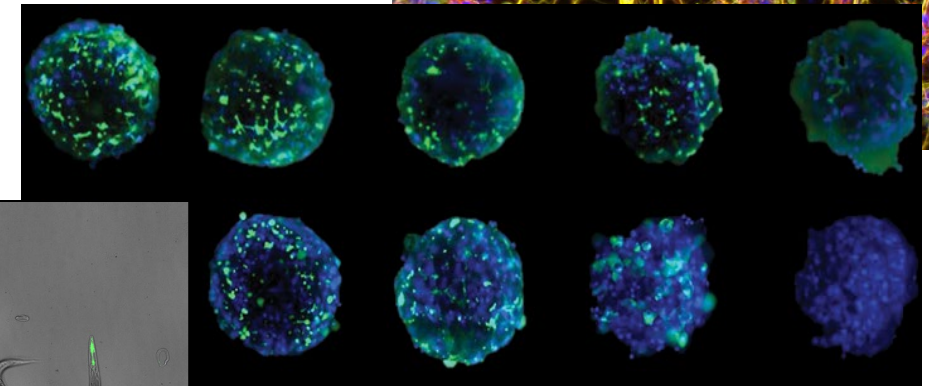
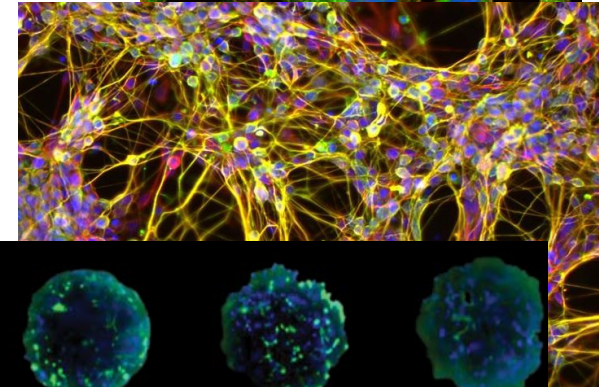
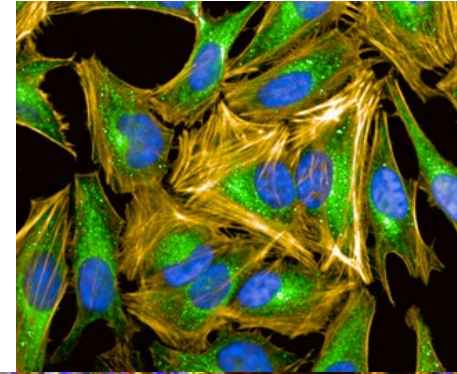
Plant
Libraries

Academic
Collection

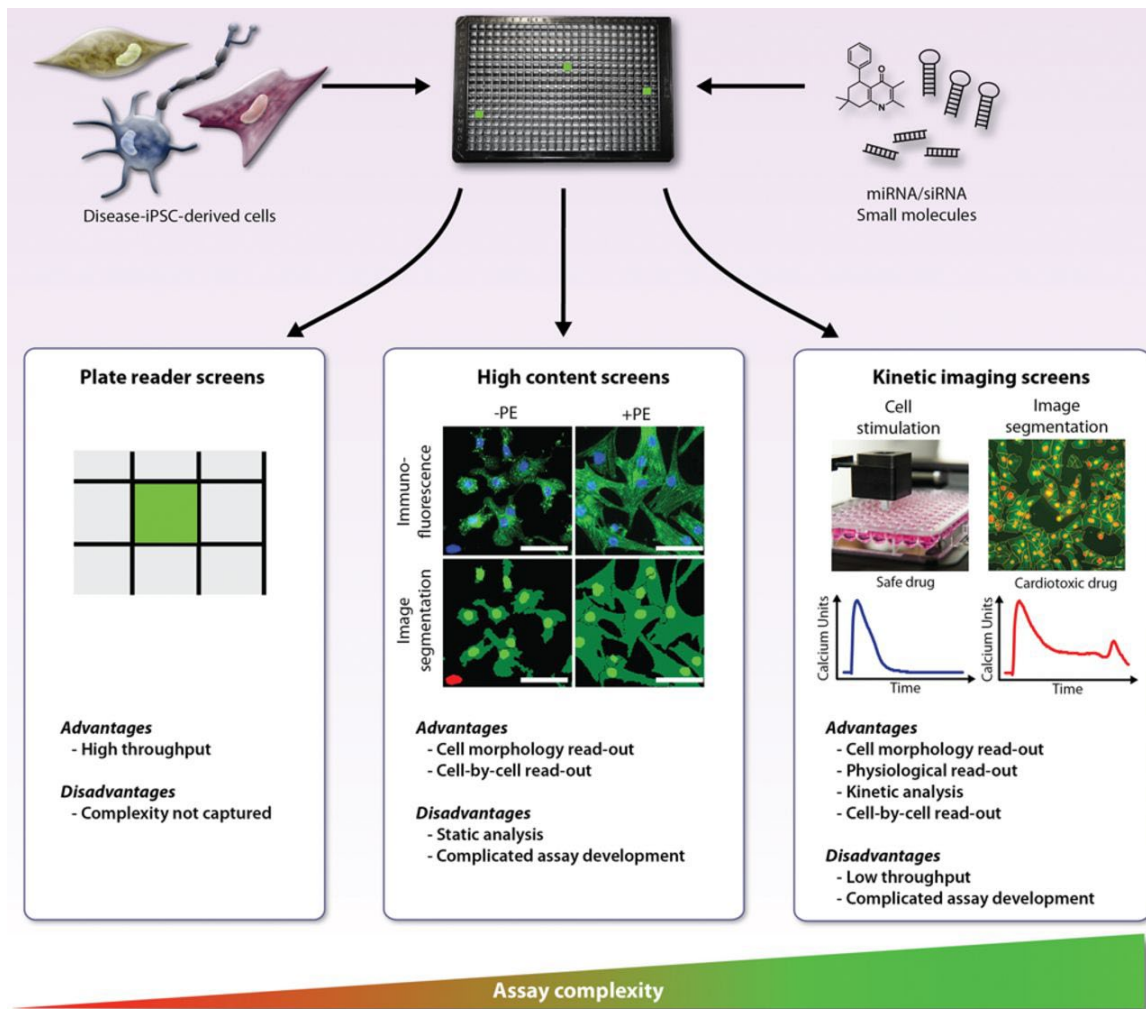
Examples of Experimental models



- Target based assays (Enzymatic, GPCRs, Ion channels)
- Bacteria
- (Cancer) cell lines
- Primary mouse epithelial fibroblasts/ bone marrow derived mast cells
- Human Patient-derived cancer cells populations
- Human pluripotent cells
- Spheroids and Organoids
- Whole organisms: Plants, C.elegans, Zebrafish
- BSL3 capabilities



More than 50% of the screens are phenotypic based



Examples of Phenotypic assay read outs

- Cell viability
- Signaling pathway activity
- Gene and Protein expression
- Protein localization
- Morphological changes
- Live cell imaging

Mark Mercola. Circulation Research, Volume: 112, Issue: 3, Pages: 534-548

A Screening project

- Project start up meeting

- Set up and sign **user agreement**

- ✓ **Assay development (PI)**

- Assay transfer, experiments at CBCS
- Assay formatting (384) and test of automated liquid handling (CBCS)

- ✓ **Pre-screen:** one or more test runs with ≈ 10 plates (CBCS)

- ✓ **Screening usually at single concentration (10 microM) (CBCS)**

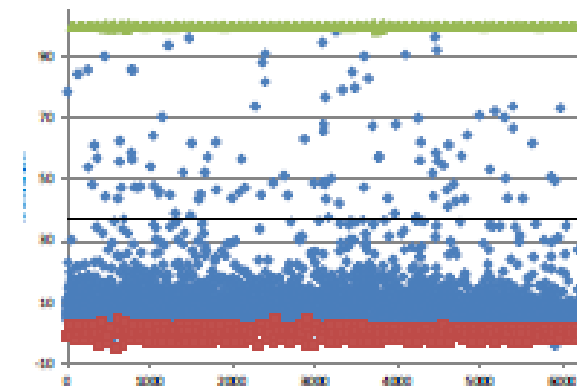
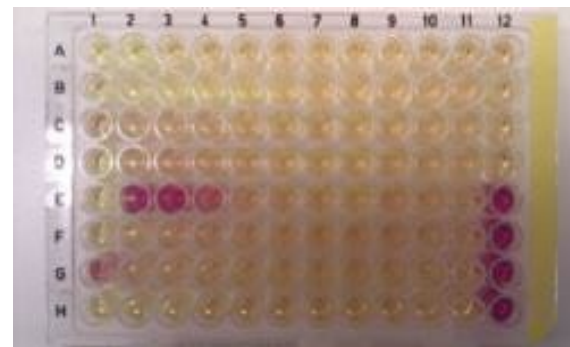
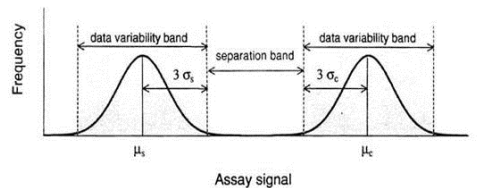
- 3 concentrations hit confirmation and **counterassay**, estimating ~ 150 -200 compounds)(CBCS)
- 11 concentration dose response curves, estimating 30-60 compounds (CBCS)

- ✓ **Evaluation of confirmed hits by CBCS medicinal/computational chemists and selection of possible analogs (CBCS)**

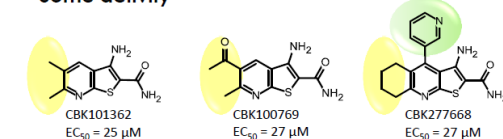
- Test of analogs, estimating 56 compounds (CBCS)+ commercially available => establish crude SAR
- Re-synthesis of hits and some analogs (CBCS)

- ✓ **Further hit validation (PI, or PI+CBCS) and down stream assays**

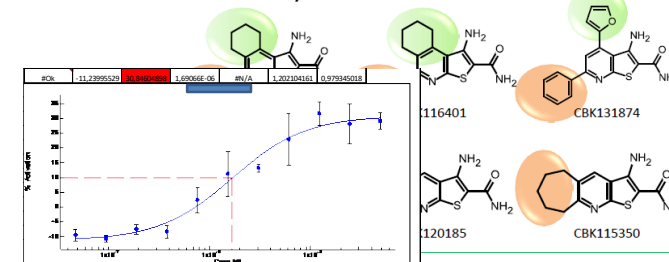
- Project closure



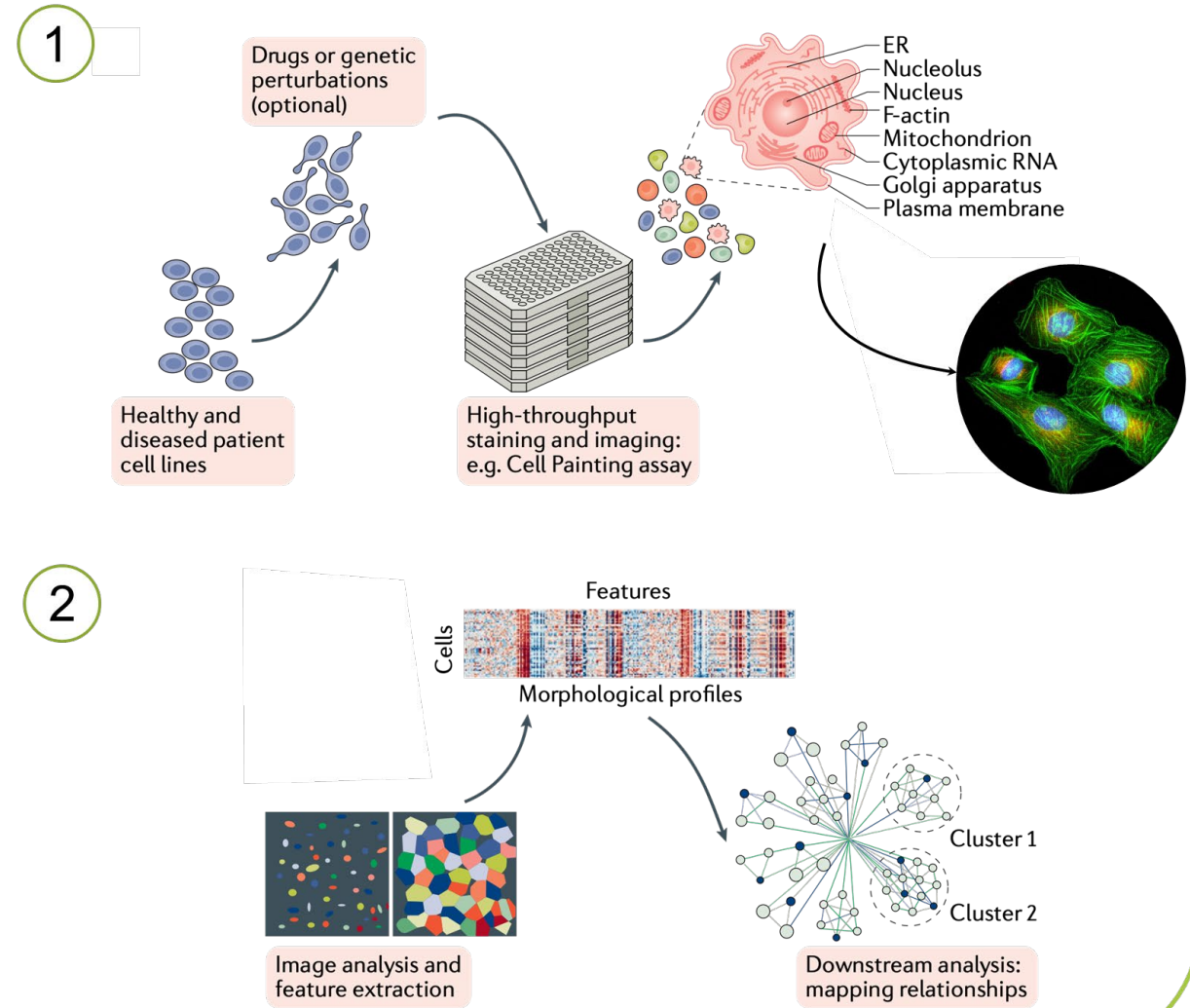
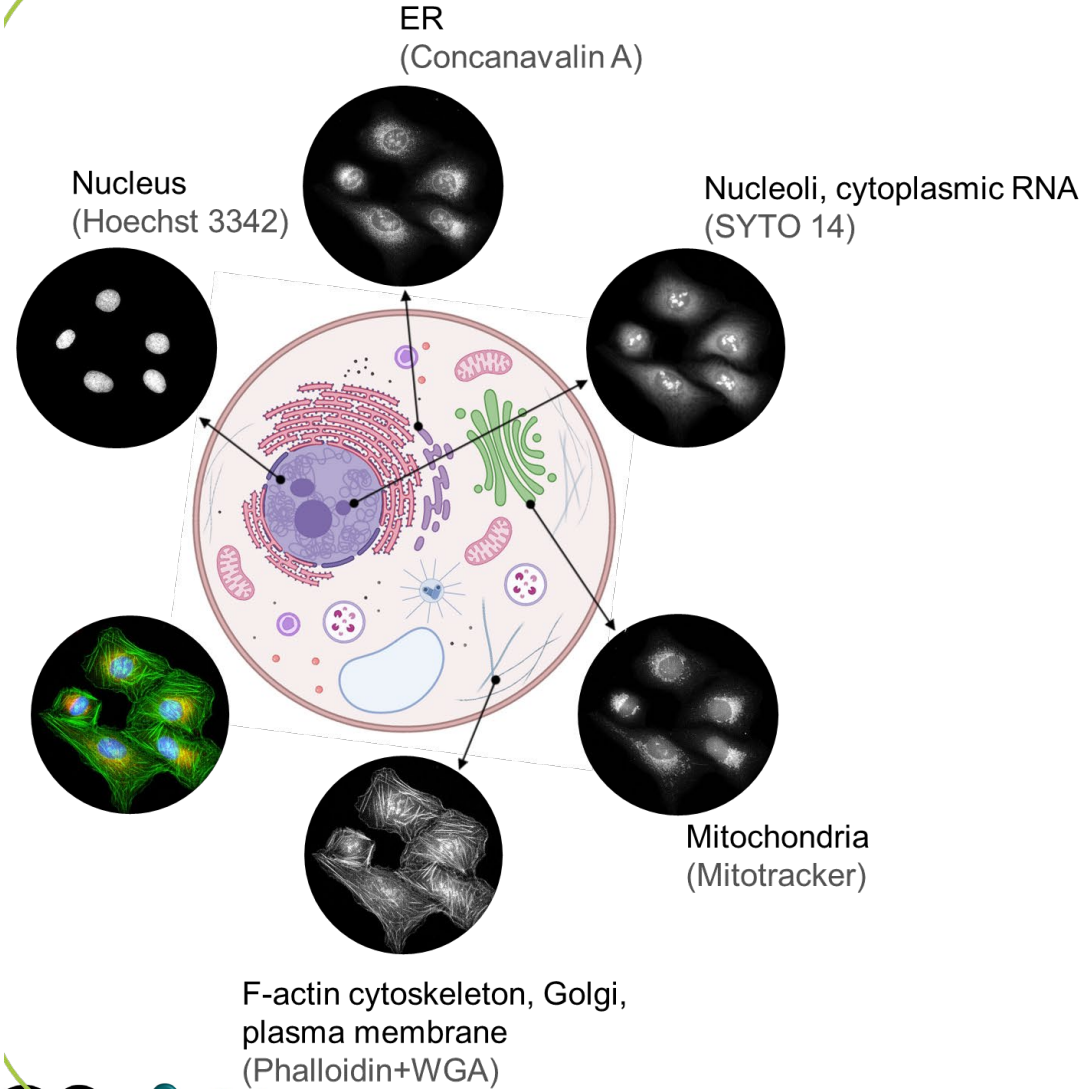
Some activity



No activity



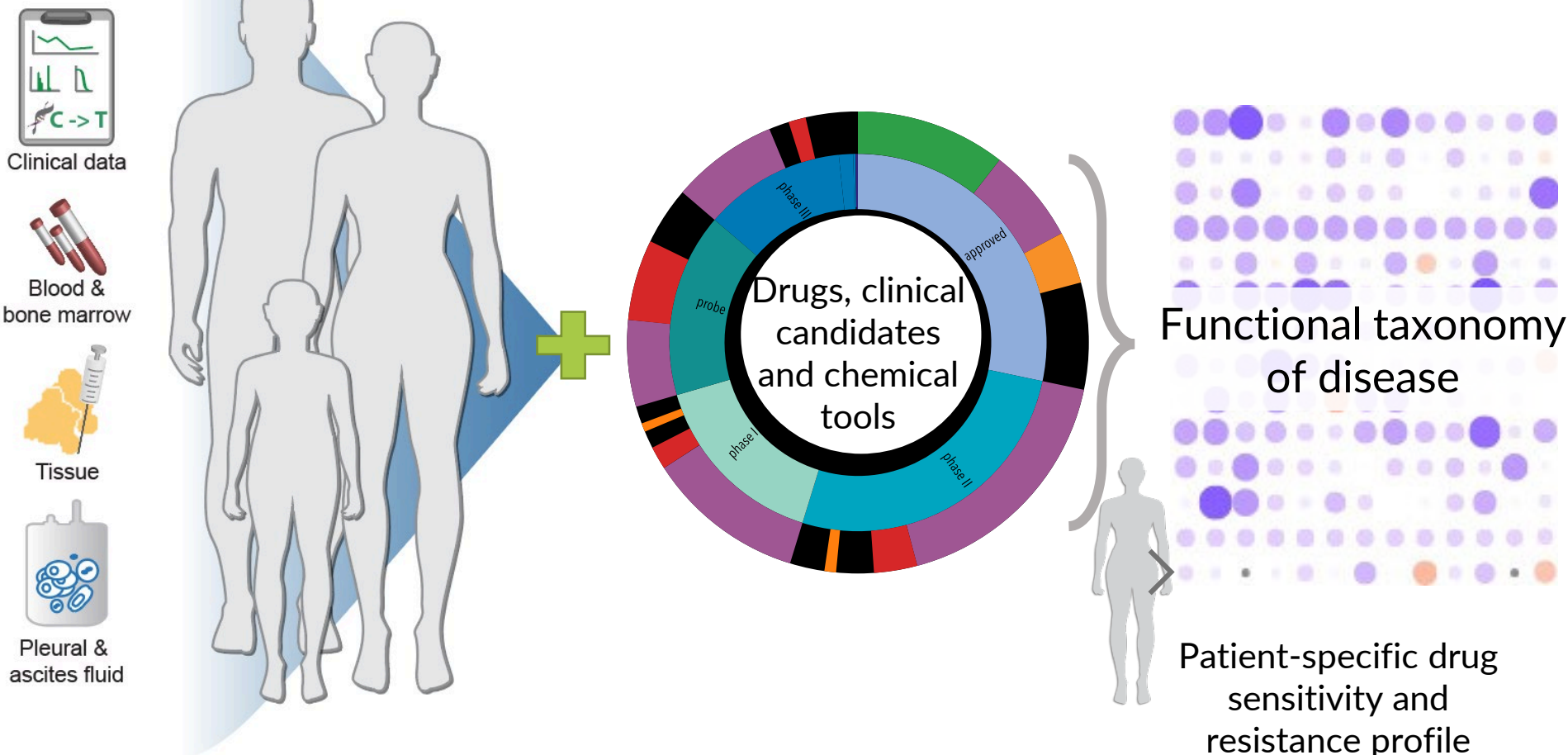
Compound and Disease profiling – Morphological profiling – Cell painting



Compound and Disease profiling – Functional precision medicine



Profiling of primary, patient-derived or complex cell models to better understand the drug sensitivity patterns in human disease.



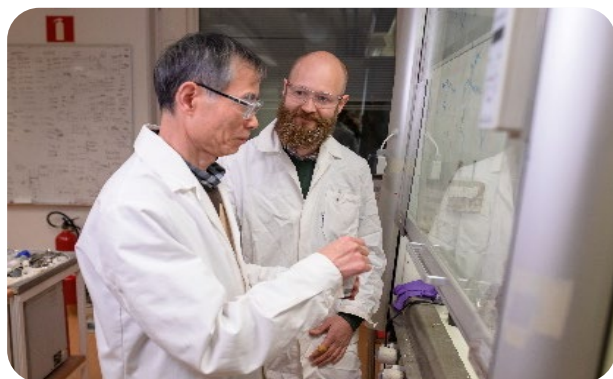
Current Services

- Drug library design and delivery
- Assay development
- Guidance and support regarding sample logistics, ethical permits, best practices

Enabling Chemistry support

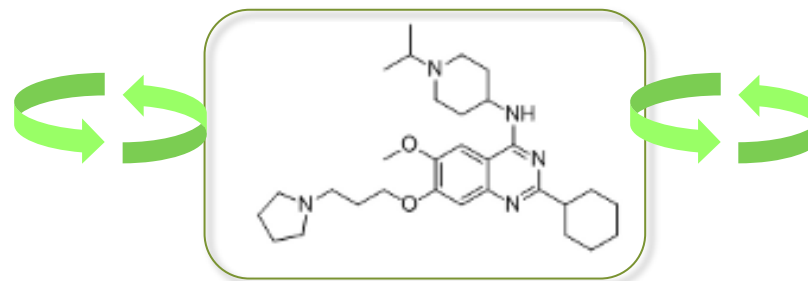
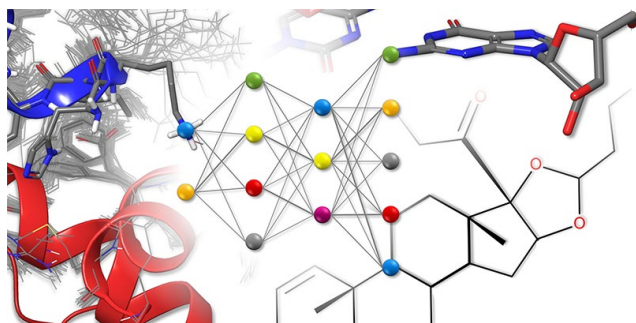


Virtual Screening - Docking
Hit Evaluations
Design - Make - Test - cycles



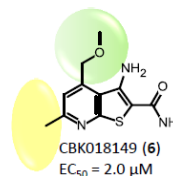
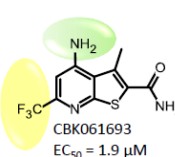
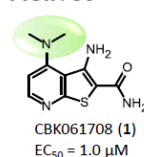
Medicinal
Chemistry

Computational
Chemistry

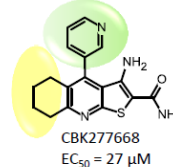
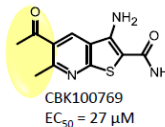
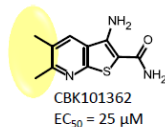


Biological
Assay

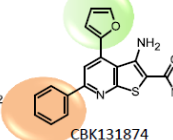
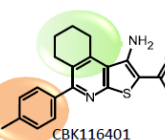
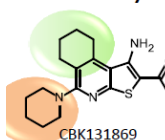
Actives



Some activity



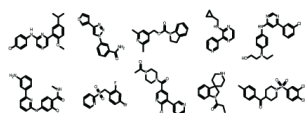
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CBCS Research Services



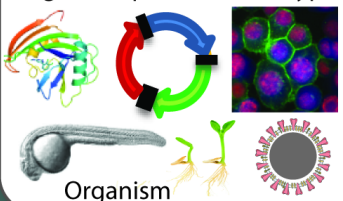
High-quality chemical libraries



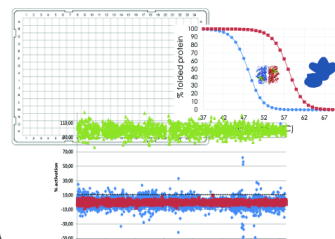
~ 350,000 compounds,
chemically diverse to
chemogenomics libraries

Industry-standard Assay development

Target Reporter Phenotypic



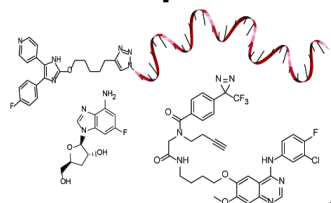
Small molecule screening



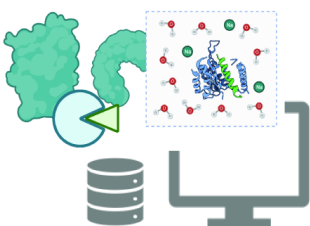
Chemical Biology Services



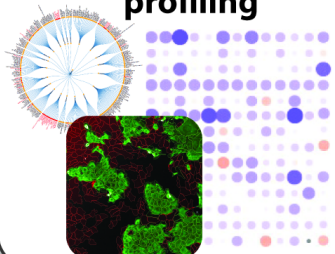
Enabling chemistry & quality assurance of hit compounds



Virtual Screening & Chemoinformatics



Disease & compound profiling



High-quality data & knowledge fueling biological discovery & innovation

Understanding of fundamental biological processes

Contribution to basic science

High impact publications

Drug Discovery & Development



Pharmaceutical industries

Innovation offices at universities

Incubation system for start-ups

Project types



- Pre-projects/ Consultancy
 - intellectual input from CBCS staff scientists
 - limited experimental support
 - delivery of limited number of test compounds
 - access to instrumentation
- Open Access – after training access to our instruments
- Service project
 - limited in time (~2 weeks of CBCS staff scientist support)
 - access to Compounds or Screening sets
- “Large” projects
 - more of CBCS resources is needed, 6 month – 2 years,
 - Assay development, Screening and/or Chemistry based or profiling projects

“first come – first serve”

PROJECT REVIEW COMMITTEE (PRC)
External and objective,
representatives from academia and pharma industry

Project Review Process



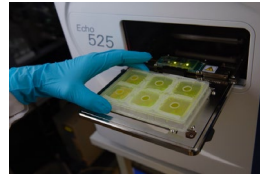
1



PI: Introduce project and goal

CBCS: Review technical feasibility, introduce working model

2



PI: Pre-project assay work

CBCS: Intellectual input, limited experimental work, delivery of test compounds, access to instrumentation

→ **pre-Project – to find out: Service project? Open Access? Larger project?**

3



Project proposal with Chemical Biology Consortium Sweden

Instructions: Project proposals are uploaded directly as a pdf file into Anubis in the open call for larger CBCS project support. All material is considered confidential, and access is restricted to a limited group of CBCS Project Review Committee members and CBCS personnel under conditions of confidentiality, solely for the purpose of evaluating the proposed research.

The scope of the collaborative CBCS projects varies significantly and the different project types require different competencies from CBCS. To ensure that we can deliver support to prioritized projects, we categorize the project proposals as either of the types 1-3 below.

PI: PRC application using CBCS template

CBCS: technical feasibility, resources and time estimates, database searches - novelty

PROJECT REVIEW COMMITTEE (PRC)
External and objective,
representatives from academia and pharma industry

Application deadline
Autumn 2023
September 18th

5



PI: Sign agreement including project plan and cost estimates, deliver reagents

CBCS: Initiate work on the project

→ **Project start**

4



1. PRC meetings bi-annually, gives **priority A-E**
2. CBCS node leaders plan work and **gets steering group approval** for the plan

PRC evaluation



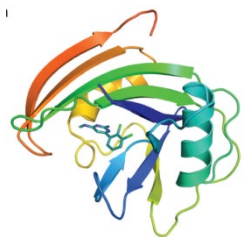
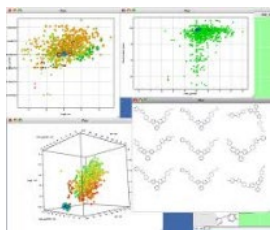
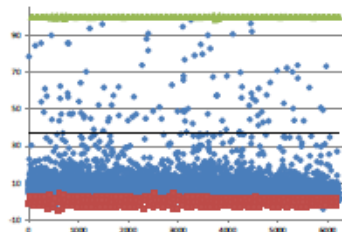
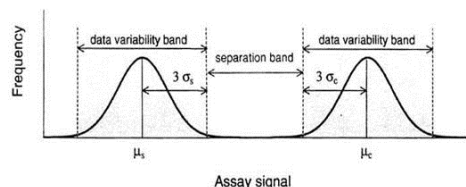
- Biological rational and potential scientific impact:
 - Research/technological quality with comments
 - Novelty and originality with Comments
 - Relevance with Comments
 - Overall score with Comments
- Importance of CBCS efforts
- Availability of described assays, resources and funding incl. follow up and validation studies
- Scoring of publication plans

CBCS evaluation

- Is the requested work from CBCS feasible?
- How many full-time months of work from CBCS?
- Are there already small molecules available?
- List secondary assays suggested

- Monitor national spread and gender perspective

CBCS collaborative research services



- Assay design and development
- Formating 96 - 384 well plates

PI & CBCS

Pre-project /
Assay
development
project

- The "Screen"
 - Pre-screen
 - Full deck screen
 - Follow up in several concentrations
 - Counter screen

CBCS (PI)

Screening
project

- Hit Confirmation
- Orthogonal assays
- In silico profiling
- Re-Synthesis of hits
- Test analogs - crude SAR

CBCS (PI)

- Medicinal chemistry to establish SAR and optimizations for further studies

CBCS & PI

Chemistry based
project

CBSC Large Projects Call Fall 2023

← ↻ 🏠 <https://anubis.scilifelab.se/call/CBCSLP23F>

SciLifeLab Anubis Calls Documentation About

Call for proposals CBCS Large Projects Call Fall 2023

Identifier CBCSLP23F

Opens 2023-07-02 00:00 Europe/Stockholm **Open.**

Closes 2023-09-18 14:00 Europe/Stockholm **45 days remaining.**

My proposal You need to be logged in to create a proposal. [Login](#)

Description

The unit for Chemical Biology (Chemical Biology Consortium Sweden - [CBCS](#)) at SciLifeLab is looking for chemical biology expertise to academic groups across Sweden in a collaborative project model.

The support may include:

- Assay development and screening of small molecules and drugs, including projects in BSL2/3
- Synthetic organic and medicinal chemistry support (functionalized molecules for pulldown, activity based probes)
- Computational chemistry (such as virtual screening, chemoinformatics, machine learning)
- Access to small-molecule and annotated drug libraries.
- Drug and/or disease profiling using Cell Painting -Support for functional precision medicine projects monitoring

All applications are ranked by our external project review committee based on scientific potential and feasibility. Priorities are given to projects with high scientific potential and feasibility. We require a demonstration of technical feasibility thus we require that you contact CBCS well in advance (at minimum 2 weeks before deadline) to discuss your project and application. Projects are expected to start Spring 2024. See www.cbcs.se for your nearest point of contact.

Labels

-

Documents

Template CBCS project proposal_Autumn_2023.docx [Download](#)

Template for the description of the project proposal.

Dummy example CBCS project proposal.pdf [Download](#)

A dummy example proposal illustrating the level of detail expected for proposals within this call.



Contacts us
minimum **2 weeks**
before deadline to discuss
your project and application!

www.cbcs.se