











SRC funded National Infrastructure for Chemical Biology at six universities

Anna-Lena Gustavsson

www.cbcs.se













# Infrastructure Capabilities



#### **Platforms**



### Capabilities

- Pandemic Laboratory Preparedness
- Precision Medicine and Biomarkers
- Planetary Biology
- Systems Biology
- Spatial and Single Cell Biology
- Structural Biology
- Data-driven Life Science
- Drug Discovery and repurposing etc.













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# **CBCS Mission – Chemical Biology**



The mission of CBCS is to, in collaboration with research groups, develop and utilize high-quality small molecular tools to address important biological questions within all areas of life science.

- Explore biology!



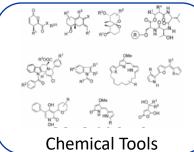
**Research Community** 



**CBCS** Infrastructure



**Basic Research** 





**Environment** 



**Human Health** 



**Veterinary Medicine** 



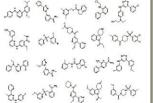
Plant Physiology



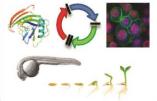
### **CBCS Services**

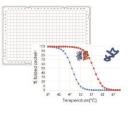






Assay development

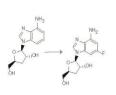




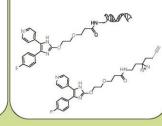
Small molecule Screening



Hit and SAR exploration



Mechanism of Action studies



Understanding of fundamental biological processes

Contribution to basic science

High impact publications

### **Chemical Biology**

Biological / medical questions & hypotheses **Basic Research** 

Validated research tool compounds & biology

Drug Discovery & Development



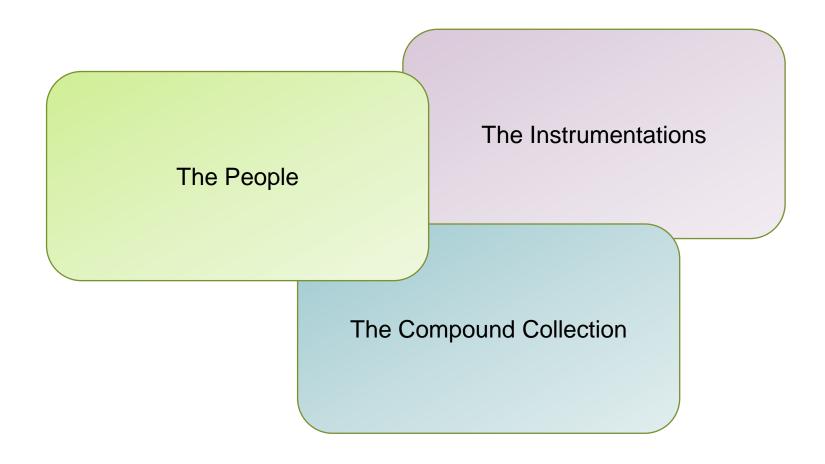


Pharmaceutical industries Innovation offices at universities Incubation system for start-ups



### **CBCS** Resources







# The People

# Karolinska Institutet

#### **CBCS** Staff scientists:

- Assay development
- Screening
- Compound Management
- Medicinal chemistry
- Computational chemistry
- Target ID

With both academic and "pharma" experience.

Highly linked to strong research community!





























## The Instrumentations & Lab @







#### Assay development and screening

- Liquid handlers
- Plate readers
- High content screening

#### Echo 525&550 Multilabel plate readers FLIPR Tetra HTS **EnVision** system Multidrops Victor3 Robotic arm ImageXpress Micro XLS high PreciseFlex 400 content microscope navigating our screening hub Bravo AquaMax Pipetting robot **Molecular Devices**

#### **Synthetic Chemistry**

- Fully equipped chemistry laboratories
- Chemical stores w/ 17,000 reagents
- NMR spectrophotometers, HPLC-MS, prep-LC, microwave reactors







## The Instrumentations for fragment-based screening



- Swedish NMR Centra.
- Some Users Drug Discovery & Development platform SPR
- Under discussion with Metabolomics platform RapidFire MS
- MAX IV



# **The Compound Collection**



High-quality chemical libraries

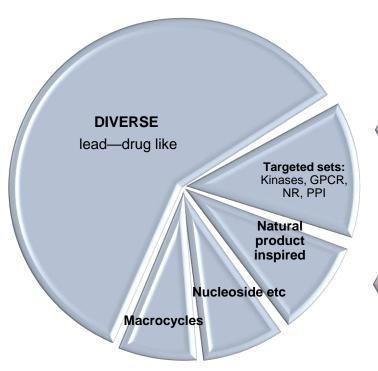
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Enabling chemistry of hit compounds

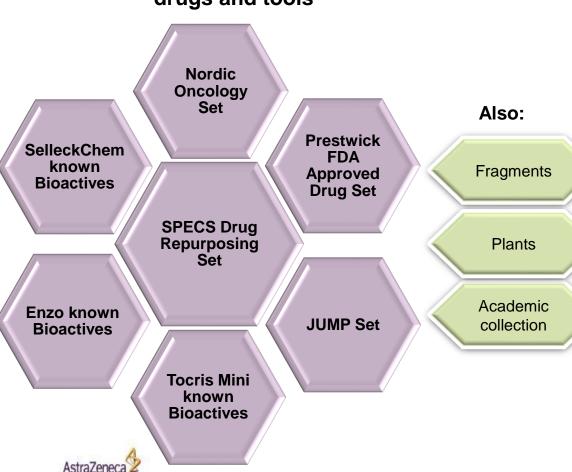
~350 000 compounds
Donations from
ex-pharma and biotechs
Commercial vendors

### Primary Screening Set – 35 k compounds

Diverse representatives includes sub-sets focused on target classes or chemotypes



## Annotated Compounds – drugs and tools





Phenotypic Screening Collection 14 000 compounds covering 1700 targets



### Fragments

### 4 sets of Fragments:

- Scilifelab Chemical Inventory storage 1000 cmpds, 50 mM DMSO
- MayBridge fragment set (UmU NMR) 1000 compounds, 100 mM d-DMSO
- F-fragments (NMR)
  - Scilifelab Chemical Inventory Storage 96 compounds, 100 mM DMSO
  - Key Organics Bionet (DTU collaboration)- 462 compounds; 200 mM DMSO



# The Compound Center @ Karolinska Institutet





A multidiciplinary team with expertise in:

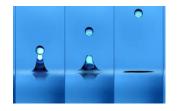
- Technical proficiency
- Chemistry
- Process engineering
- QA/QC
- · Automation solution development

Logistics





10 mM DMSO stock solutions stored @ - 20 °C, humidity control instrument: LiCONiC Kiwi



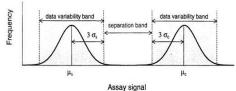




https://compoundcenter.scilifelab.se/

## **CBCS** collaborative project model

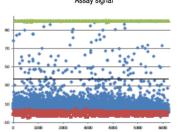




Assay design and development

PI & CBCS

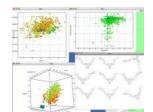
Months/ years Pre-project /
Assay
development
project



• Screen

CBCS (PI)

Days



Data analysis

- Hit confirmation
- · In silico profiling
- etc

CBCS (PI) Weeks

Screening project



- Medicinal chemistry
- Compound profiling
- Biological profiling
- Target ID /MoA

CBCS & PI Months/years

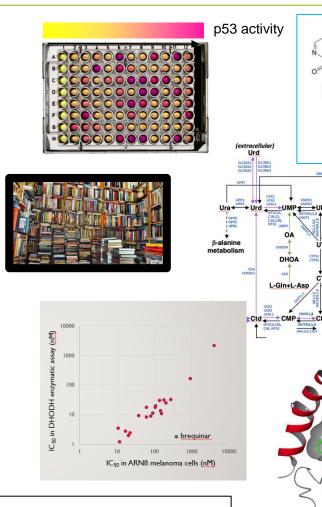
Chemistry based project

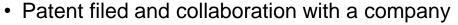
### PI: Sonia Lain, Karolinska Institutet



- Background: research group with strong interest in the tumor suppressor p53 biology
- Aim: to identify compounds that activates p53 to possible cancer therapies
- Method: Phenotypic screen
- Results:
- Several chemotypes identified => SAR established
- Mechnism of Action Elucidations Knowledge based strategy
  - DHODH identified as primary target
  - Linked PI with SAROMICS => structure-based optimization of lead series
- Project continued with
  - DDDp at SciLifeLab
  - Karolinska Innovation AB







• Published: Nature Com. 2018; J Med Chem 2020



### CBCS achievements 2010-2021



- Supported more than 230 individual users from all major Swedish universities.
- 170 publications
- > 10 patents
- ~10 projects advanced into innovation systems
- 7 start-up companies
- New project proposals from PIs every week (480 entries in project database)

















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