Drug Discovery and Development Platform

Turning Discoveries into Innovations

Information event 2023-01-24

Call for new drug discovery pilot projects at SciLifeLab DDD with special emphasis on new modalities and antibiotics

DDD platform Directors:
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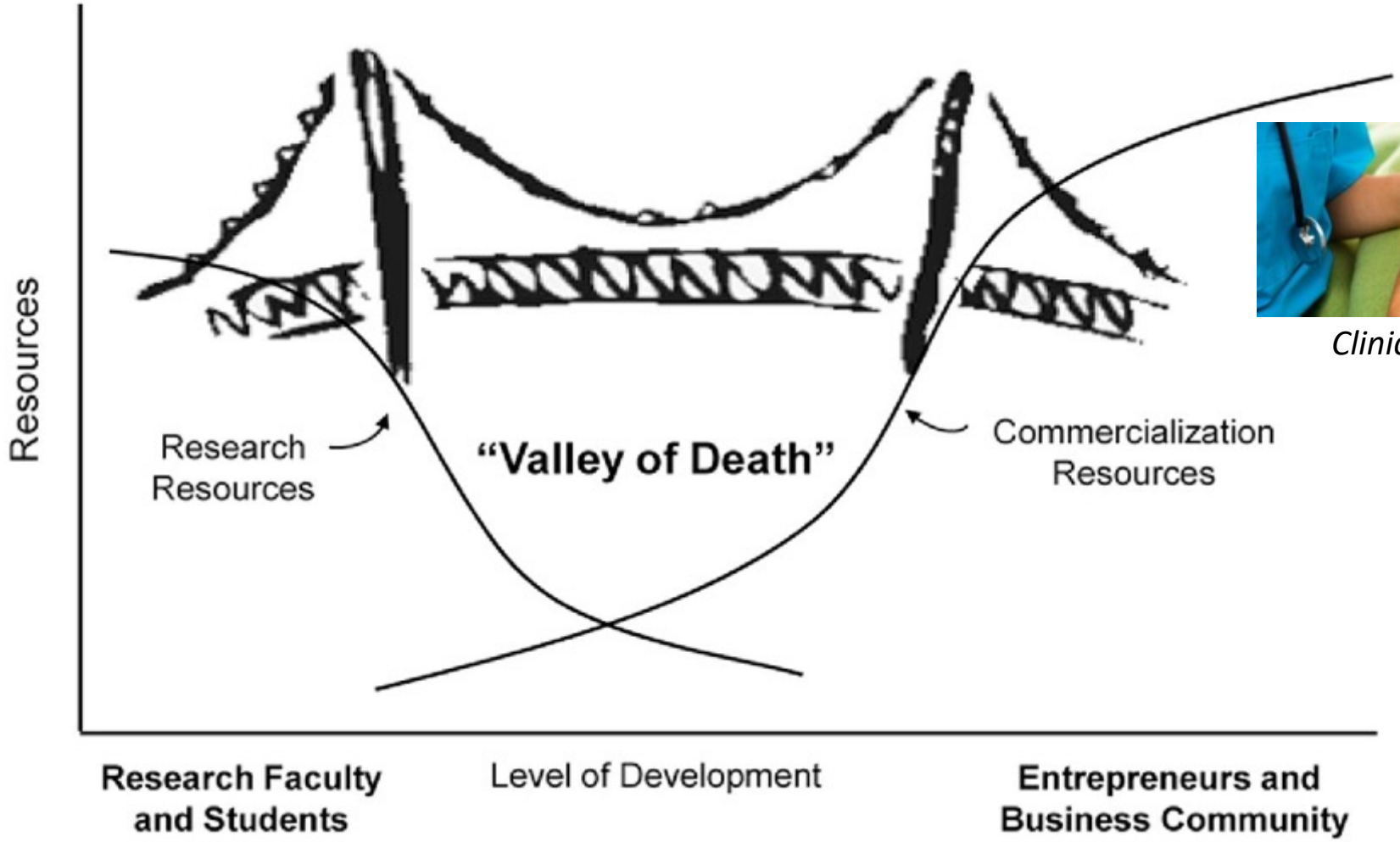
SciLifeLab DDD Objective

"Turn academic discoveries into innovations"

Drug Discovery?

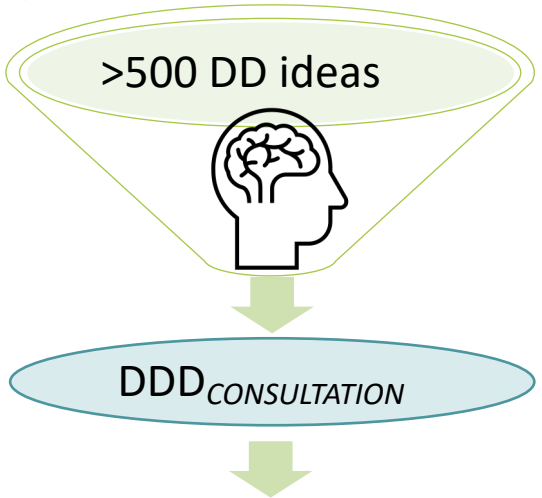
Validation?
Proof-of-concept?
Safety?
Competition?
Need?
Biomarkers?
Clinical?
….



Clinical use

SciLifeLab DDD Capabilities

"Provide State-of-the-art Drug Discovery & Development knowledge in Sweden to support innovations"



DDD *PROGRAM* **DDD *SERVICE***

HAND OVER

- **Small molecules**
- **Antibody therapeutics**
- **Oligonucleotides**
- **New modalities**

SciLifeLab

CBGE, Integrated Structural Biology, Cellular and Molecular Imaging, Metabolomics, Genomics, Bioinformatics, DataCenter, etc.

Host Universities

UU, KTH, SU, KI, LU, GU

DDD *COLLABORATIVE*

- **Contractual ability**
- **Partnerships**
  - InnoPharma (Vinnova)
  - EUbOpen (IMI)
  - Conception (IMI)
  - ENABLE2 (VR)
  - MURYXIN (JPIAMR)
  - Nevermore Covid (SciLifeLab/KAW)
  - …

Validated DD programs

Exits: 2 Programs & 40 Service / year

4 Clinical
4 Internationally partnered
9 Swedish biotechs (3 listed)

elicera THERAPEUTICS · AlzeCure Pharma · LIPUM

Consultations and Project Review

- *CBCS/CBGE*
- *ELF/EU Open screen*
- *CRO's*

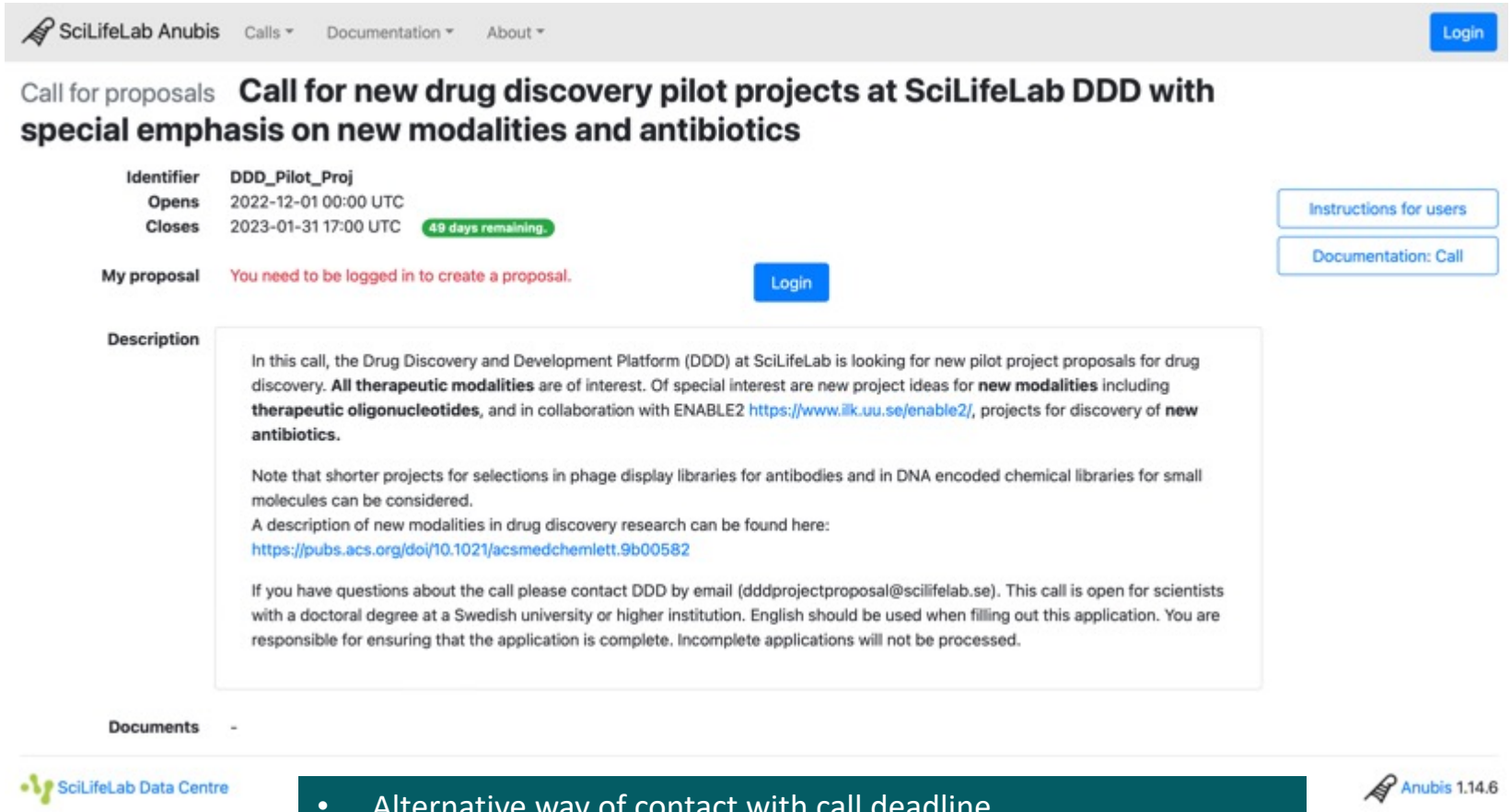
"Beginning with the goal in mind"

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 & publication strategy
6. The feasibility to conduct a phase 2 study
7. Competence and ability of PI team
8. Technical feasibility to develop a drug
9. PI entrepreneurship

Academic customers - Personnel & Infrastructure included, user pay for consumables

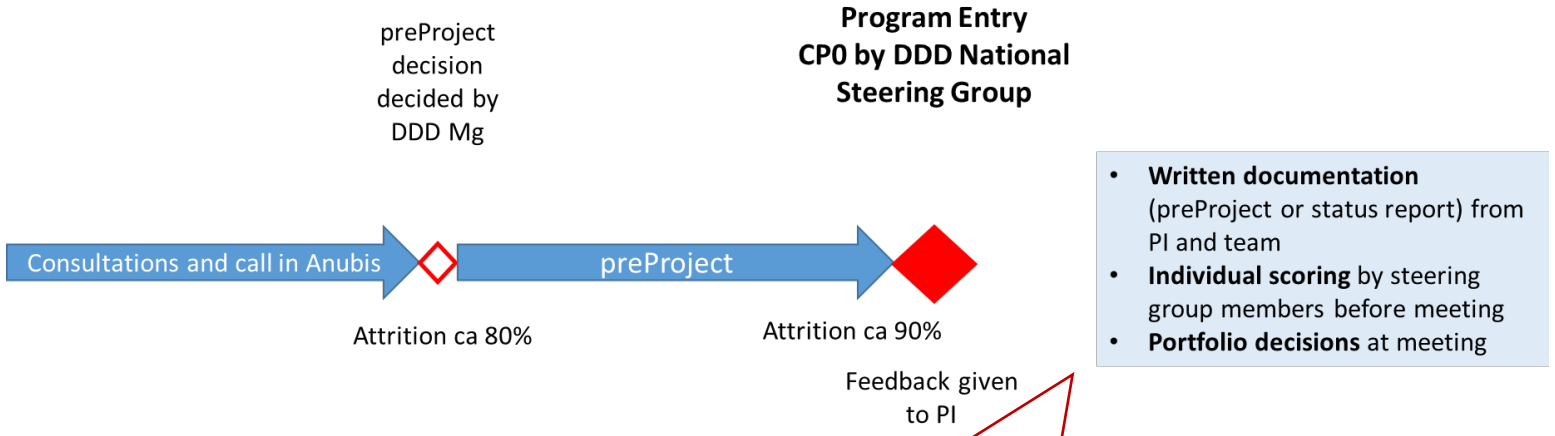
Anubis call for pilot-projects

https://anubis.scilifelab.se/call/DDD_Pilot_Proj



- Alternative way of contact with call deadline
- Provides suitable level of background
- Used to prioritize consultation meetings
- Used for external pre-review of Oligonucleotide projects

Timelines Q1/Q2, 2023

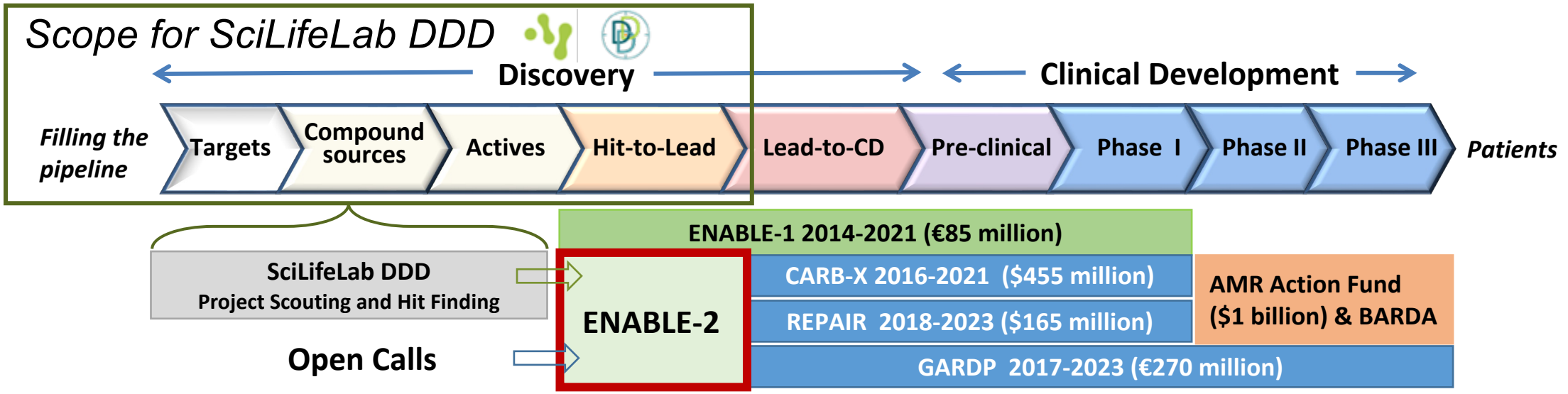


Important timelines early 2023

- National call in Anubis December 1st – January 31st
- preProject decision mid-February
- preProject phase: mid-February – late March
- Start of new programs: June 1st

Focus 1: ENABLE2 – antibacterial drug discovery

ENABLE2 – VR funded continuation of the IMI program for antibacterial drug discovery with focus on the early stages of antibiotic discovery and development.



Enable2 entry thresholds

- Molecules/series with a novel mode of action targeting in-scope pathogens
- Minimum inhibitory concentration (MIC) ≤ 16 µg/mL vs. at least one of the key ENABLE-2 pathogens *E. coli, K. pneumoniae, P. aeruginosa, A. baumannii, S. aureus, E. faecium*
- Potential for optimization

Application and details:

https://www.ilk.uu.se/enable2/apply/

Call currently (Jan 2023) closed but projects fulfilling critera is still encouraged to contact Anders Karlén

Focus 2: Tomorrows therapeutic modalities?

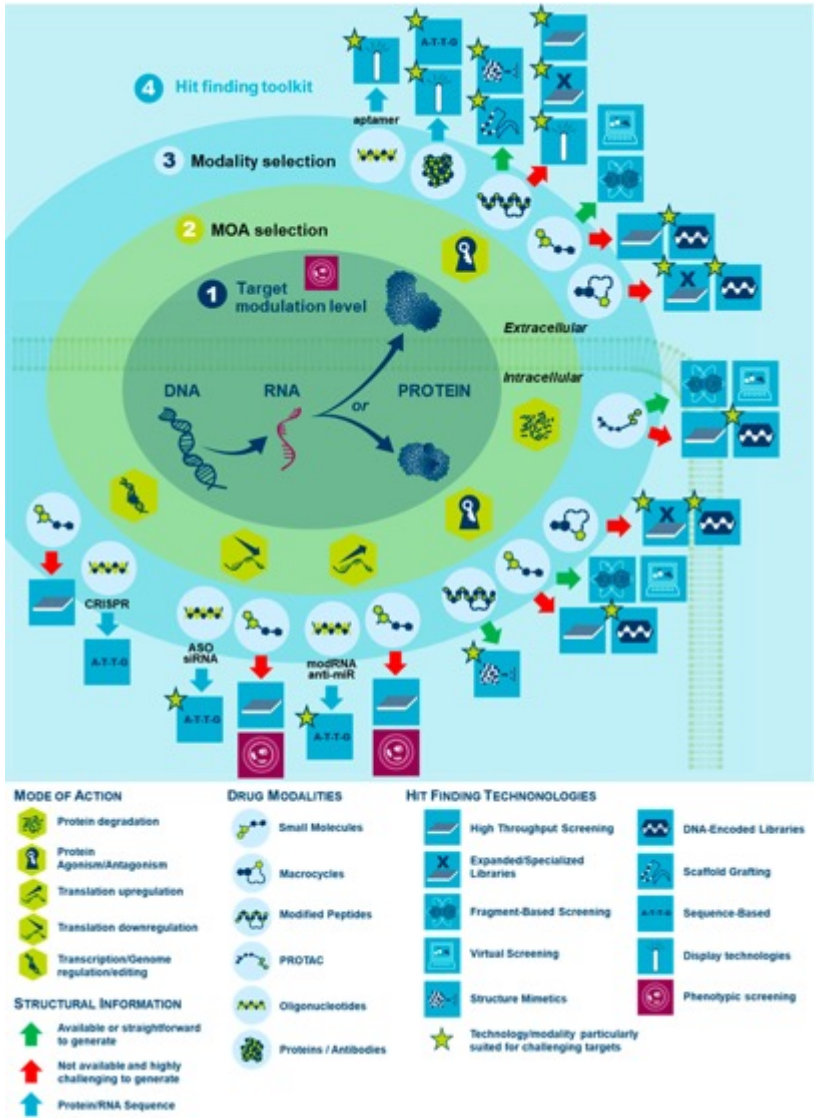
20 000 proteins

3824 disease linked

1265 “druggable”

672 “drugged”

<20% of disease-linked proteome



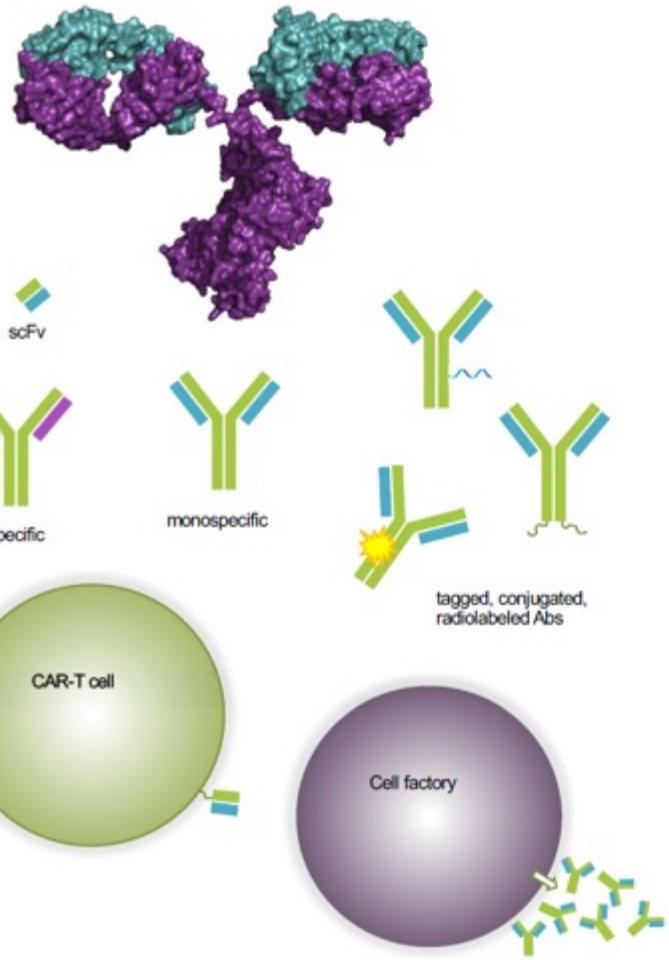
Drugging the ”undruggable”

New modalities
&
New technologies

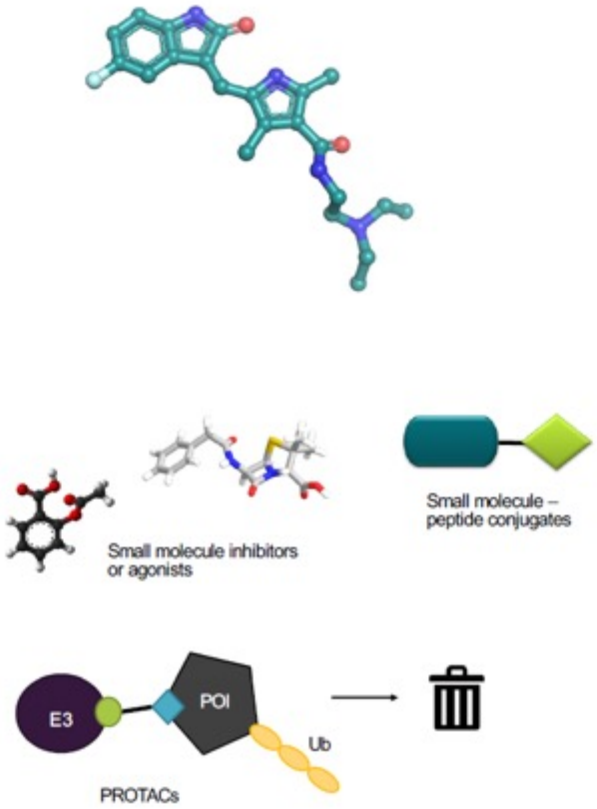
E. Valeur; P. Jimonet *J. Med. Chem.* 61, 9004, DOI: 10.1021/acs.jmedchem.8b00378

DDD Toolboxes allows exploration of new modalities

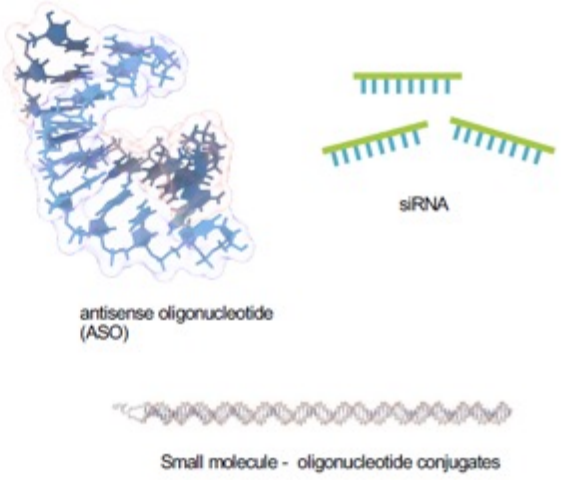
Antibodies



Small molecules



Oligonucleotides



The modalities shown here are examples of past and present DDD projects

Hub*

Centre for developing therapeutic oligonucleotides: medicines of the future

KAW, GU, SciLifeLab >100M investment in 2021

OligoNova

Professor Pär Matsson

Scientific Director of the OligoNova Hub

A **national research platform** that provides academic researchers in Sweden with the support and capabilities essential to transform ideas and discoveries into new therapeutic oligonucleotides.

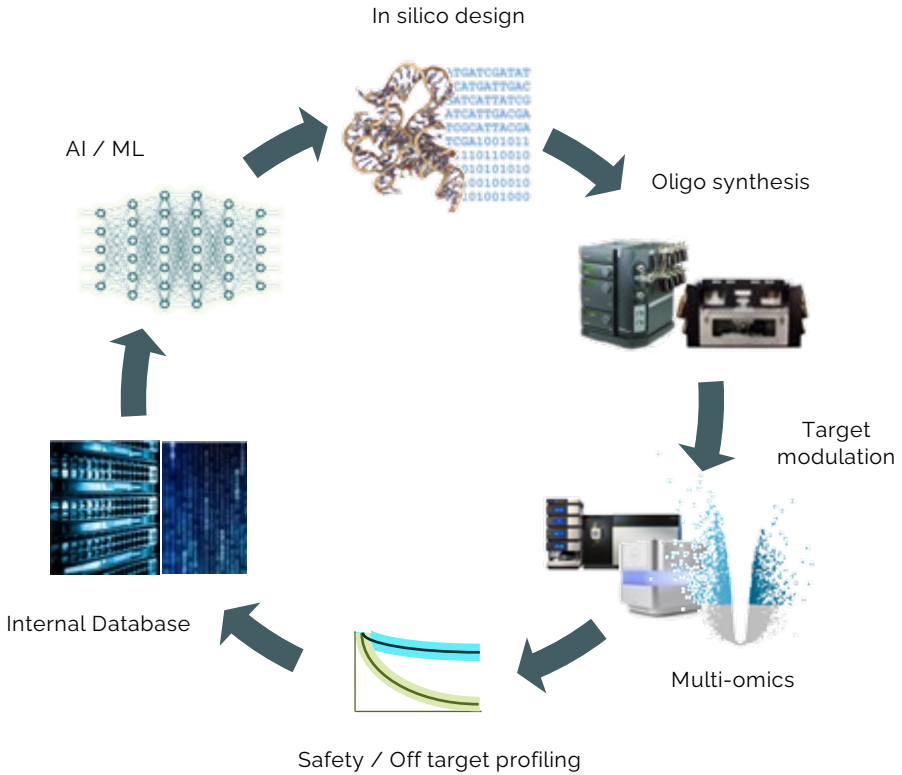
Part of the **SciLifeLab Drug Discovery and Development (DDD) platform** tasked with driving ideas for and research on novel therapeutic targets in Academia to preclinical Proof of Concept.

Home to 8–10 experts on oligonucleotide design, synthesis, and optimization, as well as assay development and oligonucleotide screening and imaging expertise.

Prioritized ideas and projects can access the entire infrastructure, services and knowledge via both the OligoNova Hub and the SciLifeLab DDD platform with around 40, highly motivated experts and scientists available for support.

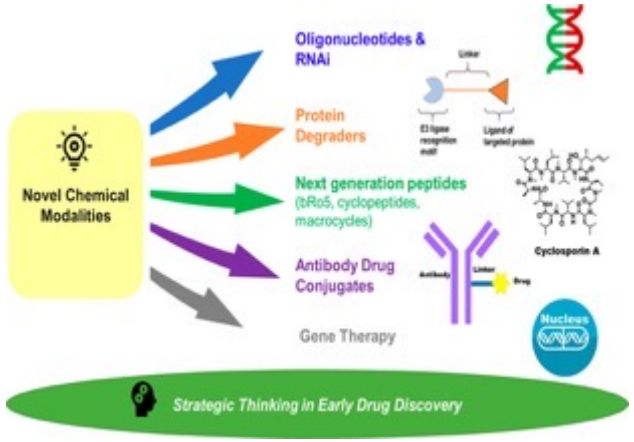
Established at the University of **Gothenburg** Core Facilities and physically located at the **AZ BioVentureHub** in the heart of **GoCo Health Innovation City**.

Expert capabilities on the design, synthesis, testing, and evaluation to drive drug projects.

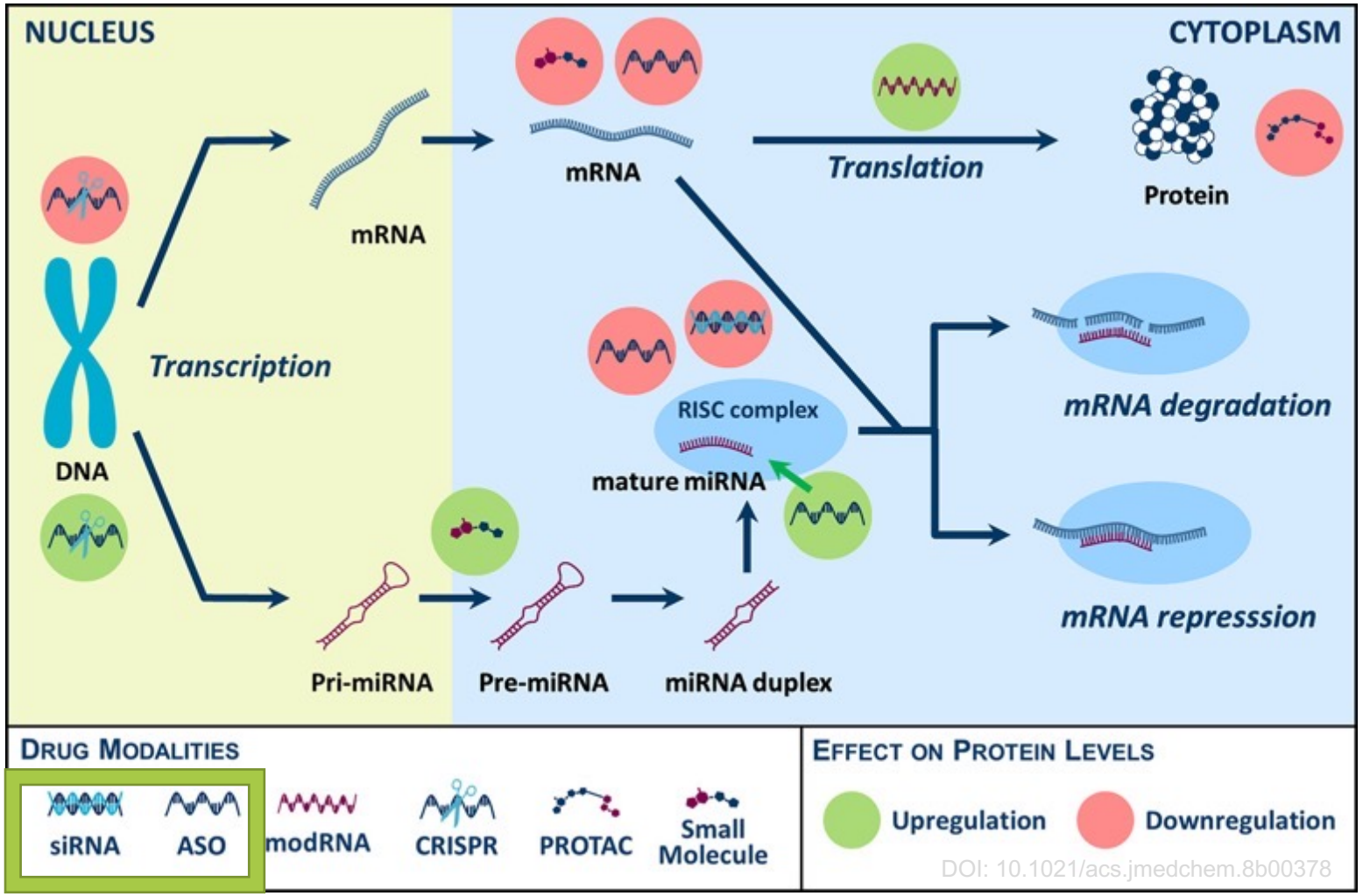


*All IP associated with research conducted at the OligoNova Hub belongs to the respective researcher according to the "Teachers' Exemption" applicable in Sweden.

siRNA and ASO Oligonucleotides



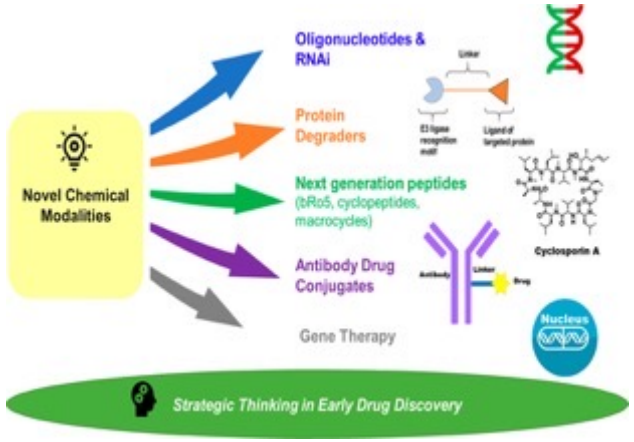
DOI: 10.1021/acsmedchemlett.9b00582



DOI: 10.1021/acs.jmedchem.8b00378

- Effect on protein protein levels – not activity
- Modify RNA splicing

Targeted Protein Degradation



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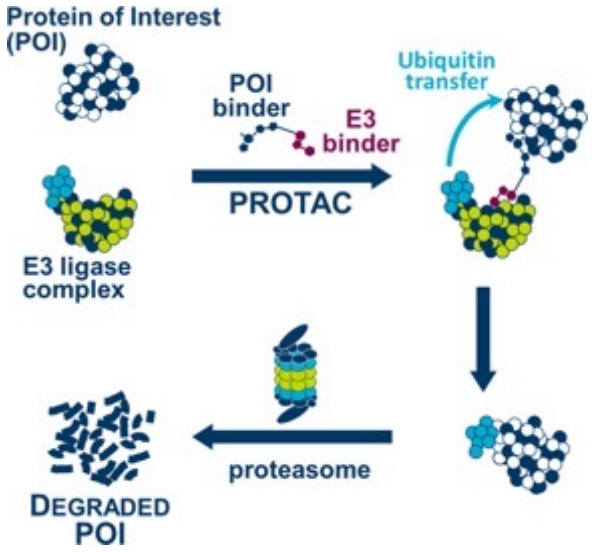

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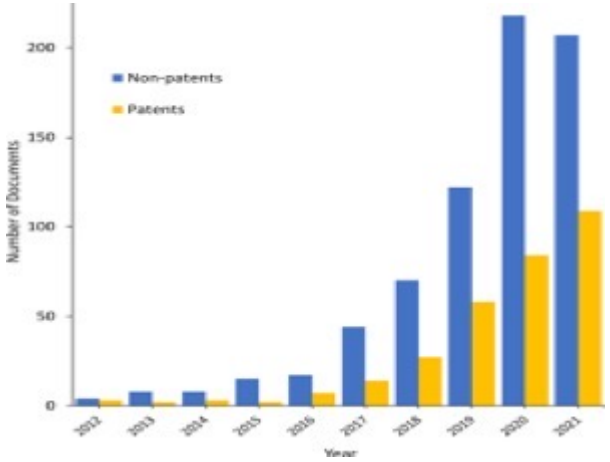
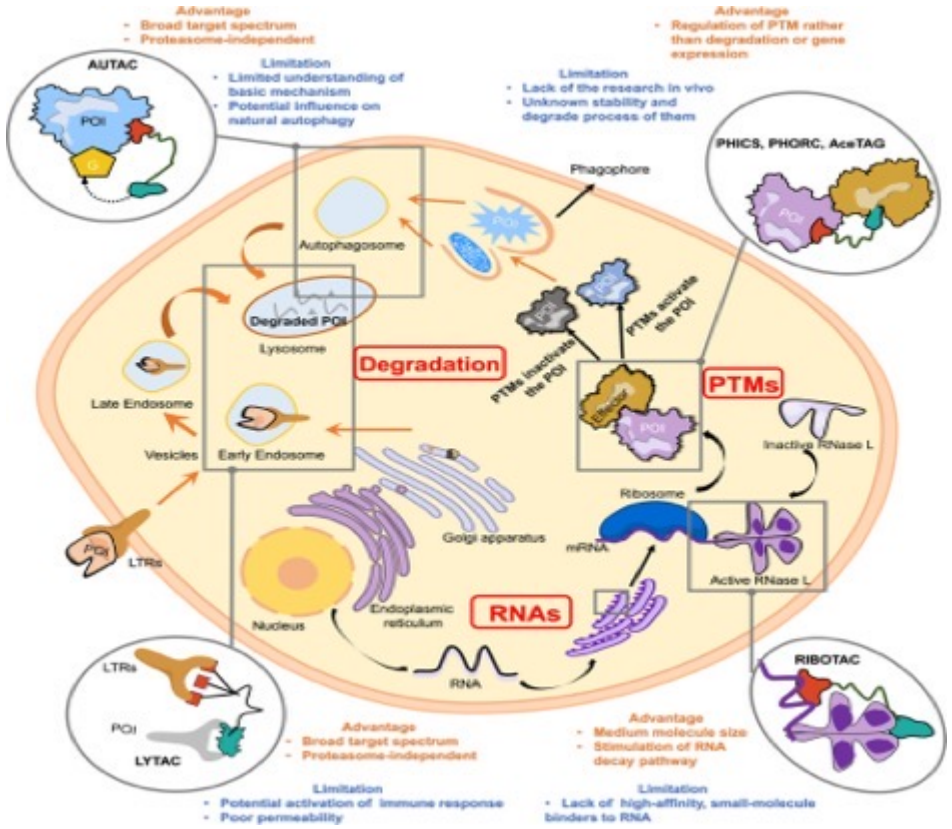


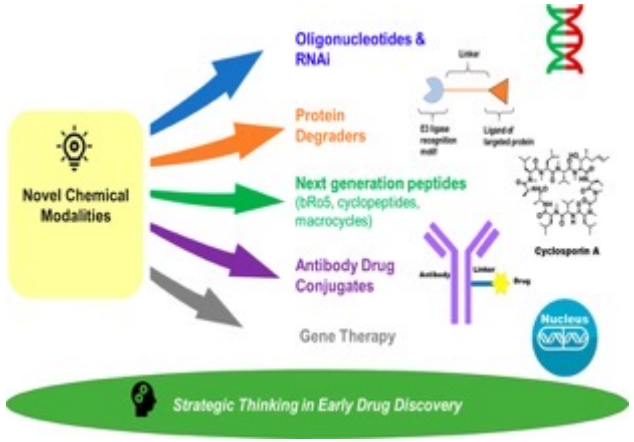
Sasso et al, Biochemistry 2022, in press



Hue et al. *J. Med. Chem.* **2022**, *65*, 8091–8112

- Intra- or extra-cellular
- Small molecule TPD clinically validated
- LYTAC and AbTACs for non-proteosomal TPD

Conjugates & Theranostics



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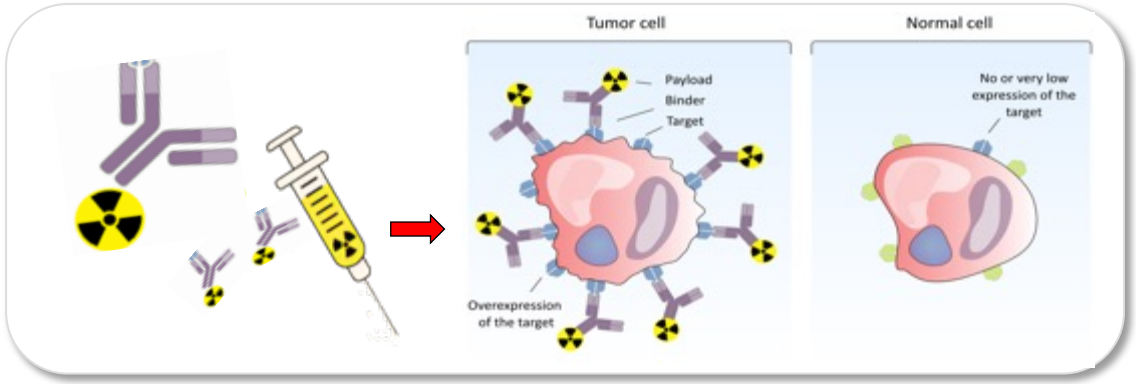
DDD exit in May 2022



Marika Nestor, UU
Associate Professor,
Department of Immunology, Genetics and Pathology, Uppsala University

Akiram Therapeutics

(68M SEK 230112)

New modalities – New Technologies

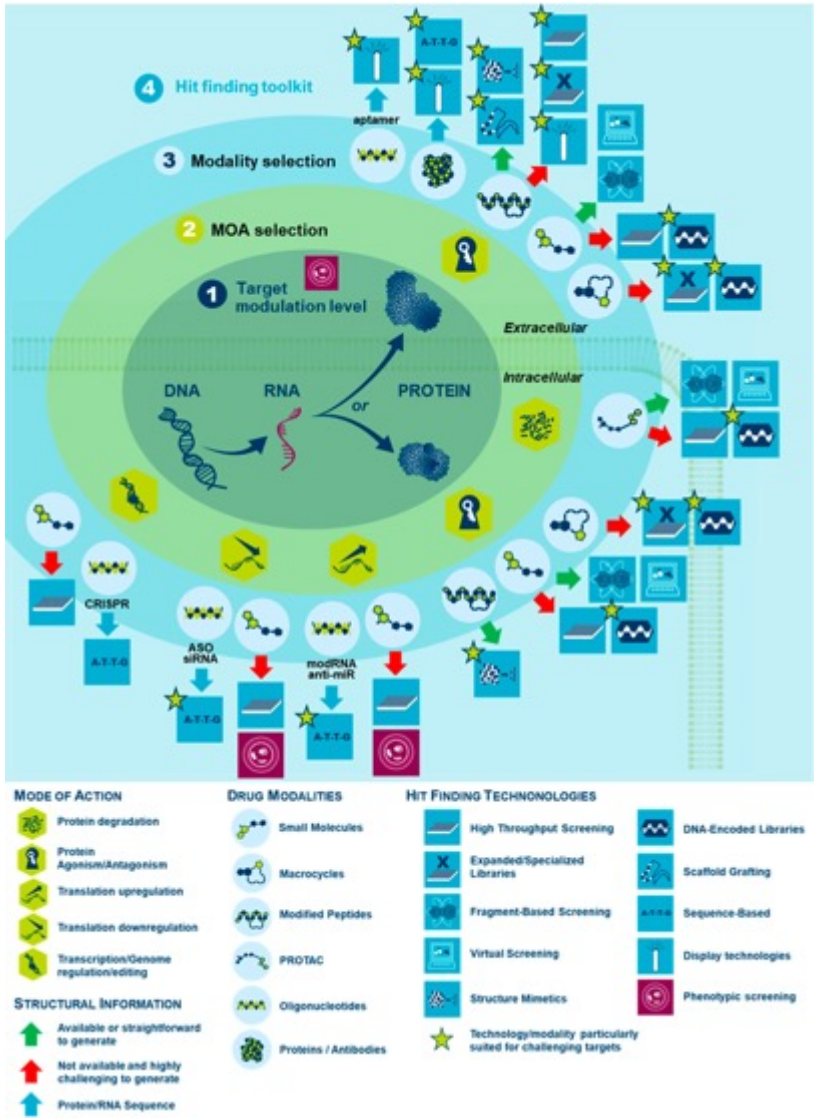
20 000 proteins

3824 disease linked

1265 “druggable”

672 “drugged”

<20% of disease-linked proteome

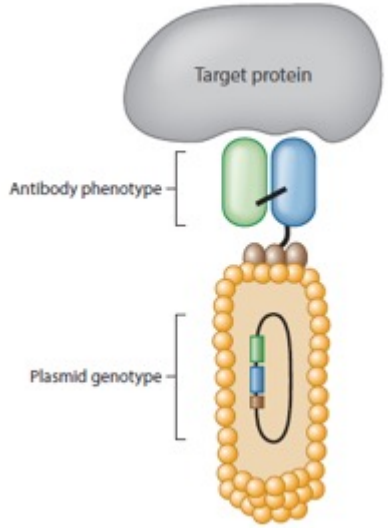


Drugging the ”undruggable”

New modalities
&
New technologies

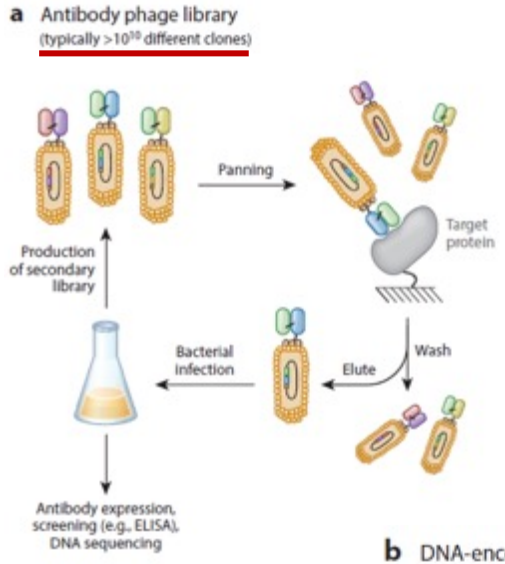
E. Valeur; P. Jimonet *J. Med. Chem.* 61, 9004, DOI: 10.1021/acs.jmedchem.8b00378

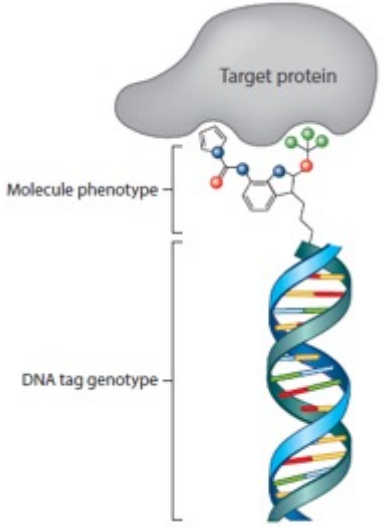
New technology: Display & Selection Hit-finding



Phage display for mAbs

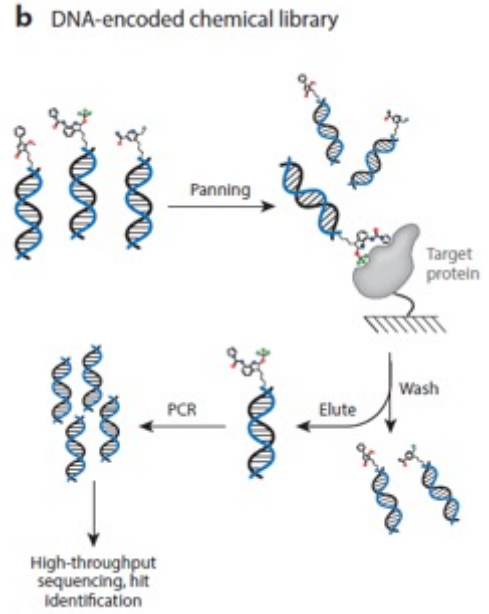
SciLifeLibs 1-5





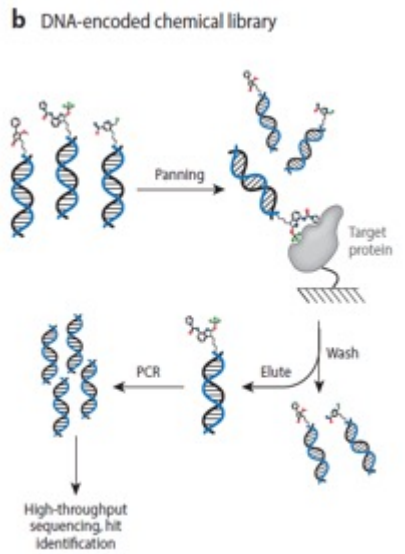
DEL affinity selection for small molecules

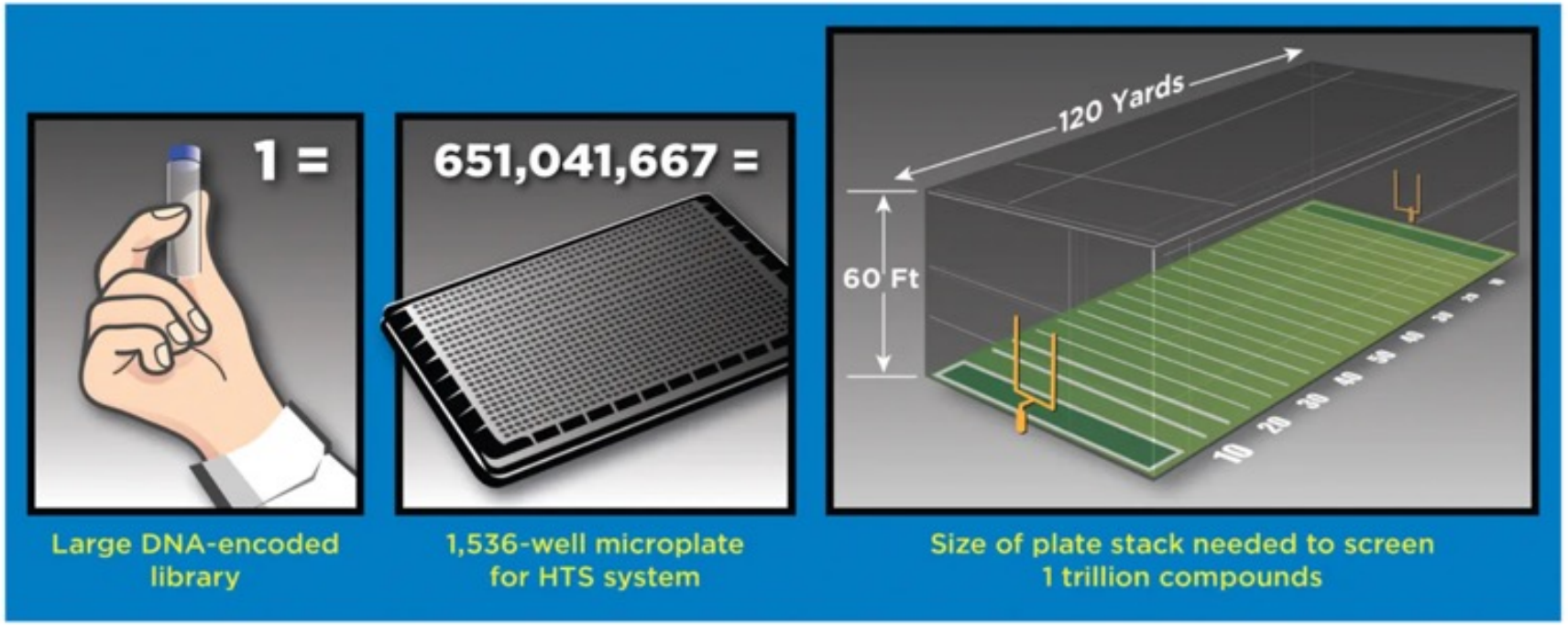
New SciLifeLab DDD capability



Neri & Lerner Annu. Rev. Biochem. **2018**

Hit-finding technologies: Display & Selection





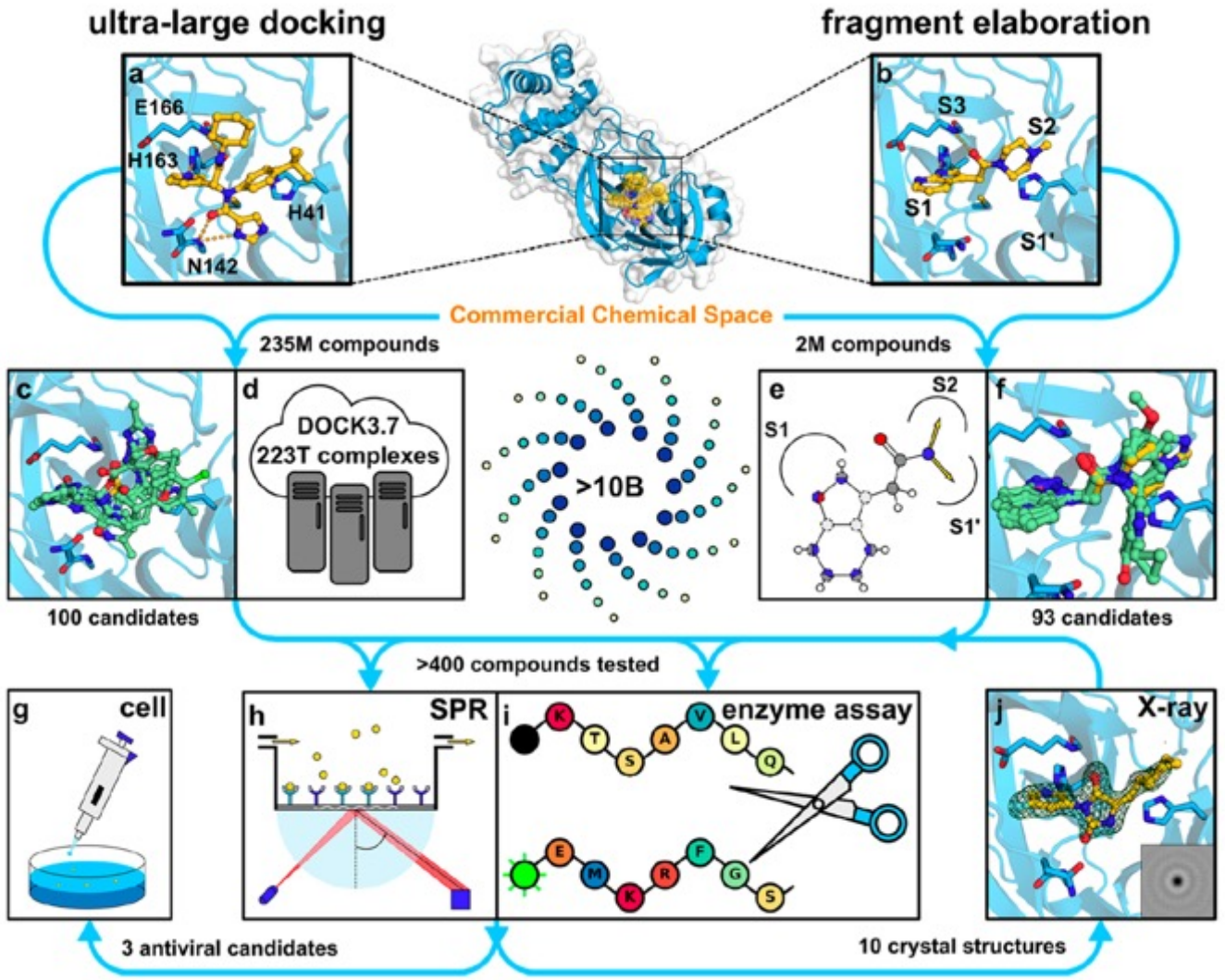
With DEL technology, you can make and screen libraries of up to a trillion or more compounds. What would it take to screen that many compounds with a conventional system? Using standard 1,536-well plates, you'd need a stack of plates large enough to cover an American football field—to a height of 60 feet. At the standard speed of 100,000 compounds a day, completing one full screen would take more than 27,000 years.

Combine with ML to probe SM-POI affinity SAR directly from the screen

Image from Amgen, https://www.amgen.com/stories/2019/11/dna-encoded-libraries-will-drive-new-drug-design-paradigm

Hit-finding 2: In silico screen & Make on demand

- DDD & CBCS Technology Dev. Project with NBIS for exploring ultra large chemical space



J. Am. Chem. Soc. 2022, 144, 2905–2920
https://doi.org/10.1021/jacs.1c08402

SciLifeLab Capabilities for Hit-finding

HTS Library	”Make on Demand” Libraries	DEL
Size: $<10^7$	Size: $<10^{10}$	Size: $<10^{13}$
Screening in microwell plates	In silico screening	Affinity selection in a tube
Functional cellular screen	Experimental evaluation	Recombinant protein

Technologies complement each other!

DDD Call: SM, mAbs, ONs, New modalities

https://anubis.scilifelab.se/call/DDD_Pilot_Proj

Important timelines early 2023

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- preProject decision mid-February
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SciLifeLab

Karolinska Institutet

KTH

Stockholms universitet

UPPSALA UNIVERSITET

SciLifeLab has been created by the coordinated effort of four universities in Stockholm and Uppsala: Stockholm University, the Karolinska Institutet, KTH Royal Institute of Technology and Uppsala University.