

Drug Discovery and Development Platform

Turning Discoveries into Innovations



Information event 2023-08-16

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

DDD platform Directors:

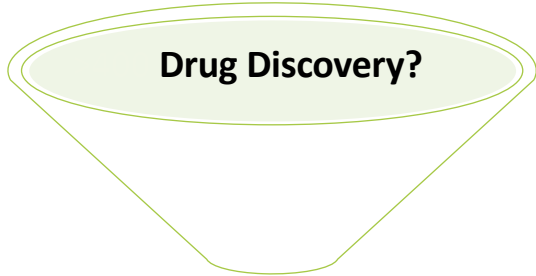
Per Arvidsson, KI: per.arvidsson@scilifelab.se

Kristian Sandberg, UU: kristian.sandberg@scilifelab.uu.se

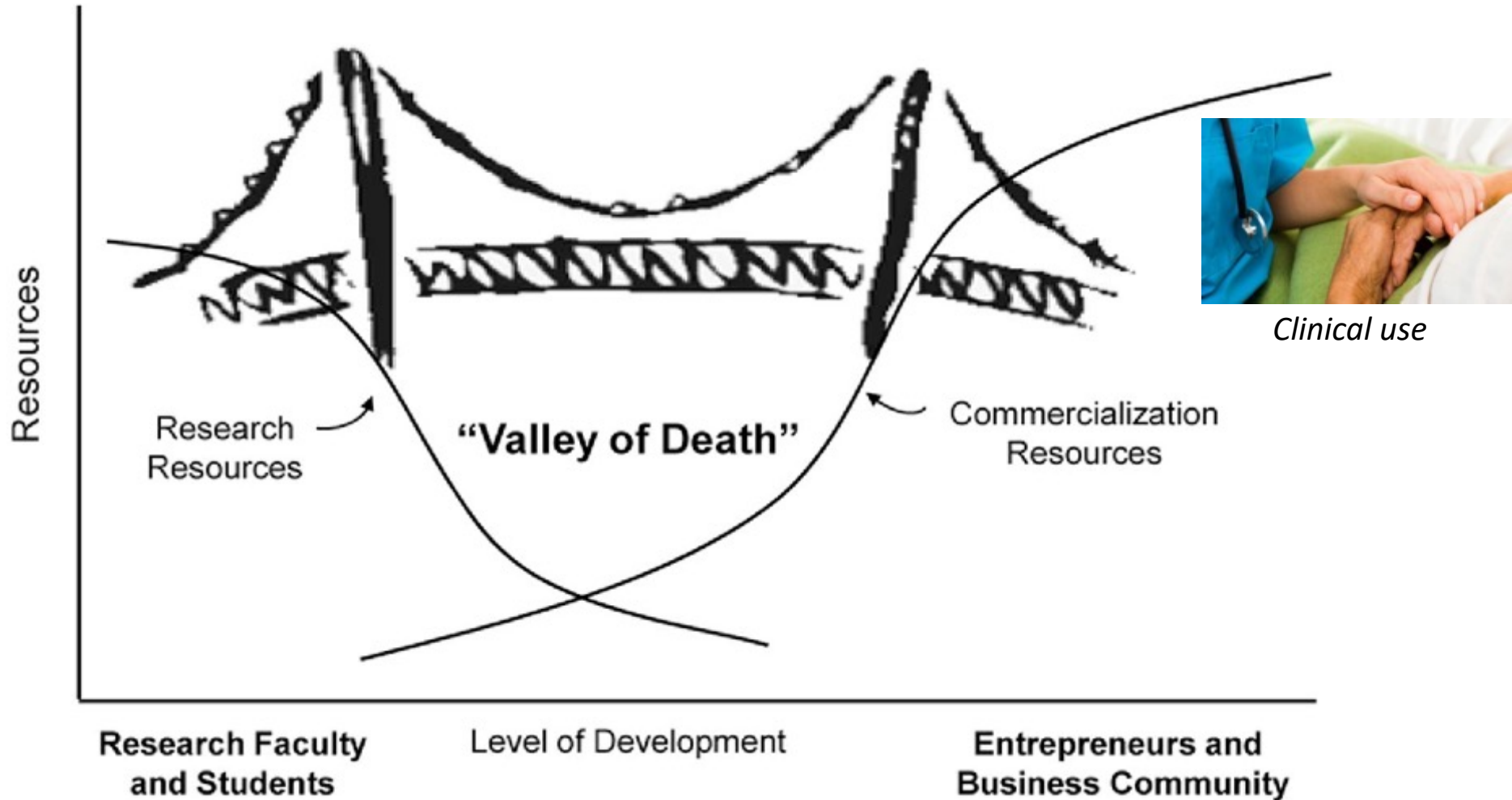


SciLifeLab **DDD** Objective

“Turn academic discoveries into innovations”



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



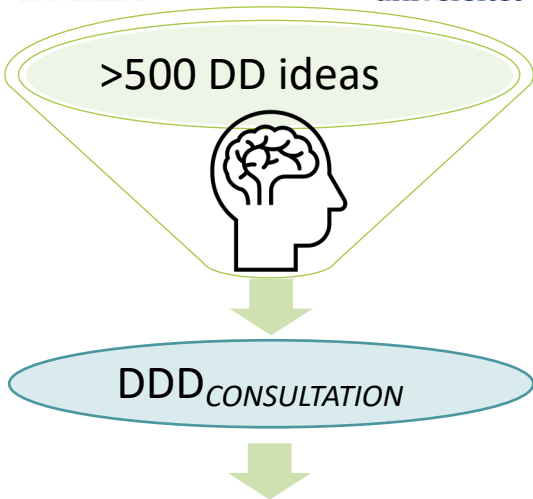
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SciLifeLab DDD Capabilities



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



DDD PROGRAM

DDD SERVICE

HAND OVER

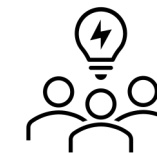


- **Small molecules**
- **Antibody therapeutics**
- **Oligonucleotides**
- **New modalities**



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
- 11 Swedish biotechs (3 listed)





DDD Collaborative models



DDD_{CONSULTATION} – confidential second opinion of project’s DDD potential

DDD_{preProject} - preparatory work before a **DDD_{PROGRAM}**

- Up to 10 months and may include QC of protein, in vitro ADME profiling, selections in phage-display or DEL, ONs for target validation

DDD_{PROGRAM} - only for academics

- In average 4 years with full support from DDD

DDD_{COLLABORATIVE} - access to infrastructure

- DDD as collaborator in research consortia. Primarily focus on technologies

DDD_{SERVICE} - access to spare resources

DDD National Steering group
External and objective,
representatives from
academia and pharma industry



Consultations and Project Review



”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



Anubis call for pilot-projects



https://anubis.scilifelab.se/call/DDD_Project_Call_summer_2023

SciLifeLab Anubis Calls ▾ Documentation About ▾

Call for proposals

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

Identifier DDD_Project_Call_summer_2023

Opens 2023-06-16 00:00 Europe/Stockholm Open.

Closes 2023-08-24 17:00 Europe/Stockholm 58 days remaining.

My proposal You need to be logged in to create a proposal. Login

Description

The DDD platform at SciLifeLab supports academic drug discovery project with expertise and technical capabilities. We have, for example, platforms to develop small molecule drugs, therapeutic antibodies, oligonucleotide therapeutics, proximity-inducing agents such as bispecific antibodies and PROTACs.

In this call, the Drug Discovery and Development Platform (DDD) at SciLifeLab is looking for new pilot project proposals for drug discovery. **All therapeutic modalities** outlined above are of interest. Of special interest are new project ideas for (multispecific) **biologics**, and in collaboration with ENABLE2 <https://www.ilkk.uu.se/enable2/>, small molecule projects for discovery of **new antibiotics**.

Note that small projects for selections in phage display libraries for antibodies, selections in DNA encoded chemical libraries for small molecules or limited screening for antisense or siRNA molecules can be considered.

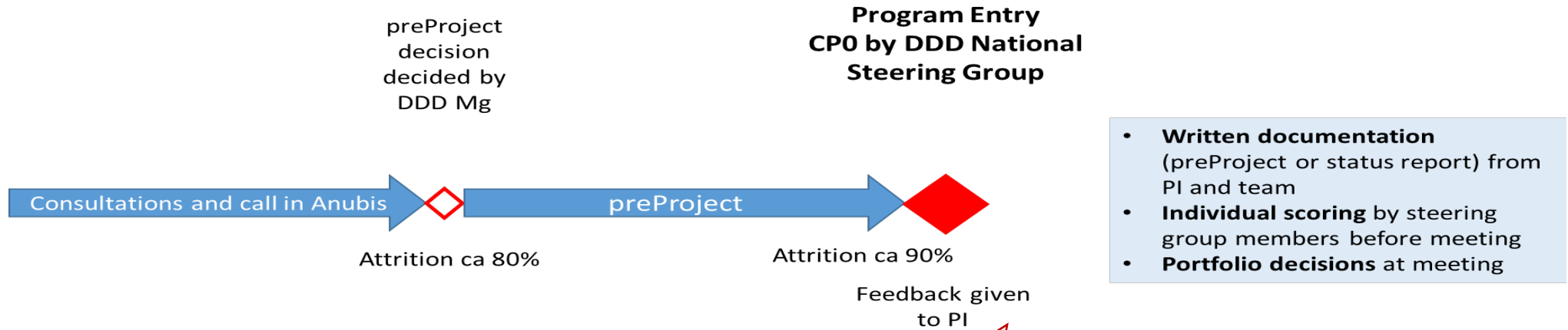
A description of new modalities in drug discovery research can be found here:
<https://pubs.acs.org/doi/10.1021/acsmedchemlett.9b00582>

If you have questions about the call please contact DDD by email (dddprojectproposal@scilifelab.se). This call is open for scientists with a doctoral degree at a Swedish university or higher institution. English should be used when filling out this application. You are responsible for ensuring that the application is complete. Incomplete applications will not be processed.

- 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 Q3/Q4, 2023



Important timelines 2023

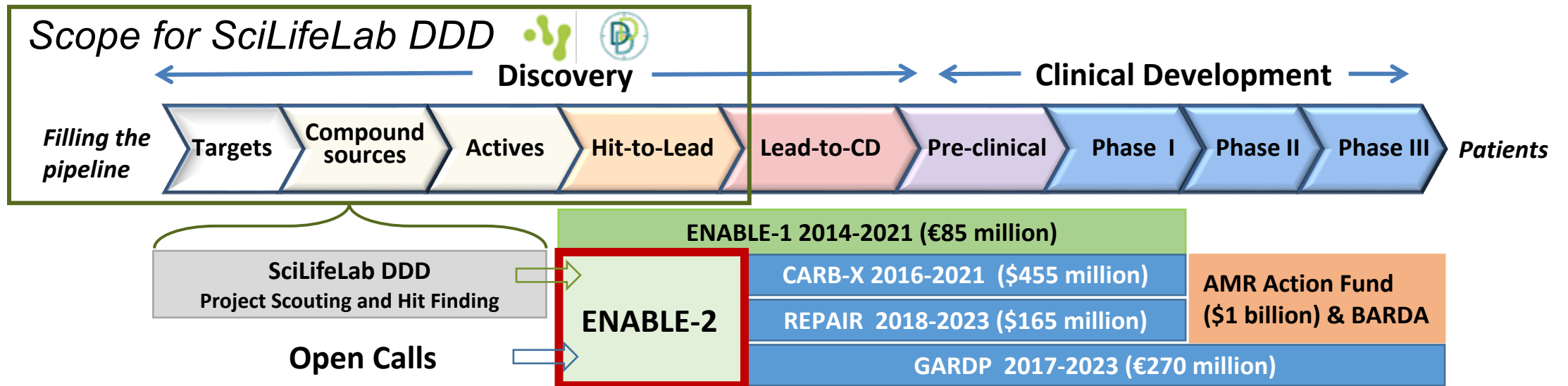
- National call in Anubis June 16th – August 24th
- preProject decision early-September
- preProject phase: early September – early October
- Start of new programs: December 1st



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) $\leq 16 \mu\text{g/mL}$ 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.ilkk.uu.se/enable2/apply/>

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



Focus 2: Tomorrow's therapeutic modalities?



20 000 proteins

3824 disease linked

1265 “druggable”

672 “drugged”

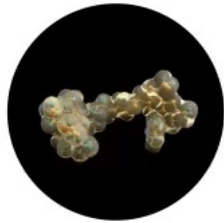
<20% of disease-linked proteome

CREATING NEXT GENERATION THERAPEUTICS

SMALL MOLECULES



Small molecules



PROTACs

ANTIBODY THERAPEUTICS



Monoclonal antibody



Antibody drug conjugate



Bispecific antibody

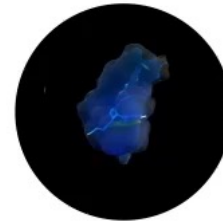


Fragment antibody

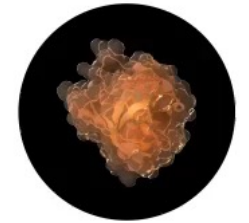
PEPTIDE OR PROTEIN THERAPEUTICS



Cell therapy

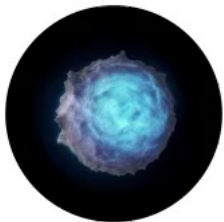


Peptides

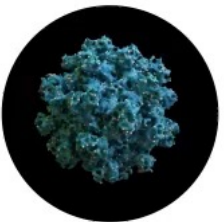


Anticalin[®] protein

CELL BASED THERAPEUTICS



Cell therapy

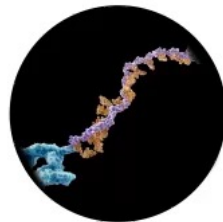


In vivo expressed biologics (IVEBs)

NUCLEOTIDE-BASED THERAPEUTICS



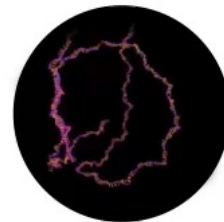
Antisense oligonucleotide



Oligonucleotide conjugate



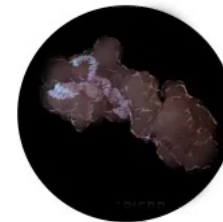
siRNA



mRNA



saRNA



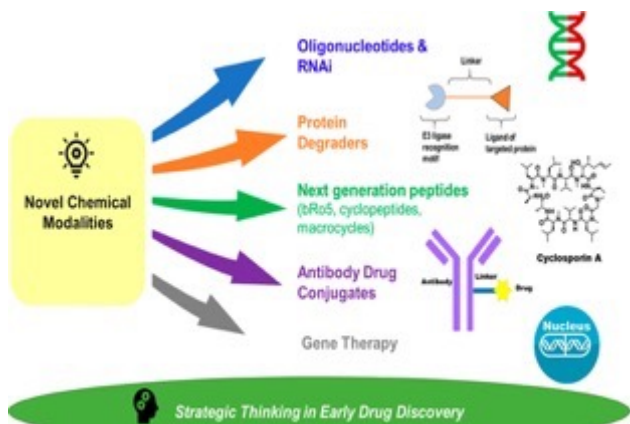
Therapeutic gene editing



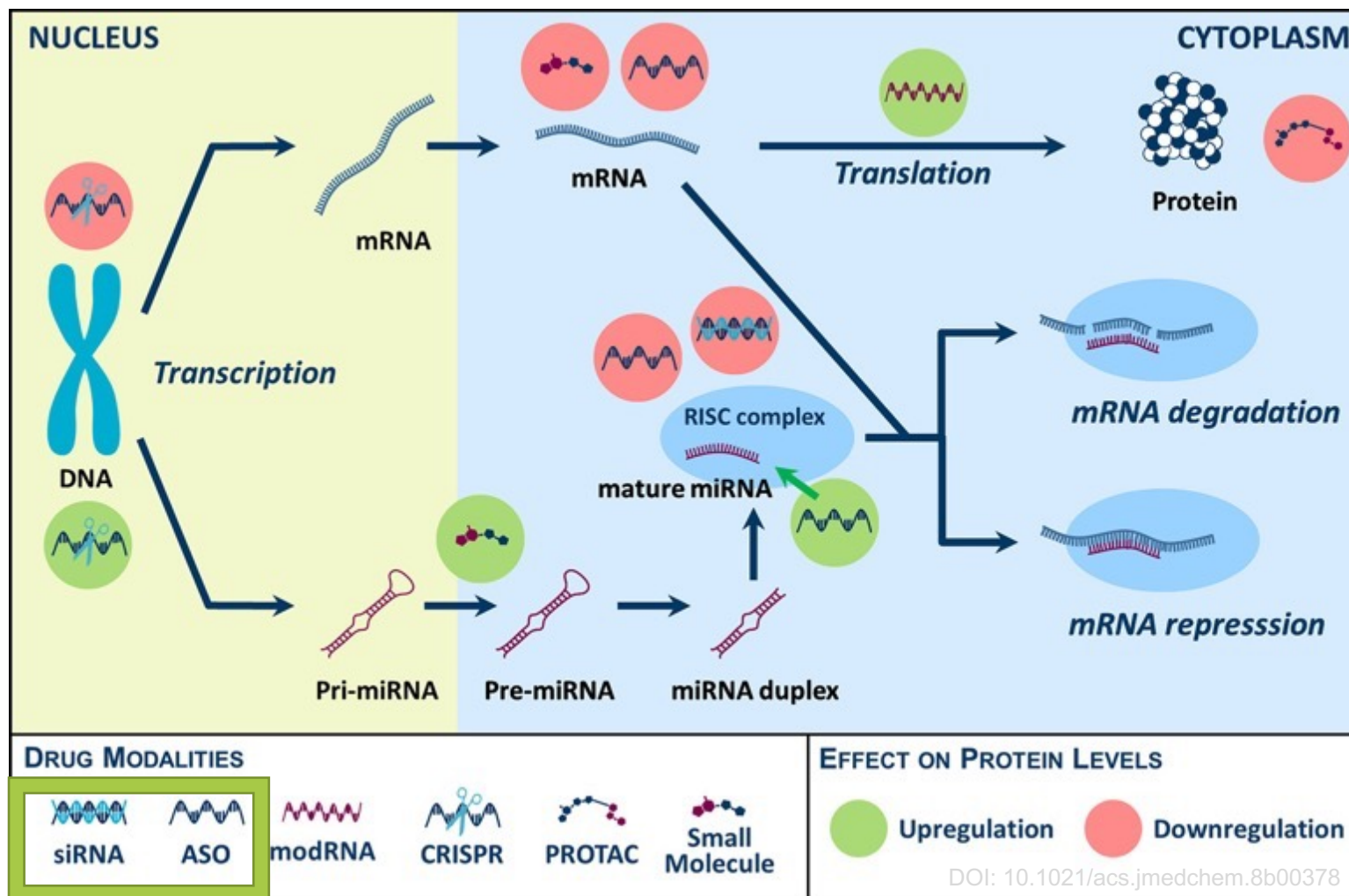
DNA



siRNA and ASO Oligonucleotides



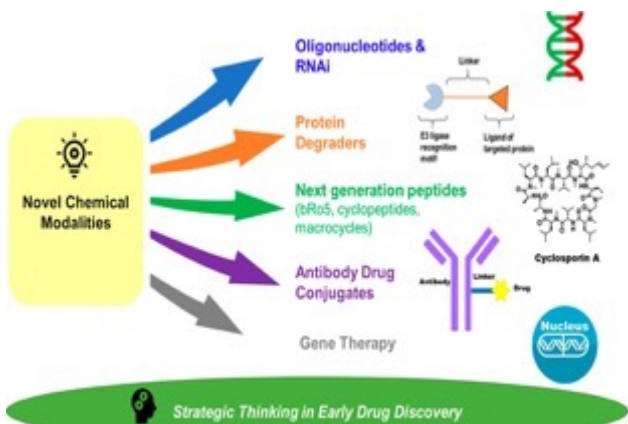
DOI: 10.1021/acsmedchemlett.9b00582



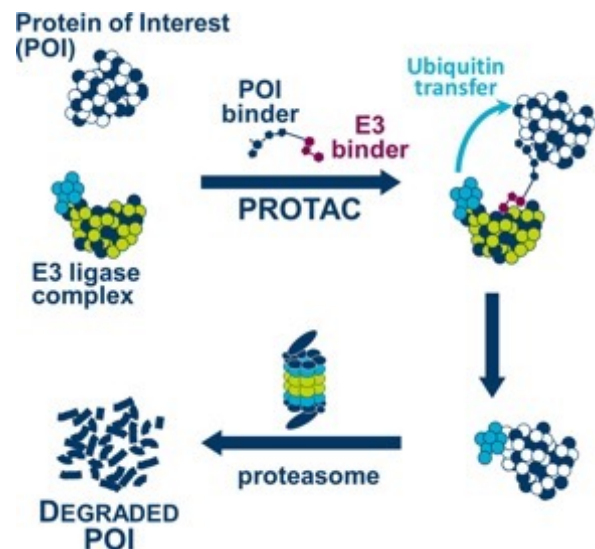
- Effect on protein levels – not activity
- Modify RNA splicing



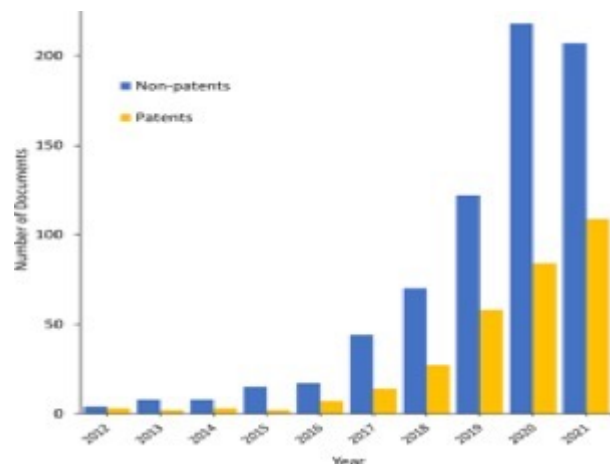
Targeted Protein Degradation



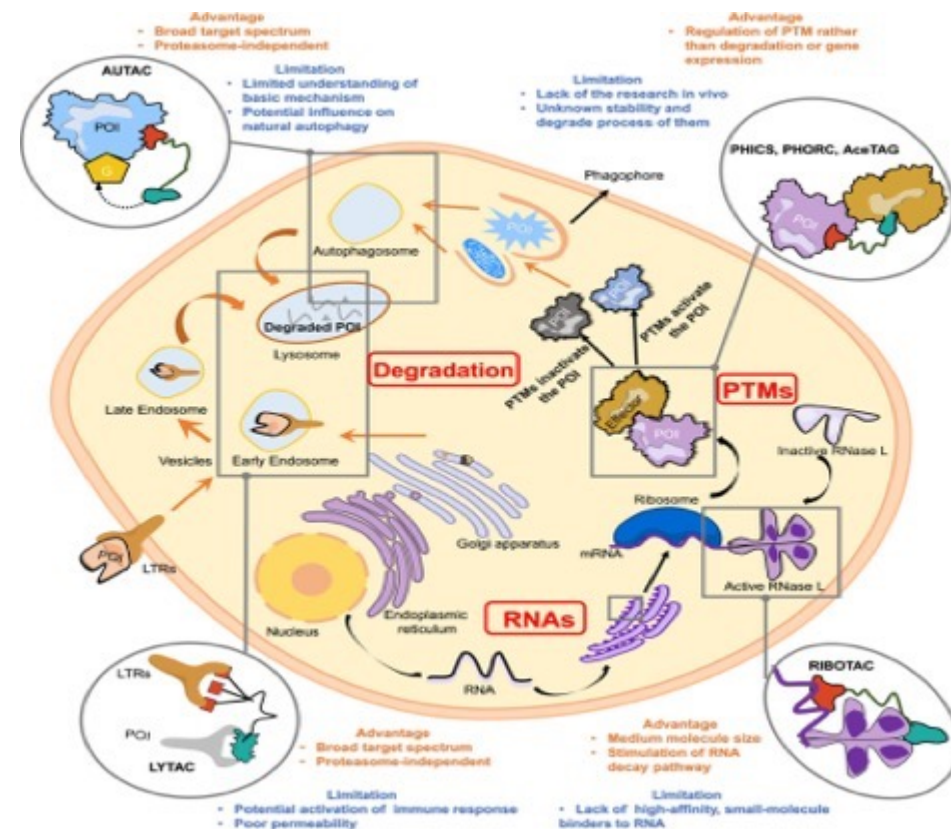
DOI: 10.1021/acsmchemlett.9b00582



DOI: 10.1021/acs.jmedchem.8b00378



Sasso et al, Biochemistry 2022, in press



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

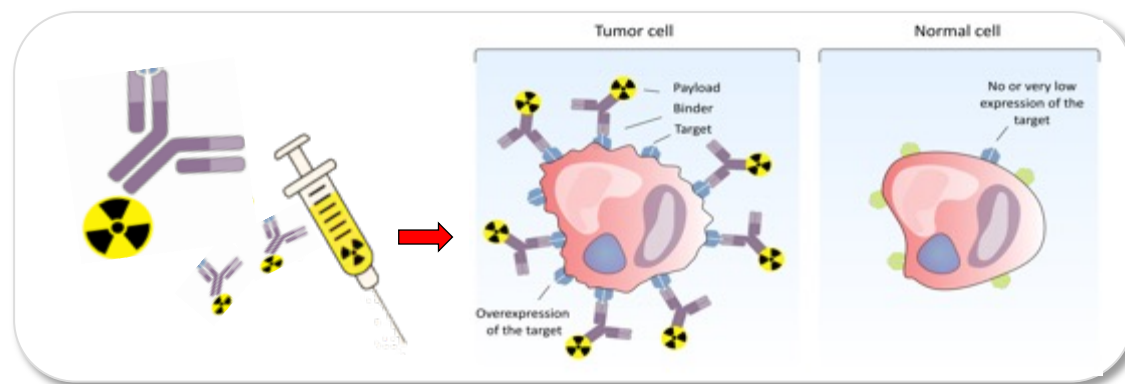
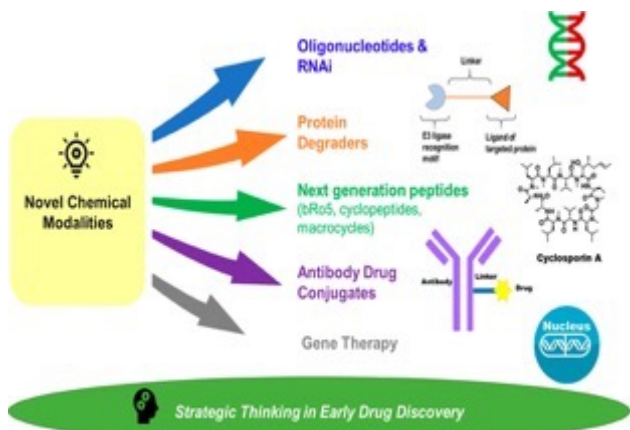
- Intra- or extra-cellular
- Small molecule TPD clinically validated
- LYTAC and AbTACs for non-proteosomal TPD



Conjugates & Theranostics



DDD exit in May 2022



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

Akira Therapeutics

(68M SEK 230112)

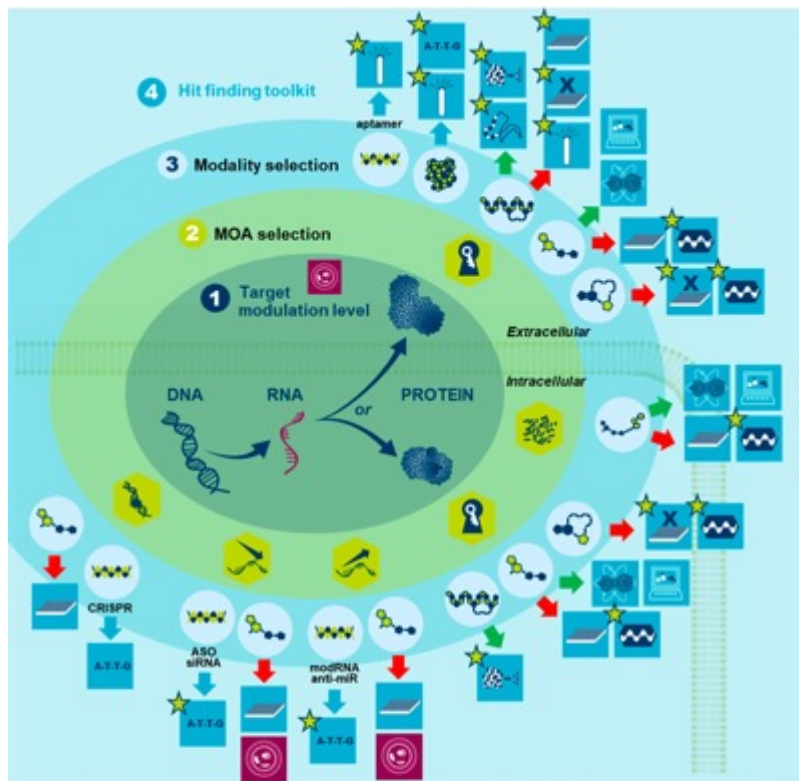
DOI: 10.1021/acsmchemlett.9b00582



New modalities – New Technologies



20 000 proteins
 3824 disease linked
 1265 “druggable”
 672 “drugged”



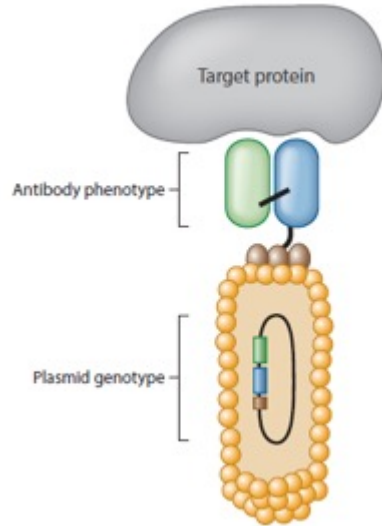
Drugging the
 ”undruggable”
 New modalities
 &
 New technologies

<20% of disease-linked proteome

MODE OF ACTION	DRUG MODALITIES	HIT FINDING TECHNOLOGIES
Protein degradation	Small Molecules	High Throughput Screening
Protein Agonism/Antagonism	Macrocycles	Expanded/Specialized Libraries
Translation upregulation	Modified Peptides	Fragment-Based Screening
Translation downregulation	PROTAC	Virtual Screening
Transcription/Genome regulation/editing	Oligonucleotides	Structure Mimetics
STRUCTURAL INFORMATION	Proteins / Antibodies	DNA-Encoded Libraries
Available or straightforward to generate		Scaffold Grafting
Not available and highly challenging to generate		Sequence-Based
Protein/RNA Sequence		Display technologies
		Phenotypic screening
		Technology/modality particularly suited for challenging targets

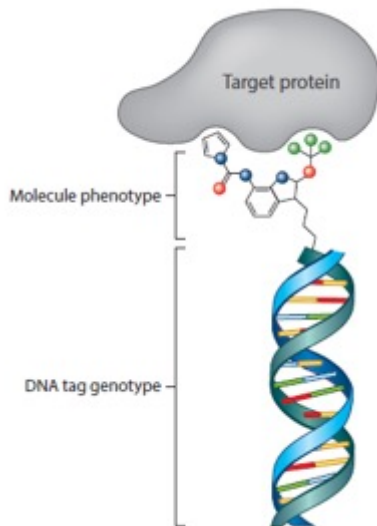


New technology: Display & Selection Hit-finding



Phage display for mAbs

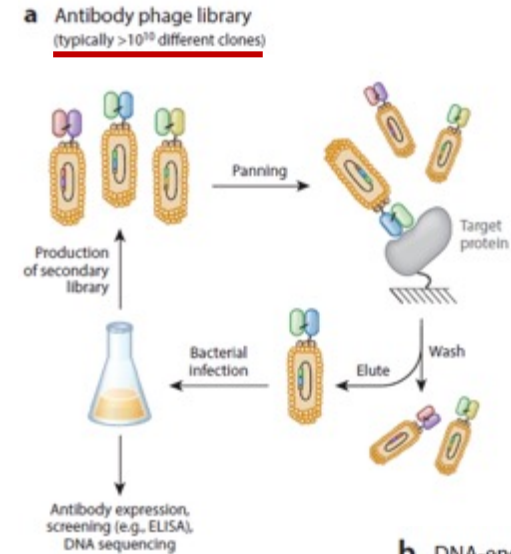
SciLifeLabs 1-5



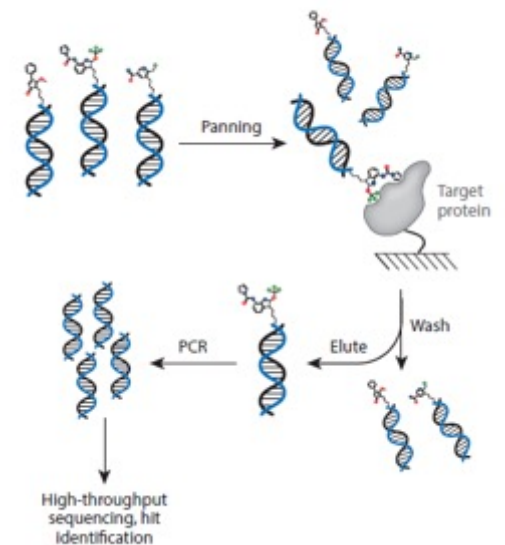
DEL affinity selection for small molecules

New SciLifeLab DDD capability

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



b DNA-encoded chemical library

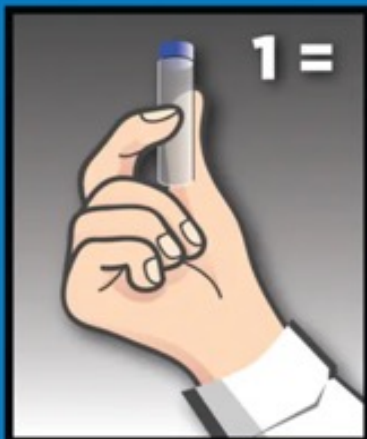
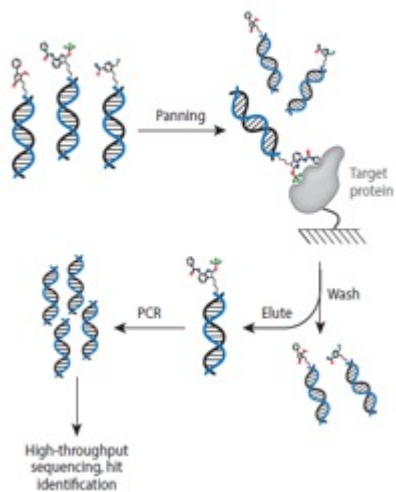




Hit-finding technologies: Display & Selection



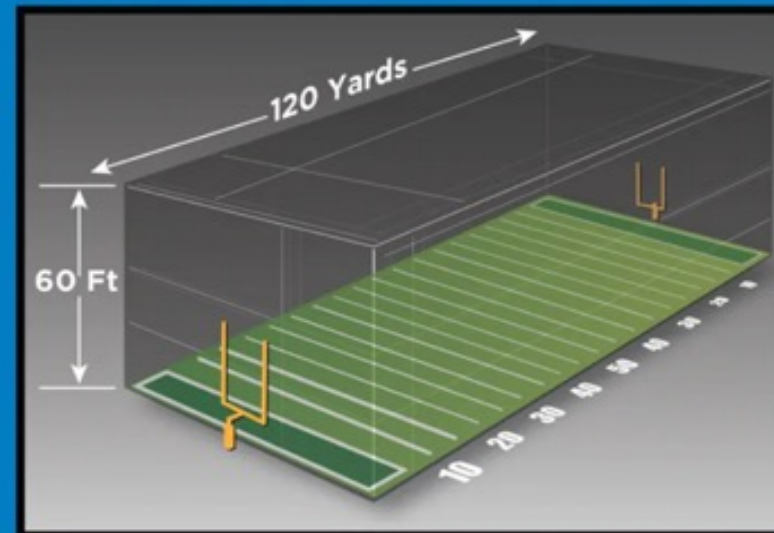
b DNA-encoded chemical library



Large DNA-encoded library



1,536-well microplate for HTS system



Size of plate stack needed to screen 1 trillion compounds

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



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_Project_Call_summer_2023

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- preProject decision early-September
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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.