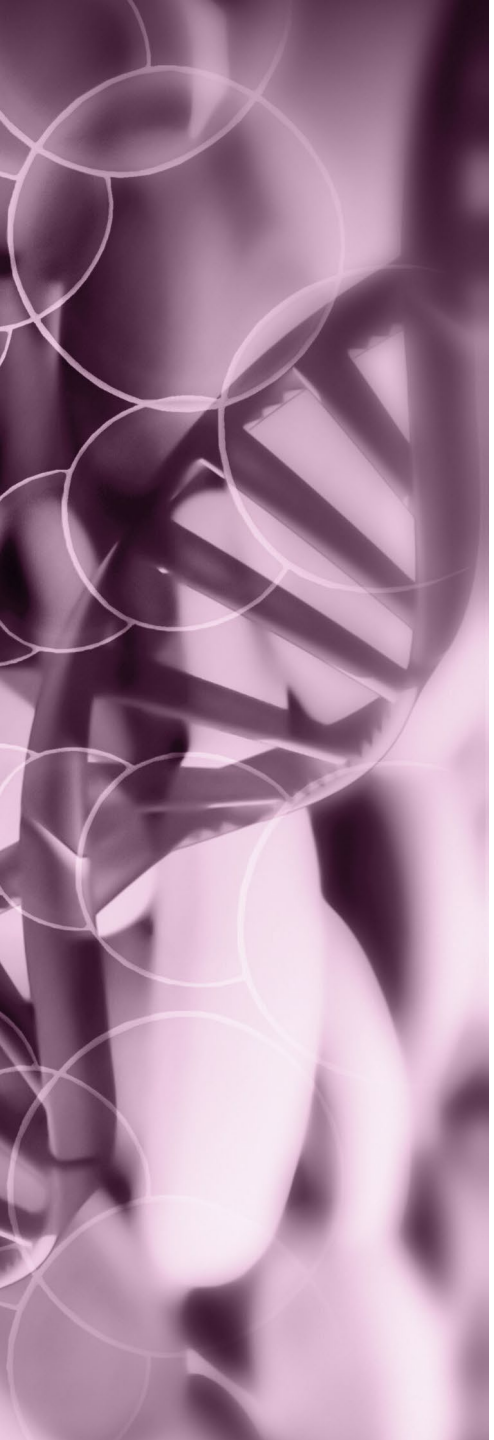


The Chemical Biology and Genome Engineering Platform

Call for Platform Pipeline Projects (PPPs)

Bernhard Schmierer, Karolinska Institutet

Platform Co-Director and Coordinator
Unit Head *CRISPR Functional Genomics (CFG)*

The Chemical Biology and Genome Engineering Platform consists of three independent units

Chemical Biology Consortium Sweden (CBCS)


Anna-Lena Gustavsson, KI
Erik Chorell, UmU
New nodes at LU, UU, GU, LiU

CRISPR Functional Genomics (CFG)

Bernhard Schmierer, KI

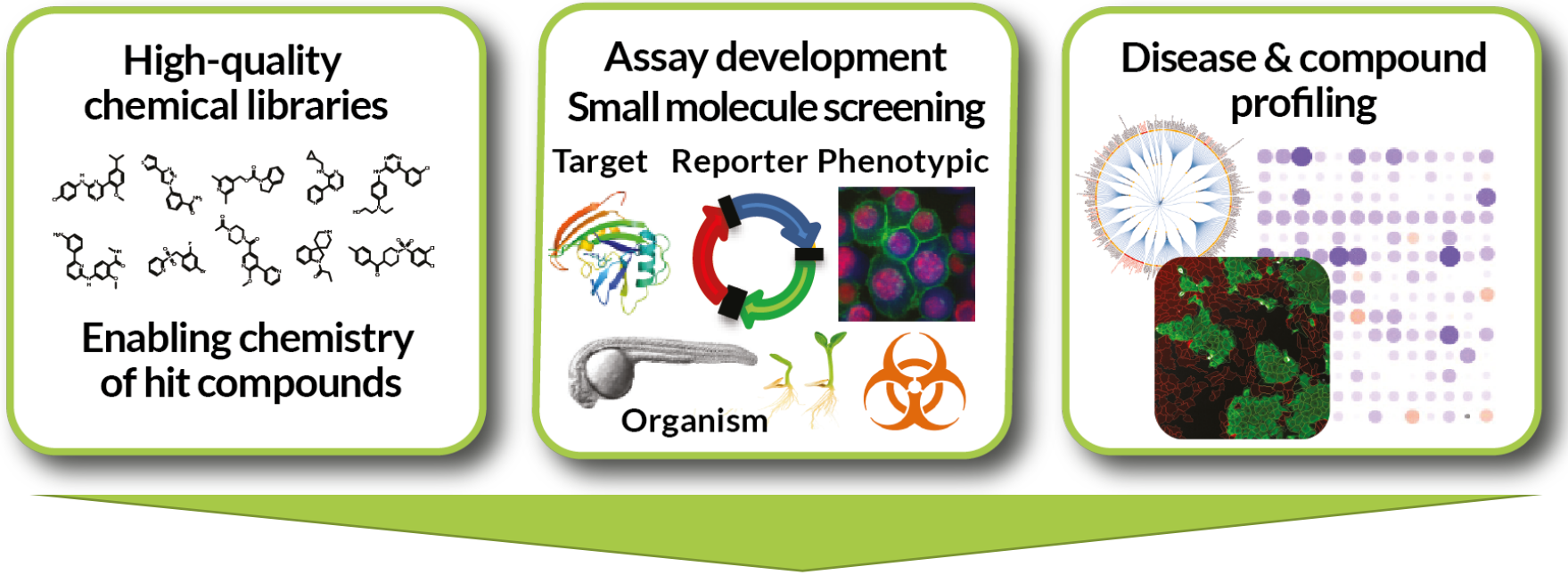
Chemical Proteomics (ChemProt)

Massimiliano Gaetani, KI

We have a common mission:

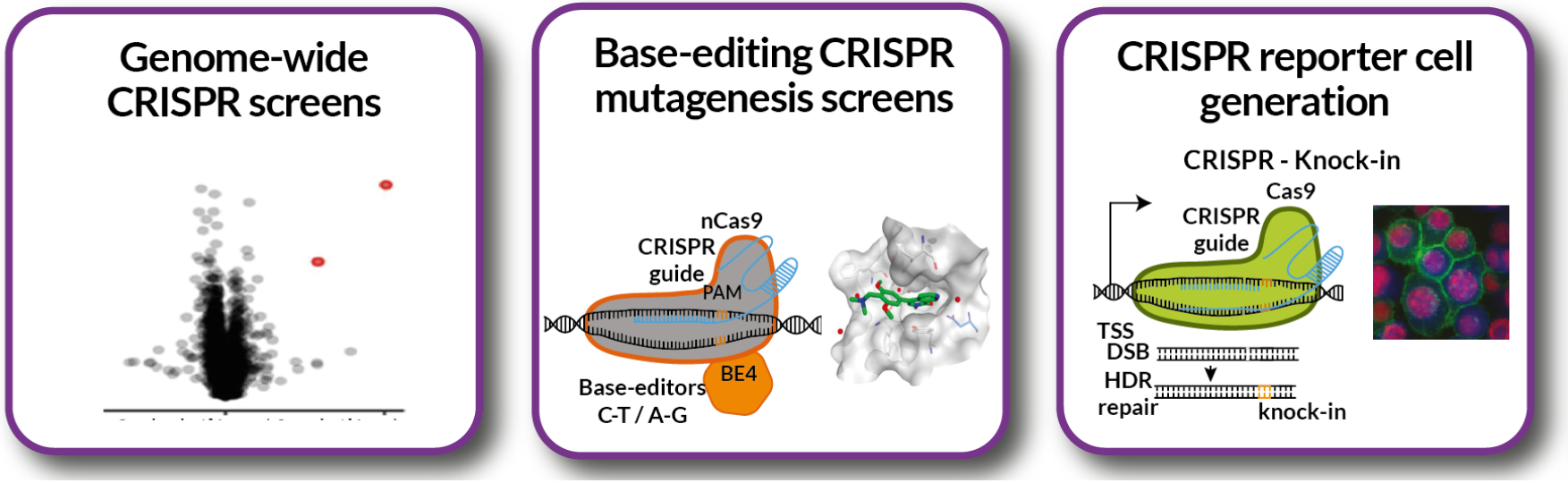
Turning phenotypic observation into mechanistic insight

Chemical Biology Consortium Sweden



- Create **small molecule tools** for basic research
- Unravel **biological function and mechanisms** by using known small molecules/drugs (e.g. AZ compound collection)
- **Probe "ligandibility"** of target proteins with small molecules
- Identify and **optimize small molecules** that modulate a phenotype of interest
- Establish a **structure-activity relationship** by synthesizing and testing analogs
- **Profile small molecules phenotypically and multi-dimensionally** (viability, cell-type specificity, cell painting, transcriptomics, proteomics)

CRISPR Functional Genomics



Toolbox

Cas9, dCas9 fusions, Cas12a, Cas13d

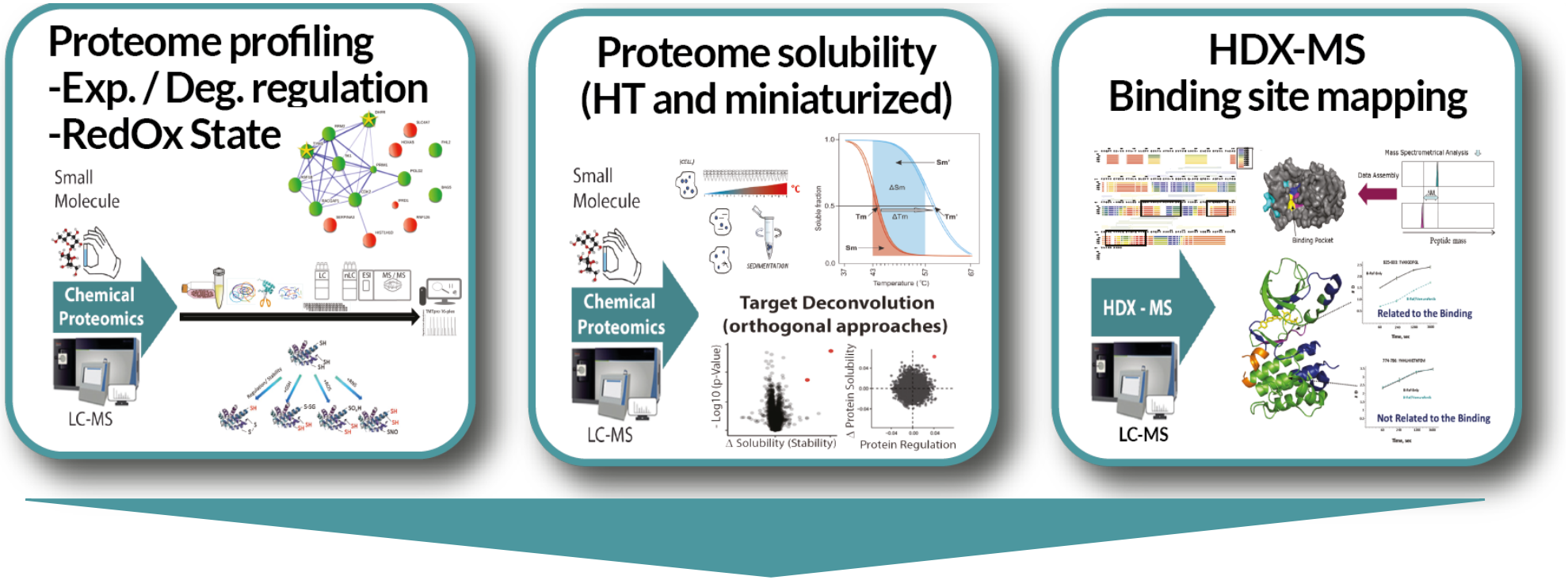
CRISPR-KO, CRISPR-I, CRISPR-A,

CRISPR-X, Perturb-Seq, CROP-Seq

KO, KI, base-editing, prime-editing

- Create **disease-relevant cellular models** or **reporter cell lines** (precision editing)
- Interrogate **protein-coding genes**, l**ncRNAs, miRNAs** and **non-coding DNA elements** – both genome-wide or focused
- **Identify genomic loci** regulating **viability**, proliferation, differentiation, **drug-response**, infection, signal transduction, cell-cell interactions, etc., etc.
- Map **small molecule-target interactions** by CRISPR-guided base-editing screens

Chemical Proteomics

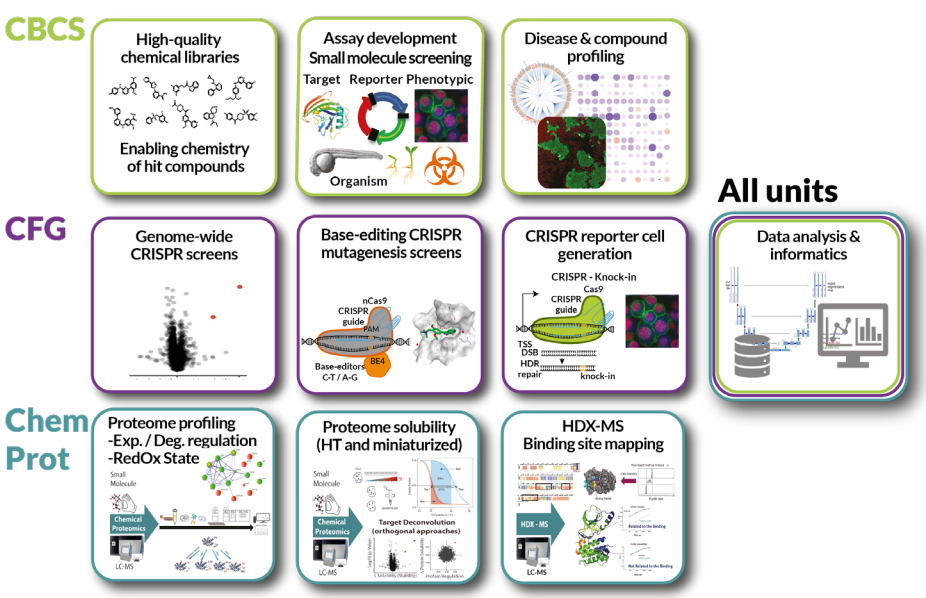


- Identify **small molecule targets by deep-profiling** (8,000 – 10,000 proteins)
- Study **proteome regulation/function** at a multidimensional level (expression, PTM, thermal stability, RedOx balance)
- Identify small molecule targets by combining **orthogonal proteomic approaches** based on physicochemical properties
- **Map binding and interaction sites** (for compounds and antibodies)
- Narrow down **targets of several small molecules in parallel** (multiplexing)

The platform technologies provide synergies for target discovery and mode-of-action elucidation

Target Discovery.
Target identification and validation downstream of a phenotypic screen **is challenging**.
Combining chemical, genetic, and proteomic methods is often needed to approach the problem.

Mode-of-Action Elucidation.
How does a small molecule elicit its effect? Which pathways are affected?
How does the compound interact physically with the target protein?
Are there Off-targets?



Target Discovery
Mode-of-Action Elucidation

Small molecule – target pair

Call for proposals:

Access CBGE's technologies at significantly reduced cost

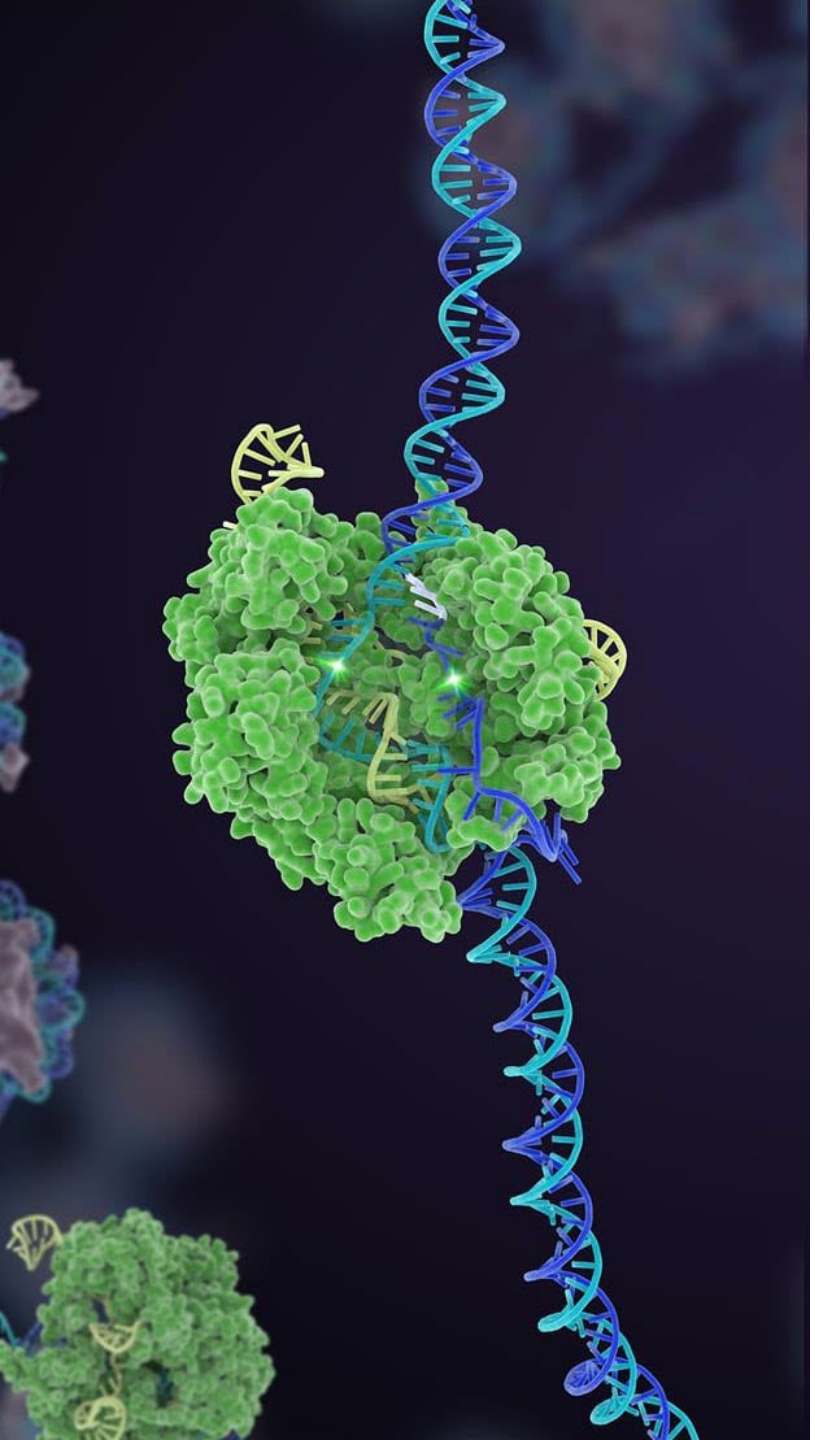
Platform pipeline projects (PPPs) that engage **two or more** of the platform units

Researchers from any Swedish university, any area in life science

Up to **100,000 SEK** extra subsidy per project.

Deadline Feb 20th, 2023

cbge-ppp@scilifelab.se



International Symposium

CRISPR as a research tool

Karolinska Institutet, Solna

May 25-26, 2023

John Doench, Broad MIT
Neville Sanjana, NY Genome Center
Randall J. Platt, ETH Zurich
Tuuli Lappalainen, KTH and NY Genome Center
Douglas Ross-Thriepland, AZ & CRUK
Yumeng Mao, Uppsala University
Eric Shifrut, Tel Aviv University
Jacob Corn, ETH Zurich

Organized by CRISPR Functional Genomics and the Wermeling Lab