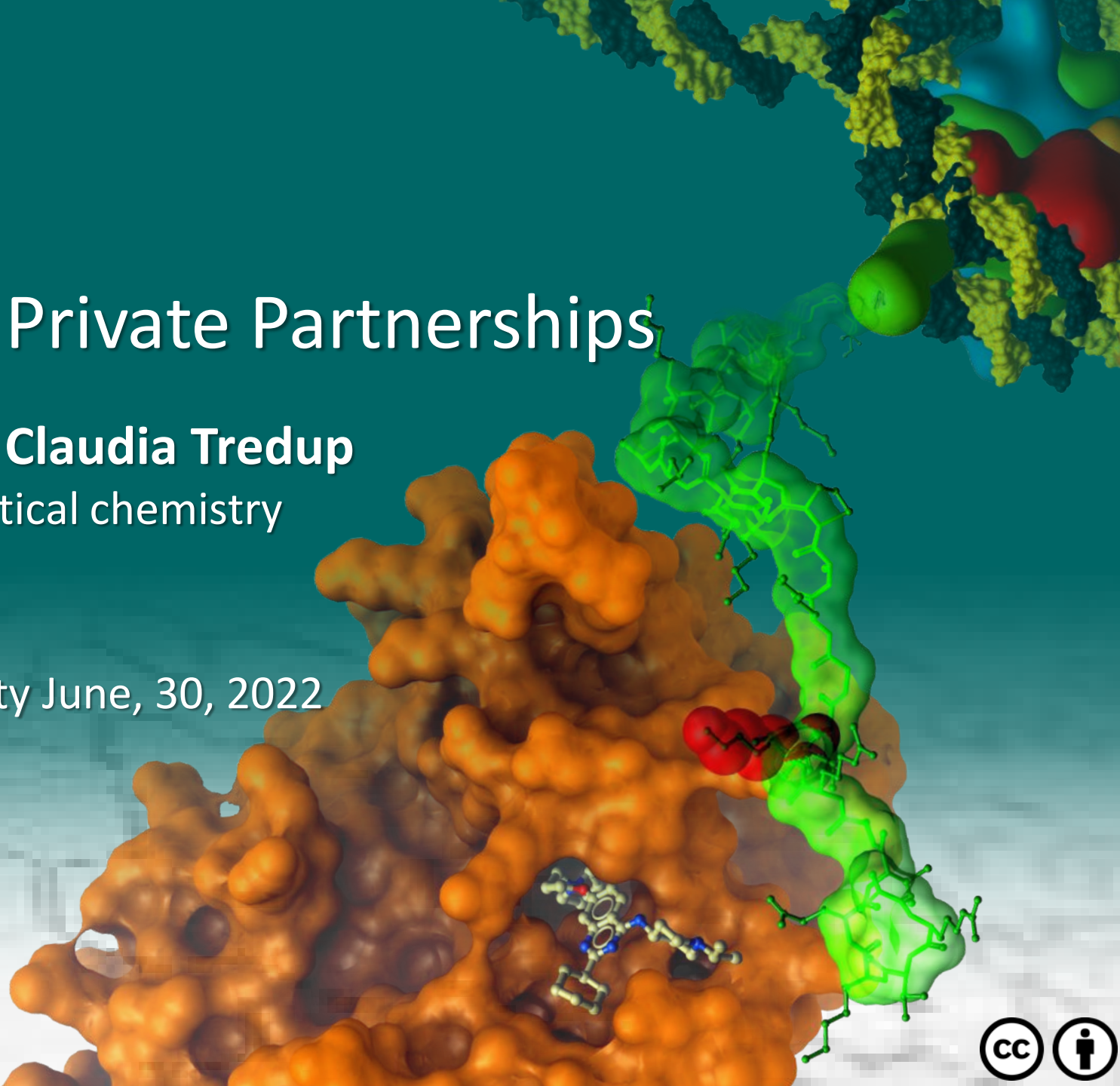
Open Science in Public Private Partnerships

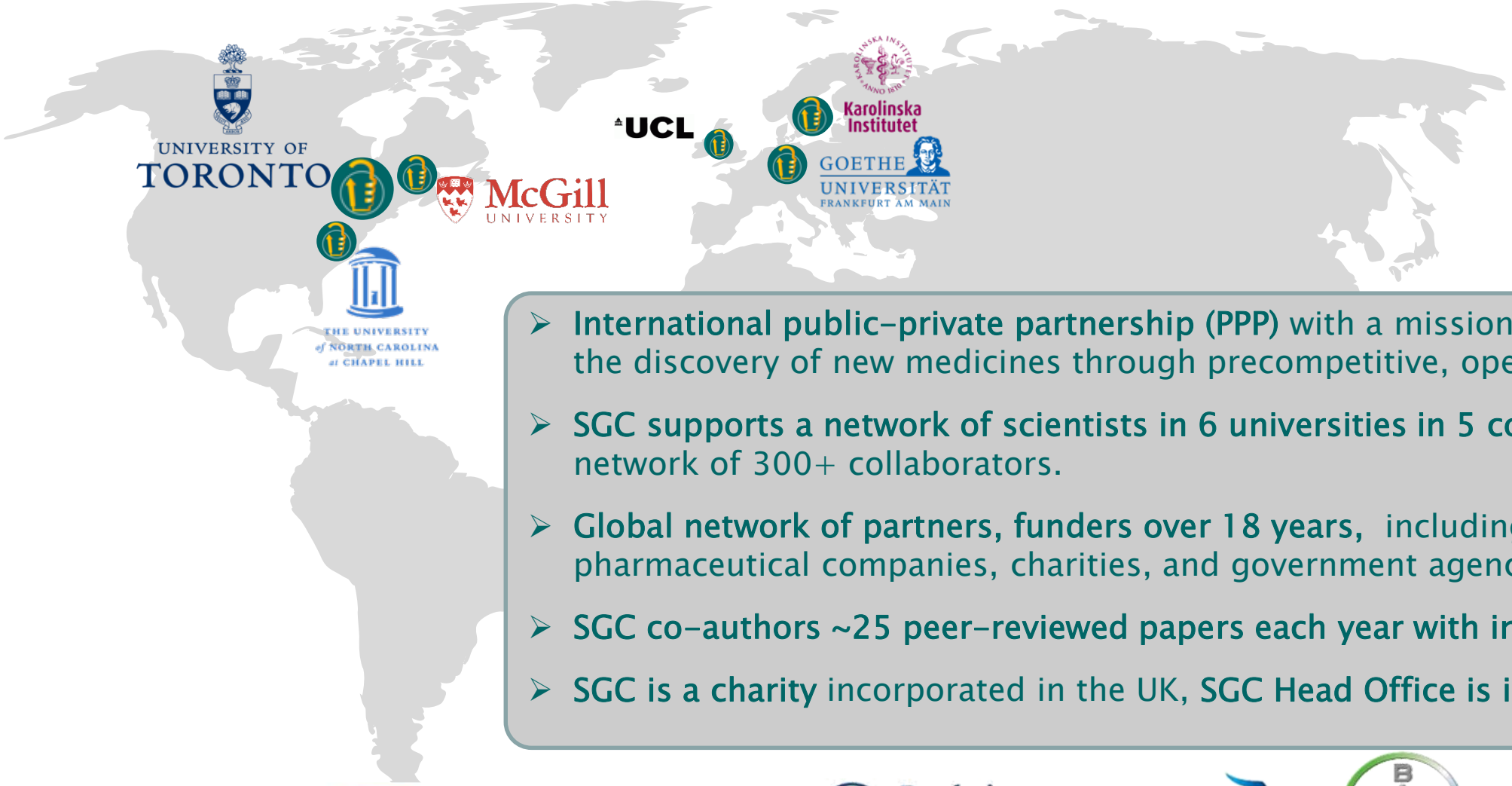
Dr. Susanne Müller-Knapp & Dr. Claudia Tredup
SGC Frankfurt, Institut für pharmaceutical chemistry
Goethe University Frankfurt

Open Science Forum, Goethe University June, 30, 2022



The Structural Genomics Consortium (SGC) is a global public private partnership dedicated to open science

SGC



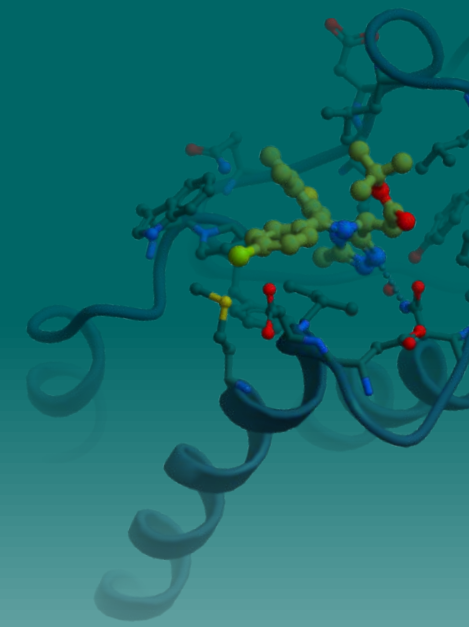
- **International public-private partnership (PPP)** with a mission to accelerate the discovery of new medicines through precompetitive, open science.
- **SGC supports a network of scientists in 6 universities in 5 countries** plus a network of 300+ collaborators.
- **Global network of partners, funders over 18 years,** including pharmaceutical companies, charities, and government agencies.
- **SGC co-authors ~25 peer-reviewed papers each year with industry.**
- **SGC is a charity** incorporated in the UK, **SGC Head Office is in Canada.**

GenomeCanada
Innovative Medicines Initiative
imi
Ontario
Bill & Melinda Gates foundation
The Esheman Foundation Wilmington • North Carolina
Boehringer Ingelheim
janssen
BAYER
Pfizer
Takeda
Genentech
Bristol Myers Squibb
MERCK

SGC at a glance

Main outputs:

- High Throughput Structural Biology (>4000 structures deposited)
- Renewable Antibodies/Binders
- Patient-Cell Derived Assays
- Chemical Probes (~190) and Chemogenomics Libraries
- Data driven research (ML)



Our Ethos: Open Access

Promptly placing results, reagents and know-how in the public domain

We agree **not** to file for patent protection on any of our research outputs

(and encourage our collaborators to do the same)

OPEN ACCESS

www.thesgc.org

Why Do We Need SGC?

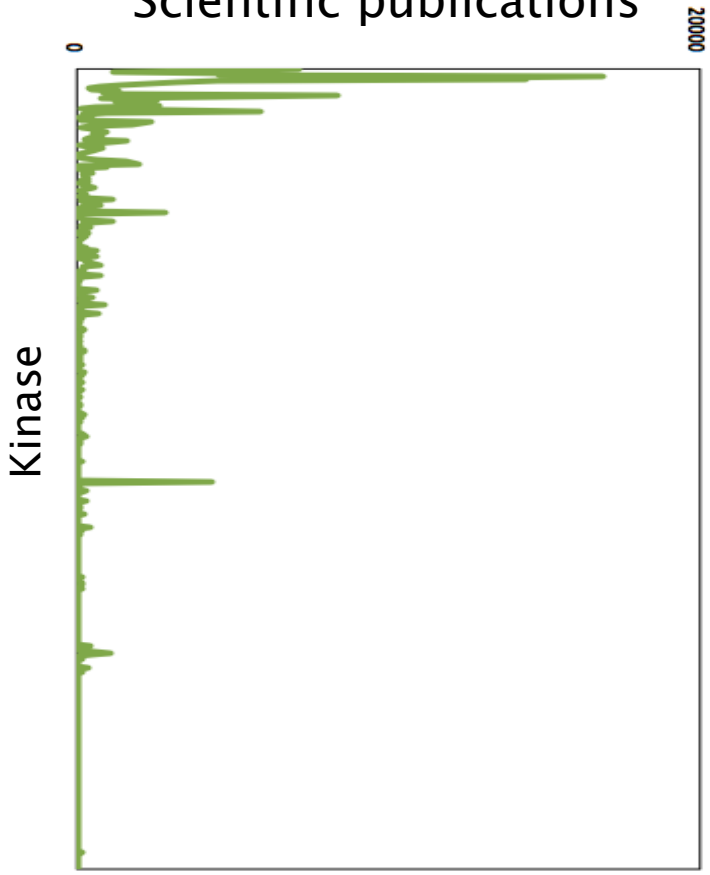
>$250B a year invested in biomedical research

- No new medicines for schizophrenia since 1950's
- No new treatment for Alzheimer's since early 80's

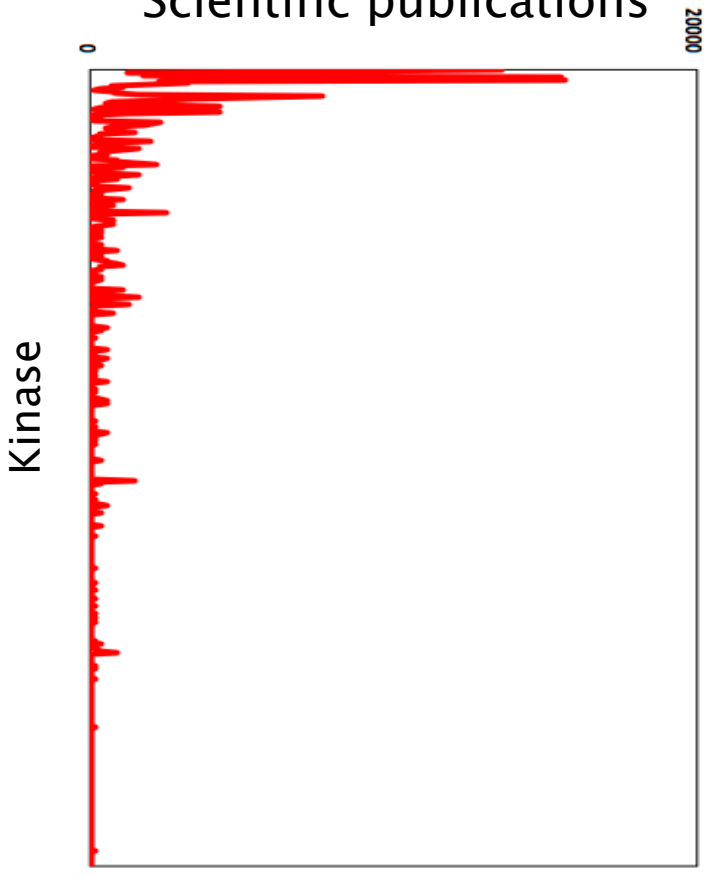
Medicines are not affordable for most people in the world

Most Science Is Redundant

Global Effort (2019)



German Effort (2019)



COMMENT

ANTHROPOLOGY Call for unity in the science of human beings p.180 | GENETICS Reviewed: two primers on personal genomics p.180 | POLICY Sanitation, not vaccination, is most important in Haiti p.175 | OBITUARY Jack Oliver, key player in proof of plate tectonics, remembered p.170

Too many roads not taken

Most protein research focuses on those known before the human genome was mapped. Work on the slew discovered since, urge **Aled M. Edwards** and his colleagues.

When a draft of the human genome was announced in 2000, funders, governments, industry and researchers made grand promises about how genome-based discoveries would revolutionize science. They promised that it would transform our understanding of human biology and disease, and provide new targets for drug discovery. Yet more than 75% of protein research still focuses on the 10% of proteins that were known before the genome was mapped — even though many more have been genetically linked to disease.

We performed a bibliometric analysis to assess how research activity has altered over time for three protein families that are central in disease and drug discovery: kinases, ion channels and nuclear receptors. For all three, we found very little change in the pattern of research activity — which proteins are associated with the highest number of publications — over the past 20 years[1]. Even those proteins that have been directly associated with disease remain 'hidden in plain sight,' with scientists proving very reluctant to study them.

Where there has been a shift in research activity, it was often spurred by the emergence of tools to study a particular protein, not by a change in the protein's perceived importance. We believe that ensuring high-quality tools are developed for all the proteins discovered may be all that is needed to drive research into the unstudied parts of the human genome — even within funding and peer-review systems that are inherently conservative.

We searched for mention of every human ▶

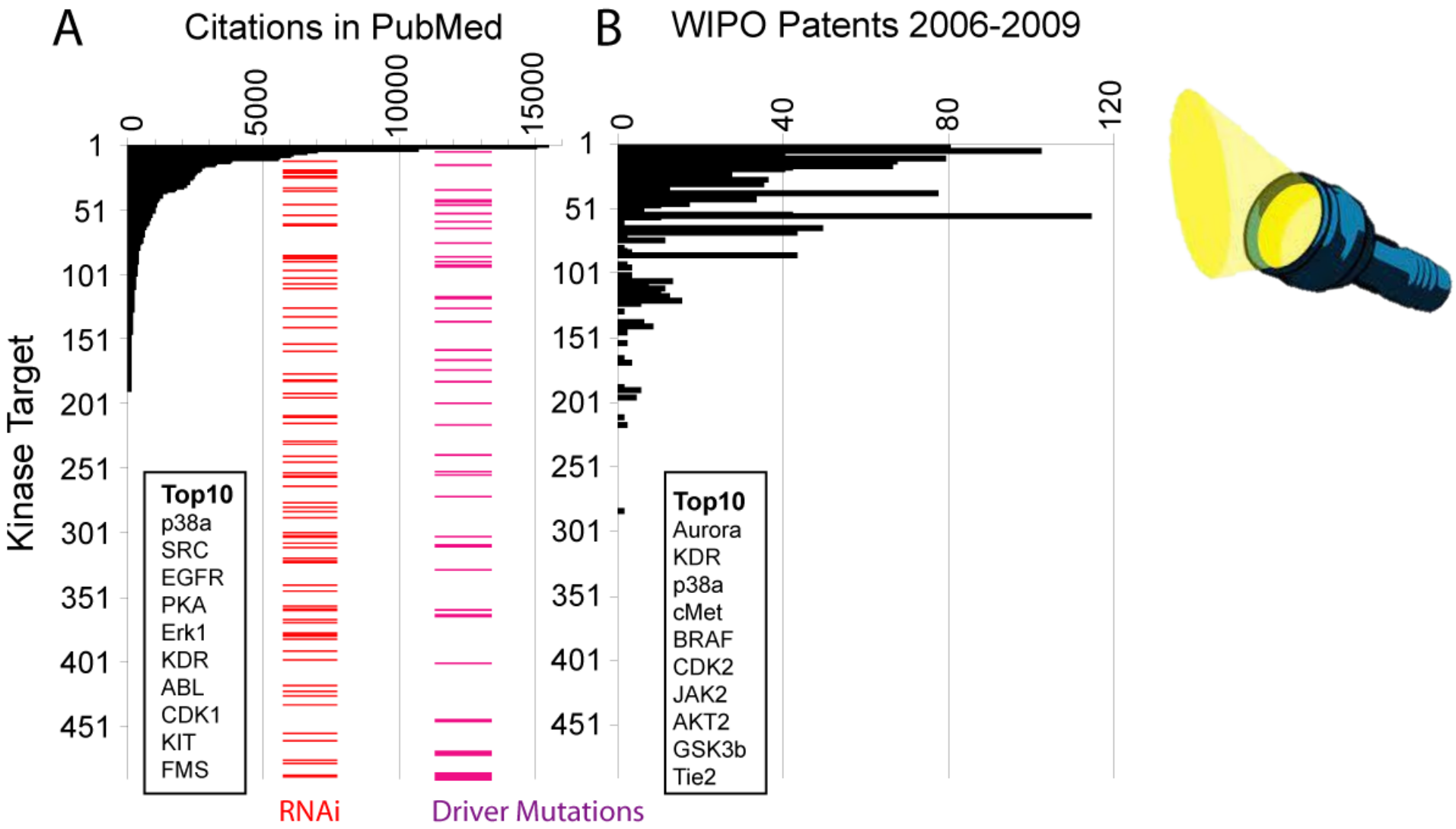
NATURE.COM Protein mapping gains a human focus: go.nature.com/vbqctf

The System Is The Problem

- Funding based on published results
- Lack of funding for truly innovative ideas
- Small increments
- Agreements/IP – time consuming

charitably, mixed. A recent Bloomberg report shows how quickly university patent incomes plunge once we look beyond the megastars. In 2014, just 15 US universities earned 70% of all patent royalties. British science policy researchers Paul Nightingale and Alex Coad conclude that 'Roughly 9/10 US universities lose money on their technology transfer offices... MIT makes more money from selling T-shirts than it does from licensing'. A report from the Brookings institute

WHERE ACADEMIA SHINES LIGHT, INDUSTRY SEARCHES



The (un)targeted cancer kinome. Fedorov O, Müller S, Knapp S. Nat Chem Biol. 2010 Mar;6(3):166-169.

Evolving science and partners to address pressing global

SGC

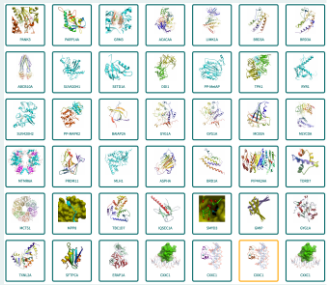
2004 | 2007 | 2011 | 2015 | 2020 | 2025

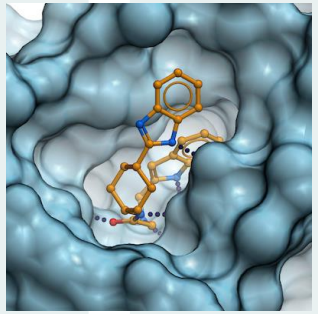
PHASE I | Phase II | Phase III | Phase IV | Phase V

SCIENTIFIC FOCUS

STRUCTURAL GENOMICS

Human Protein Families
Human Parasite Proteins





Bio-active Chemical Tools

CHEMICAL GENOMICS

TARGET 2035

DATA DRIVEN DD

Machine Learning

Patient-derived disease assays

INDUSTRY PARTNERS

GlaxoSmithKline

GlaxoSmithKline, Pfizer, MERCK, NOVARTIS

GlaxoSmithKline, Takeda, Pfizer, janssen, Lilly, abbvie, Boehringer Ingelheim, BAYER, NOVARTIS

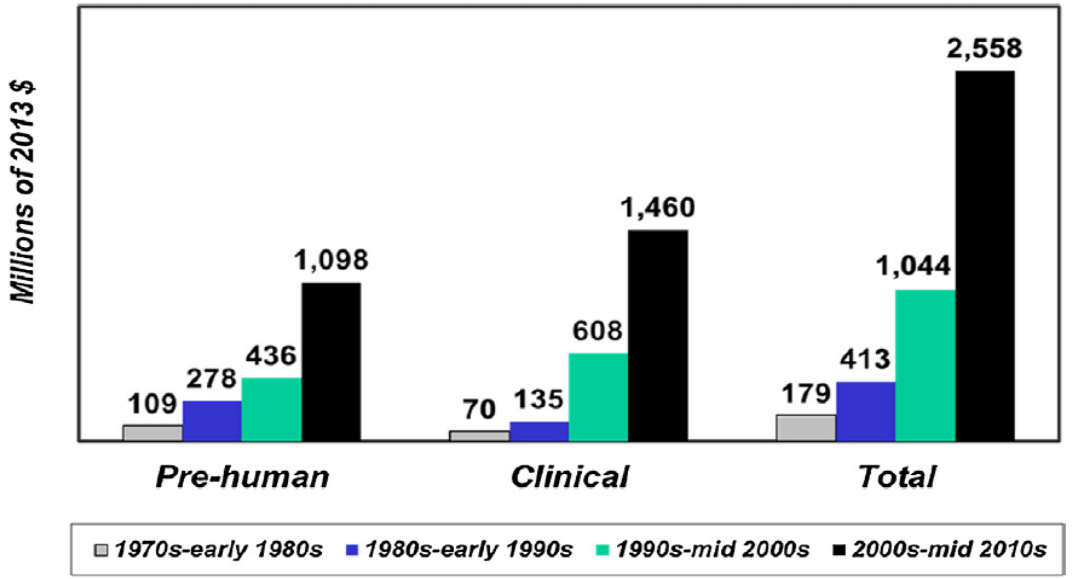
Takeda, Boehringer Ingelheim, janssen, Pfizer, MERCK, abbvie, BAYER, MSD, NOVARTIS

EUbOPEN
Enabling & Unlocking Biology in the OPEN

Genentech, janssen, MERCK, Pfizer, Boehringer Ingelheim, Takeda, BAYER, Bristol Myers Squibb

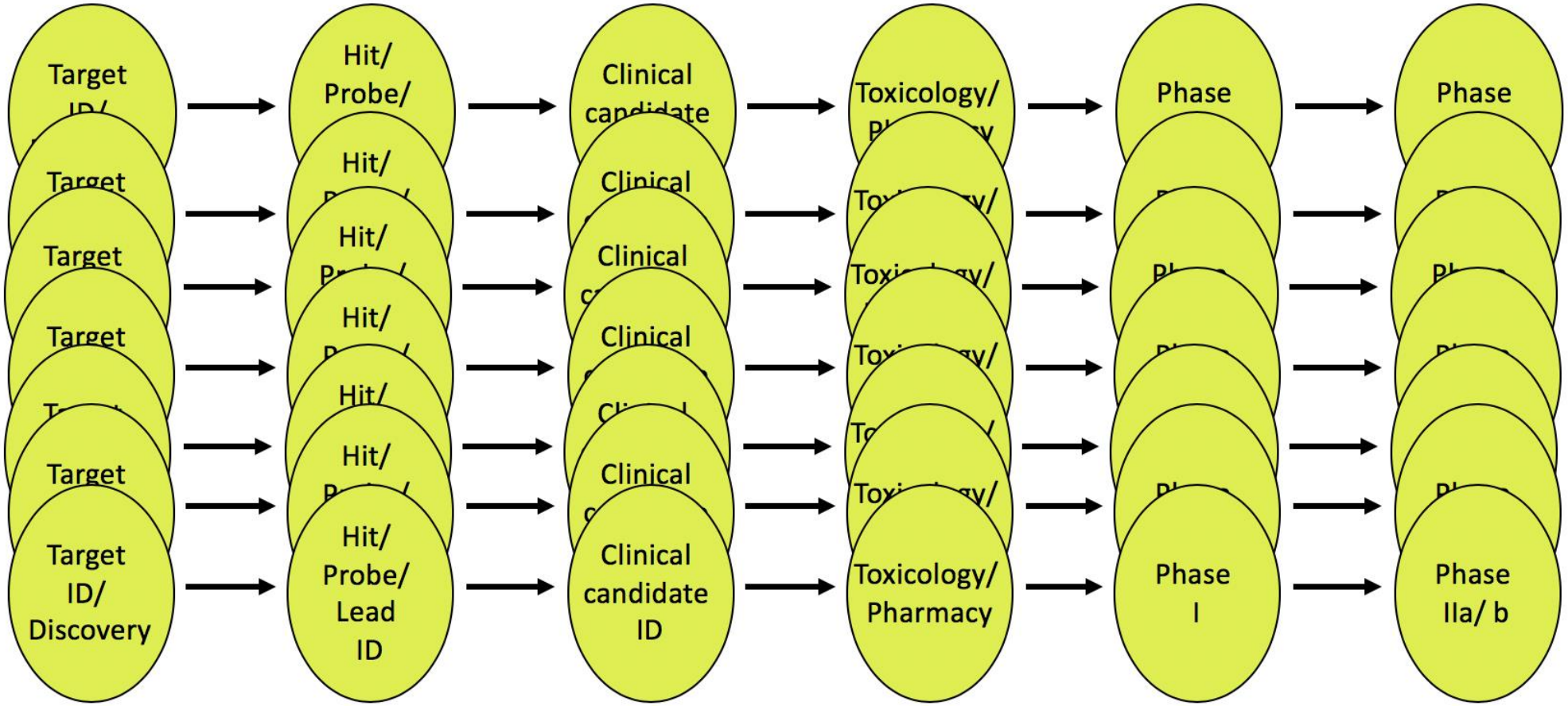
What Does Industry Gain?

- New medicines are exorbitantly expensive
- >$2.5B in private sector R&D costs per approved new drug
- # new drugs approved per $1B halved every 9 years since 1950s
- clinical attrition rates



- Launches at $100,000's per patient per year the new normal
  - Kalydeco® (Ivacaftor); Orkambi® (Lumacaftor/Ivacaftor) for genetic subsets of CF ->$300K/year
  - Rare disease drugs now launching at almost $1M/year in some cases
  - Targeted cancer therapies – mAbs, kinase inhibitors $$$
  - Glybera example (gene therapy for lipoprotein lipase disorder developed at UBC) – $1M for one dose
- Trends exacerbating pricing:
  - Increasing development costs, costs of failure, and clinical attrition – YES
  - BUT ALSO: patient population sizes getting smaller with better genetic characterization
- Sustainability for public and private payers?

Siloed Proprietary Development Leads to Redundancy



Examples of failed parallel late-stage clinical programs: NK1 receptor antagonists for analgesia; matrix metalloproteases and farnesyltransferase inhibitors for cancer; cholesterol ester transfer protein for CVD; beta-amyloid for AD; aurora kinase inhibitors for breast cancer

Precompetitive Research – from lab to patients?

SGC

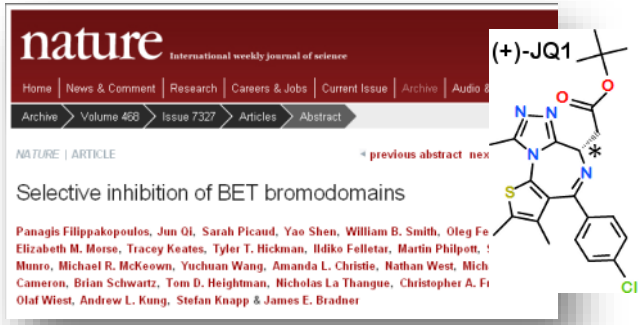
2 Years and 2 months

6 Months | 11 Months | 1 Month | 6 Months | 3 Months

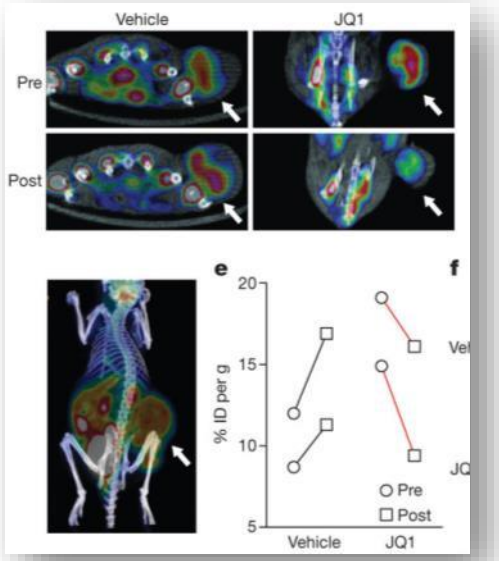
July 2009 | Jan 2010 | Dec 2010 | Jan 2011 | July 2011 | Oct 2011 | Mar 2012

GSK collaborati on starts

Oxford and Harvard start collaboration BET /NMC

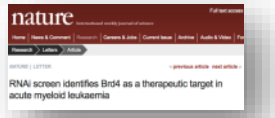


GSK carries out first in man study (open)

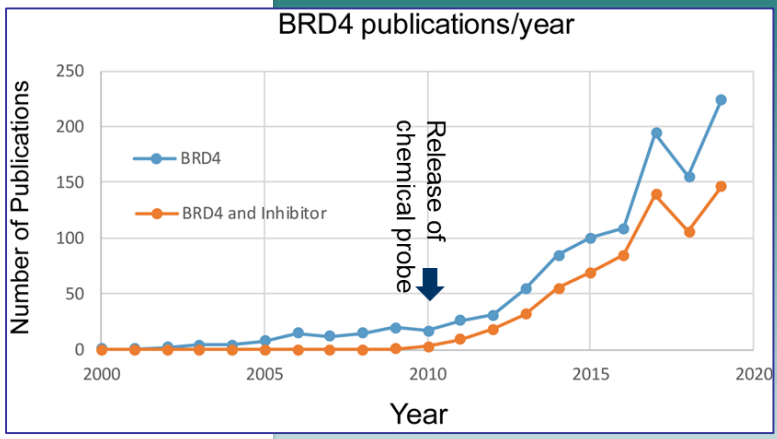


Co – publication of JQ1 probe (SGC; cancer) and I-BET probe (GSK; inflammation)

JQ1 distributed to 100+ labs

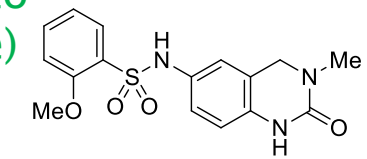


Booming interest in Academia and Industry



Brd4 linked to AML (Nature) MM (Cell)

Pfizer BET probe announced



Currently >30 clinical trials

SGC Model for Pre-Competitive Chemical Probes for Drug Disc

Creative commons

Public Private Partnership

SGC

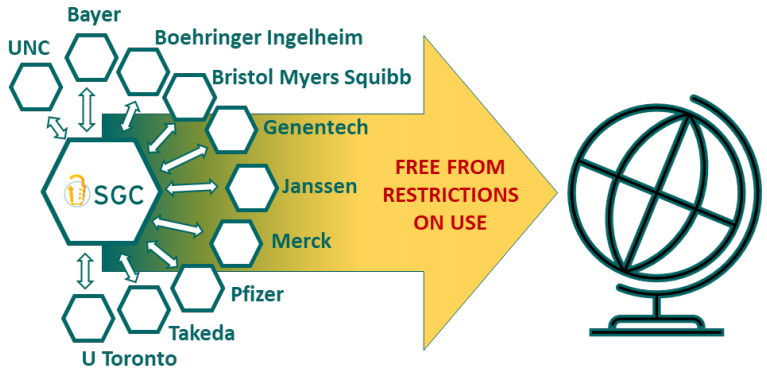
Public Domain

Chemical Probes

Proteins,
Assays/Screening
3D Protein Structure
Medicinal Chemistry
Target Engagement in cells

Target Validation

Disease studies
No restrictions
Publication
Tools for all



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Proprietary

Private Sector

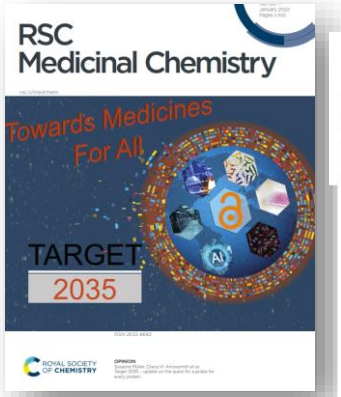
Drug Discovery Development

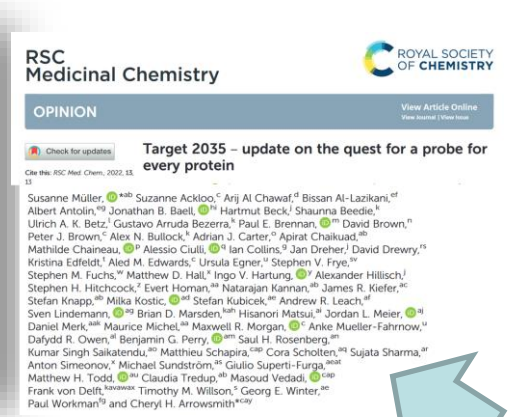
Lead optimization
Pharmacology
DMPK
Toxicology
Chemical development
Clinical development

Edwards et al, Nature Chem Biol, 2009

PUSHING THE OPEN SCIENCE BOUNDARIES

SGC




RSC Medicinal Chemistry

ROYAL SOCIETY OF CHEMISTRY

OPINION

View Article Online

Check for updates

Target 2035 – update on the quest for a probe for every protein

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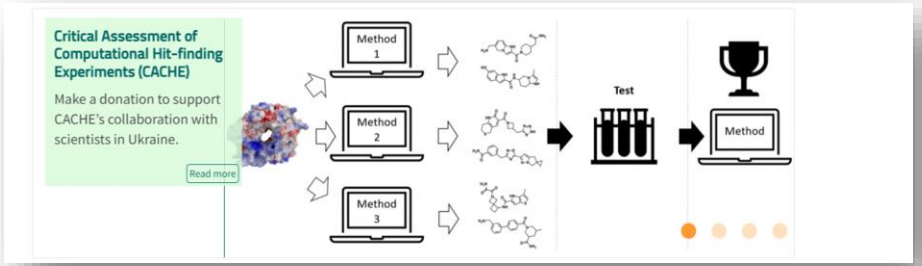
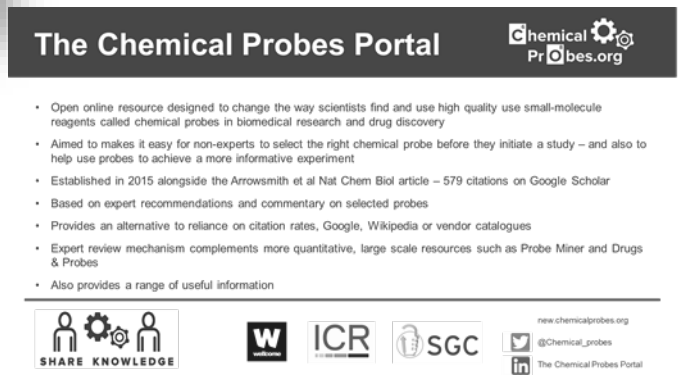
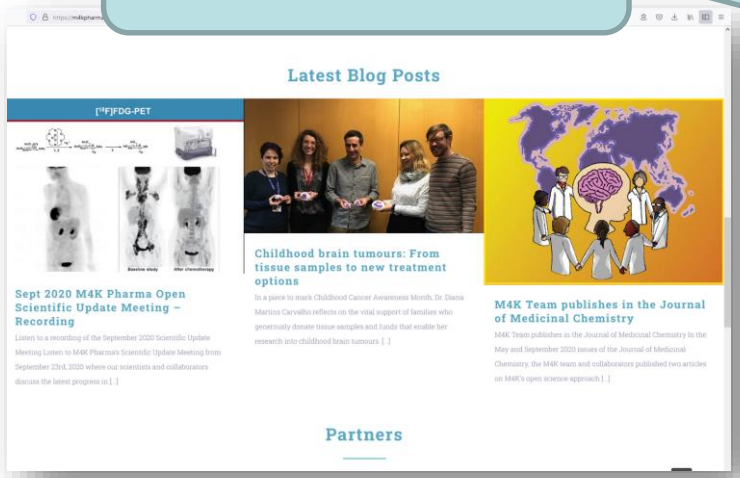
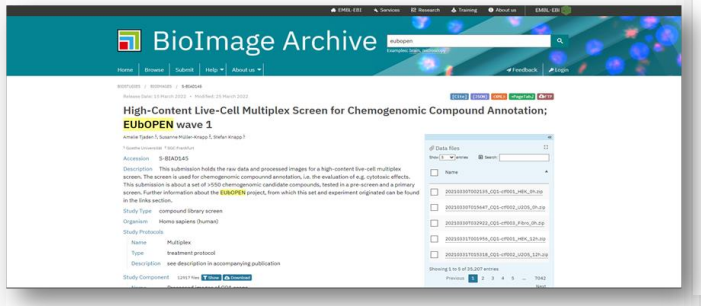




… crowd-sourced evaluation of research tools

Agora Open Science Trust (Charity)





… deposition of metadata

Open Lab Notebooks

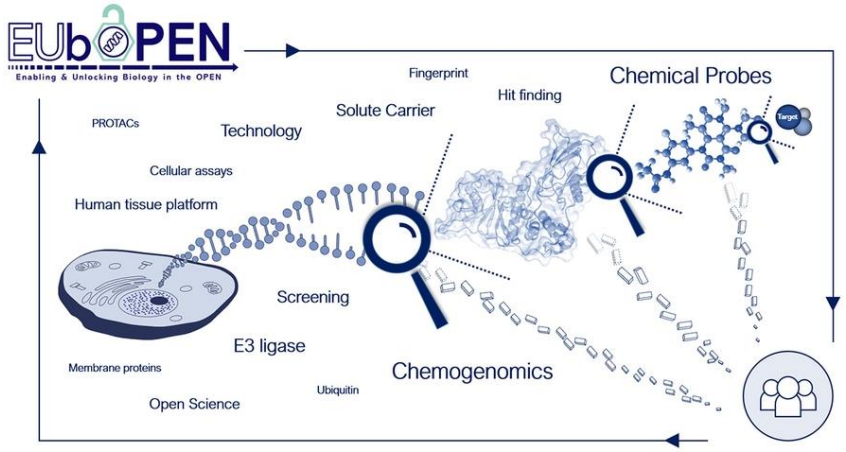
Extreme Open Science Initiative: SGC scientists around the world are starting to post their lab notebook online in real time.

… University of British Columbia, Emory University, Sick Kids Hospital…

SGC in Numbers

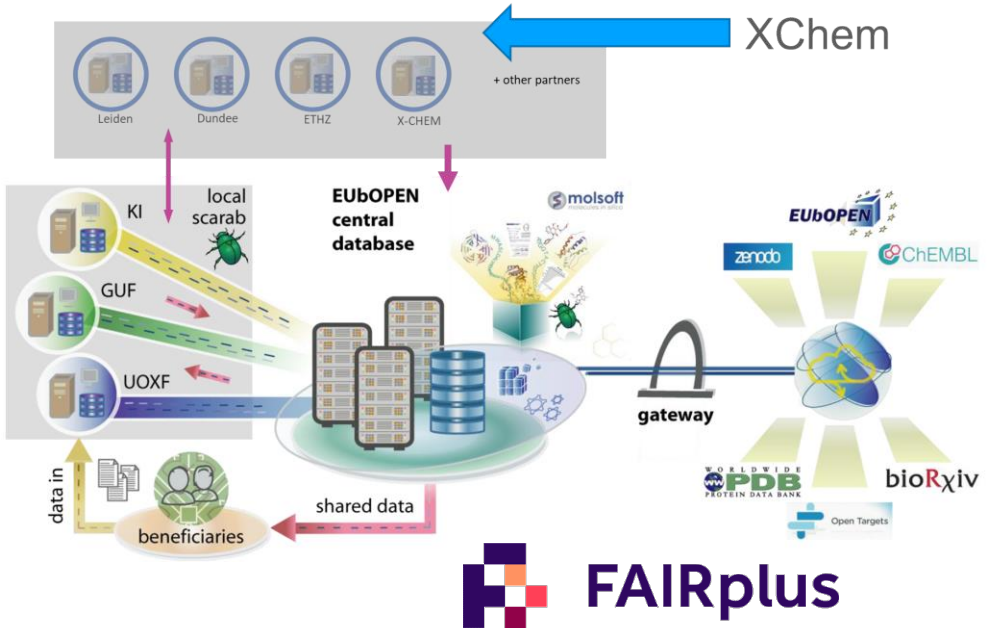
- Publication of more than 2 manuscripts per week (many in high impact factor journals)
- More than 4000 protein structures deposited in the PDB contributing 12% of all known structural information for human proteins
- 2 Spin-out companies
- > 190 chemical probes
- Common development of assay platforms with biotech companies (e.g. Eurofin, Promega, DiscoverX, Sigma)
- Worldwide network of collaborators

EUbOPEN



- The EUbOPEN consortium is an **Innovative Medicines Initiative** (IMI) funded project to **enable and unlock biology in the open.**
- **22 partners** from academia and industry
- five years (2020–2025)
- **Total budget of 65.8 million euros** covered by a grant from the IMI and cash and in-kind contributions from the EFPIA companies, IMI Associated Partners and non-EU partners.
- **Coordinated by GUF**
- **Open Science Policy**

GOETHE UNIVERSITÄT FRANKFURT AM MAIN



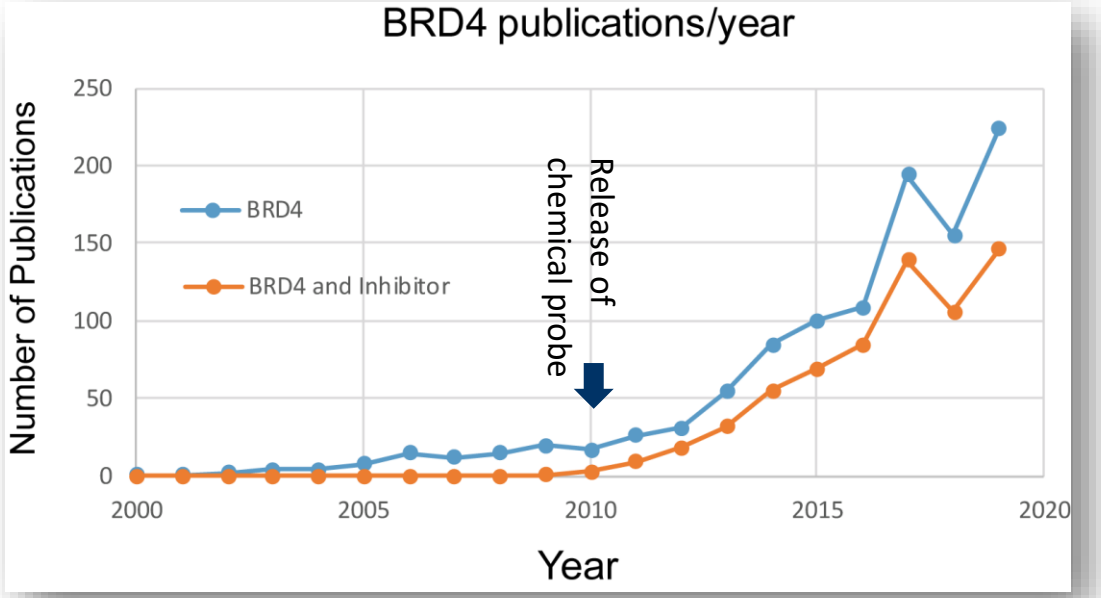
FAIRplus

- Open access requirement for **all** EUbOPEN and SGC publications
- Depositing publications in repositories
- Subject-based/thematic repository (e.g., arXiv, Europe PMC), **OR**
- Zenodo the OpenAIRE repository hosted by CERN
- FAIR Guiding Principles

  Findable, Accessible, Interoperable, Reusable

OPEN SCIENCE AS SOLUTION

- Encourage innovation
- Engage industry
- Accelerate science
- Increase reproducibility
- Reduce redundancy
- Engage patients
- Mobilize funding
- Develop new technologies through crowed sourcing



SGC CHEMICAL PROBES

- 20 years after deciphering the human genome, our understanding of human disease is still far from complete
- Lack of tools, which help understand biology and disease-relevant processes
- In a bibliometric analysis, we found that chemical probes were the most impactful tools to enable researchers to work on new genomics targets
- Freely available probes to human proteins will enable discovery of new medicines

Chemical probe = a drug-like small molecule that selectively modulates the activity of a specific protein in cells

Impact of SGC chemical probes

Discovered

190+

Chemical probes discovered by SGC or with pharma or academics

Distributed

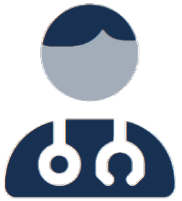
42,662+

Samples of chemical probes distributed globally by SGC and trusted vendors

Citations

7,285+

SGC chemical probes used by scientists around the world



Clinical Trials

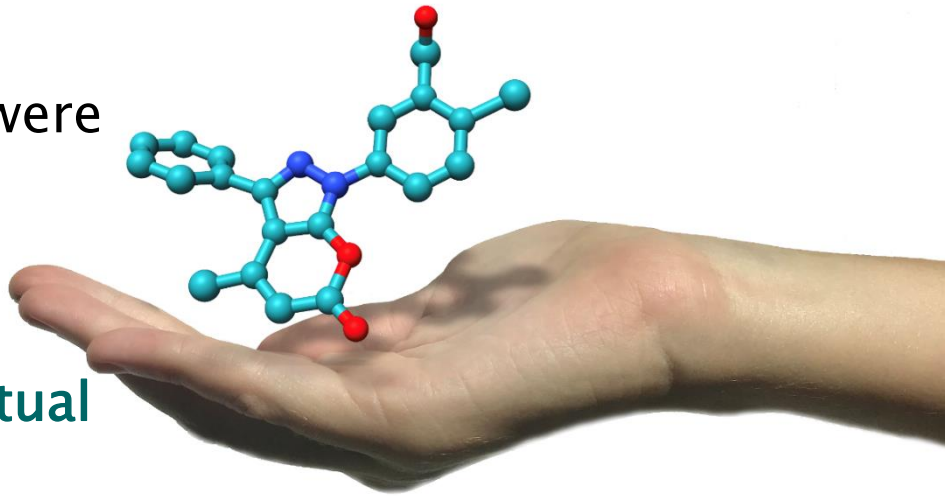
25+

Clinical trials and late-stage preclinical programs based on therapeutic hypotheses generated with SGC chemical probes

Hundreds of papers using SGC probes resulting in therapeutic hypotheses

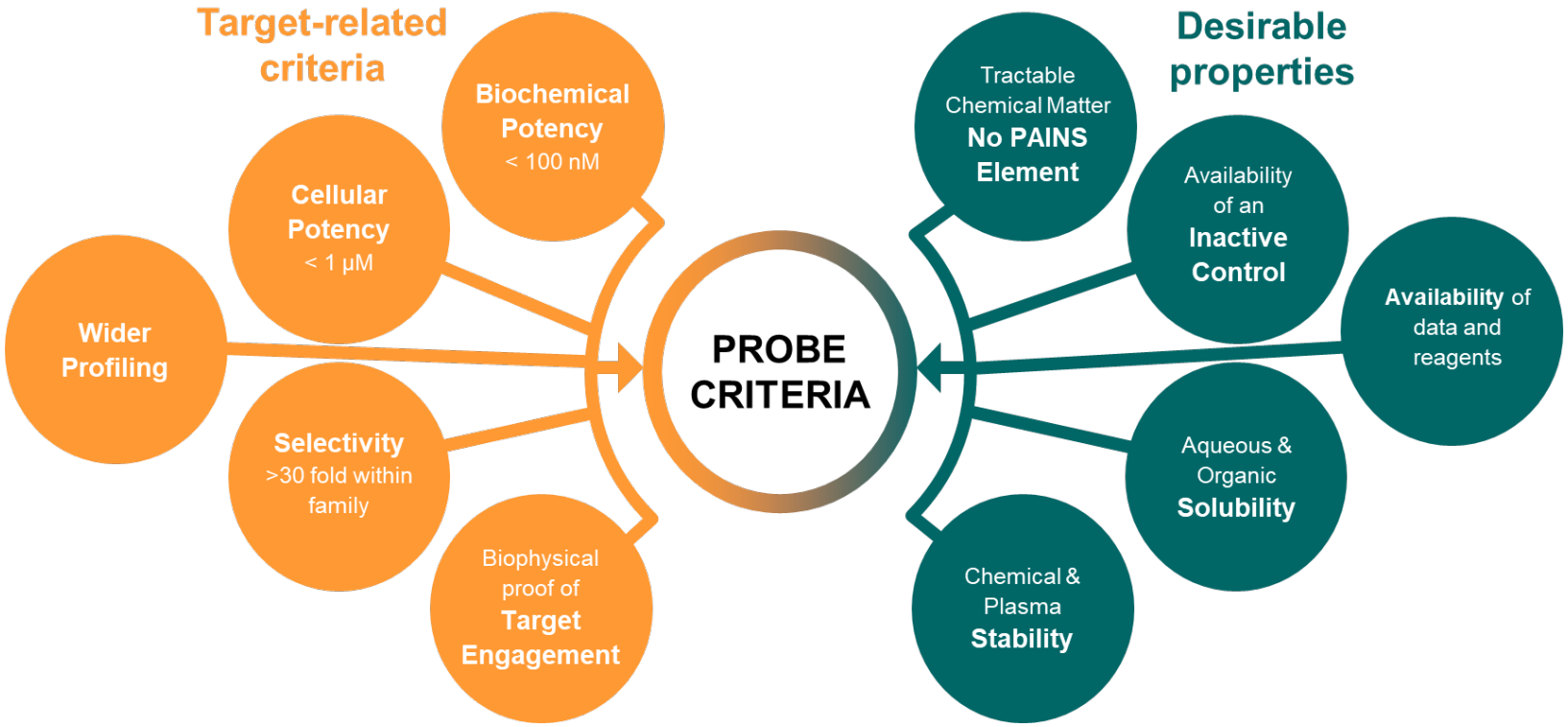
Donated Chemical Probes Program

- Initiated 2017 by SGC pharma partners (AbbVie, Bayer, Boehringer Ingelheim, Janssen, MSD, Pfizer, and Takeda) and led by SGC Frankfurt
- A collection provided by the pharmaceutical industry to the global scientific community
- Make openly available chemical probes, many of which were previously not in public domain
- Initially donations from pharma, later academics joined
- Available to all researchers without complicated contractual restrictions
- Make available through chemical vendors



Müller et al. Donated chemical probes for open science. Elife. 2018 pii: e34311. doi: 10.7554/eLife.34311

Review and Dissemination Process

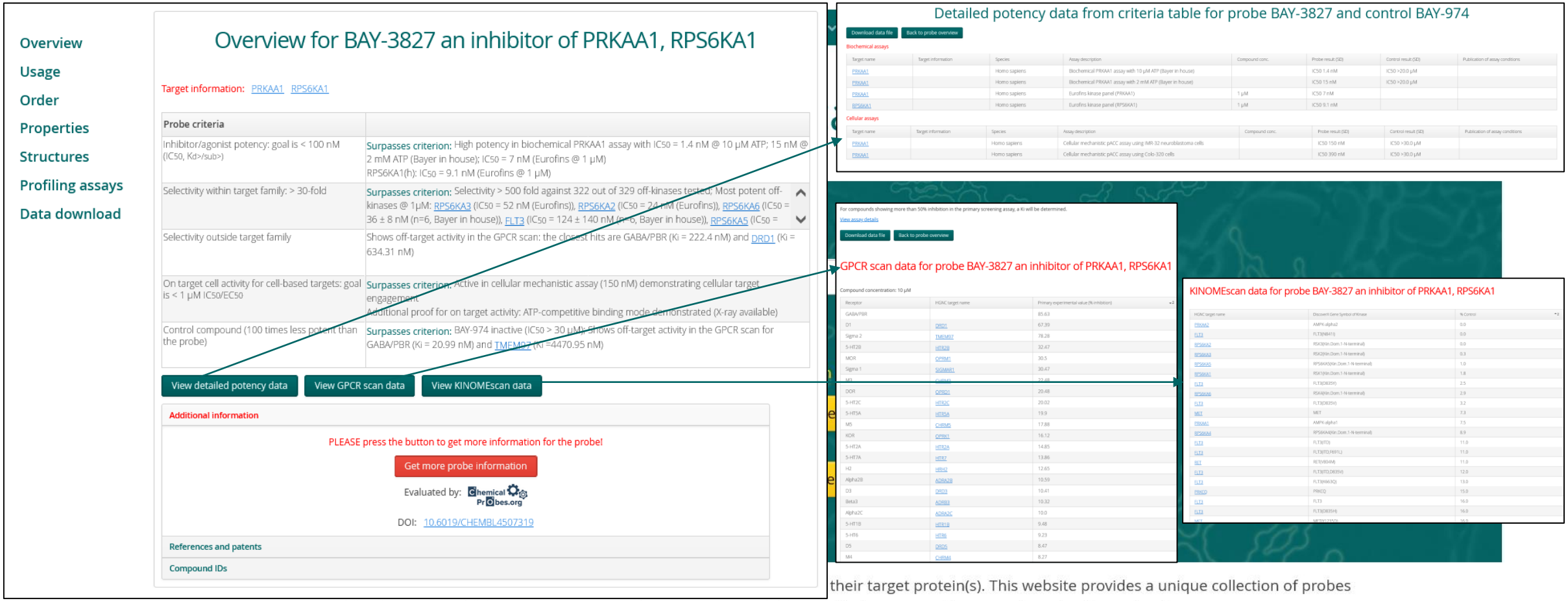


Probe proposal → Review and approval by independent committees → Database → Distribution by SGC and vendors

Donated chemical probes for open science, eLife 2018;7:e34311 doi: 10.7554/eLife.34311

Database – Website

All data in a publicly available database



their target protein(s). This website provides a unique collection of probes with their associated data, control compounds and recommendations on their use as well as a way to order the molecules.

DCP Data is Findable, Accessable, Interoperable and Re-usable

Findable
- specific URL for each probe, DOI number

Accessable
- DCP database website is open and free
- Data accessible though ChEMBL

Interoperable
- use a formal, accessible, shared, and broadly applicable language for knowledge representation
- link to other sources of knowledge / open repositories such as ChEMBL, PubCHEM, OpnMe, chemicalprobe.org

Re-usable
- Data update history
- CC-BY
- Metadata publication, modification and versioning not possible

Reagents and uptake from research community

SGC

DCP probes in numbers

105
DCP PROBES

92
INDUSTRY PROBES

13
ACADEMIC PROBES

12500
COMPOUNDS SHARED

28
COUNTRIES

Contributors

Takeda
BAYER
Pfizer
Boehringer Ingelheim
janssen
MERCK
Genentech
abbvie
NOVARTIS
MERCK Be well
gsk
MONASH University
EBERHARD KARLS UNIVERSITÄT TÜBINGEN
Institut Pasteur
ICR The Institute of Cancer Research
LUMC
KAROLINSKA INSTITUTET ANNO 1810
technische universität dortmund
UNIVERSITY OF NORTH CAROLINA CHAPEL HILL
UCSF
FOGHORN THERAPEUTICS
TECHNISCHE UNIVERSITÄT DARMSTADT

TARGET 2035: AN SGC-LED GLOBAL INITIATIVE

WHAT IS TARGET 2035?

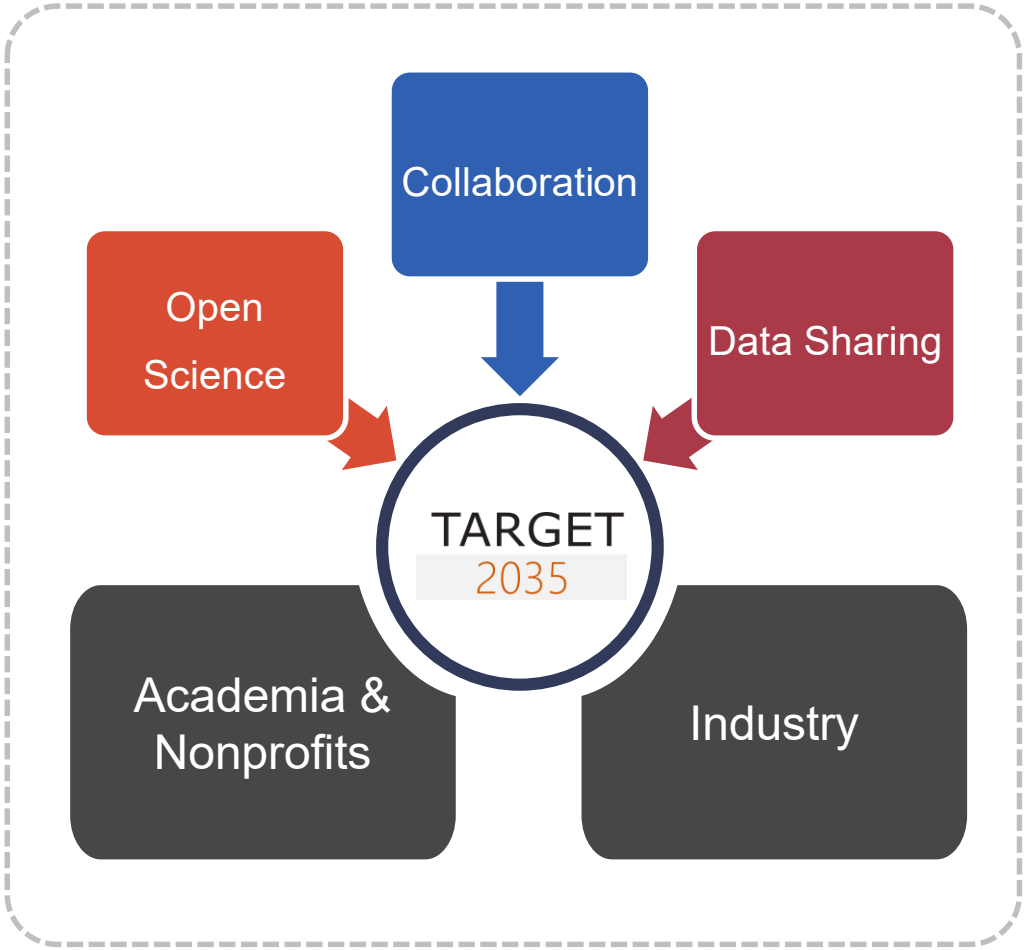
Open science global movement, focusing on the creation of chemical and biological tools to study human proteins and inform drug discovery.

OUR MISSION

Development of a pharmacological modulator for every human protein by 2035.

OUR VISION

Global collaborative effort to create open access tools to study each human protein and gene.



www.target2035.net

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