

Target 2035 - a global, open science initiative that aims to develop pharmacological modulators for each human protein

TARGET
2035

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www.target2035.net

@Target2035

What is Target 2035?

The human genome was mapped 20 years ago but most proteins remain understudied. Illuminating this "dark proteome" is key to better understanding human biology and disease, including uncovering new therapeutic targets and strategies.

Chemical probes are amongst the most effective tools to study proteins [1-6], but their development (especially for understudied proteins) is expensive and can take multiple years.

Target 2035:

- 1) Formalizes the goal of developing pharmacological tools for each human protein
- 2) Is an open science movement catalyzed by a global federation of scientists

EuBOPEN.org, ReSOLUTE (re-solute.eu), FAIRplus (fairplus-project.eu), Structural Genomics Consortium, are large-scale initiatives which have the objective of contributing to Target 2035.



Pharmacological Tools

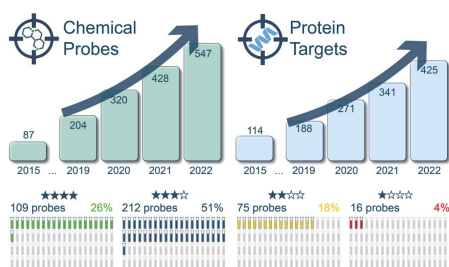
- Chemical probe**
Drug-like, potent, selective, cell active
- Biological probe**
Potent and selective affinity reagent e.g. monoclonal antibody
- Chemogenomic tool**
See KCGS (sgc-unc.org), EuBOPEN.org
- Chemical handle**
Tool for degrader development

- x Toxic
- x Reactive
- x Promiscuous

Pharmacological Tool

- ✓ Unencumbered for use
- ✓ On-target modulation
- ✓ Cell permeable
- ✓ Selective

Chemical probe development rate is slow.



Schematic of the data growth of the Chemical Probes Portal and assessment of their quality [3].

Some ways to solve this?

- Increase awareness of the value of chemical probes
- Build the federation of scientists
- Create opportunities to participate in the open science movement

~ Opportunities to participate ~



❖ Benchmark computational methods with experimental data

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❖ Community-based chemistry to accelerate probe discovery

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- The SGC provides the biochemistry (proteins and assays).
- Chemists worldwide provide the molecules.
- All data and ideas are freely shared in real time.
- All the work conducted within the OCN will be open and patent-free.



PUBLIC DEL LIBRARY

❖ Large, public, open DNA-encoded library

Peter J. Brown, peter.brown@unc.edu

- Need chemists willing to contribute to creating the library



Donate chemical probes

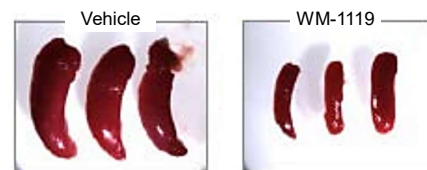
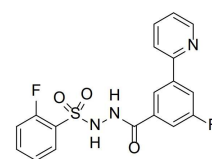
Claudia Tredup
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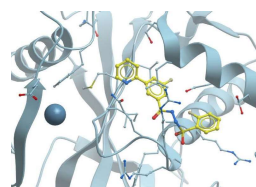
Nominate & review chemical tools

Susanne Mueller-Knapp
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Value of chemical probes: WM-1119 enables researchers to explore the therapeutic potential of KAT6A/6B



Spleen in mice



KAT6A (PDB 6CT2)

- KAT6A, KAT6B
- acetylate histone, and non-histone proteins
- regulate diverse biological processes and play essential roles in AML, lung, and breast cancers.
- WM-1119 is effective in preventing the progression of lymphoma in mice [7].

Chemical probe resources



<https://www.chemicalprobes.org/>



<https://www.sgc-frm.uni-frankfurt.de/#/start>



<https://thesgc.org/>



<https://opnme.com/>

→ Interested to share hit-finding, biophysical, biochemical assays, knowledge and/or results?

→ Contact: Target2035@thesgc.org



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References

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