

Target 2035 – Probing the human proteome to discover biology and drug targets

Executive Summary of Berlin meeting

Background: Among all the available techniques and reagents, bibliometric evidence unequivocally shows that pharmacological modulators (such as chemical probes) have the greatest influence on subsequent publications (Edwards et al, Nature 470:163 2011). Pharmacological modulators are also key parts of the pharmaceutical industry's target validation arsenal as they have a variety of features that are complementary to genetic approaches: they are often reversible, have immediate action, can target specific functions, provide dose-dependent response, more closely mimic therapeutics, can be used on many cell types, including primary cells, may be useful in vivo, etc.

Hypothesis: It should be possible for an organized community to generate potent, well-characterized and reversible functional modulators for every protein in the human genome by 2035, with an intermediate goal of developing potent, well-characterized and reversible functional modulators for most druggable proteins by 2025. This would require technological improvements, the participation of the pharmaceutical sector, a commitment to open science and a well-governed, inclusive, federated and global organizational model.

Berlin meeting summary: ~50 scientists, representing funders, industry and academia met for a one-day critique of the proposal. There was general enthusiasm for the initiative, a consensus that it might provide an inspirational and community-building focus, agreement that a public domain effort was the only way forward, and strong agreement about the potential scientific impact and impact in technology development. However, there was much discussion, and some lack of consensus, on important details. Topics that needed clarification include: how to, or whether to, select targets centrally, and how to apportion work among participants; what might be the most appropriate target product profiles for the probes; whether to include other types of probes, such as antibodies; how much to invest in technology development; whether a hub and spoke model was the most effective; how/where data would be stored and made available. There was agreement to continue with the concept.

Next steps:

- Review the summary for accuracy and tone
- Prepare a position piece to be published in an open access journal, with a well-articulated rationale for the emphasis on pharmacological modulators
- Create sub-teams to focus on the following areas and create a draft action plan (or earlier). Suggested team leaders encouraged to bring in additional people.
 - Organization and governance
 - Near term technologies and implementation
 - SME involvement
 - Technology for the future
 - Computational approaches and data
 - Community building