A new venture to exploit disordered proteins as drug targets

Overview

Many incurable diseases (cancer, neurodegeneration) involve intrinsically disordered proteins. Considered undruggabble by the mainstream pharmaceutical industry, disordered proteins continuously change their three-dimensional shapes and lack long-lived sites to which drug-molecules can attach themselves (Figure 1). Our mission is to make disordered proteins druggable. We will screen millions of disordered protein/drug-molecule pairs to learn the rules of drugging disordered proteins. Building on our expertise and working with academic/industrial partners, we will leverage cutting-edge biology, engineering, and artificial intelligence (AI) to deliver new drugs and tools. To accomplish this in a manner for maximum societal benefit, we will establish a non-profit Focused Research Organisation (FRO).

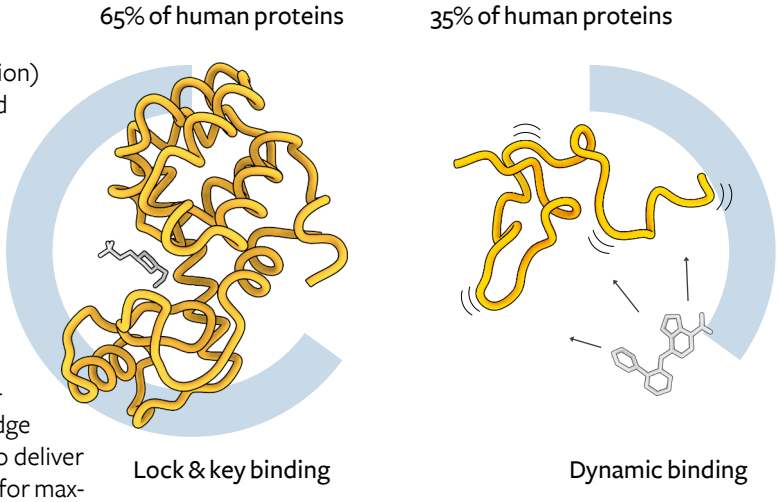

Figure 1. Our current understanding of how to develop small molecule drugs is limited to the interactions between ligands and structured proteins (left), whereby drugs are often simply described as fitting snugly into well-defined binding pockets. Nevertheless, many full-length (and extensive regions of structured) proteins lack such long-lived binding sites for small molecules. For example, disordered proteins (right) are highly dynamic, rapidly interconverting between different shapes, and are abundant in humans. Highly dynamic proteins like disordered proteins can indeed bind small molecules; however, the mechanisms of these interactions remain elusive & differ from traditional drug binding. Our goal is to make highly dynamic proteins druggable.

Our vision

Our goal is to map drug-binding capacities for every disordered protein, thus catalysing next-generation drug discovery.

How we'll do this

We aim to enable prediction of small-molecule binders from disordered protein sequences alone. We will first build a high-throughput, parallel platform (combining experiment, computation, and AI) to increase state-of-the-art screening efficiency to probe millions of small-molecule/disordered protein interactions. We will leverage this tool to create an enormous dataset and ultimately build an AI system that, given any disordered protein sequence, will predict promising drug candidates.

Why this can't be done in academic labs

The funding/infrastructure required to engineer an integrated, high-throughput, interdisciplinary platform (instrumentation that does not yet exist) and create an extremely large dataset exceeds academic resources/norms. Academic salary and contract limitations also restrict top engineering talent recruitment (software/hardware).

Why VC/large pharmaceutical companies won't do this

We will create a large, publicly-available dataset for the benefit of the UK R&D ecosystem. Pharmaceutical companies and start-ups are disincentivised from sharing their tools, hits, and understanding of general binding mechanisms, even though doing so could dramatically accelerate drug discovery and improve societal health.

A Focused Research Organisation

Our mission—make disordered proteins druggable—and the scale of our science are bold, rooted in public good, and require a strong engineering focus without academic publishing nor industrial profit pressure. To maximise impact, we will create a UK-based FRO to achieve technical milestones (creation of high-impact tools, datasets) within 7 years. We are committed to sharing our work publicly (tools, AI software, data), while also maximising translational impact by protecting IP of specific therapeutic molecules to ensure they can be accessed by medical professionals/patients. Upon completion, we will have the tools/expertise to launch new, non-profit initiatives and/or start-ups.

We are seeking £15M from a variety of sources and 1:1 match funding from DSIT should we be successful in the Research Ventures Catalyst programme, up to a final total of £30M.

Contact us at *info@bindresearch.com*.