

Project Proposal: A “Focused Research Organization” to Characterize Antibodies Through Open Science

Many antibodies that scientists purchase from commercial manufacturers to conduct their research do not work as advertised, because most have never been validated properly. This project brings together the public and private sectors to conduct independent, third-party testing of commercial antibody manufacturers’ catalogs and publish the results in the public domain, such that no scientist ever uses an ineffective antibody again.

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Problem Statement

Thousands of scientists use antibodies – each of which targets one of the 20,000 human proteins – to develop fundamental theories of human biology, and to identify targets for new medicines. These antibodies are often purchased from commercial antibody manufacturers, whose combined catalog contains between 3.5 million and 4.8 million products. But for more than 30 years, the scientific community has been aware that many of these antibodies do not work as advertised, meaning that they do not recognize the intended protein target, or recognize the target but also recognize non-specific targets that confound their use. This occurs because many if not most antibodies have never been validated, or have been validated using inferior or outdated scientific methods, and because academics do not have resources or skill sets to test them themselves. When an antibody binds to a non-targeted protein, a researcher may believe that the target protein, perhaps a drug target, is present in a particular cell type or subcellular organelle when in reality it is not. These erroneous results lead to a vast waste of time, resources, and human capital.

Project Concept

The science on the optimal antibody testing methodology is largely settled: using an appropriately selected wild type human cell and a CRISPR knockout version of the same cell as the basis for testing yields the most rigorous and broadly applicable results. However, the cost of testing for an individual target or antibody is often prohibitive for any individual academic lab or company. Our organization, YCharOS (Antibody Characterization through Open Science), couples the settled science with a unique open science business model, in which a consortium of antibody manufacturers provide, in-kind, all their renewable antibodies (i.e. monoclonal or recombinant, which once tested are of value in perpetuity) to any given target to YCharOS for use in direct, head-to-head comparisons. This centralized testing model creates massive economic efficiencies for the sector while also providing immense scientific benefit to the



public. Moreover, since all data will be released into the public domain using the principles of open science, the benefits accrue to all. We envision a world where no scientist ever uses an antibody that has not been rigorously tested by an independent third party. We believe that renewable antibodies for all 20,000 human proteins can be knockout validated in many applications for a one-time total budget of approximately \$100 million.

What is a Focused Research Organization?

[Focused Research Organizations \(FROs\)](#) are time-limited mission-focused research teams organized like a startup to tackle a specific mid-scale science or technology challenge. FRO projects seek to produce transformative new tools, technologies, processes, or datasets that serve as public goods, creating new capabilities for the research community with the goal of accelerating scientific and technological progress more broadly. Crucially, FRO projects are those that often fall between the cracks left by existing research funding sources due to conflicting incentives, processes, mission, or culture. There are likely a large range of project concepts for which agencies could leverage FRO-style entities to achieve their mission and advance scientific progress.

This project is suited for a FRO-style approach because antibody characterization is a time limited project that, once completed, will identify high-performing antibodies that can be produced and used in perpetuity. Antibody validation itself is unlikely to generate papers, but will create a public good that enables the production of new research results using properly validated antibodies.

How This Project Will Benefit Scientific Progress

Academic and pharmaceutical scientists laboring to advance our understanding and treatment of human disease will be able to save time and money and produce higher quality research using validated antibodies. Monetarily, scientists spend an estimated \$1 billion per year on ineffective antibodies that could otherwise be spent on conducting further research. Furthermore, there is a not insignificant volume of faulty research publications that have resulted from scientists unknowingly using ineffective antibodies.

Key Contacts

Authors Chetan Raina, CEO of YCharOS, chetan.raina@ycharos.com
 Al Edwards, CEO of the Structural Genomics Consortium,
aled.edwards@utoronto.ca
 Peter McPherson, McGill University, peter.mcpherson@mcgill.ca

Referrers Matt Hourihan, Federation of American Scientists, mhourihan@fas.org
 Alice Wu, Federation of American Scientists, awu@fas.org