

Title of proposed idea:

Coordinated social groups of Human Proteome disease network focused efforts to enable targeted proteomic translational research.

Nominator:

Robert Moritz, PhD, Institute for Systems Biology

What is the major obstacle/challenge in the field? What is needed to overcome this obstacle/challenge?

A major obstacle is the unfocused and biased nature of proteomics research through small programs that do not contribute to the larger picture of the Human Proteome. Proteomics cannot be reliant on one technique, all have their advantages and failings so as to create a successful project, one must select components of many techniques to tackle the problem of defining solutions for translational research. The goal of the program should be a broad based accessible suite of technologies, focused on efforts that can be applied to translational research. These techniques must be available for many groups to participate rather than small super groups and the techniques must be supported by robust bioinformatics to enable a system approach to understanding disease at both the proteomic and genomic level and be able to be applied to large enough numbers to be statistical valid. To overcome this impasse, a general framework of technology selection and data repository to a selection of poorly addressed disease settings as well as well studied focus areas needs to be established.

What emerging scientific opportunity is ripe for investment by a Trans-NIH program (e.g. the NIH Common Fund)?

All NIH funded research would contribute to a network of data repositories (Tranche, Peptide/SRMAAtlas, Peptidome (should be reconstituted) etc) with the general focus on data quality and dissemination. The technologies are mature enough today to provide whole proteome analysis (deep shotgun, targeted SRM) to contribute to a Trans NIH program to provide analysis in a disease agnostic manner but contribute to the development of the understanding of the whole human proteome collectively. These efforts would at the barest minimum be quantitative and include all aspects of proteins (PTM's etc) and be measured spatially and temporally. Emerging efforts in capture reagent development can be focused on proteins that are determined to be the most valuable (e.g., cancer associated networks, membrane receptors) and work hand in hand with proteomic methods.

What are the potential Trans-NIH investments that could accelerate scientific progress in this field?

Given the development in whole proteome analysis has culminated in two complementary technologies that can deliver highly reproducible quantitative measurements, Trans NIH investments can take these developments in the technology capabilities across many types of samples and disease focus. The potential development and sharing of reagents through additional investments in the technologies and

reagent production (i.e. new affinity reagents that are inexpensive and robust) to allow many researchers to apply these technologies in a focused manner is worthwhile.

Specifically, investment in coordinated proteomic groups tackling common efforts as put forth by each division. Groups can be part of one or multiple groups depending on the level of effort and focus. These would be groups of bioinformatic approach to data (i.e., repositories etc), groups in data generation to mine the human proteome based on disease networks and groups on data generation for translational studies.

If a Trans-NIH program on this topic achieved its objectives, what would be the impact?

Deeper understanding of protein network associated with disease or specific perturbations. Application of bioinformatic developments in understanding genomic measurements and translation into protein measurements for robust predictions to measurable protein effects across disease focuses of NIH divisions. A defined US involvement in the Human proteome and continued leadership in the development of technologies to tackle the next generation of data developments.