

Title of proposed idea: Connecting genetics with proteomics

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

In a short time, it will be possible to obtain full genome sequence for everyone. Rare variants that change protein sequence will be identified, and we will want to connect these variants with disease and disease risk. If a variant occurs only once, however, there is no statistical power to link it to disease.

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

The scientific opportunity is to develop methods that combine information from whole-genome or exome sequencing with information about protein structure, function and evolution to connect rare variants to disease and disease risk.

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

Investments in sequencing large cohorts.

Investments in developing algorithms for joint analysis of sequence data and structure.

Synthetic biology approaches for direct testing of the function of rare variants.

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

Improved ability to annotate personal genomes.