Title of proposed program: ***Undiagnosed Diseases Program***

Submitting Source: NIH

What is the major obstacle/challenge/opportunity that the Common Fund should address?
An unrecognized gap in the delivery of medical care involves the diagnosis of rare and novel disorders. The NIH Office of Rare Diseases Research reports that 6% of individuals seeking its assistance have an undiagnosed disorder. Even among rare-disease patients who have obtained a diagnosis, 15% have spent at least 5 years carrying the "undiagnosed" moniker (JAMA 305:1904-5, 2011). These individuals need and deserve investigation, both for their own care and for the insights they provide to biomedical research. The ability to diagnose them has, in recent years, been revolutionized by the use of genetic and genomic analyses, yet training remains needed in the interpretation of genome sequence and other genomic data as applied to the diagnosis of rare diseases. Therefore, the needs are the diagnosis of extremely rare disorders, the training of experts in the analysis of contemporary genomics data for the study of rare diseases, and the discovery of new diseases. Several obstacles stand in the way of addressing these needs. First, the medical profession often takes a fragmented approach toward dissecting the etiology of undiagnosed diseases, often sending patients on multi-year diagnostic odysseys. Second, there exists a dearth of experts qualified to analyze and interpret contemporary genomic data for clinical applications. Third, once discovered, intriguing and informative new diseases are rarely linked to appropriate basic science researchers for further study. Finally, there is widespread denial of reimbursement for diagnostic testing by third-party payers. The NIH Undiagnosed Diseases Program (UDP), inaugurated in the NIH Intramural Research Program in 2008, has demonstrated that it can address the above-mentioned needs, circumnavigate the obstacles, and capitalize on the possibilities to reveal novel mechanisms of disease and to expand the spectrum of explained human phenotypes. The UDP provides proof-of-principle for this proposal.

What would the goals of the program be?
The goals of the program are to propagate the UDP model to the extramural community, meld basic researchers to clinical projects, train medical genomicists in rare disease diagnostics, and make new biomedical discoveries.

Why is a trans-NIH strategy needed to achieve these goals?
A national network for UDPs is synergistic with the missions of all the NIH Institutes/Centers (ICs) by increasing the use of genomics in translational science and generating basic discoveries of medically relevant genes and pathways. It is cross-cutting in that the lessons learned will be applicable to any disease or organ system of interest to NIH ICs.

What initiatives might form the strategic plan for this topic?
The first initiative would establish UDPs around the United States through the creation of a new network with the NIH UDP acting as a coordinating center. The second initiative would be to train physicians and scientists to interpret contemporary genomics data for medical purposes. The third would be to set an example for how the NIH can provide a model to catalyze translational investigations by linking basic researchers to newly discovered disease-causing genes.

If a Common Fund program on this topic achieved its objectives, what would be the impact?
A national network for UDPs would bring undiagnosed patients, whose management is currently fragmented, to medical specialists organized in a systematic framework for discovery, diagnosis, and often treatment. The network would also provide a new a model for integrating genomic medicine and basic research for diagnosis and clinical care. Finally, the program will make new discoveries relevant to medical genomics.