Title of proposed program: *In Silico* **Modeling of Chronic Human Diseases**

Submitting IC: NIH

What is the major obstacle/challenge/opportunity that the Common Fund should address?

The NIH and US Corporations combined are investing more than $130 billion dollars every year in biomedical research and development, yet the number of drugs reaching Biological Licensing Agreement status is constantly declining. Although considerable improvements have been made, Biotechnology and Pharmaceutical Industries often lack rational approaches to develop and test new drug candidates. Although the constant input of basic scientific knowledge, new methods, approaches and tools for discovering, developing and testing new drug candidates is considerable, the complexity of many chronic human diseases is such that most efforts aimed to safely and permanently modify chronic human conditions are unsuccessful. Currently, research in human biology is experiencing an increased use of system biology, systems mathematics and computer simulations. Over the past decade, a new field of research, *in silico* biology, i.e. the use of computerized models to predict outcomes in biological studies, has emerged. The concept of using *in silico* biology for the modeling of human diseases is still in its infancy, but may eventually facilitate a better understanding and prediction of chronic human disease pathogenesis, and ultimately help to design better and more rational approaches for developing and testing new drug candidates.

What would the goals of the program be?

The overall goal is the standardization of data types and terms and the development of modeling methodologies in the context of an actual large-scale multidimensional molecular and physiological dataset, with the ultimate goal of providing a more comprehensive network view of chronic human diseases that can be used to define causal relationships and construct predictive models. Demonstration projects will examine the concept that the generation of predictive *in silico* models of chronic human diseases will be instrumental in facilitating the understanding and prediction of human disease pathogenesis and result in better and more rational approaches to develop and test new drug candidates.

Why is a trans-NIH strategy needed to achieve these goals?

Modeling approaches that are capable of predicting biological behavior at the organismal level still need to be developed and validated using real data. In addition, the concept of using *in silico* modeling of chronic human diseases to better understanding and predict human disease pathogenesis needs to be examined in many different chronic diseases areas, which are the core mission of different NIH IC.

What initiatives might form the strategic plan for this topic?

1. Generation of large-scale multidimensional human molecular and physiological datasets.
2. Generation of *in silico* models of human diseases.
3. Development of *in silico* based approaches for developing and testing new drug candidates.

If a Common Fund program on this topic achieved its objectives, what would be the impact?

The success of this CF program would provide standards and methodologies that would enable IC-funded projects focused on the generation of disease-specific models. These new models would improve understanding of disease pathophysiology and the development of enhanced capabilities to predict and select the best therapies for treatment and prevention, thereby providing better personalized medicine for patients.