Title of Proposed Program: Synthetic Biology for Functional Understanding of Biological Processes and Clinical Applications

Submitting Source: NIH

What is the major obstacle/challenge/opportunity that the Common Fund should address?
Enormous progress has been made in understanding the genetic, molecular, and cellular basis of human health, development and disease. High throughput biology, including genomics and transcriptomics have accelerated the discovery rate and systems biology has emerged as a method to combine multi-dimensional experimental data with computational approaches to make sense of the data and generate biological or clinical hypotheses. A major bottleneck in this process is elucidating the function particularly from the large number of putative networks and pathways that arise from these efforts. Current molecular biology methods such as RNAi are inadequate to keep pace with the new discoveries and new hypothesis testing and are of limited direct clinical utility. The emerging field of synthetic biology combines engineering design principles with chemistry and molecular biology to create new molecular tools and entire synthetic systems. Synthetic biology differs from molecular biology both in its scope and its conceptual approach: designing individual functions or entire synthetic biochemical or metabolic networks with desirable structural or enzymatic functions and properties that do not exist in nature or molecular functions that are too difficult to reproduce or too expensive to purify from natural sources. By building molecular circuits and studying their behavior in cells, biologists can gain insight into biological design principles. Synthetic biology offers promise in engineering vaccines and drugs with new and specific capabilities, the microbiome, cellular and regenerative therapies. Specific examples of recent successes include the ability to create proteins with pre-modified amino acids that can be expressed in prokaryotic systems where post translational modification is normally ineffective, engineering entire new multi-step metabolic networks to drugs, and engineering bacteria which sense or home to specific biochemical or biological cue before releasing a therapeutic.

Why is a trans-NIH strategy needed to achieve these goals? strategic plan for this topic?
Synthetic biology is a relatively new field. While other agencies (DoE, DARPA, NASA) all support programs in synthetic biology, NIH has no focused effort in this area. Individual grants on this topic are not uncommon but are scattered across multiple ICs and the biomedical research community is relatively unaware of these tools. The NIH members from a current trans-agency interest group on Synthetic Biology could form the nucleus for a new trans-IC working group which would gather information on the existing portfolio, galvanize and coordinate scattered efforts, and explore the potential for biological and clinical demonstration projects, the Ethical, Legal and Social implications, and the need for resources of standardized molecular tools and the potential for synthetic biology to enable a new era of biomedical research. Major technical challenges in biomedical research, intractable using current methods, could be identified through an RFI and a challenge (prize) mechanism could be proposed to stimulate risky high impact solutions to the most pressing and difficult technical hurdles.

If a Common Fund program on this topic achieved its objectives, what would be the impact?
The impact of such a program would be to show the utility of synthetic biology as an approach for studying human health and disease and feasibility of using these approaches for clinical applications. A common fund program in this area would leverage advances made in other fields, coordinate with programs currently supported by other agencies, unify the sector of the synthetic biology development community that is currently attempting to focus on biomedical applications and begin to provide these tools to the biomedical research community.