

Common Fund Idea Nomination Template

Title of proposed program: SaME Therapeutics: Targeting Shared Molecular Etiologies underlying multiple diseases

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

Developing drugs for patients is a slow and costly process. There are about 7000 human diseases and approximately 250 treatments. The FDA approves three to four rare disease interventions per year. At this rate, it will take more than 1,000 years to treat all diseases. At present, the paradigm for therapeutics development focuses on one disease at a time. However, based in large part from insights gained by NIH-funded biomedical research, a limited number of known molecular pathways have been identified. Moreover defects in these pathways underlie a common molecular etiology for multiple diseases. A sensible approach would be to identify diseases with Shared Molecular Etiologies (SME) and screen for therapies targeting these common pathways thus potentially impacting several diseases rather than one individual disease at a time. This approach can also increase the numbers of patients eligible for clinical trials.

Examples of possible areas where molecular etiologies are shared by a number of diseases are discussed in a recent commentary (Brooks, Tagle, & Groft Nature Biotechnology, June, 2014 in press).

This proposed Common fund initiative also represents an opportunity for NIH to align therapeutics development with the taxonomy of disease based on molecular biology, as outlined in a recent IOM report (http://www.nap.edu/catalog.php?record_id=13284).

This proposed initiative characterizes the elements of a Common Fund supported program.

Transformative: This initiative has the tremendous potential to dramatically change current therapy development approach of one disease at a time.

Catalytic: This initiative can catalyze the development and/or use of new drugs, devices and biologics, and can bring therapies to patients, especially those with rare conditions, that may not have garnered research attention but may share SME with other more common disorders.

Synergistic: This proposed initiative cuts across multiple scientific disciplines, and will require partnerships with other stakeholders, such as the FDA, pharma and patient groups. The goals of the proposed initiative support and advance the individual missions of NIH Institutes and Centers (ICs) and will tap on the NIH's investments in systems biology, infrastructure for pre-clinical and clinical studies.

Cross-cutting: The proposed initiative seeks to develop therapies that would be relevant to multiple diseases or conditions that affect many organs and systems, and thus will necessitate a coordinated, trans-NIH team for implementation.

Unique: This proposed initiative is innovative but tractable and has generated interest from potential partners, like the FDA.

What would the goals of the program be?

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The primary goal of the proposed initiative is to streamline and accelerate the number of new therapeutics that can be made available across a wide range of diseases. Aligned with this goal would be the identification of new therapeutics that target SME underlying multiple traditional diseases.

A second goal would be to anticipate and address potential scientific and regulatory science hurdles that might arise in this paradigm-shifting approach. Related to this goal would be to undertake pre-clinical and clinical studies that underlie therapeutics development targeted to SME, in patient populations encompassing multiple diseases.

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

Nearly all NIH ICs have an interest in the development of therapeutics, and therefore a better and more efficient approach in therapy development is of broad interest. Moreover, perturbations in a particular pathway can also affect multiple diseases that span the interest of several ICs. However, any single IC would only focus on those diseases that are relevant to its mission. In contrast, SMEs that underlie several diseases will most likely cut across the interest of multiple ICs. In addition, growing knowledge of the molecular pathways that underpins the shared molecular etiologies of disease crosses many multiple ICs.

What initiatives might form the strategic plan for this topic?

- 1) One initiative would be to identify and screen for new therapeutics to target SME. Examples of SMEs that might be targeted under this initiative include: protein misfolding and disorders of protein homeostasis, abnormalities in ubiquitination/deubiquitination, defects in signaling pathways such as RAS, AMPK, mTOR, and defects in cellular energetics resulting from mitochondrial dysfunction. Importantly, therapeutics screened under this initiative would not be limited to small molecules, but could also include devices and biologics that target SMEs.
- 2) A second initiative would be to undertake pre-clinical and early stage clinical studies of therapeutics targeted to SME. These studies would be fundamentally different than current approaches focused on single diseases. Recent interactions with the FDA in this area have been very positive, and includes an interest in partnering with the NIH should this initiative come to the implementation stages.

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

The success of this Common Fund program would fundamentally change the paradigm for pre-clinical and clinical studies and therapeutics development, from the current focus on individual diseases to SME. This change would align therapeutics development with the developing taxonomy of disease based upon molecular biology. It is likely that such an approach would be attractive for venture capital pharmaceutical companies and biotech, as well as venture capital firms.

The success of this CF program would also address regulatory challenges that are associated with changing the concept of disease and therapeutics development.