Title of proposed program: Off Target Helpful Effects Registry (OTHER) Project

Submitting Source: NIH

What is the major obstacle/challenge/opportunity that the Common Fund should address? What would the goals of the program be? It is well established in pharmacology, toxicology, and clinical practice that all drugs affect multiple targets, and have multiple effects, in humans. These "off target" effects can be beneficial, leading to repurposing opportunities where a drug approved for one indication finds utility in another, or can be harmful, leading to adverse events which can lead to limitation in use or withdrawal of the drug. The FDA has launched the Sentinel effort through large health care systems to capture adverse events. No one is capturing unexpected, serendipitous beneficial effects which could be useful for repurposing of marketed drugs. Many current efforts are focused on drug repurposing utilizing rational, computational, or screening approaches, but no systematic effort is being put on the most obvious and relevant experience with approved drugs, which is the patients who currently take them.

Since over half of all Americans now take at least one prescription drug, and one in six takes three or more medications, an enormous experiment in polypharmacology and off-target effects is now being done in the U.S., but those data are not being captured. This program would create a user-friendly social media platform and database to allow patients to enter disease, medication, and effects information anonymously, tools to analyze the data, and a data portal to allow researchers to query the database for improvement in symptoms of a second disease upon starting a new medication for a different ailment. While a large amount of "noise" will undoubtedly be present in the database due to many biases in selection, collection, and reporting, it is anticipated that signal of off-target beneficial effects will be identifiable, and if successful it will lead to new therapeutic hypotheses that can be rapidly tested in preclinical models and/or clinical settings. Note that this project is, in some ways, the inverse of the FDA's Sentinel initiative which monitors over 100 million people for adverse events. The OTHER project would crowd source positive experiences with medications (although harmful effects could be collected as well) to identify unexpected beneficial new uses of approved drugs.

Why is a trans-NIH strategy needed to achieve these goals? What initiatives might form the strategic plan for this topic? This program will require a very broad array of expertise from informatics to pharmacology to disease biology across the spectrum of NIH, so is ideally suited to be a trans-NIH program. The program's initiatives would include (a) conceptualization, design, development, and implementation of the database, (b) an outreach component to educate the public about the utility of the project and encourage participation, (c) programs to pilot the utility of the database to generate testable hypotheses, and (d) programs to test the hypotheses generated in preclinical models or clinical settings, to test the veracity of the data and the hypotheses generated from it. The FDA should be engaged with this project as well.

If a Common Fund program on this topic achieved its objectives, what would be the impact? If successful, this program would generate many new uses for existing therapies based on real-world patient experience, would lead to new avenues of investigation of disease biology based on the pharmacology of the drugs found to be effective, and would lead to a very beneficial participatory trend whereby the public contributes in very real ways to biomedical research and the development of new therapies.