

CONCEPT CLEARANCE

FISCAL YEARS 2016-17 RESEARCH INITIATIVES — NCATS

TITLE: Drug Repurposing/Repositioning

OBJECTIVE: The purpose of this concept is to develop a set of funding opportunity announcements (FOAs) to support robust, pre-clinical (to establish rationale for a clinical trial), clinical trial planning and clinical trial implementation. Funding will be used to repurpose drugs where the hypothesis originates from the use of a publicly available method for identifying new indications for existing drugs such as independent crowdsourcing strategies for investigational drugs or computational algorithms. The pre-clinical studies to establish rationale for a clinical trial will serve as “use cases” to test the utility of the method that identified the drug/indication pair. Support will separately be provided for clinical trial planning and clinical trial implementation. Separating funding into three stages allows investigators to apply for funding at multiple on ramps to test a new therapeutic use, depending on the current stage of their particular project.

BACKGROUND: Therapeutic development is a costly, complex and time-consuming process. The average length of time from target discovery to approval of a new drug is about 14 years. The failure rate during this process exceeds 95 percent, and the cost per successful drug can be \$2 billion or more. The high therapeutic development failure rate means there are many existing, partially developed therapeutic candidates that could be repurposed for use in a new disease indication. Data available through the FDA Rare Disease Repurposing Database, which is a compilation of drugs that have been repurposed from use in a common disease to use in a rare disease, suggest that approved drugs have high potential for use in multiple indications [1].

These FOAs are intended to complement the ongoing NCATS New Therapeutic Uses initiatives. The previous New Therapeutic Uses initiatives tested two successful process improvements: 1) using NCATS template agreements to accelerate establishment of academic and pharmaceutical partnerships and 2) publicly posting industry assets to solicit ideas from the academic community (i.e., “crowdsourcing”) for new therapeutic uses.

One of the lessons learned from publishing the New Therapeutic Uses funding opportunity is that many investigators are using computational algorithms and other innovative processes to identify drug/indication pairs for experimental drugs and for drugs approved by the Food and Drug Administration (FDA). However, they struggle finding support to test the new drug indications through standard NIH funding mechanisms. NCATS mission is focused on process improvements and is disease agnostic. The Center emphasizes innovation and deliverables, relying on the power of data and new technologies to develop, demonstrate and disseminate improvements in translational science. These initiatives are intended to demonstrate the usefulness of process improvements that could lead to dissemination of effective methods to the broader scientific community.

DESCRIPTION: NCATS seeks to support robust, pre-clinical repurposing studies that are testing a hypothesis that originates from the use of a published or publicly available method for identifying new indications for existing drugs. The pre-clinical studies will serve as “use cases” to demonstrate the usefulness of the drug/indication pairing method.

While the goal of an individual project will be to explore the potential new use of existing investigational and FDA-approved drugs, NCATS seeks to identify strategies that may improve the efficiency of drug repurposing and repositioning studies.

Goals:

- Assess a variety of methods for identification of new drug/indication pairs or new combination therapies for drug repurposing/repositioning studies by supporting “use cases.”
- Improve the translational efficiency of clinical trials for drug repurposing studies.
- De-risk future exploration of existing drugs for use in new diseases.

- Uptake of systematic drug repurposing methods that, when successfully implemented, can result in getting more drugs to more patients more quickly.

IMPORTANCE: This effort will provide an opportunity to test the usefulness of a publicly available method for identifying new indications for existing drugs that can be adapted in other drug repurposing studies to accelerate the rate that new therapies get to patients.

HISTORY: From 2012 to 2015, NCATS supported 13 projects in 12 disease areas by crowdsourcing new therapeutic uses ideas for a total of 76 pharmaceutical assets. Use of NCATS template agreements successfully shortened the time to establish collaborations between academic medical centers and pharmaceutical development partners to 3-4 months, from a typical year or more.

Many prospective applicants are seeking funds to repurpose additional drugs that are not on the NCATS posted list of agents.

CURRENT PORTFOLIO OVERVIEW: NIH drug development FOAs tend to focus on new molecular entities in specific disease areas (e.g., the National Institute on Drug Abuse, the National Institute of Mental Health, the National Institute on Alcohol Abuse and Alcoholism, Blueprint Neurotherapeutics). The National Cancer Institute's Cancer Therapy Evaluation Program supports repurposing of investigational drugs specifically targeted toward cancer. The National Institute of Neurological Disorders and Stroke's NeuroNEXT program will support repurposing of existing drugs. The National Institute of Arthritis and Musculoskeletal and Skin Diseases; the National Institute of Allergy and Infectious Diseases; the National Eye Institute; and the National Heart, Lung, and Blood Institute have clinical trial planning grant solicitations that could be used for planning trials (if pre-clinical studies are successful). However, in some cases, these FOAs are for large multisite trial planning. Outside of New Therapeutic Uses, there are no FOAs that seek drug repurposing hypotheses that are the result of innovative processes for pairing drugs with indications.

COLLABORATIVE ACTIVITIES: NCATS works with other Institutes and Centers (ICs) in the management of New Therapeutic Uses projects and will do the same for these FOAs. Specifically, we rely on program staff from other ICs to provide subject matter expertise. We try, whenever possible, to align our goals with those that are consistent with the categorical IC as long as NCATS' standards of research are maintained. NCATS sought input from program staff across NIH to identify areas of greatest need.

REFERENCE:

[1] <http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/HowtoapplyforOrphanProductDesignation/ucm216147.htm>

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