TO: UCSD Clinical and Translational Research Institute (CTRI) General Members

FROM: CTRI Translational Research Technologies (TRT) Division

REQUEST FOR PROPOSALS

Title

Assay Development and Pilot Screens Grants to Accelerate Early Lead Discovery: Generating Preliminary Data for the NIH R01/R21 FOA “Solicitation of high-throughput screens (HTS) to discover chemical probes”

Overview

The UCSD CTRI has committed $25,000 – $50,000 to “Seed Funding” 5-10 high-throughput screening (HTS) assay development projects, thus encouraging early steps of translating breakthrough discoveries in the laboratory towards clinical applications. Funds will be dedicated to the services provided by the Conrad Prebys Center for Chemical Genomics (CPCCG) at the Sanford-Burnham Medical Research Institute (SBMRI) in La Jolla, California. Services offered by the CPCCG include conversion of investigator’s prototype assays into a robust, scalable and automatable high-throughput screening assays and generation of pilot screening data from small test libraries.

Over the past 7 years, CPCCG has assembled unique drug discovery capabilities, impressive laboratory robotics infrastructure, veteran pharmaceutical talent, and experience in attracting and executing successful academic-industry partnerships. CPCCG successfully competed for a multimillion dollar collaborative research 6-yr grant (U54) to be 1 of 4 Comprehensive Centers of the NIH’s Molecular Libraries Probe Production Centers Network (MLPCN), as well as for designation of 1 of 5 Comprehensive Centers of NCI Chemical Biology Consortium (CBC). Through the MLPCN, CPCCG has had over 4 years experience of attracting, mentoring collaborators and co-applying for competitive NIH FOAs (R03, R21, R01, R33, SBIR) and managing over 25 projects/year with multiple PIs from many institutions, while participation in NIH Steering committees has afforded access and knowledge of additional funding opportunities and programs targeted toward rare and neglected diseases (TRND), and translational research (CAN, NCATS). Additionally, through the CSC, CPCCG has extensive experience and success in an aggressive deliverable driven contract research environment, and intimate knowledge of the NIH’s NeXT program.

To learn more about the CPCCG and this seed funding program, attend a lecture by Dr. Michael R. Jackson, Associate Professor and VP Drug Discovery and Development at CPCCG, on the topic of “Drug Discovery: Generating drug candidates to novel targets”, August 23rd, 3:00 – 4:00 PM, Leichtag Building, first floor lecture hall.

Seed Funding Goal

The goal of this seed funding is assist UCSD CTRI investigators in fulfilling the multiple technical requirements leading to successful application for two new NIH Funding Opportunity Announcements (FOAs) for using developed high-throughput assays to interrogate large chemical collections of small molecules for the purposes of finding validated hits against translational targets or pathways related to human diseases [http://grants.nih.gov/grants/guide/para-12-058.html; http://grants.nih.gov/grants/guide/para-12-059.html]. Both of these FOAs expire on September 8, 2014.

How to Apply

A one to two page application may be submitted at any time using the "Application for Funding" button on the CTRI TRT website [http://ctri.ucsd.edu/laboratory/Pages/default.aspx]. Proposals will be reviewed by an HTS Assay Advisory Board composed of CTRI and CPCCG leadership. Current plans envision awarding 5-10 applications per year during the life of the NIH FOAs. It is highly recommended that prior to submission of an application, PIs should establish dialog with Dr. Thomas “T.C.” Chung, Director of Outreach and Project Manager (tcung@sanfordburnham.org) who will arrange discussion of the project, explore various options for assay design, and agree on the most suitable assay format with the appropriate HTS Assay Development or High Content Screening (HCS) Core Directors.

The 1-2 page proposal should briefly describe the biology of the project, the proposed assay format and the development plan with a timeline (including any resources required from CPCCG), the relevance and novelty of the target/assay to drug discovery, and the reasons why an HTS screen using the assay proposed is likely to be funded by the NIH.

The current seed grants are for UCSD faculty who are CTRI General Members to use CPCCG services. For UCSD faculty who are not CTRI members, CTRI membership applications can be found at http://ctri.ucsd.edu/about/membership/Pages/default.aspx.

Review Criteria

1. Novelty of the assay. Assays proposed must be “de novo” assays – i.e. where new reagents need to be generated to generate feasibility data. (Slight reconfigurations of existing assays or commercially available assays will not be funded).
2. Relevance to drug discovery. The target of the assay should ideally be implicated in a disease or disease process and thus have a plausible clinical application.
3. Probability that the HTS assay meet the criteria for funding by NIH Special Emphasis Panel for the PAR-12-058 (R01) or PAR 12-059 (R21) Grant Applications. The proposed final HTS assay should fit the criteria outlined by the respective FOAs. Preference will
be given to those applicants that are at a more robust level of technical readiness. Applicants agree to lead an R01/R21 application and agree to work with the CPCCG team to generate the preliminary HTS data required for submission.

Benefits and Obligations of the Funding Program

If awarded, this Seed-funding program has two phases:

In Phase I the investigators collaborate with the HTS Assay Development Core in the CPCCG to review assay concepts, know-how, reagents, and protocols for the investigators prototype assay to then develop a practical assay concept, and work plan to generate the required reagents, and deliver a workable at least 384-well prototype HTS assay. The professionals in the CPCCG HTS Assay Development or HCS Cores may further miniaturize and optimize to a 1536-well format, then generate pilot HTS data in this final format. The data generated by the Core includes confirmation of automated assay robustness ($Z' > 0.5$, $S/B > 4$, $CV < 10\%$); pilot screening of a small (~2K compounds) library to establish the approximate hit rate for the primary assay. Furthermore, CPCCG will assist the PI in developing a plan for a cascade of follow-up assays (orthogonal, counterscreen, selectivity), demonstration that these assays can support quantitative dose-response studies, and where possible generate actual data on pilot hits through this cascade.

Phase II is preparation and submission of the NIH R01 or R21 grant application. Using the HTS data generated by the Core, the PI prepares the background and research plan of the grant application. The CPCCG will co-apply and assist in drafting the specific aims, screening cascade, timelines, and provide a subcontract budget. The application is accompanied by a letter of support (LOS) from Dr. Thomas "T.C." Chung, Project Manager, for the NIH Roadmap program at CPCCG and/or Dr. Michael R. Jackson, VP Drug Discovery and Development at CPCCG. Dr. Chung is available as a resource to help guide PIs in preparing the R01 or R21.