NIH Roadmap ACCELERATING MEDICAL DISCOVERY TO IMPROVE HEALTH

Molecular Libraries and Imaging Initiative

RFA-Assay Development for High Throughput Molecular Screening

Program Objective. This RFA is one component of the NIH Molecular Libraries and Imaging Roadmap Initiative (http://nihroadmap.nih.gov/molecularlibraries/index.asp), a major NIH effort to broaden access to rapid assay technologies. This program funds the development and adaptation of biological assays for use in automated high throughput molecular screening (HTS). A further component of this Roadmap Initiative (PAR-06-545) recommends appropriately configured biological assays for HTS within the Molecular Libraries Screening Centers Network (MLSCN), which employs a large library of chemical compounds that are part of the Molecular Libraries Small Molecule Repository. It is intended that this RFA promote the development of automated screening projects that can be submitted to the MLSCN via this mechanism. The overall goal of the Initiative is to facilitate the creation of a public database of biological information about small molecule chemical structures (*PubChem*), which then seeds the further development of small molecule pharmacological tools for biological research.

Aim to Improve HTS Access. High throughput molecular screening (HTS) is the automated, simultaneous testing of thousands of distinct chemical compounds in models of biological mechanisms. Active compounds identified through HTS can provide a starting point for the design of powerful research tools that allow pharmacological probing of basic biological mechanisms. These probes can be used to establish the role of a molecular target in a disease process, or, assess its ability to alter the metabolism or toxicity of a therapeutic. The immense potential of HTS to impact our understanding of biological mechanisms is largely untapped because access to automated screening facilities and large compound libraries is limited in academic, government and

non-profit research sectors. The NIH Molecular Libraries Roadmap Initiative will provide unprecedented access to these resources and allow the broad application of HTS in NIH-supported research.

Program Information. The Goal of the RFA is to initiate a continuously evolving stream of scientifically novel and technologically outstanding assays that can be miniaturized, automated and used for screening small molecules. This Program is open to all areas of biological and biomedical research, with the goal of encouraging the submission of well developed HTS screening projects to the MLSCN. ***Investigators are asked to state a biological question that is appropriately addressed through the use of a pharmacological small molecule probe, further define the properties that should be captured in its design, and develop assays that can be incorporated into a screening plan aimed at identifying small molecules with essential probe attributes.***

Funding is provided to enable investigators to develop promising assay protocols for novel molecular targets (supported by a 1 year R21 with up to $125,000 available in direct costs), and transform them into a plan for automated screening by demonstrating the responsiveness and robustness required for use in HTS. Emphasis is placed on screening targets for which an inadequate array of selective and potent small molecule modulators are available to the public.

In 2007 it is expected that 40-50 projects will be funded for approximately $8 million. The first submission date for 2007 (RM07-001) recently closed. However, another announcement is expected later in 2007, and additional announcements are planned for following years. Abstracts from previous year awards (RM04-012, RM05-011, RM06-004) can be viewed at the Roadmap website: http://nihroadmap.nih.gov/molecularlibraries/fundedresearch.asp

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