Request for Applications
WARF Strategic Technology Enhancement Program
Lead Discovery Initiative
2006-2007

WARF, in conjunction with the Keck-UWCCC Small Molecule Screening Facility (SMSF), has created a new initiative for assay development and small molecule screening through its new Strategic Technology Enhancement Program (STEP). WARF's STEP is intended to move early stage technologies closer to realization. Within STEP, the Lead Discovery Initiative addresses the development and application of high throughput screening assays suitable for identification of small molecules that interact with a given target.

This initiative is directed at investigators who have identified either:

1) putative regulatory elements, other drug targets, and/or a biological assay for high throughput screening of available chemical compound libraries, or
2) a new chemical entity or collection to be screened in one or more available biological assays.

The Wisconsin Alumni Research Foundation (WARF) will fund the selected projects. All work will be carried out at the SMSF, and all funds will be directly paid to the SMSF on a contract research basis. It is anticipated that laboratories providing a biological assay or target would be responsible for providing biological reagents (purified proteins, engineered cell lines, etc.) for assay development and screening with the chemical libraries at the SMSF and would work with the SMSF to develop secondary biological assays to evaluate hits**. Selection of the project does not result in funds being awarded to the applicant's laboratory but instead provides contract services for the laboratory through the SMSF.**

The SMSF will provide the following services for those technologies accepted into this program.

1. Assay Implementation: The SMSF will adapt, optimize and automate existing target-based and cell-based phenotypic assays obtained from the UW laboratory to 96-well or 384-well plate format as appropriate to the specific assay, screening approach, and level of throughput anticipated. The SMSF is capable of implementing assays using a variety of detection readouts such as absorbance, fluorescence, luminescence, fluorescence energy transfer (FRET), and cell-based imaging screens.

2. Compound Library: The SMSF has a compound collection of 43,000 compounds with known or unknown biological activities and diverse chemical structures. This library will be expanded to 60,000 during the next few months.

3. HTS Screening: The SMSF will screen the compounds for biological activity in HTS assays to identify and confirm hits. Secondary assays, using a different readout, will be performed on initial hits in order to minimize false-positive results.

4. Optimization Chemistry: In consultation with the UW investigator, the SMSF will provide a moderate level of optimization by identifying analogs of initial hit compounds from commercially available small molecules as represented, for example, in the ZINC database. These compounds will be assayed for improved properties such as potency and solubility. Additional chemistry efforts involving synthesis of analogs may be available to UW investigators by applying to the WARF Lead Optimization Program.

5. HTS Informatics: The SMSF will provide informatics support to track compounds, assays, and screening data. All data will be held in confidence at the SMSF and provided to the UW investigator.

6. Biological Assays: For UW chemists providing collections of synthetic or natural product compounds, the SMSF will provide biological assays. Available assays include mechanism of action assays currently provided by the SMSF and custom assays developed in response to accepted applications. Representative assays currently available through the facility are listed on the SMSF website at http://www.hts.wisc.edu/Resources/nonscreening_info.htm. The SMSF will identify active members of the collection in preliminary studies and determine the IC50s for selected hits in consultation with the UW investigator.

Proposal Submission Deadlines
Applications will be accepted on a continuous basis and will be reviewed once each month.

Eligibility
Applicants must be University of Wisconsin researchers. In order to be eligible for consideration, all applications must submit, or have previously submitted, an Invention Disclosure Report (IDR) to WARF detailing the nature of the technology to be considered for the program.

Final Report Required
A report summarizing your findings and results generated both at the SMSF and in follow up work performed outside of the facility is due upon completion of the project.

Application Process
Interested researchers should complete the Lead Discovery Initiative Application Form and send it to Laura Heisler at the address below by email attachment or U.S. mail. This form is intended to solicit information needed for both a technical and a technology transfer evaluation of the proposal. If a UW Invention Disclosure Report (IDR) has not been filed with WARF for this technology, a completed IDR must also accompany the application. If you have any questions regarding the status of a previous disclosure to WARF, contact your WARF Intellectual Property Manager or the WARF STEP Manager (see below). Instructions regarding the submission of an IDR to WARF as well as the IDR form are available at http://www.warf.org/inventors/index.jsp.

Evaluation Process
A core committee comprised of SMSF, Pharmacy, and WARF staff will meet once a month to evaluate proposals. Only proposals relating to inventions already disclosed to WARF (either disclosed in advance or at the time of proposal submission) will be considered.

Proposals will be evaluated and ranked based on the following criteria:

1. Novelty of the putative target, assay design or new chemical entity
2. Anticipated potential of the research to lead to a licensable invention
3. Technical feasibility of developing and implementing a selective high throughput screen (for new targets)

Inquiries
For questions concerning the Lead Discovery Initiative or the application process, contact
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For questions concerning the UW CCC SMSF or specific SMSF services, contact
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