

### **Purpose of the Program**

The UMASS-Chemical Screening Initiative (UMASS-CSI) provides investigators access to experienced professional and state of the art technological resources at the Small Molecule Screening Facility (SMSF) for the discovery of exceptional chemical probes, potential diagnostic and therapeutic candidates of high impact, as well as research tools. The program is funded by the UMASS Office of the President's Science and Technology Fund.

### **Executive Summary**

- To permit the discovery of high impact chemical compounds with therapeutic benefits in the academic setting
- To provide drug screening and development support for meritorious projects from across the UMASS system
- Facilitate external funding
- Facilitate industry-academia collaborations by demonstrating 'druggability' of biological targets
- Generate Intellectual Property for UMASS

### **Objective of this Call for Proposals**

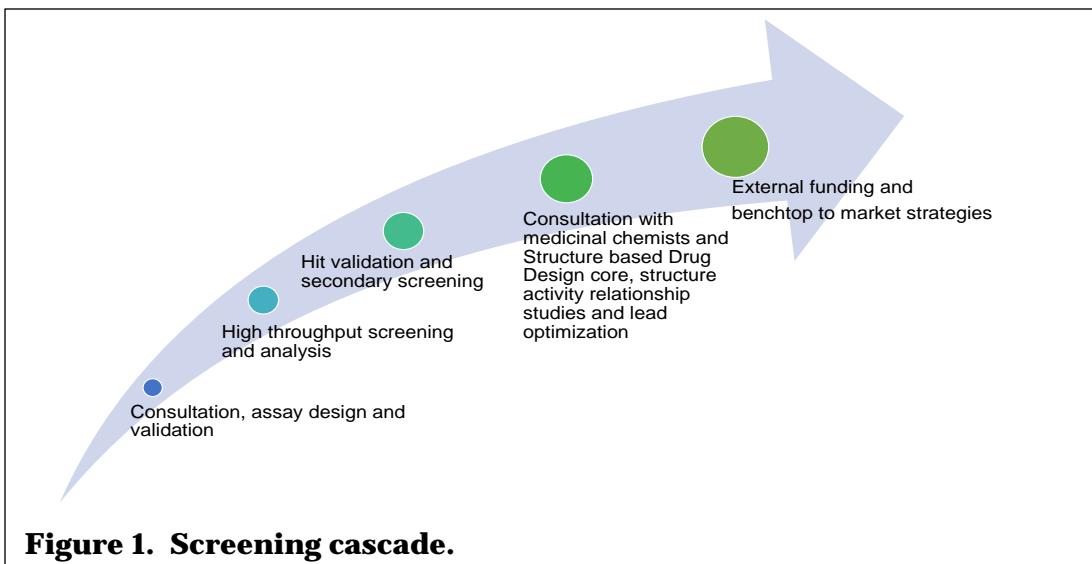
The objective of this announcement is to invite applicants with a well-developed assay used in basic research and therapeutic development programs suitable for HTS to submit the assay for consideration by the UMASS-CSI to identify hits and probes from the SMSF compound library.

**Tier 1 projects** encompassing pilot experiments would be awarded \$7,250 each for screening any library of choice, up to a total of 5,000 compounds (e.g., a partial Diversity set and/or a combination of the LOPAC and international drug collection to name a few).

**Tier 2 projects** would involve comprehensive screening of the entire 58,000 compound library. Tier 2 projects would be awarded \$22,500 each.

In both cases, the awards would cover all costs involved. These awards would cover not only assay development and high throughput screening costs, but also secondary and counter screening, hit validation, compound picking, and consultation with medicinal chemists at UMASS Amherst (Dr. Sergey Savinov) and the Structure-based Drug Design core at UMASS Medical for further developing these compounds into potential therapeutics (**see the screening cascade in Figure 1**).

Dr. Sangram S. Parelkar, who is the manager of the SMSF and has broad expertise in drug discovery and development, would be responsible for assay development and all aspects of screening. Dr. Thompson, the SMSF Core Director, will also provide input into assay design and compound prioritization.



### **Small Molecule Screening Facility Core Strengths**

- **Expertise:** Medicinal chemistry and HTS assay development
- **State of the art automation:** dual arm Biomek Fxp (Beckman Coulter) liquid handler and BioTek MultiFlo FX Multimode fluid dispenser equipped with RAD™ technology for individual well dispensing
- **High throughput capabilities:** rapid plate transfer and stamping with high precision for volumes as low as 100 nL into 96, 384 and 1536 well plates – Biomek FxP
- **HEPA enclosure on instrumentation:** sterile and particulate free environment for cell based assays
- **Limitless assay capabilities:** cell based and biochemical assays, automated ELISA's, PCR setup, high throughput DNA extraction to name a few
- **Screening libraries:** collection of 58,000 unique pharmacological small molecules (included targeted libraries) occupying novel chemical space
- **Detection in multiple formats:** ability to conduct Absorbance, Fluorescence Intensity, Fluorescence polarization, Time Resolved Fluorescence, TR-FRET, and Ultra-sensitive luminescence plate reader assays – EnVision Plate reader (Perkin Elmer)
- Hit to lead capabilities

### **Small Molecule Screening Facility Compound Libraries**

- Diversity Set consisting of 15,360 (5,000 + 10,000) unique drug-like compounds (Life Chemicals)
- Central Nervous System targeted library of 5,000 compounds (Life Chemicals)
- Epigenetics Screening library (virtual docking and similarity search based) consisting of 2,601 compounds (Life Chemicals)
- Fsp3-enriched fragment-based library consisting of 2,600 compounds (Life Chemicals)
- LOPAC consisting of 1,280 compounds (Sigma)
- FDA-approved US and International drug collection consisting of 1,280 compounds (Microsource)
- DIVERset library of 30,000 drug like compounds (Chembridge)

### **Guidance for HTS Assay Application**

Proposals submitted in response to this announcement must have the following:

- 1) **Readiness for High Throughput Screening:** Assays submitted for HTS should be miniaturized into 96, 384 or 1536-well format, should be well established and characterized. Assays should have simple procedures readily adaptable to automation. Steps such as centrifugation, filtration, and extraction should be avoided. "Mix and measure" assays are preferable.

- 2) **Assay Performance and Robustness:** Assays should be robust i.e. remain unaffected by small changes in assay parameters, reproducible and meet minimum statistical threshold for robotic screening. Assays with Z' parameters greater than 0.5 are typically HTS-compatible assays. Also, a detailed description of assay protocol include DMSO tolerance, time, temperature, protein concentrations, cell-culture media, plate type, and detection methods to name a few.
- 3) **Diversity of Assay types:** Each proposal should include a primary HTS assay and secondary, confirmatory, or orthogonal assays (counter screens).

### ***Application Requirements***

All applications must contain the following elements:

Application Elements	Suggested Length
<b>Project Narrative</b>	2-3 Sentences
<b>Project Summary/ Abstract</b>	20 lines
<b>Technical Proposals</b>	Limit of 2 pages total
• Project Description	
• Technical Feasibility	
• Assay Configuration	
• Schematic of the Screening Plan	
• Description of Criteria for a Validated Hit Compound	
• Future Plans	Limit of ¼ page
• Potential Commercialization	Limit of ¼ page
<b>NIH Biosketch</b>	Limit to 4 pages PI + Co-PI (if applicable)
<b>References/Publications</b>	

### ***Selection Process***

Proposals received shall be ranked and selected based on the following criteria:

- **Assay feasibility:** Proposals would be evaluated for high throughput screening feasibility as configured using the existing infrastructure and capabilities of the SMSF. Proposals deemed not suitable would not be considered further.
- **Medical relevance:** Proposals would be evaluated for scientific merit, novelty of the target and potential for meeting an unmet medical need.
- **Commercialization potential:** The committee will consider the commercial potential of inhibitors for a specified target and use this factor, along with the unmet medical or biotechnology need, during its prioritization of meritorious proposals.

### ***Project Leadership***

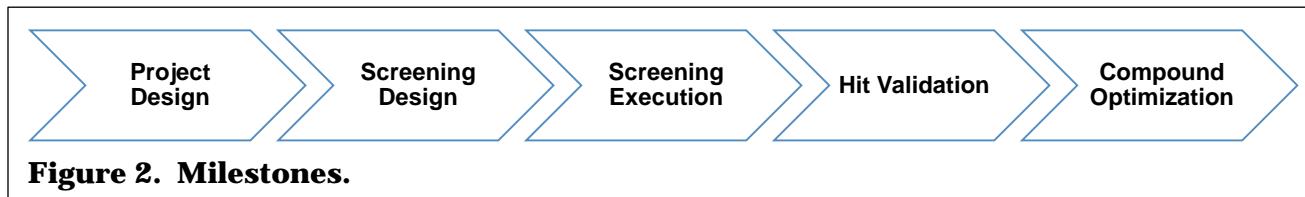
Drug screening proposals shall be critically reviewed by the following panel of experts:

- **Dr. Paul Thompson**, SMSF Core Director and medicinal chemist with numerous years of expertise in target based drug design and HTS approaches for drug discovery
- **Dr. Celia Schiffer**, expert in structure-based drug design and virtual screening
- **Katherine Luzuriaga MD**, Professor, Program in Molecular Medicine; Director, UMCCTS, has expertise in the discovery and clinical development of drugs and biologics
- **Dr. Brendan O'Leary**, Executive Vice Chancellor, Innovation and Business Development, has several years of experience in early-stage venture capital, biotech industries, industry-academia collaborations and expertise in commercialization efforts within academia

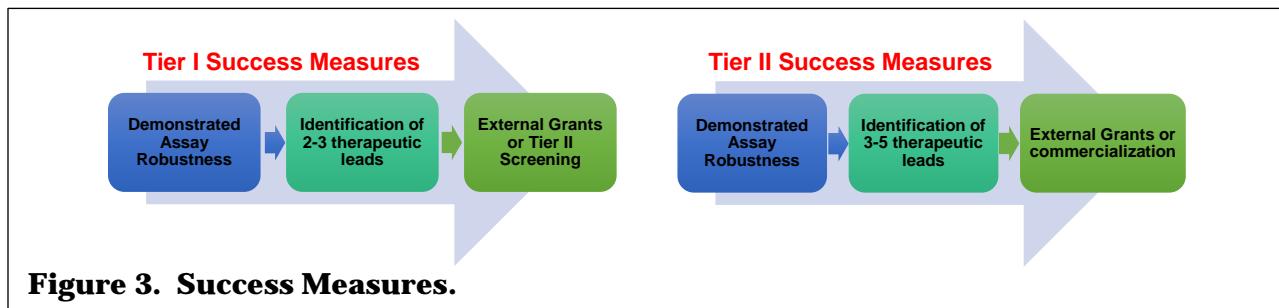
- **Dr. Peter Reinhart**, Director, Institute of Applied Life Sciences, has extensive experience in academic and industrial biomedical research, business development, licensing deals and implementation of industry partnerships
- **Dr. Sergey Savinov**, Extension Associate Professor, having expertise in drug discovery and development, management of compound libraries, cheminformatics, and molecular modeling

#### **Milestones and Success Measures**

To run a timely and efficient screening support, multiple project milestones would be created (**Figure 2**). Prior to initiating screening campaigns, the awardees would meet with the Dr. Thompson and Dr. Parelkar to design the screening approaches. Once the screening has been executed with successful hit validation, the awardees would work with medicinal chemists and the Structure Based Drug Design Core for hit optimization.



Depending upon the Tier level, program success would be measured by the ability to demonstrate assay robustness, to identify 2-5 therapeutic hits, to obtain external funding and or to be commercialized (**see in Figure 3**).



#### **Key Dates for this Call for Proposals**

Call open: **06/01/2016**

UMASS-CSI team available for questions and project mentoring: from 06/01/2016

**Proposal Deadline: 07/01/2016, 5:00 p.m. Eastern time**

Awards Announced: on or about **08/31/2016**

**Application Submission:** Please email the completed applications to [Keiko.Dion@umassmed.edu](mailto:Keiko.Dion@umassmed.edu)