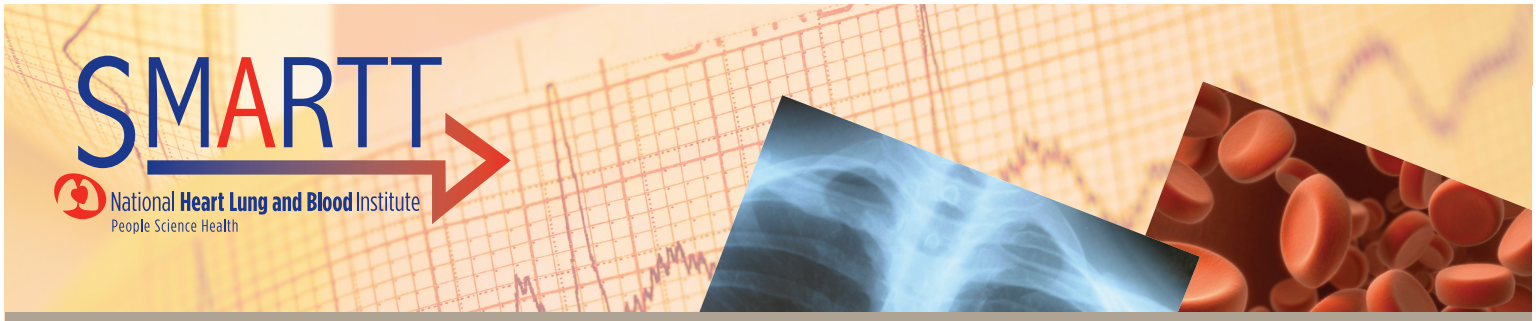

SMARTT

National Heart Lung and Blood Institute
People Science Health

Science Moving towArds Research Translation and Therapy

Accelerating the Translation of Therapeutic Agents from Discovery to the Clinic

SMARTTnews

October 2012

In this Issue

Our Team

National Heart Lung and Blood Institute

RTI International
Coordinating Center

ABL, Inc.
Biologics Production Facility

SRI International
Pharmacology/Toxicology Facility

Small Molecule/
Non-Biologics Production Facility

National Heart Lung and Blood Institute
People Science Health

www.nhlbismartt.org

Conversation with a SMARTT Investigator

Cynthia Lander, PhD, is the Chairman and Chief Executive Officer of Moerae Matrix, Inc., a biopharmaceutical company focused on the development of therapeutics for fibrotic diseases. Prior to founding Moerae, Dr. Lander was a partner in Nascent Enterprises, LLC, a venture capital partnership specializing in commercialization of medical inventions. She received her doctorate in neuroscience from Yale University and conducted postdoctoral research at the Rockefeller University as a Revson Fellow. SMARTT is assisting Dr. Lander with the development of MK2 for treatment of idiopathic pulmonary fibrosis (IPF), a serious and fatal lung disease for which there are no approved treatments in the United States. We asked Dr. Lander to share her experiences while getting started with the SMARTT program.

1. How did you find out about the SMARTT program?

I heard about the program through one of your colleagues at NHLBI, Dr. Traci Mondoro, who has been very supportive of Moerae's work and pointed us toward the new SMARTT program. It's nice to have a BrIDGs-like program targeted specifically to cardiovascular and pulmonary projects that address significant unmet medical needs. We are very proud to be associated with SMARTT.

2. Tell us about your experience with the program so far.

I can summarize the experience in two words: refreshing and rational. With a traditional grant proposal, you submit an application and that's the only opportunity you have to state your case. With SMARTT, it's nice to be able to engage in an iterative process, where there can be an open dialogue with program officials and SMARTT staff. The review time is shorter, and it was great to host a webinar and be able to answer clarifying questions in real time. The opportunity to collaborate with experts in the field is also like expanding the company's team. You don't get those opportunities from a traditional grant program.

3. Tell us about your experience with the SMARTT website.

The website has a clean, attractive appearance and a user-friendly design. Navigation is simple and straightforward, and the content is comprehensive and clarifying. Application entry/content upload is easy and straightforward.

I would suggest adding a link that allows users to print out all of the questions on both preliminary (screening) and full applications, so that they can be distributed to applicant team members prior to uploading content.

4. Now that you've been through the application process, do you have any advice for future investigators?

Establish a dialogue and interact with program officials. Having conversations with NHLBI program officers is a win-win situation because both sides can get their needs met by tailoring the application submission. The SMARTT Coordinating Center, the facilities, and NHLBI have been very interactive, receptive, and willing to help. In the typical grant submission process, there is no chance to have that dialogue. SMARTT has transformed grant submission and review in a very refreshing, rational way.

5. We are about one-third of the way through the SMARTT program. Do you have any suggestions for NHLBI as we move forward?

Keep up the good work! Please let me know if you need letters of support from award recipients, if SMARTT requests funding beyond 5 years. It would be my pleasure to be able to help such a worthwhile program continue.

Project Profile – Dr. Kenneth Rock

Dr. Kenneth Rock at the University of Massachusetts Medical Center was among the first investigators to use SMARTT's services. Dr. Rock is studying the association of the NLRP3 (NALP3 or cryopyrin) inflammasome with atherosclerosis.

Recently, he found that mice deficient in NLRP3 or interleukin 1b (IL-1b) appear to be protected from developing atherosclerosis. Cholesterol crystals can stimulate IL-1b release by macrophages through a cathepsin B (CatB)- and cathepsin L (CatL)-dependent mechanism that induces activation of NLRP3. In addition, CatB- or CatL-deficient mice have reduced inflammation secondary to administration of cholesterol crystals. Consequently, an inhibitor of CatB or CatL has the potential to to significantly reduce inflammation induced by cholesterol crystals and atherogenesis.

Dr. Rock has identified such a CatB and CatL inhibitor, K777, which inhibits NLRP3 inflammasome-dependent IL-1β release in response to cholesterol crystals. K777 injected intravenously significantly reduces neutrophil influx into the peritoneum, an in vivo indicator of reduced IL-1β release.

In response to Dr. Rock's Request for Services Application (RSA), NHLBI's SMARTT program provided him with sufficient amounts of the inhibitor to continue preclinical studies in further pursuit of a treatment for atherosclerosis. Dr. Rock noted that "the material we obtained through the SMARTT program will be essential for allowing us to proceed with our preclinical models."

ABOUT SMARTT

- Please contact the SMARTT Coordinating Center to answer questions about the program.
- SMARTT is accepting applications for preclinical development services.
- We are seeking scientists to serve on the SMARTT Scientific Review Board to evaluate the scientific merit of Request for Service Applications (RSAs). (A small honorarium is provided for serving on the SRB.)

Please contact:

Sudie Rowshan
SMARTT Coordinating Center Project Director
Phone: 919-541-8722
Email: srowshan@rti.org
Get started **here**

SMARTT PROGRESS

Completed

- Synthesis of small molecule inhibitor of NLRP3 for use in atherosclerosis

In Progress

- Pharmacology/toxicology and regulatory affairs for a 22 amino acid peptide inhibitor of MK2, used for chronic treatment of pulmonary fibrosis
- Pharmacology/toxicology and regulatory affairs for a peptide inhibitor of PAR1, used to inhibit thrombosis
- Biologic manufacturing of recombinant human lecithin-cholesterol acyltransferase, used for the treatment of familial lecithin deficiency
- Pharmacology/toxicology, regulatory affairs, and biologic manufacturing of scuPA, used for treatment of pleural loculation
- Regulatory affairs for MK2-AP, used for treatment of acute lung injury

Advocacy Awareness – Genetic Alliance

SMARTT News recipients should be aware of the Genetic Alliance, the world's leading nonprofit health advocacy organization committed to transforming health through genetics. Their network includes more than 1000 disease-specific advocacy organizations, as well as universities, private companies, government agencies, and public policy organizations. The network is a dynamic and growing open space for shared resources, creative tools, and innovative programs.

One of the programs is the Genetic Alliance Registry and BioBank (GARB), a centralized, clinical data registry and sample repository that enables translational research. Founded in 2003, this cooperative venture provides shared infrastructure and customized solutions for disease advocacy organizations to lead sophisticated research initiatives. GARB sends a monthly update to keep investigators informed of developments in the field of registries and biorepositories. It also highlights relevant funding announcements, training opportunities, scientific meetings, and recent literature updates.

Registration/Application

Investigators interested in SMARTT may register to receive program updates, including this newsletter, and may apply for SMARTT services at https://www.nhlbismartt.org. To apply for SMARTT services, the following criteria must be met:

- US-based academic investigator or small company that meets the NIH Small Business Innovation Research Grant criteria
- Identification of a lead therapeutic candidate for treatment of heart, lung, or blood diseases
- Identification of a therapeutic indication for which services are being requested
- Proof of efficacy in an animal model appropriate for the selected indication

Conferences

NHLBI staff and SMARTT contractors exhibit at many conferences throughout the year. Please visit our booths to learn more about the program.

Conference	Date	Exhibitor
Contact Pharma	Sep. 20–21, 2012	ABL, Inc.
CACO Pharmaceutical and Bioscience Society (CACO-PBS)	Oct. 5, 2012	SRI International
IBC Bioprocess Meeting	Oct. 8–12, 2012	ABL, Inc.
Society for Neuroscience	Oct. 13–17, 2012	SRI International, RTI International
American Association of Pharmaceutical Scientists Annual Meeting	Oct.14–18, 2012	SRI International, RTI International
American Heart Association	Nov. 3–7, 2012	NHLBI
American College of Toxicology	Nov. 4–7, 2012	NHLBI
American Society of Hematology	Dec. 8–11, 2012	NHLBI

Frequently Asked Questions

One regular feature of SMARTT News will be to provide pertinent FAQs that may be helpful to investigators as they prepare to apply to the program. A complete list of FAQs is available on the SMARTT website.

Q. Is SMARTT a grant program?

A. No. SMARTT will provide access to preclinical development services and resources at no cost to the investigator.

Q: Is there a deadline to apply for SMARTT services?

A: No. Applications for SMARTT services may be submitted at any time, and they are evaluated in the order received.

Q: Does SMARTT provide services to all organizations?

A: No. SMARTT services are limited to academic institutions, nonprofit organizations, and small businesses.

Q: Does SMARTT support basic research on heart, lung, and blood diseases?

A: No. SMARTT services are intended primarily for studies that support submission of an Investigational New Drug (IND) application to the FDA. Studies involving identification or proof of concept for a drug substance/product would be considered premature for the SMARTT program.

Q: Does SMART fund preclinical research for diagnostic tests?

A: No. SMARTT does not fund preclinical research for diagnostic tests, except for imaging agents or other substances requiring an IND application to the FDA.

Q: Does SMARTT provide regulatory affairs support services?

A: Yes. Assuming the scope of work is within the mission of NHLBI, the SMARTT program provides regulatory affairs support to investigators with promising drug substances/products.

Q: Does SMARTT provide non-GMP/GMP manufacturing and pharmacology-toxicology services?

A: Yes. Assuming the scope of work is within the mission of NHLBI, the SMARTT program provides non-GMP/GMP manufacturing and pharmacology-toxicology services.

Q: What are the minimum eligibility requirements for SMARTT services?

A: The minimum eligibility requirements for SMARTT services are twofold: (1) the subject of the research must be within the mission of NHLBI; and (2) the proposed project must support preclinical studies leading to submission of an IND application, including amendments or extensions of existing INDs. In this context, "Translational Research" is narrowly defined as activities occurring between discovery of a biologic or non-biologic/small molecule drug substance/product effective for the treatment of a specific disease, and initiation of a Phase I clinical trial.

Q: What are the minimum requirements for GMP manufacturing or GLP pharmacology-toxicology services?

A: Assuming the scope of work is within the mission of NHLBI, the minimum requirements for GMP manufacturing or GLP pharmacology-toxicology services are (1) demonstration of efficacy in an animal model and (2) a pre-IND meeting with the FDA, the outcome of which provides a reasonable expectation that the drug substance/product will progress toward an IND application if the project is successful. Investigators who have completed in vivo efficacy studies may apply for regulatory affairs services/consultations to support preparation for a pre-IND meeting. SMARTT does not have sufficient resources to support proof-of-principle or discovery-phase activities. Please refer to the SMARTT website for additional information on SMARTT's Role in Translational Research.

Q: What are the minimum requirements for non-GMP manufacturing or non-GLP pharmacology-toxicology services?

A: Assuming the scope of work is within the mission of NHLBI, the minimum requirement for non-GMP manufacturing or non-GLP pharmacology-toxicology services is demonstration of efficacy in an animal model. SMARTT does not have sufficient resources to support proof-of-principle or discovery phase activities. Please refer to the SMARTT website for additional information on SMARTT's Role in Translational Research.

Q: How do investigators request services from the SMARTT program?

A: The request process begins with completion of an online application that asks for a general description of the project and services being requested. If the project is deemed eligible, investigators are asked to complete a more detailed Request for Services Application (RSA).

Q: How will Request for Service Applications be evaluated?

A: First, RSAs are evaluated by NHLBI program staff to confirm they meet minimum eligibility requirements and to verify that the requested services are within SMARTT's capabilities. Next, applications are reviewed and scored by a panel of expert investigators familiar with the field of study. Successful applicants work with the relevant SMARTT facility to develop a project schedule and budget, which undergoes a final approval step by NHLBI prior to initiation of the work.