

Merck Research Laboratories

SSF Emerging Discovery Science (SEEDS) Program

Bringing together the most promising academic research with Merck R&D capabilities to validate and advance emerging therapeutic targets, pathways and technologies that show potential relevance to treat human disease.

About Us

Merck Research Laboratories (MRL), the arm of Merck & Co., Inc. focused on discovering and developing therapies to improve patients' lives, has expanded its discovery capabilities in South San Francisco (SSF) by opening a new, cutting-edge research facility.

The new nine-story, multi-disciplinary discovery research hub, accommodates more than 300 scientists and support research spanning exploratory biology through early clinical development. The building was custom designed with an open atmosphere that encourages collaboration and team work. The site also boasts a large auditorium to provide space for nearby academics, scientists and entrepreneurs to convene and engage in scientific dialogue.

About the MRL SEEDS Program

The MRL SEEDS program is a new MRL SSF initiative seeking research collaborations with academic researchers to advance the most innovative discoveries for therapeutic targets, pathways and technologies.

The MRL SEEDS program will launch in 2020 with the selection of 5 – 10 research collaborations with 3 of the premiere San Francisco Bay Area universities: **Stanford University, the University of California, Berkeley and the University of California, San Francisco**. The MRL SEEDS program and subsequent collaborations underscore the importance of industry and academic interactions in the early discovery space.

As a first step in a potential collaboration, ideas for proposed projects should be submitted for evaluation by the MRL SEEDS Scientific Review Committee (SRC) comprised of MRL Scientists. Ideas are to be submitted in the form of a brief **non-confidential pre-proposal form by December 2, 2019**. Pre-proposals will be evaluated for selection for full proposal development as a 1-year pilot program (up to \$125,000 USD in direct costs plus institutional indirect costs) based on recommendations by MRL SEEDS SRC. 1-year pilot programs have the potential opportunity for extension at the discretion of the MRL SEEDS program SRC.

At the discretion of Merck, MRL Scientists will work closely with investigators to make available relevant capabilities and technologies that will enhance the success of the joint research program. As part of the full proposal development process, scientists from MRL will engage with lead investigators to ensure expertise and capabilities of both parties are incorporated into the project plan as applicable.

To define the current research areas of interest and/or specific challenges to address, Merck has published 4 Active Requests for Proposals (RFPs) in Section 3 of this document.

MRL SEEDS Research Project Proposals

Who can apply?

MRL SEEDS program RFPs are open to researchers at the following universities collocated in the San Francisco Bay Area with our MRL SSF Discovery Hub: **Stanford University, the University of California, Berkeley and the University of California, San Francisco.**

Why apply?

The MRL SEEDS program is an effort to jointly advance high-quality science. All proposals submitted will be reviewed for scientific merit, tractability for drug discovery and alignment with the published areas of interest. The strongest proposals with the most compelling cases to experimentally address areas of significant medical benefit will be considered for funding, collaboration and/or sharing of Merck's R&D capabilities.

1. Getting Started

Review the current active MRL SEEDS program RFPs (Section 3). To respond to an RFP please complete the pre-proposal form. The pre-proposal form includes the required elements for completing and submitting your initial 1-2 page response.

Requirements for Submitting a Pre-proposal Form

A pre-proposal form is a brief 1-2 page non-confidential summary of your project proposal that should provide sufficient information for a pre-review by the MRL SEEDS Scientific Review Committee. If the pre-proposal is of interest to MRL, you will be notified that your pre-proposal has been selected. As required, you may be contacted by an MRL SEEDS program representative for clarification of the pre-proposal or further discussion of the concept. A full project proposal and plan will be developed by the applicant or may be co-developed with Merck's Scientists and the applicant.

A pre-proposal must not contain any confidential information. Merck will not be responsible for the confidentiality of any information that is included in the pre-proposal.

A detailed view of the request for proposal process can be found in the RFP Process section (Section 4).

Submission of a full proposal does not imply or guarantee approval. Financial and/or reagent support is contingent upon full execution of a contract between Merck and the academic institution in accordance with standard practices and terms for sponsored research agreements.

2. MRL SEEDS Contact Information

To learn more or to ask a question, please contact the Merck SEEDS Program at mrlseeds@merck.com

3. MRL SEEDS: Active Requests for Proposals

The current MRL SEEDS Requests for Proposals (RFPs) are described below. All proposals submitted will be reviewed for scientific merit and tractability for drug discovery. The strongest proposals with the most compelling cases to experimentally address areas of significant medical benefit will be considered for funding, collaboration and/or sharing of MRL capabilities.

▪ RFP-01: Age-Related Macular Degeneration (AMD)

Age-related macular degeneration (AMD) is the leading cause of adult blindness in the developed world. AMD is often classified as neovascular (“wet”) and atrophic or nonexudative (“dry”). Neovascular AMD is currently treated with anti-VEGF therapy, whereas there are no approved therapies for dry AMD. The dry form of the disease progresses over 5 – 15 years, involving the central macula last, in the absence of neovascularization. Human genome wide association studies (GWAS) has provided insight into pathways that contribute heritable risk for AMD. These offer a starting point for identifying new drug targets or developing a better understanding of mechanisms associated with disease phenotypes. We are soliciting proposals for projects exploring new targets anchored in human genetics related to retinal diseases, especially atrophic AMD, with specific interest in understanding the underlying biology, and developing translational in vitro and in vivo model systems.

▪ RFP-02: Heart Failure with preserved Ejection Fraction (HFpEF)

Heart failure (HF) is a major healthcare and socioeconomic burden affecting approximately 26 million individuals worldwide. Heart failure with preserved ejection fraction (HFpEF) accounts for 50% of heart failure patients, who have poor prognosis and quality of life. There are no effective therapies for HFpEF. HFpEF is a heterogenous disease characterized by impaired cardiovascular reserve with exercise intolerance, microvascular dysfunction, cardiomyocyte dysfunction, cardiac fibrosis, and high left ventricular filling pressures. We are seeking proposals that investigate the importance of cardiac inflammation, cardiac extracellular matrix remodeling, microvascular and mitochondrial dysfunction, sexual dimorphism, and alterations in adipose/epicardial tissue in the pathogenesis of HFpEF with the ultimate goal of identifying therapeutic pathways and targets.

▪ RFP-03: Lipid Biology (NASH)

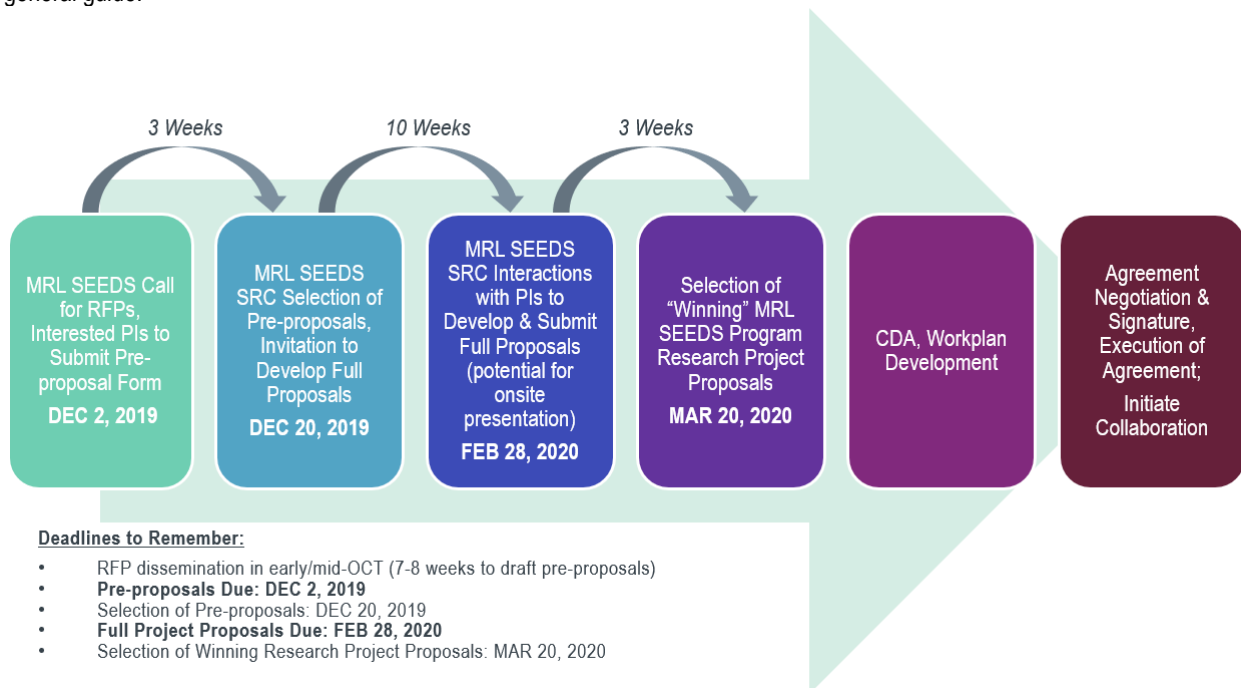
Nonalcoholic fatty liver disease (NAFLD) and Nonalcoholic steatohepatitis (NASH) are complex metabolic diseases that are rapidly becoming the leading cause of cirrhosis in the developed and developing world. We are interested in understanding the underlying mechanisms that contribute to the pathogenesis and progression of NAFLD/NASH. In particular, we are seeking proposals that address the following areas: pathways and mechanisms that couple and uncouple steatosis from hepatic inflammation and fibrosis; molecular, cellular, and microbial predictors of progression of NAFLD to NASH; clinical biomarkers of fibrosis in NASH; and the importance of lipid droplets in progression of NAFLD/NASH. Studies utilizing lipidomics, proteomics, and metagenomics to address these and other related questions are welcome.

▪ RFP-04: Inflammation, Fibrosis, and Immunometabolism

Chronic cardiometabolic diseases are characterized by the presence of extensive tissue fibrosis. Although fibrosis is an evolutionarily conserved response to injury, excessive fibrosis disrupts organ function and is a common feature of many chronic diseases. In the heart, fibrosis contributes to systolic and diastolic dysfunction, and correlates with the incidence of arrhythmia and cardiac death events. In the kidney, tubulointerstitial fibrosis is a hallmark of ESRD, and is strongly associated with renal function decline in patients with chronic kidney disease (CKD). In the liver, fibrosis leads to progression from NASH to cirrhosis and hepatocellular carcinoma. Currently, there are not effective therapies that specifically target tissue fibrosis in chronic cardiometabolic diseases. We are seeking proposals that will interrogate and understand the core molecular pathways involved in cardiac, lung, kidney, and liver fibrosis. We are particularly interested in tissue-specific immune-stromal cell interactions that contribute to development of pathogenic fibrosis. Interdisciplinary proposals using orthogonal approaches and unbiased “Omics” platforms to address immune and stromal crosstalk during pathogenic fibrosis are welcome. We are also interested in identifying and targeting metabolic checkpoints in immune and stromal cells to modulate the effector functions of innate and adaptive immune cells in chronic diseases. Proposals aimed at identifying metabolic checkpoints in immune and stromal cells and validating their mechanism of action in preclinical disease models are particularly encouraged.

4. MRL SEEDS: Request for Proposal (RFP) Process

The MRL SEEDS RFP process involves several steps illustrated in the diagram below. The timeline outlined below is meant as a general guide.



MRL SEEDS: Frequently Asked Questions

Questions and responses are divided by each phase of the MRL SEEDS program. To learn more or to ask a question, please contact the Merck SEEDS Program at mrlseeds@merck.com. Your disclosure of information does not grant you any ownership interest in future Merck company inventions.

Submissions

1. Is there any flexibility regarding the identified Active Request for Proposal statements (RFP 01 - 04)? If so, how is this determined and who might an investigator speak to about this?

The vast majority of funded requests for proposals will fall within the Active Request for Proposal descriptions; However, the MRL SEEDS SRC may consider proposals outside the defined problem statements if they are scientifically relevant. Before submitting a proposal that is outside the published Active Request for Proposals, it is best to contact the Merck SEEDS Program at mrlseeds@merck.com to bring any requests to the attention of the MRL SEEDS SRC.

2. Is there someone within Merck I can speak with to see if there is interest in my study idea (before submission of a pre-proposal form) or in case I have any questions in preparing the pre-proposal?

Yes. Please contact the Merck SEEDS Program at mrlseeds@merck.com

3. How do I submit a proposal?

Review Section 3, MRL SEEDS: Active Requests for Proposals and submit a completed pre-proposal form to the Merck SEEDS Program at mrlseeds@merck.com by December 2, 2019.

4. What is the difference between a pre-proposal and a full proposal?

A pre-proposal is a brief 1-2 page form outlining a non-confidential summary of your proposal that will be reviewed by the MRL SEEDS SRC. The pre-proposal will provide sufficient information for a pre-review of your proposal. Therefore, if the pre-proposal is rejected, requestors will not have spent a significant amount of time developing the proposal. If the pre-proposal is found to be of interest, the SRC will request a full proposal for further review. The SRC also may potentially contact the requestor for additional information and/or to co-develop the full proposal with the requestor. Full proposals may or may not be accepted for approval and therefore are not guaranteed funding. As part of the full proposal, there may be a request from the MRL SEEDS SRC for an optional onsite presentation at the MRL campus in South San Francisco, CA.

5. Who should I contact if I need information regarding the MRL SEEDS program?

Please contact the Merck SEEDS Program at mrlseeds@merck.com

6. Will Merck contribute any capabilities to the project?

Access to specific capabilities will be discussed and agreed upon for accepted proposals as part of the confidential discussions and workplan development process after acceptance of the pre-proposal.

7. Will Merck contribute any funding to the project?

Funding for approved collaborative 1-year pilot research projects is anticipated (up to \$125,000 in direct costs plus institutional indirect costs) in order to facilitate execution of the agreed upon specific aims of the project in the principal investigator's laboratory or at a third-party establishment. The amount of funding will be project-specific and will be discussed and agreed upon for accepted proposals as part of the confidential discussions and work plan development process after acceptance of the pre-proposal. Our goal is to enable the specific aims of the selected proposals.

8. How should I manage and communicate confidential information?

Only non-confidential information should be included in the pre-proposal form. If your pre-proposal is selected to develop a full proposal requiring disclosure of confidential information, please contact the Merck SEEDS Program at mrlseeds@merck.com so that a Confidential Disclosure Agreement (CDA) can be put in place to protect any confidential information.

Review & Decision

9. Who reviews the applications?

A Scientific Review Committee (SRC) comprised of Merck Research Laboratories Scientists will review all proposals.

10. What does Merck expect from investigators submitting a pre-proposal?

The MRL SEEDS program funds proposals of scientific interest that can be conducted professionally and within the agreed timeline. Our expectations: 1) to receive a well-written pre-proposal that is scientifically relevant and concise; 2) that investigators demonstrate the ability to conduct a study within the agreed timelines; 3) that, if approved, investigators agree to provide quarterly status updates and a final report of manuscript quality; 4) that part or all of the results generated during the collaboration are disseminated in peer-reviewed publications.

11. What can investigators expect from Merck?

Prompt and courteous response to submitted pre-proposals or full proposals; 2) thorough scientific review of the pre-proposal and proposal; 3) timely decision on acceptance or rejection; 4) confidentiality of information under a Confidential Disclosure Agreement (CDA) as applicable

12. What scientific points are considered when assessing a submitted protocol?

The following scientific points are considered: 1) the study is aligned with the published Active RFP statements; 2) the specific aims answer the scientific/medical questions with a well-organized study plan 3) a data analysis plan is included with the full proposal and work plan.

13. If there are questions regarding the pre-proposal, will I have a chance to address them prior to a final decision being made?

Yes. If your pre-proposal is not rejected and questions arise or clarifications are needed, you have the option of interacting with the MRL SEEDS SRC before a full proposal and work plan are completed.

Contract Negotiations and Terms

14. How much will my lab be awarded if my full proposal is selected for collaboration?

After a sponsored research agreement is executed between Merck and the academic institution, in accordance with standard practices and terms, Merck will fund up to \$125,000 USD in direct costs for a 1-year pilot program plus institutional indirect costs.

15. What are the terms of the sponsored research agreement between Merck and the academic institution if my full proposal is selected for funding?

Once your full proposal is selected for contract negotiation and funding, a Merck Discovery Transactions Manager will contact the academic institution's Technology Transfer Office to negotiate a sponsored research agreement in accordance with established and reasonable practices and terms. Financial and/or reagent support of a full proposal is contingent upon execution of a contract between Merck and the academic institution.