

Merck Research Laboratories – Discovery Biologics (MRL DB) 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 research 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 an initiative seeking research collaborations with academic researchers to advance the most innovative discoveries for therapeutic targets, pathways and technologies. The MRL SEEDS program and subsequent collaborations underscore the importance of industry and academic interactions in the early discovery space.

The MRL SEEDS program was launched in 2020 with initial focus on Cardio/Renal/Metabolic/Ophthalmic diseases and platform technologies for the discovery and development of protein and antibody therapeutics.

As a first step in a potential collaboration, ideas for proposed projects should be submitted for evaluation by the Scientific Review Committee (SRC) comprised of scientists from Discovery Biologics (DB). Ideas are to be submitted in the form of a brief **proposal form by August 6, 2021**. Proposals will be evaluated by the MRL DB SEEDS Scientific Review Committee (SRC) and may be selected for awarding a 1-year research grant (up to \$125,000 USD in direct costs plus institutional indirect costs). The 1-year grant can potentially be extended at the discretion of the MRL DB SEEDS 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 proposal and workplan 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. During the grant period, the investigator and MRL scientists will meet at least quarterly for updates. A final report is required and it is expected that part or all of the results generated during the collaboration are disseminated in peer-reviewed publications.

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

Who can apply?

MRL DB SEEDS program RFPs are open to researchers at the following universities co-located in the San Francisco Bay Area with our MRL DB SSF Discovery Hub: Stanford University, the University of California, Berkeley and the University of California, San Francisco. Master agreements have been put in place with these three universities. At the discretion of the MRL DB SEEDS SRC, proposals by researchers from other academic institutions may be considered.

Why apply?

The MRL DB SEEDS program is an effort to jointly advance high-quality science. All proposals submitted will be reviewed for scientific merit, tractability and alignment with the published areas of interest. The strongest proposals with the most compelling cases to experimentally address areas relevant for the discovery and development of protein and antibody therapeutics will be considered for funding, collaboration and/or sharing of Merck's R&D capabilities. Please consult Section 5 for other "Frequently Asked Questions".

1. HOW TO APPLY

Please review the current active MRL DB SEEDS program RFPs in Section 3. To respond to an RFP please complete the proposal form at the end of this document.

In the proposal form, please provide sufficient information for a review by the MRL DB SEEDS SRC. Please describe significance, objectives, background, details and workplan of the proposed project. Please limit the description to 3 pages. Any preliminary data, references and figures will not count toward the 3-page limit. Please also include project budget, timelines and deliverables should your research proposal be awarded a SEEDS research grant of up to \$125,000 in direct costs plus institution's indirect cost (not to exceed a total of \$200,000) for a duration of 1 year.

You may contact a MRL DB SEEDS program representative for clarification of the submission process or a non-confidential discussion of a project idea. MRL DB scientists may contact you to non-confidentially discuss a project idea. The proposal will be treated confidentially.

A view of the request for proposal process can be found in Section 4. Submission of a 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.

The submission deadline is 5:00 PM PT on Friday, August 6, 2021. Please send your proposal to dbseeds@merck.com and Bernhard.Geierstanger@merck.com. Winning proposals will likely be selected by Friday, August 27, 2021.

2. MRL DB SEEDS Contact Information

To learn more or to ask a question, please contact the Merck DB SEEDS Program at dbseeds@merck.com and Bernhard.Geierstanger@merck.com.

3. MRL DB SEEDS: Active Requests for Proposals

The current MRL DB SEEDS Requests for Proposals (RFPs) are described below. All proposals submitted will be reviewed for scientific merit and tractability. Proposals most closely related to the RFP are of highest interest but other proposals on platform technologies may also be considered for funding, collaboration and/or sharing of MRL capabilities.

■ DB-RFP-01: Lysosomal Processing and Transfer of ADC payloads

Antibody drug conjugates are degraded in lysosomes where the linker payloads are released. For some payloads transporter proteins have been identified that facilitate transfer of ADC catabolites across the lysosomal membrane. However, processing and catabolite accumulation inside of lysosomes and transfer out of the lysosome are poorly understood. We are seeking proposals for projects that will study these mechanisms and will help to predict the efficiency of payload delivery through ADCs.

■ DB-RFP-02: High-throughput Characterization of Protein Biophysical Properties

Current methods of protein characterization are limited by the amount of purified material that can be produced using recombinant systems. Therefore, the data that can be generated for screening or analysis linking sequence to biophysical assays is limited to the hundreds for even the largest initiatives. A methodology, perhaps leveraging microfluidics technology, to rapidly measure the biophysical protein properties of thousands to tens of thousands of sequence variants prior to recombinant expression would revolutionize the field of protein engineering and biologic development. We are requesting proposals aimed to establish technology to measure for example melting temperatures for tens of thousands of mAb. Other high-throughput biophysical assays to measure hydrophobicity or non-specific interactions in nanoliter wells would also be of interest.

▪ DB-RFP-03: Mining Natural Peptide Diversity as Antibody Cargo: Antibody Natural Product Fusions

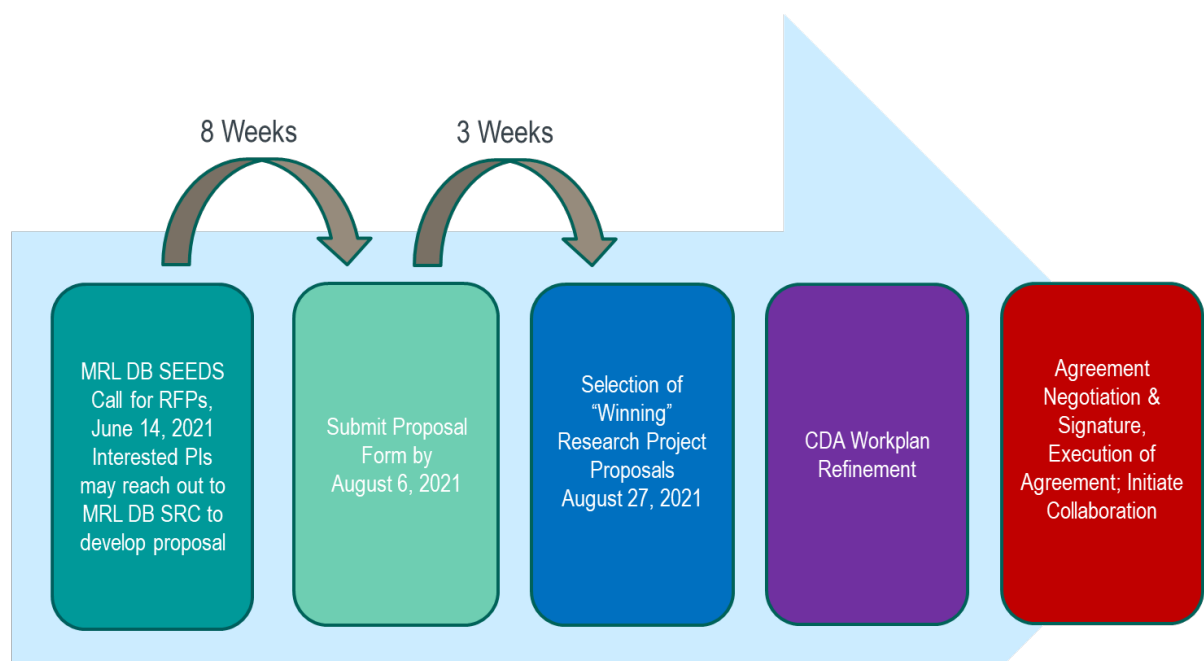
The utility of antibodies to deliver cargo to a target site has widely been accepted as an exciting modality. This has been spotlighted by the surge in Antibody-Drug Conjugates (ADCs) research. Beyond inducing cell-death, we have an exciting opportunity to modulate more finessed effects. In this call, we are interested in ideas to mine natural products that can be used as conjugates with antibodies or other fragments. We are open to ideas for different classes: pure peptides (e.g. melittin, helminth peptides) to post-translationally modified content (e.g. RiPPs).

▪ DB-RFP-04: Function-Based HT Screening for Agonists and Antagonist Antibodies

High-throughput function-based screening methods are needed to quickly identify antibody antagonists and agonists. An example is a GPI-anchored antibody cell display combined with β -arrestin recruitment-based cell screening (Ren H. et al. 2020, Nat. Comm.). We are seeking proposal for projects that enable HT function-forward screening and antibody identification using reporter gene assays and monitoring downstream signaling pathways. Ideally, the screening method will link antibody genotype with phenotype and could be applied to a variety of different targets.

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

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



Deadlines to Remember:

- Proposals Due: August 6, 2021
- Selection of Winning Research Project Proposals: August 27, 2021

5. MRL DB SEEDS: Frequently Asked Questions

Questions and responses are divided by each phase of the MRL DB SEEDS program. To learn more or to ask a question, please contact the Merck SEEDS Program at dbseeds@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 (DB-RFP 01 - 04)? If so, how is this determined and who might an investigator speak to about this?

The majority of funded requests for proposals will fall within the Active Request for Proposal descriptions. However, the MRL DB 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 to bring any requests to the attention of the MRL DB 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 proposal form) or in case I have any questions in preparing the proposal?

Yes. Please contact the Merck SEEDS Program.

3. How do I submit a proposal?

Review Section 3, MRL DB SEEDS: Active Requests for Proposals and submit a completed proposal form to the Merck SEEDS Program by August 6, 2021.

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

Please contact the Merck SEEDS Program at dbseeds@merck.com and Bernhard.Geierstanger@merck.com.

5. 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.

6. 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.

7. How should I manage and communicate confidential information?

Submissions will be treated as confidential. If your proposal still requires a Confidential Disclosure Agreement (CDA), please contact the Merck SEEDS Program.

Review & Decision

8. Who reviews the applications?

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

9. What does Merck expect from investigators submitting a proposal?

The MRL DB 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 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.

10. What can investigators expect from Merck?

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

11. What scientific points are considered when assessing a submitted proposal?

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.

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

Yes. If questions arise or clarifications are needed, you have the option of interacting with the MRL DB SEEDS SRC before a proposal and work plan are completed.

Contract Negotiations and Terms

13. 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.

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

Once your 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 proposal is contingent upon execution of a contract between Merck and the academic institution.

MERCK RESEARCH LABORATORIES – Discovery Biologics (MRL DB) SSF Emerging Discovery Science (SEEDS) Program

PROPOSAL Form

Please use the following form to develop your Merck Research Laboratories (MRL) SEEDS Proposal and submit your completed form **no later than 5:00 PM PT on Friday, August 6, 2021** to dbseeds@merck.com and Bernhard.Geierstanger@merck.com.

PROJECT TITLE:	
PRINCIPAL INVESTIGATOR NAME(S):	INSTITUTION AFFILIATION:
PRINCIPAL INVESTIGATOR EMAIL:	PRINCIPAL INVESTIGATOR ADDRESS:
PRINCIPAL INVESTIGATOR PHONE:	
TECHNOLOGY TRANSFER OFFICER: <i>Please include contact information including email, phone and address</i>	
ACTIVE RFP FOCUS AREAS: <i>Please select all that apply to the proposal</i>	
<input type="checkbox"/> Lysosomal processing and transfer of ADC payloads <input type="checkbox"/> High-throughput characterization of protein biophysical properties <input type="checkbox"/> Mining natural peptide diversity as antibody cargo: antibody natural product fusions	<input type="checkbox"/> Function-based high-throughput screening for agonist and antagonist antibodies <input type="checkbox"/> Other: (if selected indicate here) <input type="checkbox"/> Renewal
EXECUTIVE SUMMARY: <i>Please provide a BRIEF few sentences statement summarizing the research proposal</i>	

PROPOSAL <i>Please describe significance, objectives, background, details and workplan of the proposed project. Please limit the description to 3 pages. Any preliminary data, references and figures will not count toward the 3-page limit. Please also include project budget, timelines and deliverables should your research proposal be awarded a SEEDS research grant of up to \$125,000 in direct costs plus institution's indirect cost not to exceed a total of \$200,000 for a duration of 1 year. The proposal will be treated confidentially. The submission deadline is 5:00 PM PT on Friday, August 6, 2021. Please send your proposal to dbseeds@merck.com and Bernhard.Geierstanger@merck.com.</i>
1. PROJECT SIGNIFICANCE <i>Please provide a BRIEF statement summarizing the research proposal and how it relates to human disease and disease mechanism(s).</i>

2. PROJECT OBJECTIVES

Please provide research objectives and specific aims.

3. PROJECT BACKGROUND, DETAILS AND WORKPLAN

Please provide a description of the research plan to be carried out within one year. Please include background, project details, deliverables and any preliminary data and references.

4. BUDGET JUSTIFICATION:

The SEEDS grant if approved provides \$125,000 in direct costs plus institution's indirect costs up to a total of \$200,000 for the duration of 1 year.

5. BIOGRAPHICAL SKETCH OF PRINCIPAL INVESTIGATOR:

Please provide a brief bio-sketch of the PI and listing of key publications. (NIH Biosketch is acceptable).