Regenerative Medicine Minnesota
Discovery Science Award Program

APPLICATIONS DUE 3/10/2023

Objective of Discovery Science Awards

The objective of the Regenerative Medicine Minnesota (RMM) Discovery Science Award program is to support rigorous studies addressing critical basic knowledge gaps in the biology of stem cells and regenerative medicine approaches and to advance stem cell-based tools. Projects funded through this program should propose research that culminates in a discovery or technology that would:

- Advance our understanding of the biology of stem or progenitor cells that is relevant to human biology or disease; or
- Advance the application of genetic research that is relevant to human biology and disease and pertains to stem cells and regenerative medicine; or
- Advance the development or use of human stem cells as tools for biomedical innovation; or
- Lead to the greater applicability of regenerative medicine discoveries to communities representing the full spectrum of diversity.

Award Information

What is the award amount and duration?

RMM will fund total (direct and indirect) project costs of up to $100,000 per year for up to two years. Project costs must be adequately justified and are subject to adjustment prior to the issuance of an award.

How will the funds be awarded?

An RMM award is a formal contract that defines the terms and conditions of an award and documents the commitment of the funds from RMM. Projects will be monitored by RMM for progress and adherence to the project milestones, timeline and budget. If at any time RMM determines that a project is not complying with the terms of the program, or is unable to advance the project, a project may be closed and the unused funds returned to RMM.

Costs resulting from a delay or failure to meet milestones will be the sole responsibility of the recipient. Successful applicants will have thoughtfully accounted for foreseeable project risks and developed contingency plans that do not involve additional funding from RMM.

What activities will RMM support?

RMM has special interest in broadening the portfolio of research that can help relieve chronic, genetic, and/or rare disorders that impact patients and health care costs in Minnesota.

RMM funds <u>will</u> support activities under this opportunity including, but not limited to:

- Basic research into stem cell mechanisms as they relate to human biology
- Investigating stem cells or their derivatives as tools for discovering and enabling therapeutic or other innovations, e.g., for studying or modeling disease
- Basic genetic research relevant to human biology and as it pertains to stem cells or regenerative medicine
- Research and tools related to diversity, equity, and inclusion in science, i.e., extending or validating the applicability of regenerative medicine discoveries to underserved populations (e.g., use of human induced pluripotent stem cell (hiPSC) lines or omics analysis from diverse

groups of individuals, target diseases or disease subtypes more are frequently experienced by underserved groups)
- Basic research and development of tools to address bottlenecks in the development of stem cell-based and gene therapies, such as cell/tissue targeting, immunogenicity and toxicity, in vivo gene therapy delivery, engineering human pluripotent stem cells (hPSC) to evade the immune system
- Studies to better understand human cells and tissues to be modeled in vitro or targeted with regenerative medicine approaches (e.g., omics and other profiling, human cell/tissue atlases), a human stem cell/regenerative medicine component (wet lab and/or data-related) must be included in the project
- Auxiliary research activities that support regenerative medicine science (e.g., biomarker discovery, genome and epigenome editing tools, imaging tools, mechanism of disease to enable rational design of stem cell- or gene therapy-based treatments, data science and computational approaches), a human stem cell/regenerative medicine component (wet lab and/or data-related) must be included in the project

RMM resources cannot be used to support the following activities under this opportunity:
- Projects that propose solely or mainly to derive new pluripotent stem cell lines without a larger novel objective
- Any project involving the use of embryonic stem cells

Eligibility

What types of projects are eligible for funding?

To be eligible, the proposed project must satisfy the following requirements:

(1) The applicant must
   a. define a key knowledge gap (including bottlenecks in the field) (1) in our understanding of the biology or application of stem cells, or (2) in the application of genetic research as it pertains to stem cells or regenerative medicine;
   b. propose research that addresses this knowledge gap; and
   c. validate any discoveries made in nonhuman cells with a relevant human cell equivalent.

(2) Projects that generate molecular omics data must include an experienced Data Project Manager on the team.

(3) The applicant must be ready to initiate work on the funded project within 90 days of approval.

(4) Co-funding is not required.

If the project does, however, require funding over and above that which RMM provides, documentation demonstrating the commitment of funds to cover the proposed co-funding amount must be provided at the time of application submission.

(5) In keeping with the spirit of this program, the funds should remain and the work be performed in Minnesota. Exceptions may be made for materials or services not available within the state, and such exceptions should be noted in the budget.

(6) Partnerships with other institutions are allowed.

Collaborations may include research subcontracts or consulting agreements with laboratories, universities, medical centers, industry partners, etc. in the state of Minnesota. If planning to use a portion of requested funds to support a project at another institution, such as the University of Minnesota or Mayo Clinic, then the application must include that institution's indirect cost rate. The

submitted budget should reflect this and include separate indirect costs for the primary organization and any other institution with a different indirect rate. Other institution budgets should be shown separately.

(7) Application must be accurate and complete.

Who can apply for RMM funding?

(1) Only Minnesota-based academic institutions and small-businesses performing scientific and/or medical research in the state of Minnesota are eligible for this opportunity. Small businesses (the "Entity") must be based, owned (≥50%), and operating in the state of Minnesota. For this definition, a small business must have at least 2 and no more than 100 affiliated full- or part-time employees. Entities must be registered with the state of Minnesota's Secretary of State Office (http://www.sos.state.mn.us/business-liens) prior to the application being submitted.

(2) The PI and applicant organization are responsible for being in compliance with federal, state, and institutional research regulations at all times during the funding period, including having active approvals from all regulatory agencies (e.g., Institutional Review Board). A copy of the approval document(s) must be available upon request.

(3) Applicant must be in "good standing"

The PI, key personnel named in the application and any business leadership of small businesses must not have been convicted of, or are under investigation for, crimes involving fraud/misappropriation or research misconduct. The performance of applicants previously supported through the RMM program will be taken into account in funding decisions.

Who can serve as the Principal Investigator (PI)?

RMM encourages early stage investigators from diverse backgrounds to apply. To be eligible, the PI must:

- Be an employee of the applicant organization.
- Be authorized by the applicant organization to conduct the research and assume the responsibilities of the PI.
- Applications can have **only one** PI.
- PIs can only hold one RMM award at a time.
- Not currently have another application pending review or approval under this funding opportunity.
- Not currently have another application that is substantially similar or has overlapping activities pending review or approval under any RMM opportunity.

Schedule and Deadlines

Applications Due	March 10, 2023 at 5 pm
Application Review	March through May 2023
Awards Announced	Late May 2023
Earliest Start Date	July 1, 2023

Application Components and Submission

How does one apply?

Applications must be completed and submitted online at https://umnodat.infoready4.com/#competitionDetail/1893388

Any prospective PI must create a login in the system to access application materials and apply. A PI may submit only one RMM application in a given review cycle.

The main components of the application include the following key sections:

1. **Principal Investigator Information** (Responsible Party; there can only be one principal investigator)
2. **Institution Information** (responsible for receiving and disbursing grant funds)
3. **Application Preview Page/Abstract:** This section will be utilized by reviewers to prescreen applications and select a subset to move forward to the next stage of the review process.
   a. Knowledge Gap/Bottleneck/Outcome
   b. Project Summary
   c. Disease Indication or Area of Impact
4. **Resubmission Statement:** If this application is a resubmission from previous RMM review cycles, the applicant will provide a brief statement on how this application addresses the previous reviewers' critiques.
5. **Statement of Significance and Impact:** Description of how the proposed research, if successful, could: a) address a critical basic knowledge gap in the biology of stem cells or regenerative medicine approaches that is relevant to human biology or disease, or b) advance the development or use of human stem cells as tools for biomedical innovation, addressing a major bottleneck to the discovery, development or use of stem cell-based or gene therapies, or c) lead to the greater applicability of regenerative medicine discoveries to communities representing the full spectrum of diversity.
6. **Objective and Specific Aims:** A concise description of the project objective and project aims, and criteria for success.
7. **Rationale:** Description of the scientific rationale for the proposed research and preliminary data.
8. **Research Plan:** A concise but detailed description of the methods and techniques to be employed to achieve aims, and potential pitfalls and alternative approaches.
9. **Data Sharing and Management Plan:** A description of the proposed plan to share and manage data generated from the project.
10. **Timeline:** Activities-based timeline for achieving project aims.
11. **Principal Investigator and Team:** A description of the PI and team's roles, expertise, and experience.
12. **Resources and Environment:** A brief description of the resources available to the project and environment.
13. **New Jobs:** An estimate of the number of new jobs that will be created with this funding (if awarded) and plan for sustaining these jobs after the award has ended.
14. **Intellectual Property:** A brief summary of any intellectual property related to the proposed project, including protection status and ownership/assignment.
15. **References**
16. **Budget Information:** Completed budget form (template provided in online application portal).
    a. **Direct** costs requested

b. **Indirect** costs requested (see: https://oamp.od.nih.gov/dfas/indirect-cost-branch/indirect-cost-submission/indirect-cost-definition-and-example. These should be included in the budget at the established NIH-negotiated rate or, in the absence of a federally-negotiated rate, at 10 %.)
c. **Total combined** costs requested (must be ≤ $100,000/year, $200,000 total)
d. Start date requested (between July 1, 2023 and July 30, 2023)
e. Length of award (1 or 2 years)

17. Biosketches/CVs for Key Personnel

Application Review Information

What criteria are used to evaluate the applications?

1) *Does the project hold the necessary significance and potential for impact?*
    a. Does the project define and address a key knowledge gap in our understanding of the biology or application of stem cells, or in the application of genetic research as it pertains to stem cells or regenerative medicine?
    b. Does the project define and address a major bottleneck to the discovery, development, or use of stem cell-based or gene therapies?
    c. Would the project, if successful, have a major impact on scientific knowledge in the stem cell/regenerative medicine field or on potential applications of stem cell or genetic research to regenerative medicine, rather than incrementally advancing the field?
    d. Will the outcome ultimately contribute to the advancement of world class science?
    e. To what extent does the project address chronic disorders that impact patients and health care costs in Minnesota?
2) *Is the rationale sound?*
    a. Is the proposed project based on sound scientific rationale?
    b. Are preliminary data compelling and supportive of the proposed project?
    c. Is the project significantly relevant to human biology and disease?
3) *Is the project well planned and designed?*
    a. Is the project appropriately planned and designed to give meaningful results?
    b. Are potential pitfalls identified and alternative approaches presented?
4) *Is the project feasible?*
    a. Are the proposed aims and expected project outcome logical and likely to be achieved within the proposed timeline?
    b. Is the proposed team appropriately qualified and staffed?
    c. Does the team have access to all the necessary resources to conduct the proposed activities?
    d. Is the budget appropriate for the research proposed?

What is the process for evaluating an application?

Pre-submission Consultation

RMM is committed to helping develop promising stem cell-based technologies by partnering with researchers. Therefore, prospective applicants are encouraged to contact RMM with questions or to discuss their project's eligibility before applying.

Eligibility Review

RMM will assess whether the proposed project meets eligibility requirements sought under this program. If RMM determines that an application does not meet the eligibility requirements of the program, RMM will notify the applicant of its decision and, if RMM deems it is appropriate, allow an opportunity to

remedy. If RMM deems it inappropriate, or if the applicant does not remedy the error in a timely manner, RMM will remove the application from further review and funding consideration.

Scientific Review

The scientific merit of each application will be assessed by RMM Board members and scientific reviewers from outside Minnesota. Applications will be evaluated according to scientific and technical merit, applying the review criteria described above. The review will be conducted in three stages. In the first stage, RMM Board members will conduct a pre-review of applications to identify applications that the Board believes are most responsive to the funding opportunity and hold the most potential for impact. Since the selection process is focused on quickly identifying promising proposals rather than identifying deficiencies in applications, no reviewer comments are collected at this stage.

Selected applications advance to the second stage of review, which involves assignment to specific scientific reviewers outside of Minnesota. Applications are scored according to the review criteria and review comments are collected and discussed by the Application Review Committee, which is made up of the RMM Board and RMM program leadership.

In the final stage of the review, all applications will undergo a review by the Application Review Committee in which applications of high scientific and technical merit will be carefully scrutinized to allocate the funds available to support the award mechanism as wisely as possible. Applications that have the highest potential to help achieve the vision and goals of the RMM program (programmatic relevance, portfolio balance, adherence to the intent of the mechanism) will be selected for funding. Although the evaluations of the scientific reviewers are a key factor, the additional consideration of programmatic intent and portfolio balances means that applications are not funded using an established "pay line" based solely on a numeric scoring system.

Consideration of Past RMM Award Information (If Applicable)

RMM may consider information from a previously funded and related RMM award as part of its review. This includes but is not limited to achievement of specific milestones, data, and outcomes for a related RMM award or awards. A “related RMM award” includes: (1) an award for which the applicant PI served as the PI, a co-investigator, or otherwise substantially participated in the conduct of the award; (2) an award involving the same research project or product; or (3) and award that includes overlapping team members.

Confidentiality and Data Privacy

RMM’s confidentiality and conflict screening policies apply to everyone who will have access to applications or who will participate in any review meeting in which confidential information is discussed. Through administration of the RMM program, the University is committed to protecting the information submitted in your proposal as allowed under state data privacy laws and University policy. Minnesota's Government Data Practices Act contains specific provisions on public grant data and protected trade secret information. In the application, you will be asked to identify specific sections that you believe qualify as your trade secret information (https://mn.gov/admin/data-practices/data/types/tradesecrets/).

Award Administration

Issuance of Award

An RMM award is issued through the Sponsored Projects Office at the University of Minnesota, via a Notice of Grant Award (NOGA) and/or Subaward Contract document, which is a formal contract that defines the terms and conditions of an award and documents the commitment of the funds from RMM. RMM reserves the right to modify or establish funded project activities and the associated budget prior to

issuance of a NOGA/Subaward Contract, including, when applicable, establishing project milestones, success criteria, and timelines at its sole discretion after consultation with the PI and based on information provided in the application.

Payments and Reporting

Payments are made on a cost-reimbursement basis. For University awards, this is done automatically up to the award amount. For non-University awardees, invoices must be submitted per the contract document. Projects will be monitored by RMM for progress and adherence to the project milestones, timeline and budget. If at any time RMM determines that a project is not complying with the terms of the program, or is unable to advance the project, a project may be closed and the unused funds returned to RMM.

Grantees will be required to provide periodic written progress and financial reports to RMM. RMM will partner with the grantee to foster the success of the project. Grantees will have ongoing communication with the RMM Program Manager throughout the duration of the award.

Award Conditions

The PI is responsible for being in compliance with federal, state, and institutional research regulations at all times during the funding period, including having active approvals from all regulatory agencies (e.g., Institutional Animal Care and Use Committee). A copy of the approval document(s) must be available upon request.

If the PI of the grant leaves the institution, a request for change in PI may be submitted for consideration. If no request is submitted or the request is denied, unused funds will revert to RMM.

If the PI of the grant is unable to use the funds for the research as proposed in application, funds will revert to RMM.

In keeping with the spirit of the awards, the funds should remain and the work be performed in Minnesota. Exceptions may be made for materials or services not available within the state, and such exceptions should be noted in the budget.

Intellectual Property

Inventions arising from RMM-funded projects are required to be reported to RMM. As with federal funding, RMM permits businesses and nonprofits (including universities) to retain ownership of the inventions, while also giving the Minnesota state government the license to practice the subject invention. In turn, the organizations are expected to file for patent protection and to ensure commercialization for the benefit of public health.

No-Cost Extensions

Timeline progress on funded projects is of critical importance to RMM. Therefore, RMM will consider a No-Cost Extension (NCE) request, submitted at least 30 days before the project end date. Such a request should properly justify how such an extension will advance the project towards its expected outcome, but Grantees should not assume RMM will approve a NCE request.

Contacts

For questions not answered in the RFP, email RegenMedMN@gmail.com.