REQUEST FOR APPLICATIONS (RFA)

MSCRF Discovery Program

INTRODUCTION:

Stem cell research offers extraordinary promise for new medical therapies and a better understanding of debilitating human diseases, injuries, and conditions. The development of new medical strategies for the prevention, diagnosis, treatment and cure of human diseases, injuries and conditions through human stem cell research is a high priority for the State of Maryland.

FUNDING OBJECTIVES

This Request for Applications is soliciting Applications for research grants that are designed to attract and support Investigators working on new and innovative hypotheses, approaches, mechanisms or models that may differ from current thinking in the stem cell field and have no preliminary data supporting the Application. Grants awarded under this RFA will fund basic and translational research involving human stem cells.

ELIGIBILITY INFORMATION

All MSCRF-funded personnel must conduct their work in Maryland and be employed or retained by an eligible Maryland-based organization while conducting such work. This employment or retainer may be permanent, temporary, full-time or part-time. Applicants from Maryland-based public and private, not-for-profit research organizations of all types (not including Federal research labs) are eligible for this Award (e.g., universities, colleges, research institutes and medical centers).

Applicants may submit a Revised Application for a Discovery applications that was previously reviewed by the Commission but not funded. Such Proposals must include in the Appendix the Application Number of the previous MSCRF submission, and a point-by-point response to the prior scientific review.

Applicants who have received prior MSCRF funding may apply for a New Award in a subsequent funding cycle on a related or different topic, under the same or a different MSCRF funding mechanism. A summary of the research progress and any publications and/or presentations that resulted from the former MSCRF funding must be included in the Appendix.

Each Application for an Award funded by the MSCRF shall have only one (1) PI, but may have multiple Co-PIs, Investigators and/or collaborators. PIs may participate as Investigators or collaborators in any number of MSCRF-funded Projects in the same funding cycle.

Any one candidate may apply to the MSCRF as the PI for only one new Award in any given cycle. PIs must register in the TEDCO online submission system at least one month prior to the Grant Submission Deadline to avoid unexpected delays. Individuals from under-represented minorities and individuals with disabilities are encouraged to apply.

ELIGIBLE RESEARCH AND CELL TYPES:

All research funded by the MSCRF **must** involve human stem cells. Animal cells may be used to supplement studies with human stem cells. Basic and translational research Projects are all eligible for funding. All types of human stem cells, as defined in the Stem Cell Act: The Stem Cell Act defines eligible human stem cells as follows: human cell that has the ability to: (1) divide indefinitely; (2) give rise to many other types of specialized cells; and (3) give rise to new stem cells with identical potential. The full text of the Stem Cell Act is available on the MSCRF Web site (see www.MSCRF.org).

OTHER ELIGIBILITY CRITERIA

Awardees will receive MSCRF funds only after providing documentation to TEDCO confirming that the research to be conducted with MSCRF funds has been approved by the relevant Institutional Review Board ("IRB") and Institutional Animal Care and Use Committee ("IACUC"). Awardees conducting research that involves human embryonic stem cells ("hESC") must provide documentation of approval by a Stem Cell Research Oversight Committee before MSCRF funds shall be released.

AWARD INFORMATION

AVAILABLE FUNDS

The MSCRF is currently budgeted to commit up to $20.5 million, in aggregate, in FY 2023 to fund Grants under all of its RFAs. The number of Grants awarded will depend upon the quality, size and mix of Applications received.

AWARD SIZE, DURATION & TERMS

Under this RFA, the total direct costs proposed may not exceed $300,000 per award for a maximum of 2 years duration. Additional MSCRF funds will cover indirect costs, not to exceed 15% of direct costs. Max amount per Award is $345,000.

Because the nature and scope of the proposed research will vary from Application to Application, the size and duration of Awards may also vary. Approved Projects may be funded at or below the requested/proposed amount, for a number or reasons, including potential reductions in State appropriations or funding otherwise available to MSCRF.

MSCRF funds cannot be used to support any Project that is or has been funded in its entirety by another funding source. However, an Applicant may receive complementary funding from another source to cover other work that is related to the same overall Project.

PIs shall assume responsibility for the planning, directing and execution of their proposed Projects. MSCRF-funded Discovery Research Grants will be subject to the terms and conditions set forth in detail in the Grant Agreement entered into between an Awardee's affiliate institution and TEDCO.

Under this RFA, MSCRF Grant Award funds may be used for the following direct costs, commensurate with the time dedicated solely to the proposed research:

- Salary and fringe benefits for the PI and essential personnel
- Equipment
- Supplies
- Consultant costs

- Contract services
- Collaboration expenses
- Travel and conference expenses
- Publications and miscellaneous costs

MSCRF funds may not be used to cover personnel costs of Investigators who are located and conduct the work outside the State of Maryland, regardless of whether such out-of-State Investigators are employed or retained by a Maryland-based or non-Maryland based organization. Applicants are permitted to include out-of-State Investigators and/or collaborators under the Discovery Research Grant if they demonstrate that no MSCRF funds will be used to support work or personnel costs for the out-of-State Investigators.

Purchase of equipment and supplies, publication costs, conference expenses, contract manufacturing and services and other non-personnel costs may be incurred outside the State of Maryland, in accordance with customary practices of researchers.

Certain pre-Award costs are allowable. Applicants may, at their own risk, and without the Commission's prior approval, incur obligations and expenditures to cover costs up to ninety (90) days before the beginning date of the initial budget period of the Discovery Research Grant, if such costs are necessary to conduct the Project and would be allowable under the Grant, if awarded.

The incurring of pre-Award costs in anticipation of Award of a Discovery Research Grant imposes no obligation on the Commission either to make the Award, or to increase the amount of the approved budget if an Award is made for less than the amount anticipated. Awardees should be aware that pre-Award costs result in borrowing against future support, and that such borrowing must not impair Awardees' ability to accomplish their Project objectives in the approved time frame or in any way adversely affect the conduct of their Projects.

Once a Grant has been awarded, up to ten (10) percent of funds can be reallocated between budget categories without prior MSCRF approval (e.g., from salaries to supplies). However, reallocations in excess of ten (10) percent must be approved in advance by MSCRF.

INTELLECTUAL PROPERTY

Invention disclosures and intellectual property developed under the Discovery Research Grant funded by the MSCRF will be owned by, and the responsibility of, the recipient PI, in accordance with standard U.S. intellectual property law on inventorship and ownership and the Awardee's affiliate institutional guidelines.

Award recipients shall determine whether to apply for patents or other intellectual property protections on discoveries or inventions developed with MSCRF funding under the Grant. In the event that an Applicant decides to apply for such intellectual property protections, the Applicant shall be responsible for all fees and expenses involved.

SHARING RESEARCH RESULTS AND NEW CELL LINES

Awardees are required to share with qualified researchers their research results and any cell lines and other materials developed with MSCRF funding. Cell lines therefore must be derived from the tissues of individuals who provided consent to such sharing. Awardees may require that the recipient researcher(s) pay reasonable compensation for such new cell lines or materials. Awardees may include in the Grant

Budget, and use MSCRF funds to pay for, reasonable expenses associated with sharing arrangements. Awardees shall determine whether and to what extent to cover such sharing of new cell lines and materials with intellectual property and contractual protections (i.e., Confidentiality Agreements, Material Transfer Agreements, Data-Sharing Agreements, License Agreements, Supply Agreements, etc.).

PUBLISHING

Applicants must commit to make the results of their MSCRF-funded research readily available to others, through publications (preferably), public presentations or other accessible means.

APPLICATION AND SUBMISSION INFORMATION

CONTENT & FORMAT OF APPLICATION

All Sections of the Application must be submitted through the TEDCO online submission system. The document must be formatted using point size 12 Arial font, with margins no smaller than one-half (0.5) inch on all sides. Uploaded file must be limited to 80 megabytes (MB).

The Application must include the following Sections:

A. Project Summary - *Limited to one (1) page*

Project Summary describing the proposed research and its potential contribution toward the goals of the MSCRF and this RFA, as set forth in this document.

B. Research Plan - *Limited to six (6) pages, including all tables, figures and charts*

A description of the Research Strategy and Design, Data in support of the Proposal, Significance, Specific Aims, Rationale, Approach and Innovation**.**

C. Key Project Personnel - ***(A table format, not included in the page count)***

A list of the names, affiliate organizations, and roles of all key personnel, defined as the PI and individuals in addition to the PI, who contribute to the scientific development or execution of the Project in a substantive way, and devote measurable effort (in person months) to the Project, whether or not salaries are requested. Typically, these individuals have doctoral or other professional degrees, although individuals at the masters or baccalaureate level should be included if their involvement meets the definition of key personnel. "Effort of zero person months" and "as needed" are not acceptable levels of involvement for key personnel.

D. Budget and Budget Justification - ***(A table format, not included in the page count)***

A detailed yearly budget and budget justification, including salaries that are within the current NIH salary range and commensurate with the time allotted to the proposed research. This budget will be used if the Application is funded. Make certain that it is complete and accurate. Applicants should request only the funds needed to complete the proposed Project. Requests for less than the maximum allowable amount will not be considered as a weakness.

E. Resources and Environment - *Limited to one half page not included in the page count*

A description of the facilities in which the work will be conducted and how the scientific environment will contribute to the probability of success, including such things as collaborative arrangements involving on-site resources, unique features of the subject population and institutional support.

F. Translational Potential and/or Plan - *Limited to one half page not included in the page count*

An explanation of (i) the relationship between the proposed research and the etiology, prevention, diagnosis or treatment of human diseases or conditions;(ii) how clinical practice and treatment of human diseases or conditions will be advanced by the proposed research; (iii) how the proposed research may contribute to new medical therapies or test new therapies in human patients; and/or (iv) how the proposed research will translate prior research results into new medical therapies or test new therapies in human patients, and the projected time line for accomplishing such clinical application(s).

G. Bioethics - *Limited to one half page not included in the page count*

A description of the ethical issues relevant to the proposed research and how these issues will be addressed, including, but not limited to, a discussion of the ethical issues related to the cell type(s) and cell line(s) to be used; animal welfare (i.e., IACUC); IRB review and related concerns regarding human subjects, if applicable; and Stem Cell Research Oversight Committee review (required of all Projects that involve human embryonic stem cells). If new cell line(s) will be created, the Application must explain how the biological materials used to create them will be obtained and how subjects will be consented. Applicants should refer to existing human stem cell research ethics guidelines and the Maryland Stem Cell Research Act.

H. Appendix - *Limited to 25 supplemental pages (Upload in the same file as the application)*

The Appendix shall include (in this order):

(1) Literature in Support of the Application

A list of scientific Literature in support of the Proposal, including Author, Title, Journal, Volume, Publication Date, and Page Numbers.

(2) Biosketches - *Limited to four (4) pages each in any format including publications*

The Biosketches, and up to five (5) relevant Publications, for key personnel, collaborators and pertinent others. Include online publicly accessible links. Manuscripts in preparation, manuscripts submitted but not yet accepted and those currently in revision cannot be included.

(3) Response to Reviewer Comments, if Applicable - *Limited to three (3) pages (not counted in the Appendix page limits)*

For Applicants Resubmitting an Application that was previously reviewed under any MSCRF funding mechanism, but not funded: An Introduction to the revised Application, including the Application Number of the previous MSCRF submission, and a point-by-point response to the prior scientific review.

(4) Summary of Prior Research Progress, if Applicable - *Limited to two (2) pages (not counted in the Appendix page limits)*

For Applicants who have had previous MSCRF funding and are requesting funding for a New MSCRF Award: The Summary of the research progress and/or findings from the previously funded MSCRF Project, including a list of any publications, new collaborations, INDs, IDEs or patents, and any additional non-MSCRF funding that resulted from this previous MSCRF funding.

(5) Letter(s) of Collaboration, if Applicable - *Limited to five (5) one-page per collaborator (not counted in the Appendix page limits)*

For Applications that involve Collaboration(s): A Letter of collaboration from each collaborator (i) agreeing to the proposed collaborative research; (ii) briefly outlining the nature of the collaboration; and (iii) agreeing that, if MSCRF funding is awarded, they shall share research results with each other and comply with the progress reporting duties under the MSCRF Grant Agreement, conditioned upon TEDCO's duty to maintain the confidentiality of the reported information to the extent reasonably permitted by Title 4 of the General Provisions Article of the Annotated Code of Maryland. Such letters

must be co-signed by the collaborators and responsible officials at the collaborators' affiliate institutions.

(6) Collaborative Plan, if Applicable - *Limited to two (2) pages (not counted in the Appendix page limits)*

For Applications that involve Collaboration(s): A detailed description of the nature and terms of the collaboration, and a management plan explaining such issues as how the Applicant and collaborator(s) will communicate and handle confidential information, use milestones to determine resource re-allocation and Project re-direction, share data and resources, prepare required reports and handle geographic separation, if applicable.

(7) Other Current Support

The Project Number(s), Title(s) and Funding Source(s) of all currently supported research, and a short paragraph summarizing each Project.

The Appendix may not be used to circumvent the length limitations of the Application. Applications that are incomplete, do not meet the format and/or content requirements, exceed specified length limits, are non-responsive to this RFA or are from ineligible Applicants will not be reviewed.

Web form Information

In addition, applicants must complete all the web form information in the online system as early as possible to avoid unexpected delays. Among other sections, this information include:

- A bioethics section (maximum 250 words)
- Impact on biotechnology in Maryland statement (maximum 250 words)
    - Briefly describe the potential of this application to impact the biotechnology sector in the state of Maryland. Some examples may include IP that may be licensed or lead to commercialization, existing or proposed collaborations, creation of new jobs, and workforce development.

University applicants must obtain approval from their research/grants administration office before submitting an application. Please attach letter or evidence of such approval along with the uploaded application.

SOURCE FOR APPLICATION INFORMATION

Application information will be available electronically on the MSCRF Web site (see www.mscrf.org).

SUBMISSION DEADLINES & REVIEW DATES

Application Submission Deadline: January 19, 2023, by 5:00 p.m.
Peer Review Date(s): March 2023
Commission Review Date(s): May 2023
Earliest Anticipated Start Date: June 2023

METHODS OF SUBMISSION

Grant Application

PIs must register in the TEDCO online submission system at least one month before the application submission deadline. Grant applications must be submitted through the TEDCO online submission system by January 19, 2023, no later than 5:00 p.m.

REVIEW INFORMATION

AWARD DECISION CRITERIA

The Scientific Peer Review Committee will review all Applications and rank them based on scientific merit. Similar to the NIH scoring system of 1-9 will be used to rate the overall impact/priority of the proposed research. In this system, "1" indicates the highest impact/priority and "9" indicates the lowest impact/priority. The Commission will then review the ranked Applications and make final funding decisions.

To receive a high scientific priority score, an Application must be judged strong in all of the following categories:

- **Meeting the Overall Objectives of The MSCRF Program:** Do the proposed studies broaden and advance the knowledge of human stem cell biology? Are they relevant to the development of commercial and or clinical application(s) to prevent, diagnose and treat human diseases and conditions? Will these studies enable, support and expedite such commercial and or clinical applications?

- **Relevance to Regenerative Medicine:** Does the proposed research use adult, embryonic, iPS or other human stem cell lines? Does the PI justify the use of human stem cells in the proposed research as necessary or advantageous as compared to other approaches? Does the Project address problems in regenerative medicine, as defined by the Commission?

- **Likelihood of Success:** Are there limitations of the proposed studies that will make it difficult to apply findings or strategies in the clinic? Are there completed or on-going clinical trials that will impede/accelerate the proposed research?

- **Translation Potential and Plan**: Does the Application include strong interactions between basic, translational and/or clinical components? Is there a clear plan for translating research results to the clinic? Will the Project lead to new medical therapies or test new therapies in patients? Will the research help explain the course of any human disease(s) or condition(s)? Will it identify new biomarkers or other methods for preventing or diagnosing disease(s) or condition(s)? Will it identify new targets for treatment? Will it develop new treatment strategies, products or tools?

- **Collaboration(s):** Does the proposed research involve collaboration(s) among scientists and/or clinicians from for-profit and not-for-profit institutions, companies and organizations? If so, is there a demonstrated commitment from each institution? Is there a management plan that addresses how the Applicant and collaborator(s) will communicate, handle confidential information, use milestones to determine resource re-allocation and Project re-direction, share data and resources, prepare required reports and handle geographic separation, if applicable?

- **Scientific Merit:** Is the Project likely to have major scientific impact and make a substantial contribution toward accomplishing the goals of the MSCRF program?

- **Research Significance:** Does this Project address an important scientific problem, relevant to human stem cells? What is the relationship between the proposed research and the etiology, prevention, diagnosis or treatment of human diseases or conditions? If the aims of the Application are achieved, how will scientific knowledge or clinical practice and treatment of human diseases or

conditions be advanced? What effect will these studies have on the concepts, methods, technologies, treatments, services and/or preventative interventions that drive stem cell biology?

- **Innovation:** Is the Project original and innovative? Does it challenge existing paradigms or clinical practice or address a novel hypothesis or critical barrier to progress in the field? Does it develop or employ new concepts, approaches, methodologies, tools or technologies in the field? What is the potential impact on the advancement of biotechnology or medical innovation?

- **Approach:** Is there adequate preliminary data to support the rationale of the Research Project? Are the conceptual or clinical framework, design, methods and analyses adequately developed, well integrated, well-reasoned and appropriate to the aims of the Project? Is relevant literature appropriately referenced? Are anticipated results discussed? Does the Applicant acknowledge potential problem areas and consider alternative tactics? Are the experiments as designed likely to significantly impact the field?

- **Investigators:** Are the Investigators appropriately trained and well suited to carry out the Project? Is the proposed Project appropriate to the experience level of the PI and other Investigators? Does the research team bring complementary and integrated expertise to the Project?

- **Budget and Budget Justification:** Is the requested period of support appropriate for the scope of the Project? Is the effort listed for all personnel appropriate for the proposed work? Is each budget category realistic and justified in terms of the aims and methodology? If equipment is requested, is it justified, cost effective and budgeted appropriately?

- **Resources and Environment:** Does the scientific environment in which the work will be conducted contribute to the probability of success? Do the proposed studies benefit from any unique features of the scientific environment or subject population? Do these studies employ useful collaborative arrangements involving on-site resources or personnel? Is the institutional support adequate?

- **Bioethics:** Does the proposed research use adult, embryonic, iPS or other human stem cell lines? If an existing line is to be used, what are the justifications for that line? If new lines are to be created, what measures will be taken to comply with the Stem Cell Act as well as existing stem cell research bioethics guidelines? If human donors are involved, have they been properly consented? If human subjects are involved, what protections will be in place to ensure their rights and welfare? If animal subjects are to be used, what measures are taken to comply with IACUC guidelines?

If the PI's work was previously funded by the MSCRF, in whole or in part, the Application will be evaluated on the following additional factors: Did the Investigator make significant scientific progress towards the goals of the previously funded research? Were results of the previously funded Project reported in scientific publications and/or presented at conferences? Did the previously funded research result in new collaborations, inventions or Project-generated resources as proposed in the original Application? Did the previous Project generate subsequent funding from non-MSCRF sources?

The Commission reserves the right to pursue collaborative funding arrangements with third parties and, in such an event, the further right to share the application materials and/or the review summaries with those potential co-funders upon the execution of a Confidentiality Agreement restricting their further disclosure.

AWARD ADMINISTRATION INFORMATION

NOTIFICATION

The PI's affiliate organization will be notified electronically when the Application is received. A formal notification, in the form of a Notice of Award ("NOA"), signed by the MSCRF Executive Director, will be sent via email to successful Applicants.

POST AWARD REPORTING

A. Annual Progress Reports

PIs must file Annual Progress Reports describing the research conducted, and the interim and/or final results of that research, at the end of each funding year. Financial reporting relevant to the MSCRF-funded Project shall be specified in the Grant Agreement executed between TEDCO and the Awardee's affiliate institution, company or organization. Progress Reports must be submitted to the MSCRF electronically through the TEDCO on-line submission system, no later than thirty (30) days after the end of the annual period covered in the report.

The MSCRF will review all Annual Reports to evaluate the progress that has been made relative to the plans, timetables and budgets proposed in the respective Applications before funding for the subsequent year is approved.

B. Annual Symposium Presentations

The Commission will conduct an in-State Annual Symposium to report to the scientific community and the public the progress of the MSCRF program. All PIs must present, orally or in poster format, their on-going or completed MSCRF-funded research at each Annual Symposium, during and immediately following their Grant period.

C. Final Report

Within forty-five (45) days after the end of the overall Grant period, PIs must file their Final Reports, describing the research conducted and the results of this research. This Final Report shall include explanations and justifications for any proposed studies that were substantially changed or not completed. The Final Report must also describe the impact, significance, translational potential and/or clinical applicability of the research results as well as a full accounting of all expenditures charged to the award in a tabular format signed by the financial officer, and a formal closeout letter prepared and signed by the ORA office. The details concerning the format, content and length of the Annual Progress Report shall be specified in the Grant Agreement executed between TEDCO and the Awardee's affiliate institution, company or organization.

COMPLIANCE

A Principal Investigator not in compliance with the reporting obligations under the Discovery Research Grant shall not be eligible to apply for continued or subsequent MSCRF funding.

AGENCY CONTACTS

Questions about this RFA must be submitted by email to: mscrfinfo@tedco.md.