JDRF Request for Applications: Collaborative Advancement of Cures for T1D

November 2022

Summary

- **The goal of this funding opportunity is to accelerate the development of therapies to prevent, slow, halt or reverse the progression of Type 1 Diabetes (T1D) and/or cure established T1D through the advancement of high-impact research carried out by coordinated, multidisciplinary teams.**
- **Proposals eligible for consideration will describe studies that accelerate T1D research by coordinating multiple (2 or more) laboratories with unique yet complementary expertise to address gaps in the field that require technological, subject-matter, or analytical expertise more expansive than what is available in individual laboratories.**
- **JDRF seeks to fund awards for collaborative projects that aim to accelerate bold courses of research to potentiate significant advances toward a Cure for T1D by leveraging increased budgets and expanded expertise. Previously established or new collaborative teams are eligible and encouraged to apply.**
- **Priority consideration will be given to proposals that outline research plans that are approaching clinical translation.**
- **Applications received in response to this RFA may request up to $2,250,000.00, for a period of up to 3 years. Budget requests must be appropriate to the scope of work, development stage of the research, and size of the collaboration. Larger/longer awards may be considered but must be discussed with JDRF scientific staff in advance.**

Funding Opportunity Description

JDRF, the world's leading non-profit organization with the mission to cure T1D, aspires to accelerate the development of therapies to prevent, slow, halt or reverse disease progression and provide insulin independence to all those at risk or affected by T1D. Major advancement continues to be made in therapies that protect beta cell survival and function, disrupt the autoimmune attack on beta cells, and provide insulin and restore glycemic control through the use of beta cell transplantation. JDRF seeks to rapidly expand upon and translate these approaches to clinical trials to benefit patients at all stages of disease. Achieving this goal and addressing major advancement of therapies will require expanded resources and broad multidisciplinary expertise, likely more than can be achieved in a single grant or by individual laboratories. Therefore, the goal of this invitation is the development of research collaboratives consisting of at least two or three laboratories aligned in constructing a multifaceted and coordinated approach to advancing the development of cures for T1D. Aligned laboratories should each contribute unique and complementary expertise, approaches, and capabilities necessary for achieving the overall aim of the proposal. Studies that describe a multifaceted approach to advance research along the development pipeline toward clinical translation will be prioritized.

Background

There are no cures yet for T1D, an autoimmune disease characterized by an immune-mediated loss of pancreatic beta cell mass and function, resulting in insulin deficiency and dependency[1]. While exogenous insulin therapy is the only established treatment, people with T1D require constant glucose management. Only 17 percent of youth and 21 percent of adults achieve optimal glycemic outcomes, and people living with T1D face significant risk of long-term complications, mental burden of 24/7/365 disease management, financial burden due to medical care, and loss of income and productivity[2,3]. The advancement of interventions to prevent, slow, or halt disease progression are urgently needed to improve outcomes for the increasing number of people diagnosed with T1D each year. Moreover, strategies to restore tight glycemic control while eliminating the need for exogenous insulin administration in those who are insulin dependent are also needed.

The JDRF Cures Program aims to develop curative therapies for patients of all ages and at all stages of T1D. Autoantibodies to beta cell antigens, proteins produced by the immune system in response to a person's own beta cells, are indicative of autoimmunity and can develop before any clinical symptom of T1D is detected. At-risk individuals having two or more autoantibodies can have normal or slightly altered blood sugar levels, as the autoimmune response has initiated the assault on, but not completely depleted, the reservoir of insulin-producing beta cells in the pancreas. Preventative therapeutic interventions for these individuals to stop the further destruction of beta cells by the immune system and promote beta cell survival, regeneration and function are needed to retain or increase endogenous insulin production and delay or halt the onset of T1D. Individuals who have progressed to new-onset symptomatic disease exhibit variable levels of insulin dependence, as their reservoir of functional beta cells has been depleted below a level capable of meeting their insulin requirements. Therapeutic approaches for these patients are needed to preserve or improve beta cell function and restore glycemic control, in addition to strategies which aim to address autoimmunity.

Finally, for individuals with long-standing T1D and little to no remaining functional beta cells, clinical islet transplantation is currently the only approach with a clinical proof of concept that demonstrates full restoration of glucose control and insulin independence. Cadaveric pancreatic islet transplantation via portal infusion under the cover of systemic immunosuppression is efficacious in improving glycemic control, preventing severe hypoglycemia, reducing or eliminating exogenous insulin requirements, and improving quality of life in patients with medically unstable T1D. Significant progress has been made in the development of alternative renewable sources of insulin-producing cells (e.g. stem cell-derived beta cells) to overcome the shortage of donor tissue. However, major scientific and technical challenges remain around the validation of alternative sites of implantation, ensuring adequate oxygenation and vascularization of implanted beta cells to promote cell survival and function, and overcoming allogeneic immune rejection and recurring autoimmunity. Development of strategies to address these barriers are needed before beta cell replacement can be widely implemented as a cure for T1D and other insulin requiring diabetes.

The discovery and advancement of therapies for all stages of disease, and progression of those therapies through the development pipeline towards clinical translation is essential for the

realization of a cure. Accelerating life-changing breakthroughs and interventions by identifying and addressing the gaps and barriers that prevent advancing research into the clinic and prioritizing the opportunities with the greatest potential to lead us to cures is a critical component of the JDRF Research Strategy. To that end, the JDRF Cures Program aims to deliver advances in screening, disease-modifying therapies, and beta cell replacement therapies that treat individuals at all stages of disease. Proposals submitted to this announcement should have goals that align with these aims of the JDRF Cures Program.

Applicant Eligibility

JDRF welcomes Letters of Intent (LOIs) from established and/or new collaborative teams of investigators, organizations, and companies with the demonstrated expertise to carry out the proposed research.

- **Teams of investigators should identify an investigator and institution to serve as the lead applicant, team coordinator and principal investigator of the JDRF application.**
- **Applications may be submitted by domestic and foreign non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, industry, units of state and local governments, and eligible agencies of the federal government. Applicants must hold an M.D., D.M.D., D.V.M., Ph.D., or equivalent and have a faculty position or equivalent at a college, university, medical school, or other research facility.**
- **There are no citizenship requirements for this program. To assure continued excellence and diversity among applicants and awardees, JDRF welcomes applications from all qualified individuals and encourages applications from persons with disabilities, women, and members of minority groups underrepresented in the sciences.**
- **JDRF's standard Terms and Conditions will apply to all non-industry grants. Please review them in advance to ensure your collaboration will be able to comply. Contact your JDRF Program Contact with any questions.**

Project Eligibility

Proposed research plans must address a major gap-filling advancement in the development of therapies and cures for T1D. Priority consideration will be given to proposals that accelerate the transition of research through the pipeline toward clinical translation.

For consideration, the work proposed should address the development and enabling of clinical testing of therapies and approaches toward one or more of the following JDRF Cures Program goals:

Screening:

- **The development of data and analysis necessary for improving the prediction of high-risk individuals.**

Disease Modification:

- **Accelerating the development of disease modifying therapies that delay, stop, or reverse the development and progression of T1D, and enables pivotal clinical testing of these therapies.**
- **Developing immunotherapy approaches that stop the autoimmune attack, enhance immune regulation, or deviate inflammatory processes.**
- **Investigating approaches focused on promoting the function, survival, regeneration, and targeted delivery of therapies to beta cells**

Beta Cell Replacement

- **Accelerating the development and validation of strategies that ensure cell survival and function in alternative sites of implantation.**
- **Research that enables the development of safe, more efficacious, and longer-lasting cell therapies without the use of broad immunosuppression.**

Further Considerations:

- **Teams that combine the expertise of established investigators in the field of T1D with those outside of the field that provide the required expertise to expand the experimental scope or capabilities of the proposed research and facilitate advancement are of high priority.**
- **LOIs and full proposals must address the role and necessity of each individual investigator or research entity for achieving the research aims. If selected for a full proposal, a clear communication and coordination plan to facilitate the cooperative and multi-laboratory scope of the described research must be included. The distribution of budget across the institutions must be clearly described and justified.**
- **Priority consideration will be given to projects that outline research plans that are approaching clinical translation (late preclinical development).**
- **Priority consideration will be given to proposals that outline courses of study that address multiple Cures Program Strategies (for example, investigation into beta cell transplantation and immunotherapy to promote transplanted cell survival).**
- **Consideration will be given to proposals that outline clinical trials; please reach out to the scientific contact below before submitting your LOI if you will be proposing clinical research (observational and/or interventional).**
- **Collaborative teams consisting of academic and industry investigators will be considered for funding and may be prioritized. Please reach out to the scientific contact below before submitting your LOI if you will be proposing an application that includes an industry or for-profit collaborator.**
- **Given the expanded nature of the resources available for projects selected for funding under this announcement, priority will be given to proposals that outline accelerated and bold courses of research to potentiate significant advances toward a cure for T1D**
- **Applicants are encouraged to share data with the scientific community, according to JDRF standards.**

Examples of projects sought for this funding notice include but are not limited to:

- **Collaborative groups that combine approaches such as targeted immunotherapy to stop the autoimmune attack with groups specializing in beta cell transplantation.**
- **Collaborative groups investigating a therapy to stop the autoimmune attack on beta cells with individual laboratories exhibiting expertise in immunology, beta cell biology, and/or a technological approach such as scRNAseq, or expertise with a tool for preclinical development such as humanized mouse models.**
- **Collaborative groups that combine expertise in screening for novel targets with targeted immunotherapy.**
- **Collaborative groups that combine expertise in cell biology with expertise in the analysis approaches necessary for the creation and utilization of big data sets.**
- **Collaborative groups combining expertise in beta cell health and stress with those developing cell delivery systems that ensure adequate oxygenation and promote vascularization to ensure maximal cell survival and function following transplantation in alternative sites**
- **Collaborative groups combining expertise in islet transplantation with novel immunotherapies to test and validate new protocols to eliminate the use of toxic immunosuppressive drugs and reduce the risk to transplant recipients**
- **Collaborative groups combining expertise in islet transplantation with novel immunotherapies and prediction of responders and non-responders to immunotherapies to identify patient populations likeliest to benefit from specific immunotherapeutic approaches.**
- **Collaborative groups combining investigators with a therapeutic target or asset in development with investigators experiences in clinical translation.**

Out of Scope for this request:

- **Projects that focus solely on advancing/developing methodology or streamlining processes.**
- **Studies focused solely on the development and/or the broad phenotyping of animal models.**
- **Studies that do not outline a clear transition from one development stage of research to the next (discovery / preclinical / clinical research).**

Budget

In response to this announcement, proposed budgets for projects should be based upon up to three years of research, with a total budget of up to $2,250,000.00, per guidelines below. Should your proposed course of research require funds greater than those listed (such as for clinical trials), please reach out to the Scientific Contact below before submitting an LOI.

Budgeting Guidelines:
Each partnership may request up to $500,000 per year for those with two partners, or up to $750,000 for three or more partners, for up to 3 years. Funds may be distributed among the partners as needed for the scope of work, and do not have to be divided equally.

Please speak with the JDRF Scientific Contact below if you have any questions about how to budget, or if your budget would significantly deviate from these guidelines. Please refer to the Cost Considerations, Section 3 of JDRF's standard Terms and Conditions for additional information about what may/may not be included in your budget.

Letter of Intent

Prospective applicants should submit an LOI, [research outline, 3 pages maximum] online via RMS360 to be considered for a full proposal request. The LOI template provided on the RMS360 website must be used to complete the application to be considered for a full proposal request. Applicants proposing clinical research should contact JDRF prior to submitting a LOI.

Letters of Intent (LOI) can be submitted under the following mechanism(s):

Strategic Research Agreement (SRA)
For proposals with applicants/principal investigators at an academic institution or similar entity, SRA applications will be accepted with proposed budgets for projects that should not exceed the guidelines above (including 10% indirect costs). The level of funding will vary depending on the scope and overall objectives of the proposal. If your project budget exceeds guidelines, please discuss with JDRF staff (contact information below). For more information on the Strategic Research Agreement (SRA) grant mechanism please refer to our website.

Industry Development and Discovery Program (IDDP)
For proposals with applicants/principal investigators from an industry entity, applicants should contact the JDRF scientific contact below prior to submitting an LOI. For more information on the IDDP grant mechanism, please refer to our website. Indirect costs are not permitted for IDDP applications. Applications from applicants from academic institutions which include an industry collaborator are also recommended to contact the JDRF scientific staff below prior to submitting a LOI.

Combination Applications that Include Academic Institutions and Industry Partners
Collaborations between industry and academic Institutions are encouraged. Applications including one or more industry partners are requested to contact the JDRF scientific staff below before submitting a LOI.

Proposal

An approved LOI is required prior to the submission of a full proposal. Upon notification of a request for a full proposal, the application must be completed using the templates provided in

RMS360. Proposal section templates in Microsoft Word, [10 pages maximum] should be type-written, single-spaced, and in typeface no smaller than 10-point font. Margins, in all directions, must be at least ½ inch. Complete information should be included to permit a review of each application without reference to previous applications.

Note that all applications involving human subject research must include supplemental information to address subject safety, study design, and investigational product information. More details can be found in the Human Subject Research Guidelines. JDRF follows the U.S. National Institutes of Health (NIH) guidelines for studies including human subjects, including the Common Rule changes.

Review Criteria

Applications will be subjected to confidential external scientific review evaluated on the following:

- **Significance**
- **Relevance**
- **Approach**
- **Innovation**
- **Environment**
- **Resource sharing plan**
- **Appropriateness of budget**
- **Feasibility of plan**
- **Strength/Suitability/Synergy of collaborative team**
- **Potential for significant advancement of T1D research**

Announcement Information Webinar and Q&A

JDRF will hold an announcement introduction meeting via Zoom on November 9, 2022 from 3-4 pm US Eastern Time to which all prospective applicants are invited. JDRF scientists will give an overview of the goals of this initiative, explain the application process, and answer initial questions on applications.

Registration for Webinar (please register by November 4, 2022):
https://jdrf.zoom.us/webinar/register/WN_jiQbL2WVQr6jiDO0U_AZ5g

**** The webinar will be recorded and available after November 9th for those unable to attend ****

Projected Timeline

Milestone	Date
Information Call	Wednesday November 9, 2022
LOI deadline	Thursday December 8, 2022
Notification of LOI Outcome	Thursday December 22, 2022
Full proposal deadline	Monday February 13, 2023
Award notification	July 2023
Earliest anticipated start	September 2023
**** Applicants that include Industry Partnerships should contact JDRF staff for custom timelines ****	

Program Contacts

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References

1. Maki, T., Gottschalk, R. & Monaco, A. P. Prevention of autoimmune diabetes by FTY720 in nonobese diabetic mice. *Transplantation* **74**, 1684–1686 (2002).
2. Wood, J. R. *et al.* Most youth with type 1 diabetes in the T1D Exchange Clinic Registry do not meet American Diabetes Association or International Society for Pediatric and Adolescent Diabetes clinical guidelines. *Diabetes Care* **36**, 2035–2037 (2013).
3. Foster, N. C. *et al.* State of Type 1 Diabetes Management and Outcomes from the T1D Exchange in 2016-2018. *Diabetes Technol Ther* **21**, 66–72 (2019).