

JDRF Request for Applications: Realignment of Established Targets and Mechanisms for Delaying or Reversing T1D

July 2022

Summary

- The goal of this funding opportunity is to identify new candidates for clinical intervention in T1D by identifying and validating targets and mechanisms from other disease indications or disciplines, and welcome new perspectives, approaches, and investigators into the search for a cure for T1D.
- Proposals eligible for consideration will describe studies that accelerate T1D research by realigning targets and mechanisms established in other diseases/foci that have not previously been interrogated for a role in the mechanisms driving disease in stages 1-3 of T1D.
- This program will award grants of up to \$750,000.00 over 3 years.

Funding Opportunity Description

JDRF, the world's leading non-profit organization with the mission to cure type 1 diabetes (T1D), aspires to establish new disease-modifying therapy clinical trials, and to foster the development of disease modifying therapies for T1D. For this endeavor to succeed, it is vital to promote and advance a broad discovery and preclinical research pipeline that is rapidly translatable to clinical trials. Given the potential for overlap in the biological processes of different diseases, research currently underway in fields such as autoimmunity, metabolism, cancer immunology, and various others may represent untapped lines of inquiry for discovery and preclinical research in T1D. The goal of this invitation is to accelerate therapy development by increasing the number of identified candidates for clinical interrogation in T1D through the realignment of targets and mechanisms under investigation in other fields or disease indications. Projects considered for funding will represent innovative ideas, perspectives, and approaches in T1D research, with the objective of providing a significant acceleration and expansion of discovery research and preclinical development. Studies investigating human and mouse gene and protein targets, pharmacological evaluation of existing interventions, and the assessment of mechanisms that play a role in related diseases in T1D-relevant model systems are of particular interest.

Background

There are no cures for T1D, an autoimmune disease characterized by an immune-mediated loss of pancreatic beta cell mass and function, resulting in insulin deficiency and dependency¹. 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}. According to the CDC's 2020 National Diabetes Statistics Report, 1.6 million Americans live with T1D in the United States, an increase of nearly 30% from 2017, with cases growing most sharply among diverse populations⁴. New 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.

The JDRF Cures Program strategy for disease-modifying therapies is to develop treatments that prevent, halt, or reverse disease progression by rebalancing the immune system and preserving or regrowing beta cells. T1D is a complex disease, suggesting success in treatment and prevention will be based upon a variety of targets and pathways. In a recent phase 2 clinical study, efficacy in the reduction of insulin dependency was observed using golimumab, a TNF α inhibitor with FDA approval for autoimmune indications such as forms of arthritis and Crohn's disease⁵. Therefore, there is a clear precedent for the successful realignment of therapeutics from other autoimmune diseases for assessment in T1D. In addition, checkpoint inhibitor therapy for cancer, such as the anti-PD1 monoclonal antibody, is associated with increased diagnosis of T1D within 3 months of treatment, indicating a connection between immune interventions in other diseases and the onset of autoimmune diabetes⁶. This highlights an opportunity to explore the onset of T1D from novel perspectives and disciplines, with the potential to identify previously unidentified targets or strategies for disease modifying therapies.

To expand target validation and preclinical research, a well-reasoned and methodological approach toward determining whether a target or mechanism is applicable to T1D is of great interest. In particular, the ability to rapidly translate current tools such as animal models, antibodies, assays, and other reagents for T1D-based discovery research represents an important opportunity for acceleration of the T1D clinical pipeline. The goal of this funding opportunity is to fast-track discovery research in target validation and identify therapeutic strategies that can be rapidly translated into clinical testing. To that end, JDRF calls for proposals to investigate targets and mechanisms established in other fields of study with clear rationale for assessment as candidates for the prevention and/or reversal of T1D. To be considered, projects should have goals that align with the JDRF Cures Program aims of delaying, halting, or reversing the onset of T1D, as outlined in the JDRF Research Strategy (available for review [here](#)).

Applicant Eligibility

- We welcome LOIs from investigators, pre-formed teams, organizations, and companies with demonstrated expertise to carry out the proposed research.
- 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.
- Collaborative projects combining the expertise and/or resources of multiple research groups are highly encouraged, as are international collaborations and other partnerships that bring together distinct expertise and abilities. Preference will be given to proposals that combine the expertise of laboratories new to the T1D field with those already established in the study of T1D. In addition, JDRF will work to connect laboratories new to the T1D field with potential collaborators and resources as needed.

Project Eligibility

- Preliminary data validating the target or mechanism in another field of study and showing availability of the proposed reagents.
- Proposed targets or mechanisms to be studied should not have been previously explored for a role in T1D.
- Clear rationale must be provided for the potential relevance of the target or mechanism to the underlying mechanisms or a potential therapeutic intervention of T1D.
- Work proposed must outline the criteria to be used for evaluation of the proposed target or mechanism in T1D and include a concise and realistic assessment of a path for the study to translate into therapeutic intervention.
- For consideration, the work proposed should address at least one of the following JDRF strategies for disease modifying therapy development in T1D:
 - Therapies to enhance regulatory immune features that protect beta cells
 - Therapies to disable the autoimmune attack on beta cells
 - Anti-inflammatory or immune deviation therapies to promote beta cell health, in particular by preserving long-term tolerance, preventing re-emergence of Teff cells, or supporting and maintain Treg function
 - Therapies to stimulate growth and derepress beta cell function
- If animal models are to be used for the assessment of the proposed target or mechanism in the context of T1D, proposals using advanced genomics techniques such as CRISPR for the timely creation of T1D-relevant animal model strains will be prioritized over those using longer-term congenic crossing of strains.
- Further Considerations:
 - As the goal of this invitation is the targeted assessment of research currently underway in other fields, researchers that are not currently working in T1D are strongly encouraged to apply.
 - Applications will be specifically assessed for the approach and criteria proposed to validate targets and mechanisms in an accelerated timeframe.
 - Preference will be given to studies focused on targets with readily available therapeutics with validated PK/PD.
 - Applicants are encouraged to share data with the scientific community, according to JDRF standards.
- Out of Scope for this request:
 - Studies that focus on targets or mechanisms (genes, proteins, etc.) that have previously been explored for a role in T1D will not be considered.

- Studies focused solely on broad phenotyping of knockout or transgenic models that do not directly measure T1D outcomes, onset, or changes in established T1D model systems (ex- NOD or beta cell depletion (STZ), etc.) will not be considered.

Funding Mechanism

In response to this announcement, Letters of Intent (LOI) can be submitted under the following mechanism(s):

Strategic Research Agreement (SRA)

For SRA applications, proposed budgets for projects should not exceed \$750,000.00 USD (including 10% indirect costs) total costs for up to three years. The level of funding will vary depending on the scope and overall objectives of the proposal. If your project budget exceeds \$750,000.00, 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 IDDP applications, 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.

Letter of Intent

Prospective applicants should submit an LOI, [2 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.

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 and have no more than six vertical lines per vertical inch. 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

Informational Webinar and Q&A

JDRF will hold an announcement introduction meeting via Zoom on July 26, 2022, from 10-11am 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 July 22, 2022):

https://jdrf.zoom.us/webinar/register/WN_hSYhAolbR5mOR2iTfAE7cw

Projected Timeline

Milestone	Date
Information Call	July 26, 2022, 10-11am EST
LOI deadline	August 23, 2022
Notification of LOI Outcome	September 7, 2022
Full proposal deadline	October 4, 2022
Award notification	February 2023
Earliest anticipated start	April 2023

Program Contacts

Strategic Fit and Scientific Inquires

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References

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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).
4. Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2020. *Centers for Disease Control and Prevention, U.S. Dept of Health and Human Services* (2020).
5. Quattrin, T. *et al.* Golumumab and Beta-Cell Function in Youth with New-Onset Type 1 Diabetes. *N Engl J Med* **383**, 2007–2017 (2020).
6. Akturk, H. K. *et al.* Immune checkpoint inhibitor-induced Type 1 diabetes: a systematic review and meta-analysis. *Diabetic Medicine* **36**, 1075–1081 (2019).