JDRF Request for Applications: Development and Validation of Non-Invasive Immune Imaging Technology to Accelerate the Development of Beta Cell Replacement Therapies

July 2022

Summary

- The goal of this funding opportunity is to catalyze the development and in vivo validation of medical imaging and theranostic technology that enables the non-invasive in vivo monitoring and modulation of immune responses towards transplanted insulin-producing cells.
- Proposals eligible for consideration will describe studies on the development of novel probes and tracers that enhance imaging specificity and sensitivity and enable multimodal and/or multiplexed imaging of immune system components of interest, and validation of such probes in in vivo models of islet transplantation. Multi-disciplinary collaborative projects are strongly encouraged and will be prioritized.
- This program will award grants of up to $750,000 over 3 years. Larger/longer awards may be considered following discussion with the JDRF scientific lead.

Funding Opportunity Description

JDRF seeks applications to support preclinical and clinical research into the development and in vivo validation of medical imaging technology for non-invasive in vivo monitoring of immune responses to transplanted insulin-producing cells. The immune response to transplanted cells is complex and dynamic, and much remains to be learned about the mechanisms of immune rejection. These technologies provide a unique opportunity to elucidate these mechanisms by enabling non-invasive longitudinal assessments and tracking of immune cell activation, trafficking, and targeting of the beta cell graft. Access to such technology would greatly accelerate the evaluation and optimization of approaches currently under development to modulate immune responses to transplanted cells so as to evade the immune response and/or promote acceptance and operational tolerance. Moreover, once translated into the clinic, these tools could be used for monitoring patients that have received beta cell transplants to identify potential adverse immune reactions that may impact the graft and enable implementation of targeted interventions to rescue the graft prior to loss of function.

Background

JDRF is committed to advancing the development of beta cell replacement therapies that are able to restore glycemic control and eliminate the need for exogenous insulin administration in people with T1D. It has been shown that cadaveric pancreatic islet transplantation is efficacious in improving glycemic control, preventing severe hypoglycemia, reducing exogenous insulin requirements, and improving quality of life in patients with medically unstable T1D. Despite significant progress in the development of alternative renewable sources of insulin producing cells to overcome the shortage of donor tissue, major scientific and technical challenges in ensuring adequate oxygenation and vascularization of beta cells implanted in alternative sites and overcoming allogeneic immune rejection and recurring autoimmunity remain which must be addressed before beta cell replacement can be widely implemented as a cure for T1D and other insulin requiring diabetes. Significant research efforts are ongoing to address these challenges, yet pace of progress is slow due to the need for longitudinal studies evaluating dynamic biological processes and reliance on traditional

histological assessments which are time consuming, require large numbers of animals for analysis of samples at various time points to achieve statistical significance, and yield a limited amount of information, thus increasing development timelines and costs.

Advances in medical imaging have been critical to track disease initiation and progression, and to inform clinical practice with diagnostic, prognostic, staging and response-to-therapy data in several disease areas. The application of various imaging modalities such as optical imaging, ultrasound (US), magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET) have enabled the gathering of anatomical and functional data for non-invasive monitoring of multiple biological processes in unprecedented precision and detail. The immune system plays a critical role in various disease states and recent advances in novel immunotherapies have sparked interest in the field of Immunoimaging. Moreover, recent advances in the field of nanomaterials have led to the development of novel probes and tracers that enable multimodal imaging, which allows leveraging the strengths of multiple imaging methods to overcome their individual limitations, as well as multiplexing, which enables simultaneous imaging of multiple targets. Furthermore, the advent of theranostic technology facilitates the simultaneous imaging of specific cell populations and localized delivery of drugs to modulate targeted cell function.

As such, JDRF wishes to leverage these advances and catalyze the development of technologies to non-invasively characterize in vivo immune responses to transplanted insulin-producing cells and support the development of theranostic technology capable of simultaneously assessing and modulating immune responses to transplanted cells. Such technology will significantly accelerate progress and reduce costs by overcoming the limitations of traditional approaches for longitudinal assessments and facilitate faster, more efficient, and more detailed characterization of immune responses to implanted cells and the impact various immune modulation and immune evasion strategies have on the immune system. These tools could then be used for non-invasive monitoring in humans recipients upon clinical translation and commercialization of beta cell replacement products.

Multi-disciplinary collaborative projects combining the resources and capabilities of multiple research groups with relevant expertise (i.e. medical imaging, immunology, T1D and islet/beta cell transplantation) are strongly encouraged and will be prioritized. All submissions should consider implications of probe mechanisms of clearance, site of islet/beta cell transplantation and ability to image immune responses, and potential for clinical translation. **Technologies with a direct path to clinical translation will be prioritized.** Additionally, the impact of probes on targeted cell viability and function and ability to accurately assess immune responses or impact of other immune targeted interventions should be taken into account.

Examples of research appropriate for this RFA include, but are not limited to:

- Development and in vivo validation of probes that enhance imaging sensitivity and specificity, and thereby increase signal to noise ratio, which enable non-invasive detection and tracking of immune cell populations which play a key role in rejection and/or survival of transplanted beta cell grafts (e.g macrophages, NK cells, various T cell subsets, B cells).
- Development and in vivo validation of probes that enable non-invasive multimodal imaging to allow simultaneous acquisition of anatomical (i.e. biodistribution) and functional (i.e. activation status) data on immune cells which play a key role in rejection and/or survival of transplanted beta cell grafts.

- Development and in vivo validation of probes that enable non-invasive multiplexed imaging for simultaneous monitoring of multiple immune cell populations which play a key role in rejection and/or survival of transplanted beta cell grafts.
- Development of theranostic technologies which enable simultaneous non-invasive characterization of immune responses and delivery of therapeutics to modulate immune responses to beta cell grafts.

In vivo validation of all of the above should be done in the context of models of islet/beta cell transplantation and rejection.

Examples of research not supported by this RFA include:

- Projects focused on T1D onset, progression, and prevention.

Eligibility

- Applications may be submitted by domestic and foreign non-profit organization, public and private, such as universities, colleges, hospitals and laboratories; units of state and local governments and eligible agencies of the federal government, for-profit entities, or industry collaborations with academia. 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.
- Please note that applications from for-profit entities or industry collaborations with academia may be submitted in response to this RFA. Additional information will be requested from for-profit entities if invited to submit a full proposal.
- For clinical studies, applicants must hold an appointment or joint appointment in a subspecialty of clinical medicine, and conduct human clinical research.
- 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.

Funding Mechanism

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

Strategic Research Agreements (SRAs)

Strategic Research Agreements are intended for support of research activities at non-for-profit entities such as academic institutions. For SRAs, proposed budgets for projects should not exceed $750,000.00 USD (including 10% indirect costs) total costs for up to three (3) years. The level of funding will vary depending on the scope and overall objectives of the proposal. If your project budget and/or timeline exceeds $750,000.00 and/or 3 years, 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 Discovery and Development Partnerships (IDDPs)

For-profit entities may apply under JDRF's Industry Discovery & Development Partnership (IDDP) funding mechanism, which entails additional requirements and typically has a modest royalty payback to JDRF. If you would like to submit an Industry Discovery and Development Partnership (IDDP) project LOI to this RFA, please check our website for additional information (https://grantcenter.jdrf.org/industry-discovery-development-partnerships/) and contact Dr. Jaime Giraldo (jgiraldo@jdrf.org) to discuss prior to submitting an application. Indirect costs are not permitted on 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 in order 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 Public Q&A

JDRF will hold an introductory meeting via Zoom teleconference on **Tuesday, August 9, 10- 11am** Eastern Standard Time, to which all interested 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. A brief introduction on JDRF's grant application portal (RMS360) will also be given.

Registration for webinar (please register by August 4th, 2022):

https://jdrf.zoom.us/webinar/register/WN_I-sfN8O3TrGSefpuJRoPNQ

After registering, you will receive a confirmation email containing information about joining the webinar.

Projected Timeline

Milestone	Date
Informational Webinar and Q&A	Tuesday, August 9, 2022 10-11am EST
LOI deadline	Tuesday, August 30, 2022
Notification of LOI Outcome	Wednesday, September 14, 2022
Full proposal deadline	Wednesday, October 12, 2022
Award notification	April
Earliest anticipated start	June

Program Contacts

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