

REQUEST FOR LETTERS OF INTENT (LOI):

RESTORING PANCREATIC ALPHA CELL FUNCTION TO IMPROVE METABOLIC CONTROL IN TYPE 1 DIABETES

PURPOSE

JDRF is committed to facilitating the discovery and translation of promising targets or therapeutics to improve and restore glycemic control in people with type 1 Diabetes (T1D). To this end, JDRF is soliciting letters of intent for research to evaluate molecular and cellular mechanisms, validate drug targets, or propose novel therapeutic interventions to correct alpha cell dysregulation and improve metabolic control in T1D.

BACKGROUND

Type 1 Diabetes is characterized by autoimmune-mediated loss of pancreatic beta cells and our understanding of the pathogenesis has traditionally revolved around insulin deficiency. However, there is an increasing appreciation of the contributions of other pancreatic cell types in controlling blood glucose levels and the consequences of their dysregulation in T1D. Alpha cells, composing 40% of the total number of cells in the islet, secrete glucagon which controls blood levels in the fasting state. Impaired glucagon secretion predisposes people with T1D to hypoglycemia, whereas hyperglycemia is associated with over secretion and hyperglucagonemia. To achieve the therapeutic objective of restoring alpha cell function and improving metabolic control in individuals living with T1D, JDRF will support applications that address the mechanisms of alpha cell dysfunction and/or present rational design of therapeutic strategies aimed at restoring alpha cell function in T1D.

OBJECTIVES

Letters of Intent are solicited for innovative approaches to discover and translate targets and pathways aimed at restoring alpha cell function. Priority will be given to translational opportunities proposing isolation/selection/validation of small molecule or biologics *in vitro*, validation of therapeutic candidates in preclinical T1D models, and translation of preclinical discoveries or other experimental systems to human cells or tissues.

Examples may include, but are not limited to:

- Preclinical proof-of-concept studies to validate novel drug targets or lead therapeutic molecules with potential to restore alpha cell function and improve glycemic control in T1D
- Identification and characterization of pathways and targets that compromise alpha cell responses to both rising and falling glucose levels in T1D.
- Understand the consequences of beta cell injury and altered paracrine insulin signaling on alpha cell physiology in T1D. How can alpha cell function be restored with limited or compromised beta cell function?
- Understand the consequences of paracrine signaling of other pancreatic cells, such as delta (somatostatin) and gamma cells (pancreatic polypeptide), as well as changes in the extracellular matrix environment of the T1D islet.
- Studies using isolated alpha cells or tissue from human donor pancreata
- Understand the role of extra-pancreatic signals (neural input, liver, etc.) in dysregulation of glucagon secretion by alpha cells
- Novel clinical strategies for T1D therapy related to alpha cell function

This RFA excludes studies that address cell transdifferentiation, or alpha-cell dysfunction in settings without partial or complete loss of beta cells (for example, as in obesity)

Applicants are encouraged to consult with JDRF Scientific Staff, Dr. Marlon Pragnell (contact information below) to discuss the alignment of their proposal to this RFA and in developing the projected study concept. Collaborations with industry and/or direct applications by companies are strongly encouraged. Those proposing studies with human pancreatic tissue are requested to contact the JDRF-supported nPOD program (jdrfnpod.org) or other tissue banks to confirm sample availability.

MECHANISM

In response to this announcement, LOI's can be submitted to our **Strategic Research Agreement (SRA)** or **Industry Development and Discovery Program (IDDP)** grant mechanisms. For more information on these mechanisms, please refer to our website:

- Strategic Research Agreements: <http://grantcenter.jdrf.org/information-for-applicants/grant-mechanism-descriptions/strategic-research-agreements/>
- Industry Development and Discovery Program: <http://grantcenter.jdrf.org/industry-partnerships/>

Up to a maximum of \$200,000 USD per year including 10% indirect costs for up to 2 years may be requested. The level of funding will vary depending on the scope and overall objectives of the proposal.

- Project proposals of up to 36 months duration and/or higher budget may be considered

Applications that are not funded in this competition may be resubmitted to other JDRF grant mechanisms according to the deadlines and guidelines described on the JDRF website: <http://grantcenter.jdrf.org/rfa/>

ELIGIBILITY

Applications may be submitted by domestic and foreign non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, 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. Please note that applications from for-profit entities or industry collaborations with academia may be submitted to this LOI, however, additional information will be requested from for-profit entities if a full application is invited.

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.

LETTER OF INTENT

Prospective applicants should submit a Letter of Intent on line via RMS360 (<http://jdrf.smartsimple.us>) to be considered for a full proposal request. The LOI template provided on the RMS360 website must be used to complete the application. Applicants will be notified approximately four weeks after the LOI deadline date if they have been approved to submit a full application.

Please see below for complete instructions. Letters of Intent should include the following information:

- Background /Rationale and Specific Aims of overall project
- Overview of hypotheses, goals, deliverables and collaborative framework as applicable
- Title, lead investigator and brief description and specific aims of individual projects (if collaborative/network)
- Expected deliverables and impact of the proposed study with potential next steps
- Intellectual Property or commercial efforts associated with the current application
- Total budget / budget by year by project
- Biosketches for all Principal Investigators

PROPOSAL

An approved Letter of Intent is required prior to 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 (<http://jdrf.smartsimple.us>). Proposal section templates in MS Word [**10 page 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 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:

http://grantcenter.jdrf.org/wp-content/uploads/2012/12/JDRF_Scientific_Guidelines_final-Aug20151.pdf

ANNOUNCEMENT INTRODUCTION AND PUBLIC Q&A

JDRF will hold an announcement introduction meeting via web and teleconference on **Monday, November 20th, 2017 from 1:00pm-2:00pm** US 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.

Click here to [join the Webinar](#)

Meeting number: 851 420 742

Meeting password: JDRF17

Join by phone

Dial in (US): 1-877-261-5012

Dial in (International): [Global call-in numbers](#)

Conference Code: 851 420 742

DEADLINES

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| • LOI Release Date | Wednesday, November 15 th , 2017 |
| • Letter of Interest Deadline | Wednesday, December 20 th , 2017,
5pm US Eastern Time |
| • Notification of Full Application Request | Wednesday, January 17 th , 2018 |
| • Application Deadline | Wednesday, February 21 st , 2018, 5pm
US Eastern Time |
| • Response to Applicants | August 2018 |
| • Earliest Anticipated Start Date | October 2018 |

SUBMISSION INSTRUCTIONS

Applicants should register and submit their completed LOI in RMS360 (<http://jdrf.smartsimple.us>).

REVIEW CRITERIA

Applications will be evaluated based on JDRF's standard confidential award policy and according to the following criteria:

- Significance
- Relevance
- Approach
- Innovation
- Investigator Experience
- Environment

CONTACTS

PROGRAMMATIC

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ADMINISTRATIVE

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If you have any grant-specific questions as you work within RMS360, please contact the administrative contact listed above.

For any **non-grant-specific** inquiries or issues, please contact SmartSimple Support Services via email support@smartsimple.com or phone (866) 239-0991. Support hours are Monday through Friday between 5:00am and 9:00pm US Eastern Standard Time.