

# JDRF Request for Applications: Development of Islet-Targeted Drug Delivery Strategies in T1D

July 2022

## Summary

- The goal of this funding opportunity is the creation and validation of reagents that convey islet cell type specificity for the purposes of targeted drug delivery.
- Respondents to this RFA should have demonstrated expertise in the development and validation of drug delivery platforms; the discovery and validation of new cellular addresses/reagents with characteristics appropriate for active drug delivery to human islet endocrine cells; and/or the ability to deliver a model payload into a human islet cell, both *in vitro* and *in vivo*.
- This program will award grants of up to \$900k over 3 years.

## Funding Opportunity Description

JDRF aims to catalyze and support innovative studies for the selective delivery of therapeutics (bioactive molecules) to human beta cells, or other major pancreatic cell types, to promote survival and restore functional beta-cell mass in type 1 diabetes (T1D). Letters of Intent (LOI) from investigators who would be interested in helping achieve this goal are being solicited. The validation of existing reagents or creation of novel reagents with islet cell specificity, and the identification of new islet cell specific cellular targets are of interest.

To safely increase functional beta-cell mass, we need to develop reagents/strategies to deliver drugs/biologics/genes specifically to the human beta cell (or other major pancreatic cell types) to promote their survival, induce proliferation, or stimulate hormone-type reprogramming. There are currently only a few identified chemical agents that induce regeneration of beta cells *in vivo* and all of them have deleterious off target effects, therefore there is a great need to produce reagents that can enable the targeted delivery of a drug payload specifically to the islet cells. Our primary objective is therefore the creation and validation of reagents that convey islet cell type specificity and enable the development of islet cell specific targeted drug delivery systems.

Examples of pertinent topics to this call include but are not limited to:

- Identification of novel surface receptors and/or other surface molecules for human islet targeting and development of reagents that can deliver payloads specifically to human beta, alpha or other islet endocrine cell types
- Development and validation of reagents for targeted drug delivery (peptide, viral construct, small molecule, etc.) to pancreatic beta cells using known beta-cell-selective receptors (e.g., GLP1R, ENTPDase3); demonstration of proof of concept of drug delivery in human islets with *ex vivo* and *in vivo* models

## Background

The JDRF Cures Program aims to halt the progression of T1D and ultimately achieve a cure through the development of disease-modifying therapies (small molecules and/or biologics) that promote the survival, function, and regeneration of endogenous insulin-producing beta cells ([Link to Strategy Document Here](#)).

Novel targets and pathways have recently been described that are able to promote beta-cell regeneration and survival. However, it has been empirically determined that many of these targets and pathways are not sufficiently specific or unique to the islet/beta cell and may present safety concerns if delivered systemically when non-pancreatic cellular targets could become deleteriously affected. Targeted drug delivery presents an opportunity to restrict a regenerative or survival therapy to the islet/beta cell and avoid or reduce deleterious effects on tissues or cells outside the pancreas.

Targeted drug delivery, also referred to as active or smart drug targeting, has most notably been successful in the oncology setting. It is likely that active drug targeting approaches, such as utilizing small molecule, biological (e.g., antibodies, aptamers, peptides, etc.), or nanomaterial drug conjugates to selectively bind to the target, could mitigate potential non-islet/beta-cell activities while increasing the potency of the therapeutic due to targeted delivery. In addition to traditional drug conjugate approaches, JDRF is also interested in gene delivery approaches via viral (e.g. AAVs, etc.) or non-viral (e.g. biomaterial scaffolds, etc.) platforms. The utility of newer generations of viruses with beta cell specific tropism are of particular interest.

However, targeted drug delivery approaches are reliant on the identification of cell type specific interactions with surface receptors or other cellular addresses (e.g., transporters) that restrict specific drug uptake, internalization, and activation within the islet to achieve desired drug effects. To date, limited data exists demonstrating successful active drug targeting to beta or islet cells. There are also few well characterized and validated human beta cell or human islet cell specific surface addresses to facilitate active drug targeting. Respondents to this RFA will possess the skills needed to identify and validate islet cell specific addresses and develop reagents for those addresses.

- Out of Scope for this request:
  - In contrast to active drug targeting, passive drug targeting refers to the accumulation of a drug around certain sites in the body and relies on distribution by blood circulation. Passive drug targeting approaches are not of interest to this call and will be excluded from this program.
  - Novel therapeutic payload development (such as chemical campaigns to optimize hit or lead molecules to drug target pathways).

## Eligibility

- We welcome LOIs from investigators, established teams, organizations, and companies with demonstrated expertise appropriate to these tasks above, paying attention to the criteria listed below.

- Examples of demonstrated expertise desired: quantitative proteomics, bioinformatics, human beta cell biology, targeting reagent generation (antibodies, aptamers, AAVs, etc.), expertise with animal models to assess beta cell regeneration and survival with an emphasis on drug metabolism and pharmacokinetics.
- 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.
- 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, LOI's can be submitted to JDRF's **Strategic Research Agreement (SRA)** or **Industry Discovery and Development 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/>
  - SRA totals can include up to 10% indirect costs;
- Industry Development and Discovery Program <https://grantcenter.jdrf.org/industry-discovery-development-partnerships/> For IDDP applications, applicants are required to contact the JDRF scientific contact below prior to submitting a LOI.
  - IDDP applications do not permit indirect costs.

The level of funding will vary depending on the scope and overall objectives of the proposal. JDRF may consider applications with increased scope (time and/or budget) where there is a strong justification, and interested applicants should discuss with the JDRF scientific contact below.

## 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](#).

## 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 **August 3, 2022, from 10-11am** 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 29, 2022):**

[https://jdrf.zoom.us/webinar/register/WN\\_PlpDp0LRQCSf1k72vc9-mw](https://jdrf.zoom.us/webinar/register/WN_PlpDp0LRQCSf1k72vc9-mw)

## Projected Timeline

Milestone	Date
Information Webinar and Q&A	August 3, 2022, 10 -11 am ET
LOI deadline	August 17, 2022
Notification of LOI Outcome	September 2, 2022
Full proposal deadline	October 5, 2022
Award notification	March 2023
Earliest anticipated start	May 2023

## Program Contacts

### Strategic Fit and Scientific Inquires

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