JDRF AND JANSSEN'S DISEASE INTERCEPTION ACCELERATOR REQUEST APPLICATIONS FOR:

BIOMARKERS OF PROGRESSION IN THE AT-RISK SETTING FOR TYPE 1 DIABETES

PURPOSE

JDRF and Janssen's Disease Interception Accelerator are soliciting applications to discover and develop candidate biomarkers of progression in the at-risk setting for type 1 diabetes (T1D). JDRF is committed and most interested in investigator-initiated proposals that focus on research with potential for clinical utility.

BACKGROUND

Validated biomarkers that detect risk, stage the disease, and predict its rate of progression in the at-risk setting for T1D are required to provide a framework for clinical trial design, benefit/risk decisions around interventions, and ultimately for the practice of predictive medicine to prevent symptomatic T1D. These biomarkers may include markers of beta cell stress, dysfunction, and damage, functional beta cell mass, autoimmune/inflammatory biomarkers, and/or biomarkers of impaired glucose and metabolic control. While progress has been made in identifying predictive markers for risk of T1D, there may be alternative molecular biomarkers (metabolites, proteomics, gene expression patterns, additional autoantibodies, etc.) that may prove to be expressed earlier, be more highly predictive, and/or more cost effective for detecting risk. Biomarkers that detect activation of innate immunity or of T cells specific for beta cells, islet inflammation or beta cell stress, dysfunction or damage may be demonstrated to serve this role. For prevention approaches to succeed it is also important to develop other biomarkers associated with progression that can be used both as prognostic biomarkers to design trials and tailor therapy and as predictive biomarkers of efficacy of preventive interventions to accelerate clinical development. Biomarkers that detect very early beta cell inflammation or beta cell stress, dysfunction or damage, beta cell specific autoimmune responses, dysglycemia, or insulin resistance may be demonstrated to serve this role. Non-invasive imaging biomarkers to detect islet inflammation and beta cell mass could prove critical for more accurate staging and monitoring progression, may help determine whether the disease can have a relapsing/remitting pattern, and may be used for assessing response to interventions. It is likely that a combination of biomarkers will be required to accurately stage and better predict rate of progression.

OBJECTIVES

Applications are sought from investigators with access to existing samples and/or patient cohorts of at-risk subjects to develop improved prognostic risk scores of progression and/or to develop new or improved screening assays. The translational potential of the investigations should be highlighted and thus, only research plans involving human samples will be considered.

The major focus of this RFA will be to identify candidate biomarkers that:

- Stage type 1 diabetes in the at-risk setting
- Provide early risk detection in the general population, with an emphasis on the pre-autoantibody stage
- Predict risk/rate of progression in autoantibody positive individuals
- Serve as surrogates of efficacy of preventive interventions
- Allow for inclusion/exclusion in clinical trials in the at-risk setting

Investigators who wish to validate candidate biomarkers in the at-risk setting are also encouraged to apply to this RFA. Here, the application should propose a vision for how the biomarker could be translated into research and/or clinical use.

Collaborative projects, where possible, to interrogate common sample or data sets are encouraged, and higher budgets may be allowed for such projects. Please contact the scientific contact listed on this RFA prior to submission of an application for approval of such projects

ELIGIBILITY

Applicants must hold an M.D., D.M.D., D.V.M., Ph.D., or equivalent academic degree and a faculty position or equivalent at a college, university, medical school, for-profit research based organization or other comparable institution.

Applications may be submitted by domestic or foreign public or private non-profit organizations, such as colleges, universities, hospitals, laboratories, units of state or local governments or eligible agencies of the federal government. Please note that applications from for-profit entities or industry collaborations with academia may be submitted to this RFA, however, additional information will be requested from for-profit entities if a full application is invited.

There are no citizenship requirements.

MECHANISM

Applications in response to this announcement can be submitted under one of the following funding mechanisms:

Pilot & Feasibility Grants (P&Fs): up to $110,000 (including 10% indirect costs) for one year only.

Strategic Research Agreements (SRAs): Up to $250,000 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. Under the terms of the grant award, written quarterly (~2 3 pages) reports will be required from the funded investigator as a basis for continued support. Progress reports will be based on milestones agreed upon by all parties prior to grant activation and go-no go decision points will be expected as part of the grant.

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 Web site: http://www.jdrf.org

DEADLINES

- **Release Date**: ..... December 7, 2015
- **Email of Intent to Submit Application**..... January 15, 2016
- **Application Due Date**: ..... February 5, 2016
- **Proof of Access to Human Samples:**……..March 18, 2016
- **Response to Applicants Date**: ..... May 2016
- **Earliest Anticipated Start Date**: ..... August 2016

RFA COMPONENTS

Applications should include the following information:

- Background and Significance of this work to Type 1 Diabetes
- Proposed research (What?)
- Rationale for proposed research (Why?)
- Research Design and Methods (How?)
- Advantages over alternative approaches that would address goal.
- Future plans if research is successful.

Proof of access to biosamples, if not included with the application, should be emailed to the administrative contact listed on this RFA by March 18, 2016.

SUMBISSION INSTRUCTIONS

On or before January 15, 2016, please email the administrative contact, Randall J. Rowe, (rrowe@jdrf.org), to inform us of your intention to submit an application. In the email, include a (1) brief (2-4 paragraphs, no more than 1 page) description of your hypothesis and experimental plan and (2) from where you intend to obtain human samples and/or data for the proposed research.

Applicants must register as an applicant and submit their application in response to this RFA using JDRF's on-line research management system RMS360 (https://jdrf.smartsimple.us).

SCIENTIFIC CONTACT

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ADMINISTRATIVE CONTACTS

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