

JDRF SPECIAL REQUEST FOR EXPRESSIONS OF INTEREST:

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

PURPOSE

JDRF is soliciting expressions of interest (EOI) 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 conduct more efficient clinical trials. 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 will prove critical for more accurate staging and monitoring progression, can help determine whether the disease can have a relapsing/remitting pattern, and can 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

Expressions of interest are sought from investigators with access to existing samples and/or patient cohorts of individuals with ≥ 2 T1D autoantibodies 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 EOI will be to identify candidate biomarkers that:

- Stage type 1 diabetes in the at-risk setting
- Predict risk/rate of progression
- Serve as surrogates of efficacy of preventive interventions
- Allow for inclusion/exclusion in clinical trials in the at-risk setting

Investigators with ideas or resources that might benefit this initiative should also submit their ideas via an expression of interest. Collaborative projects, where possible, to interrogate common sample sets are encouraged, and higher budgets may be allowed for such projects. Please contact JDRF prior to submission of an EOI for approval of such projects

JDRF recently released a request for letters of intent (LOIs) for Biomarkers of Pancreatic Beta Cell Stress and Health. This EOI is not meant as a replication of that LOI and EOIs in relation to beta cell stress and health will be considered only if they are relevant to the prevention setting. Furthermore, EOIs with a focus on autoantibody negative individuals only will not be considered.

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 EOI, 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 3 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.

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:** September 6, 2013
- **Expression of Interest:** November 1, 2013
- **EOI Notification** November 8, 2013
- **Application Due Date:** December 18, 2013
- **Response to Applicants Date:** March 2014
- **Earliest Anticipated Start Date:** June 2014

EOI COMPONENTS

Expressions of interest proposals should be no more than two pages in length including the following information:

- Name, title and institution of principal investigator (PI), co-investigator and/or key collaborator(s)
- Brief details of approach proposed, including hypothesis, scientific rationale including cohort selection (proof of access or provisional access to samples) and references to published or preliminary data (preliminary data need not be presented in detail)
- Description of potential for translation
- Biosketches of PI and co-investigators/collaborators (does not count towards page limit)

An approved EOI is required prior for submission of a full proposal. Please see below for complete instructions.

SUBMISSION INSTRUCTIONS

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

As a courtesy, please email the scientific contact, Jessica Dunne (jdunne@jdrf.org) to inform us of your intention to submit an EOI.

REVIEW CRITERIA

Submitted expressions of interest will be acknowledged with brief responses as to their suitability for further development by the JDRF no later than November 1, 2013.

SCIENTIFIC CONTACTS

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ADMINISTRATIVE CONTACTS

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