



*dedicated to finding a cure*

## **Announcement of Funding Opportunity Biomarkers in Type 1 Diabetes and its complications At least \$10 Million per Year Available**

JDRF has an unprecedented opportunity to make progress in the discovery and validation of biomarkers in Type 1 diabetes and its complications. New biomarkers will stimulate bench to bedside translation by providing measures of the biological effects of potential new treatments. The ideal biomarker can be measured in a minimally invasive way, can be measured repeatedly over time, identifies susceptibility to or early stages of disease, is indicative of disease progress, or correlates well with response to therapy.

At least \$10 Million per year will be available for this initiative, which will accommodate a variety of grant mechanisms. Duration of support will in general not exceed 3 years. However, longer studies (especially in complications) will be considered if deemed appropriate by JDRF program staff. Budgets proposed should be justified and commensurate with the type of study and the research plan; however, no specific budget limit is imposed.

Studies designed to test the validity of candidate biomarkers or new technologies to monitor candidate biomarkers in patient tissue samples or small groups of well-characterized patients are especially encouraged. For biomarkers already validated in human subjects, the effort might be to establish a precise assay prior to pursuing larger patient studies. Priority will be given to those projects with high promise for evaluating therapeutic interventions, staging clinical trials, or improving clinical care in the relatively near future. Applicants are encouraged to submit multidisciplinary approaches to address the challenges in developing a viable, clinically adaptable approach. Either academic or industry investigators may apply; JDRF encourages the submission of proposals with collaborations between academia and industry. All interested investigators are strongly encouraged to consult with JDRF Program Staff as they develop their applications.

### **Background**

A biomarker is a molecular, biological, or physical characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to therapeutic intervention. Biomarkers can be used to examine safety in animal models or humans, to make diagnoses, to indicate disease status and stage, and to predict and/or monitor clinical response. There is a critical need for biomarkers in all areas of type 1 diabetes, where current assays have limited predictive power and/or have limited acceptance by regulatory agencies.

Robust biomarkers (either a measurement from a readily obtained biologic sample or made directly in patients) would reduce the need to achieve hard clinical endpoints in clinical trials, and would therefore help to lower the associated costs of such trials by reducing the number of patients needed and the time during which they are monitored. Such biomarkers must be quantifiable and correlate well with clinical and biochemical measures of disease progression, or therapeutic response, and should be relatively inexpensive and noninvasive so that they can be measured serially over time.

This Announcement encourages the discovery and development of candidates towards validation as acceptable biomarkers. Before a biomarker can be considered as a good surrogate that would be clinically useful or appropriate for monitoring the efficacy of a therapy, effort must go toward development and validation of these biomarkers. This initiative includes but is not limited to:

- Studies of biomarkers in well-characterized patients or in biological samples from well-characterized patients
- Limited studies in human subjects to determine whether a biomarker correlates well with pathogenesis, disease processes, progression or regression of disease, response to therapy, accepted clinical endpoints, etc. Please note, extended prospective clinical trials for marker validation against hard clinical endpoints, are outside the scope of this initiative.
- Studies to design or improve the biomarker assay system to be robust, precise, quantitative and translatable to many laboratories, or to fall within costs that are appropriate for clinical use.
- Work to establish sampling or biomarker monitoring strategies that are non-invasive and/or acceptable to patients and clinical staff

Research objectives include but are not limited to:

- Biomarkers of autoimmunity in type 1 diabetes
- Biomarkers that indicate beta cell mass and function
- Biomarkers for complications of diabetes

### **JDRF requests *Expressions of Interest* for proposals to develop Biomarkers of Autoimmunity in Type 1 Diabetes**

JDRF aims to develop immune markers to: 1) improve prediction of disease risk, 2) monitor the onset, status, and stage of disease progression, and 3) predict, monitor, and assess the effect of therapeutic interventions in T1D.

Examples of pertinent topics include (not intended to be exclusive or all-encompassing):

- Identification of biomarkers and development of novel assays for evaluating susceptibility to T1D
- Identification of biomarkers that predict progression from autoimmune insulinitis to diabetes, onset and loss of a honeymoon period, status of the autoimmune response in established T1D

- Identification and assay development for immune cell-based biomarkers (T cell, B cell, DC, etc) in all aspects of T1D
- Biomarkers and assays to measure the inflammatory response in the incubation period, and at the onset and progression of T1D
- Identification of markers of immune memory in T1D
- Assays to measure efficacy of current or future therapeutic interventions
- Development of new assays or improvement of existing assays to increase sensitivity, and specificity, decrease cost, or improve functionality
- Development of technologies to detect biomarkers in easily accessible, non-invasive sites (e.g. saliva)

Applicants are strongly advised to consult with JDRF Program Staff to discuss the responsiveness of their proposal to this program. Enquiries in this area should be referred to Olivia Lou, Ph.D., [olou@jdrf.org](mailto:olou@jdrf.org), +1-212-479-7606.

### **JDRF requests *Expressions of Interest* for proposals to develop Markers of Beta Cell Mass and Function**

A comprehensive understanding of the molecular basis of beta cell development and function should generate new research tools and provide critical insights into the prevention and treatment of diabetes. JDRF aims to develop markers that are surrogates of beta cell mass and function.

Examples of pertinent topics include (not intended to be exclusive or all-encompassing):

- Markers that identify newly-formed or regenerated beta cells
- Identification of markers for monitoring pancreatic beta cell function
- Characterization of molecular markers that would delineate stem/progenitor cells of the pancreas
- Markers that elucidate mechanisms underlying the regeneration of pancreatic beta cells
- Approaches to detect and quantify beta cell-specific proteins in plasma or other patient samples that correlate with disease state

Applicants are strongly advised to consult with JDRF Program Staff to discuss the responsiveness of their proposal to this program. Enquiries in this area should be referred to Andrew Rakeman, Ph.D., [arakeman@jdrf.org](mailto:arakeman@jdrf.org), +1-212-479-7664.

### **JDRF requests *Expressions of Interest* for projects to develop Clinical Biomarkers for Complications of Diabetes**

This request seeks to provide support towards the clinical validation of promising biomarkers that can be used to predict risk, aid in early diagnosis and assess

progression of the microvascular and cardiovascular complications of diabetes. Where appropriate JDRF also seeks candidates for surrogate clinical endpoints. The overall goal is to accelerate development of biomarkers that could be used as diagnostic tools, or as outcome measures to be used in clinical trials testing new therapeutic agents. Investigators responding to this EOI may wish to take advantage of existing epidemiological or long-term clinical studies that may have been established for investigation of diabetes or of other diseases.

#### *Nephropathy*

- Approaches with potential to predict risk of occurrence of microalbuminuria
- Development of functional or biochemical (serum and /or urine) biomarkers to detect or track progression to overt nephropathy
- Development of functional or biochemical biomarkers with potential to respond to therapeutic intervention and serve as meaningful surrogate clinical endpoints

#### *Neuropathy*

- Structural or functional biomarkers to predict or track progression of peripheral or cardiac autonomic neuropathy
- Development of structural or biochemical biomarkers with potential to respond to therapeutic intervention and serve as meaningful surrogate clinical endpoints to shorten the length required for clinical trials

#### *Retinopathy*

- New imaging technologies of early stage retinopathy and macular edema
- Functional biomarker, or set of biomarkers, of retinal dysfunction useful to identify individuals with neural degeneration that correlates with microvascular structural changes and vision changes
- Structural biomarkers to detect onset, predict progression and track treatment of non-proliferative retinopathy, proliferative retinopathy and macular edema

#### *Cardiovascular Disease*

- Functional or biochemical biomarkers of accelerated cardiovascular disease in Type 1 diabetic subjects including hyperinsulinemia, elevated insulin resistance, abnormalities in coagulation factors, or platelet function

Applicants are strongly advised to consult with JDRF Program Staff to discuss the responsiveness of their proposal to this program. Enquiries in this area should be referred to Barbara Araneo, [baraneo@jdrf.org](mailto:baraneo@jdrf.org), +1-212-479-7662, for CVD and Retinopathy programs; Magdalena Eriksson, [meriksson@jdrf.org](mailto:meriksson@jdrf.org), +1-212-479-7633, for Nephropathy programs; and Helen Nickerson, [hnickerson@jdrf.org](mailto:hnickerson@jdrf.org), +212-479-7662 for Neuropathy programs.

***Expressions of Interest* are being solicited to be able to provide advice about the most appropriate grant mechanism.**

***Expressions of Interest* should be no more than two pages in length including, where applicable, the following information:**

- Brief details of approach proposed, including rationale and references to published or preliminary data (preliminary data need not exist)

- Short and long-term development goals set forth as milestones
- Access to clinical samples (JDRF is pleased to help the principal investigator identify such in advance of submission of the Expression of Interest)
- Total estimated budget and project duration (up to 3 years)

**Key Dates:**

- Expressions of Interest for the first round of assessment should be submitted no later than March 5, 2008 at 11.59 p.m. EST on proposal Central (<https://proposalCentral.altum.com/login.asp>). For questions regarding submission, please contact [grantsupport@jdrf.org](mailto:grantsupport@jdrf.org).
- Submitted expressions of interest will be acknowledged with brief responses as to their suitability for further development by the relevant JDRF Program Staff no later than three weeks from submission.

Announcement Date	EOI Deadline	Decision on EOI	Full Online Application Deadline	Notification
1/11/2008	3/5/2008	3/21/2008	4/23/2008	6/30/2008

- This is an initial announcement. Follow-on efforts are anticipated, including additional funding opportunities
- Interested investigators may access available research resources:
  - <http://www.t1diabetes.nih.gov/investigator/resources.asp>
  - <http://www.betacell.org/>
  - [http://www.jdrf.org/index.cfm?page\\_id=104491](http://www.jdrf.org/index.cfm?page_id=104491)

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Assistance can be obtained Monday through Friday between 8:30am and 5pm U.S. Eastern Time.