JDRF REQUESTS LETTERS OF INTENT FOR:

VALIDATION OF T CELL BIOMARKERS AND ASSAYS FOR T1D

PURPOSE

JDRF is soliciting projects to validate high priority candidate T cell biomarkers for T1D and to transition associated assays to fit-for-purpose status. The purpose of this RFA is to encourage the T1D biomarker community to transition widely referenced T1D relevant T cell biomarkers and assays towards validation and standardization for uniform use across the research community.

BACKGROUND

The mission of the JDRF Immunotherapies program is to establish effective immune therapies to slow down, halt, and reverse the T1D disease process. Biomarkers have the potential to play a vital role as catalysts for the clinical testing of immune therapies for T1D, by enabling the design of more effective clinical trials on the path to their approval.

In type 1 diabetes (T1D), T cells play a key role in the destruction of insulin-producing beta cells. As such, they have been widely studied, both to better understand the disease and to evaluate responses to immune therapies in subjects with or at risk of T1D. The T cell biomarker community has actively pursued two categories of T cell biomarkers; antigen-specific and non-antigen-specific. In numerous studies, T cell biomarkers have allowed the unequivocal association of T cell activity with the T1D disease process and in recent efforts, intriguing associations between patterns of T cell changes and response to immune therapies have been emerging.

Despite recent advances, a comprehensive set of easily and reliably measurable T cell biomarkers are not available. Rapidly emerging technologies, including multi-omics approaches, are increasingly being utilized to evaluate T cells and add to the need to establish harmonized SOPs for T cell measurements. Large sample volumes and sample sets are particularly needed for projects that involve replicate and reproducibility testing, or assay optimization.

Cross sectional samples (and study-derived data) from the stage 3 disease setting are available from the T1D Exchange Biobank (https://t1dexchange.org/research/biobank/) for the purposes of this RFA. Please contact the T1D Exchange directly (biobank@T1DExchange.org) for more information.
Interrogation of other appropriate sample and data sets is also welcomed.

Through this RFA, JDRF aims to establish of a set of standardized T cell biomarkers and assays for T1D that can be updated and revised as new technologies and markers emerge.

SCOPE

This RFA is soliciting projects from the T1D Biomarker community that seek to establish validated T cell biomarkers and assays. Such projects may include:

- Standardization of key T cell assays to fit-for-purpose* status
- Optimization of T cell assays
- Harmonization, standardization and distribution of SOPs
- Blinded reproducibility testing of widely accepted assays across multiple labs

- Confirmation of novel T cell biomarkers in independent sample sets
- Validation of T cell biomarkers in large studies or trials

* analytical performance of assay meets minimal acceptance criteria to support measurement of intended (T cell) biomarker in a highly feasible manner

This RFA is **not intended to support** discovery studies for novel T cell related biomarkers using boutique (single lab) T cell assays.

MECHANISM & FUNDING LEVELS

In response to this announcement, LOI's can be submitted as the following mechanisms:

Strategic Research Agreement [SRA]

Comprehensive projects that are supported by preliminary data, may be submitted under the JDRF SRA mechanism. These projects will have distinct specific aims and deliverables.

The budget proposed per project should be no greater than $250K/yr for up to 3 years. Lower budget projects for shorter scope are also welcomed. The proposed budgets will be evaluated against the nature and scope of each project at the LOI stage.

Pilot and Pilot and Feasibility [PNF]
Short term pilot projects, with potential to evolve to larger efforts, are encouraged and should be limited to $150K for a 12-18 month period. These projects may involve small confirmatory studies as pre-requisites to larger efforts or critical assay optimization steps on which subsequent decisions would be dependent.

All yearly budgets include a maximum of 10% indirect costs.

For more information on the Strategic Research Agreement mechanism, please refer to our website: http://grantcenter.jdrf.org/information-for-applicants/grant-mechanism-descriptions/strategic-research-agreements/

Pilot and Feasibility LOIs should follow the same website guidelines as the Strategic research agreements with the smaller budget and focus referred to above.

ELIGIBILITY

Applicants must hold an M.D., D.M.D., D.V.M., Ph.D., or equivalent academic degree and hold a faculty position or equivalent at a college, university, medical school, or comparable institution.

Applications may be submitted by domestic or foreign non-profit organizations, public or private, such as colleges, universities, hospitals, laboratories, units of state or local governments, eligible agencies of the federal government, or for-profit organizations.

There are no citizenship requirements. 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.

LETTERS OF INTENT

Prospective applicants should submit a Letter of Intent [1 page maximum] 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.

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, **[5 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 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-Aug2015.pdf

SCIENTIFIC REVIEW CRITERIA

Applications will be subjected to confidential external scientific review and evaluated on the following:

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

Significance: What specific biomarker need is being addressed (purpose and utility)?

Relevance: Is the proposed research relevant to the objectives of this RFA? What will be the expected impact of these studies on the JDRF's mission to accelerate the path towards widely implementable biomarkers?

Approach: Are the conceptual framework, design, methods and analyses adequately developed, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics? Is the proposed research feasible within the term of the award? Are resources and knowledge based on prior experience and know-how?

Innovation: Does the project employ novel concepts, approaches or methods? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?

Investigator Experience: Is the investigator appropriately trained and well suited to carry out the planned studies? Is the work proposed appropriate to the experience level of the principal investigator? If the investigator does not have T1D experience, are there appropriate collaborative arrangements with experts in T1D? For collaborative projects, is the project well led and coordinated?

Environment: Does the scientific environment in which the work will be performed contribute to the probability of success? Do the experiments proposed take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

PROJECTED DEADLINES

- **RFA Release Date: .....May 20, 2019**
- **Letter of Intent Deadline.....August 1, 2019**
- **Notification of Full Application request.....August 21, 2019**
- **Application Deadline.....October 1, 2019**
- **Response to Applicants.....February 28, 2020**
- **Earliest Anticipated Start Date**.....**April 1, 2020**

CONTACTS

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RMS360 (http://jdrf.smartsimple.us)

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