JDRF REQUESTS LETTERS OF INTENT FOR: DISCOVERY AND DEVELOPMENT OF IMMUNE TOLERANCE DELIVERY SYSTEMS FOR ANTIGEN SPECIFIC THERAPIES IN TYPE 1 DIABETES

PURPOSE

JDRF is soliciting letters of intent (LOI) for the discovery, development and pre-clinical testing of tolerogenic delivery systems (TDS) of diabetes-specific autoantigens designed to prevent and/or reverse type 1 diabetes (T1D). JDRF is committed to translation of research findings towards clinical results and is most interested in projects that have clinical translation potential.

BACKGROUND

Inducing antigen-specific tolerance is one of the most elusive and most highly sought therapeutic goals in autoimmune diseases. Unfortunately, several independent disease prevention and treatment trials with antigen specific immunotherapies (ASIs) have been generally disappointing with respect to metabolic disease outcomes and no treatment has been shown to induce durable immune tolerance. These studies, nevertheless, provide compelling evidence of transiently enhanced regulatory T (T_{reg}) cell number and function, and reduced effector T cell (T_{eff}) cell numbers suggesting that immune tolerance might be achieved with the appropriate improvements to ASI therapy. Because most of these ASIs were comprised of antigen only, improvements can be made to enhance the potency of ASIs with tolerance-inducing agents. Tolerance delivery systems, e.g., tolerance-inducing adjuvants, can be combined with autoantigen to achieve such an improvement in ASI potency. Several tolerance-inducing ASIs have been described and tested in preclinical models which showed an ability of ASIs to enhance various types of T_{reg} cells that could suppress specific pathogenic autoimmune responses. It should be noted that such approaches offer a platform technology that can be applied to other autoimmune and allergic conditions with the provision of disease-relevant antigen(s).

OBJECTIVES/SCOPE

Letters of interest are sought from investigators interested in discovering and developing novel tolerance delivery systems for the prevention and/or treatment of T1D. In general, such efforts include incorporation of tolerance-promoting agents with autoantigen to optimize potency of ASIs, development of tools and technologies for autoantigen delivery, and the repurposing tolerance approaches developed for other immune diseases by evaluation in T1D-relevant models. The ideal tolerance delivery system is expected to enhance potency relative to antigen alone, create a durable tolerogenic response, and show an appropriate level of safety (i.e., avoiding general immunosuppression). The clinical translation potential of the investigations should be emphasized. This initiative encourages collaborations between experts in the fields of bioengineering, immune tolerance, and T1D. However, investigators with assays or hypotheses relevant to this initiative are welcomed to apply.

Examples of relevant topics include, but are not limited to:

- Improvements in the potency of particulate delivery vehicles/substrates (e.g., nanoparticles, apoptotic cells, liposomes, etc.)
- Identification of superior tolerance-inducing agents and delivery systems by performing rigorous comparisons of potency and activity of existing and novel entities to induce immune tolerance
- Repurposing of tolerance delivery systems for use in T1D that have been used successfully in or are being developed for other autoimmune/allergic indications
- Development of existing and novel immune tolerance-promoting molecules and agents for incorporation into tolerance-delivery systems for ASIs
- Tolerance-delivery systems designed to exploit novel molecular targets to achieve immune tolerance
- Generation and evaluation of antigen presenting cell targeting systems for autoantigen delivery
- Improvements in stability and/or potency of autoantigen for delivery of mucosal tolerance
- Development of tolerance-inducing viral and bacterial delivery systems

This RFA is not intended to support: immunotherapies not of an antigen-specific nature; research on identifying novel T1D autoantigens; development (including clinical analysis) of ASIs comprised of antigen alone (i.e., “naked” antigen).

Applicants who wish to consult with JDRF Program Staff to discuss the responsiveness of their proposal to this program or to discuss ideas or resources that might benefit this initiative may do so. Enquiries in this area should be referred to contacts as shown below.

Collaborative efforts engaging investigators with complementary expertise are highly encouraged.

ANNOUNCEMENT INTRODUCTION AND PUBLIC Q&A

JDRF will hold announcement introduction meeting via web and teleconference on **November 16, 2015 at 1-2 PM** US Eastern time, to which all interested 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. A brief introduction on JDRF’s new grant application portal (RMS360) will also be given.

Click on this link: Join WebEx meeting
Meeting number: 730 077 293
Meeting password: research2015

Join by phone
Dial in (US): 877-261-5012
Dial in (Int'l): https://www.intercallonline.com/listNumbersByCode.action?confCode=5908746746
Conference code: 59 08 74 67 46

MECHANISM

Up to a maximum of $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.

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/

ELIGIBILITY

Applications may be submitted by domestic and foreign for profit and 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. Please note that additional information will be requested of applicants from for-profit entities or industry collaborations with academia if a full application is invited.

For clinical studies, applicants must hold an appointment or joint appointment in a subspecialty of clinical medicine, and conduct human clinical research.

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.

LETTER OF INTENT

Prospective applicants should submit a Letter of Intent, [**2 pages 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. Applicants will be notified approximately eight weeks after the LOI deadline date if they have been approved to submit a full 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 on the RMS360 (http://jdrf.smartsimple.us). Proposal section templates in MS 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 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://jdrf.org/grant-center/information-for-applicants/how-to-apply/application-guidelines/#human-subject-requirements

SCIENTIFIC REVIEW CRITERIA

Applications will be evaluated based on JDRF's confidential evaluation including:

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

Significance: Does this study address an important problem? Will the expected results have an impact on the performance of ASIs or IM therapeutics?

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?

Approach: Are the conceptual framework, design, methods and analyses adequately developed, well integrated 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

- **LOI Release Date**: .....October 19, 2015
- **Announcement Intro Meeting.**.....November 16, 2015
- **Letter of Intent Deadline**: .....December 3, 2015
- **Notification of Full Application Request** .....January 19, 2016
- **Application Deadline**: .....March 2, 2016
- **Response to Applicants**:.....July 2016
- **Earliest Anticipated Start Date**: .....September 2016

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