



IMMUNOTHERAPIES RFA WEBINAR

15 November 2015

Request for LETTERS OF INTENT for selection to FULL PROPOSALS

DISCOVERY AND DEVELOPMENT OF IMMUNE TOLERANCE DELIVERY SYSTEMS FOR ANTIGEN SPECIFIC THERAPIES IN TYPE 1 DIABETES

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Agenda

- Goal/Objectives of RFA
- Therapeutic rationale for improving ASIs
- Examples of investigation topics
- Proposal submission process

Long-Term Goal

To treat T1D by *restoring and then maintaining* immune tolerance to halt or reverse disease progression in prediabetes (including at-risk), new-onset, established disease*

- via potent antigen-specific immunotherapy (ASI) in combination with immunomodulatory agents

* See recent T1D staging criteria publication: Insel, R.A. (2015) *Diabetes Care* 38:1964

Objectives

To discover and develop novel Tolerance Delivery Systems (TDS) antigen-specific immunotherapies (ASIs) for the prevention and/or treatment of T1D.

The ideal TDS 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).

Therapeutic Rationale

1. Clinical Observations

- ASIs (mainly “naked antigen”) have not shown robust or durable metabolic outcomes in disease prevention or treatment trials.
- However, ASIs can lead to the desired but “transient” immune regulatory outcomes (increases in Treg/decrease in Teff cells) and sometimes slowing of metabolic decay.

2. Challenge: These observations of immune mechanistic outcomes suggest that the desired metabolic outcomes could be achieved with improvements in ASIs.

3. Solutions

- Develop more potent ASIs with novel Tolerance Delivery Systems (TDS; i.e., tolerance adjuvant)
- Create conditions better suited for ASIs to induce a robust Treg development and function that will lead to durable immune tolerance that prevents re-occurrence of autoreactivity. – covered in another RFA (see website)

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

- Improvements in the potency of particulate delivery vehicles/substrates (e.g., nanoparticles, apoptotic cells, liposomes, etc.) for TDSs of ASIs
- Identification of superior tolerance-inducing agents and ASI delivery systems by performing rigorous comparisons of potency and activity of existing and novel entities to induce immune tolerance
- Repurposing of TDSs for use in T1D that have been used successfully in or are being developed for ASIs in other autoimmune/allergic indications
- Development of existing and novel immune tolerance-promoting molecules and agents for incorporation into TDSs for ASIs
- TDS 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 ASIs for 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).

Collaborations during and after funding

- This initiative will give priority to applications that involve collaborations between experts in the fields of bioengineering and immune tolerance (with emphasis in T1D).
- The clinical translation potential of the investigations is also central to this call.
- Depending on progress, JDRF may identify synergistic projects and approach Investigators for non-confidential discussions about their projects. These discussions have in the past led to fruitful collaborations.

Funding Mechanism and Eligibility

■ Funding Mechanism

- Up to a maximum of \$250,000 USD per year including 10% indirect costs for up to 2 years
- Level of funding will vary depending on the scope and overall objectives of the proposal.
- Pilot proposals may be identified from LOIs that do not move forward to full SRA applications – applicants will be notified if so
- Projects would be funded as:

Strategic Research Agreements (SRA) (<http://grantcenter.jdrf.org/grant-center/information-for-applicants/grant-mechanism-descriptions/strategic-research-agreements/>)

■ Eligibility

- 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
- Applications from for-profit entities or industry collaborations accepted

PROPOSAL SUBMISSION PROCESS

RFA Timeline:

- **Letter of Intent Release:** Wednesday October 21, 2015
- **Letter of Intent Submission Deadline:** Thursday December 3, 2015
 - Applicants should register and submit their completed letter of intent application in RMS360 (<http://jdrf.smartsimple.us>).
- **Notification of Full Application Request:** Tuesday January 19, 2016
- **Full Application Submission Deadline:** Wednesday March 2, 2016
- **Earliest Response to Applicants:** July 2016
- **Earliest Anticipated Start Date:** September 2016

Letter of Intent/Full Proposal Application

Letters of intent and full proposal applications should be submitted via the RMS360 system (jdrf.smartsimple.us) using the research plan template provided and including the following information:

- Background /Rationale and Specific Aims of overall project
- Overview of hypotheses, goals, deliverables and collaborative framework as applicable
- Title, lead investigator and a description and specific aims of individual projects (if collaborative/network)
- Expected deliverables and impact of the proposed study with potential next steps
- Intellectual Property or commercial efforts associated with the current application
- Total budget / budget by year by project
- Biosketches for all Principal Investigators and Key Personnel

RMS360

- JDRF is using a grants management system to collect online application submissions called RMS360. The RMS360 link is as follows: https://jdrf.smartsimple.us/s_Login.jsp.
 - Please note that if you are new to the system, you must register and log in details will be generated.
- Call details and deadlines can be found in the “Funding Opportunities” tab of RMS360.
- All materials and templates pertaining to the application can be found once you’ve initiated an application in RMS360.
- It is recommended to use Google Chrome or Firefox when using RMS360, as these browsers are most compatible with the system.

Where should questions be directed?

- Questions on, scientific suitability of proposals:
 - David Alleva (dalleva@jdrf.org)
 - Simi Ahmed (sahmed@jdrf.org)
- Questions on eligibility, logistics, deadlines or submission problems:
 - Karen Ng (Kng@jdrf.org)
- 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.



THANK YOU