

JDRF REQUESTS APPLICATIONS FOR: THE ROLE OF THE MICROBIOME IN TYPE 1 DIABETES

PURPOSE

JDRF is soliciting applications to investigate the role of the microbiome in type 1 diabetes (T1D). JDRF is committed to and most interested in proposals that focus on research that provide insights into developing safe approaches to augment, accelerate, or induce robust microbiome-induced immunoregulation in childhood.

BACKGROUND

Recent evidence has demonstrated that the intestinal microbiota of young infants at risk for developing childhood-onset autoimmune and allergic disease is altered with differences in expression of LPS, a TLR-ligand, and degree of colonization with bifidobacteria. In addition, children who develop T1D have an altered intestinal microbiota with decreased diversity and greater instability to perturbations. The triggers or etiologies of these associations are incompletely understood and the mechanism(s) of their potential contribution to disease have not been elucidated. A greater understanding of the complex interactions between the intestinal microbiota and several interacting systems in the body (immune, intestinal integrity and function, metabolism, beta cell function, etc.) may provide both scientifically rational approaches to prevent development of childhood immune and allergic diseases and biomarkers to evaluate the efficacy of interventions.

The dynamic cross-talk between the microbiota and the host through signaling from both microbial metabolites and surface molecules leads to development and maturation of healthy immunoregulation. Lessons from animal models have provided some insights into critical signaling pathways activated by metabolites or by microbial associated molecular patterns signaling through conserved pattern recognition receptors. Although there are likely multiple signaling pathways, it is conceivable that signaling through a limited number of conserved pathways are required for induction of healthy immunoregulation in the young host. Vaginal delivery and breast milk likely confer or reinforce these key signaling pathways.

OBJECTIVES

A better understanding of the mechanisms of development of a healthy microbiota and microbiota-induced immunoregulation in health and its alteration in childhood-onset T1D is required. Also, associated with altered microbiota induced immunoregulation may be alteration in intestinal integrity, which could contribute to the pathogenesis of T1D. **The major focus of this RFA will be to investigate the role of the microbiome in human T1D. Potential questions to address include, but are not limited to:**

- Development.** Does perturbed development of the intestinal microbiota in early childhood contribute to susceptibility to T1D? If so, what are the mechanisms? What are the effects on intestinal integrity, immune system, metabolism and beta cell development and function?
- Microbiota containment.** Does altered intestinal permeability/integrity contribute directly to susceptibility or pathogenesis of T1D? If so, what are the mechanisms? How can its detection be refined and quantified? What interventions can correct?
- Health.** What is the basis of healthy microbiota-induced regulation? How can this be detected in the periphery? Does trained innate and adaptive immunity via epigenetic programming play a role?



Prevention and therapy. What interventions can induce or preserve the development of a healthy microbiota-induced regulation in infancy?

Collaborative projects, where possible, to interrogate common sample or data sets are encouraged, and higher budgets may be allowed for such projects. Please communicate with the scientific contact listed on this RFA prior to submission of an application for approval of such projects.

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 RFA, however, additional information will be requested from for-profit entities if a full application is invited.

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.

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 2 years may be requested. The level of funding will vary depending on the scope and overall objectives of the proposal.

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://grantcenter.jdrf.org/rfa/>

RFA COMPONENTS

Applications should include the following information:

- Background and Significance of this work to Type 1 Diabetes
- Proposed research (What?)
- Rationale for proposed research (Why?)
- Research Design and Methods (How?)
- Advantages over alternative approaches that would address goal.
- Future plans if research is successful.

PROPOSAL

The application must be completed using the templates provided on the RMS360 (<http://jdrf.smartsimple.us>). Proposal section templates in MS Word [**10 page 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.



ANNOUNCEMENT INTRODUCTION AND PUBLIC Q&A

JDRF will hold announcement introduction meeting via web and teleconference on **January 4, 2017 at 2:00pm** US Eastern Standard 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 here to Join WebEx meeting Meeting number (access code): 735 125 168 Meeting password: 4v8b3CiD

Join by phone 1-866-469-3239 Call-in toll-free number (US/Canada) **1-650-429-3300** Call-in toll number (US/Canada)

[Global call-in numbers](#) | Toll-free calling restrictions

DEADLINES

- Release Date:** December 22, 2016
- Application Due Date:** March 1, 2017
- Response to Applicants Date:** June 2017
- Earliest Anticipated Start Date:** July 2017

SUBMISSION INSTRUCTIONS

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

REVIEW CRITERIA

Applications will be evaluated based on JDRF's standard confidential award policy and according to the following criteria:

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

CONTACTS

SCIENTIFIC CONTACT

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