JDRF REQUESTS EXPRESSIONS OF INTEREST (EOI) FOR:
THE ROLE OF THE MICROBIOME IN TYPE 1 DIABETES:
PATHOGENESIS AND THERAPEUTIC UTILITY

PURPOSE
JDRF is soliciting EOs to investigate the role of the microbiome in type 1 diabetes (T1D). JDRF is most interested in research that focuses on understanding the role of the intestinal microbiome in T1D pathogenesis and utilizing these insights to develop therapeutic approaches to slow or stop T1D progression.

BACKGROUND
Recent evidence has demonstrated that alterations in several features of the intestinal microbiome are linked with the onset of T1D. These features include, but are not limited to, decreased microbial diversity, degree of colonization with strains of individual microbes, altered metabolite production, and to a lesser extent altered intestinal virome and increased intestinal permeability. Genetics and several environmental risk factors associated with T1D pathogenesis have also been shown to modify the intestinal environment and alter overall intestinal health. The interplay between the intestinal microbiome, genetics and environment is not completely understood and has made it difficult to consistently identify disease modifying features across populations. A greater understanding of the complex interactions between the intestinal microbiome (bacteria, viruses, fungi and bioactive metabolites) and several interacting systems in the body (immune, intestinal integrity and function, metabolism, beta cell function, etc.), as well as the identification of potential mechanism(s) is needed for the identification of therapeutic targets to prevent or delay the progression of T1D. Recent data from animal models and human cohorts suggest that intervening on these pathways via probiotics or direct metabolite supplementation may have beneficial disease modifying effects.

OBJECTIVES
A better understanding of the mechanisms involved in the development of a healthy microbiome and microbiome-induced immunoregulation and its alteration in T1D is required. The major focus of this RFA will be to investigate the role, function and therapeutic potential of the microbiome in human T1D. Potential questions to address include, but are not limited to:

- **Prevention and therapy.** What interventions can induce or preserve the development of a healthy microbiome-induced immune regulation? Can personalized intervention strategies be developed for those already experiencing dysbiosis? Can synthetic biology help develop probiotic strategies that are specific to the patient and T1D? Can systems biology approaches be utilized for the identification of novel therapeutic targets?

- **Development.** What is the basis of healthy microbiota-induced immunoregulation? How does perturbed development of the intestinal microbiome in early childhood contribute to susceptibility to T1D and what are the mechanisms? What are the effects on intestinal integrity, immune system, metabolism and beta cell development and function? Can genomic, proteomic, transcriptomic, and metabolomics approaches help improve our understanding of the microbiome-immune interaction? What therapeutic strategies can be implemented to prevent or delay the progression of T1D?
- **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 modify this mechanism?

- **Resolving the Microbiome Ecosystem.** What role, if any, do non-bacterial components of the intestinal microbiome (viruses, fungi, phages etc.) play in T1D pathogenesis? If one of these components is implicated, what are the mechanisms involved in disease pathogenesis? How can these be therapeutically targeted in T1D disease progression?

Collaborative projects, to interrogate common sample or data sets are encouraged, and higher budgets may be allowed for such projects and should be discussed with the scientific contact listed on this EOI prior to submission.

**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 EOI, 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.

Applicants that are currently or have previously been members of the JDRF Microbiome Consortium must be in good standing with JDRF’s data sharing policy to be considered for this funding opportunity. Successful applicants will be required to join the JDRF Microbiome Consortium.

**EOI COMPONENTS**

Prospective applicants should submit an expression of interest that is no more than 2 pages in length online via RMS360 (http://jdrf.smartsimple.us) to be considered for a full proposal request. The EOI template provided on the RMS360 website must be used to complete the application. Applicants will be notified approximately three weeks after the EOI deadline date if they have been approved to submit a full application.

**EOI proposals should include the following information.**

- Impact
- Proposed research (What?)
- Brief description of rationale for proposed research (Why?)
- Brief description of research design and methods (How?)
- Advantages over alternative approaches that would address goal, if applicable
- Future plans if research is successful and potential translational impact
- Projected deliverables for the project if successful
- Anticipated budget
- Confirmation of sample access (does not count towards page limit)

**DEADLINES**
- **Release Date**: Wednesday, September 25, 2019
- **Expression of Interest Deadline**: Wednesday, November 6, 2019
- **Notification of EOI Outcome**: Tuesday, November 26, 2019
- **Full Proposal Deadline**: Tuesday, January 14, 2020
- **Response to Applicants**: By April 30, 2020
- **Earliest Anticipated Start Date**: July 1, 2020

**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 for pilot and feasibility studies without significant preliminary data.

- **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/](http://grantcenter.jdrf.org/rfa/)

**PROPOSAL**
An approved **Expression of Interest 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 online via JDRF's on-line research management system, **RMS360** ([http://jdrf.smartsimple.us](http://jdrf.smartsimple.us)). Proposal section templates in MS Word **[12 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.

**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
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).

CONTACTS

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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 technical issues with RMS360, 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.