REQUEST FOR APPLICATIONS:
DECODING IMMUNE MEDIATED DISEASES – NOVEL APPROACHES FOR THERAPEUTIC INSIGHTS

PURPOSE

JDRF International, in partnership with the **Lupus Research Alliance** and the **National Multiple Sclerosis Society**, is soliciting Letters of Intent (LOI) from investigators across autoimmune (and other relevant) fields to advance the understanding of autoimmunity and to obtain more specific insights into commonalities and differences of immune pathways that govern these pathogenic processes. The incomplete knowledge of immune networks, pathways, disease pathogenesis and heterogeneity across multiple autoimmune diseases remains a challenge towards achieving optimal therapies to effectively treat all subjects in a given indication. The purpose of this call is to invite innovative ideas that address needs across multiple autoimmune diseases in novel ways that may allow us to make faster progress together. Applications must address one or more of the following autoimmune diseases: Type 1 Diabetes (T1D), Systemic Lupus Erythematosus (SLE) and Multiple Sclerosis (MS).

BACKGROUND

Autoimmune diseases are chronic disorders in which the immune system produces an inappropriate response against its own cells, tissues and/or organs that results in inflammation and damage. More than 100 autoimmune diseases have been identified to date. An incomplete knowledge of disease pathogenesis and heterogeneity among patients is very common in many autoimmune diseases, representing a real challenge that impacts the effectiveness of clinical trial design and the ability to predict whether a person will respond to a given treatment.

For some autoimmune diseases there are no approved immunotherapies (e.g. T1D) and for other diseases where multiple therapies are approved and already in clinical use, significant number of subjects do not respond to disease-modifying therapies. Importantly, the approved therapies in some conditions, such as SLE and MS, do not prevent disease progression and end-organ damage. While there are differences in successes and challenges across autoimmune diseases, there are overarching themes that can guide progress across multiple diseases. Common challenges, such as disease heterogeneity in SLE, MS and T1D; common features including the association of autoantibodies in the pathogenesis of SLE, Rheumatoid Arthritis (RA) and T1D, and the identification of self-antigens as key players in diseases such as MS, T1D, and Thyroiditis suggest: 1) the existence of intricate networks of autoimmune activity that may connect or differentiate these diseases from each other; and 2) the need for tools to study them.

Unraveling such overarching networks may reveal a wide selection of targetable pathways that may be shared or distinct between diseases. With the recent advances in human immunology and the advent of cutting-edge technologies, including advanced machine learning capabilities, autoimmune communities can now ask new questions or revisit old ones with new tools and for deeper, new insights. These discoveries may open new avenues of research and greatly accelerate therapeutic development.

OBJECTIVE & SCOPE

The overall objective of this RFA is to stimulate new research on common mechanisms of autoimmunity to generate new insights for novel therapeutic approaches. Letters of Intent are sought from investigators

interested in partnering to understand commonalities of autoimmune diseases by identifying networks and pathways involved in their immune-pathogenesis of diseases, in order to establish immune signatures, biomarkers and targets of effective therapies

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

- Parallel interrogation of predictive or pharmacodynamic biomarker data from existing disease specific immunotherapy trial data sets for deeper insights into therapeutic response pathways.
- Analysis of clinical samples that would allow understanding of common mechanisms using new technologies.
- Exploitation of existing datasets across autoimmune diseases using machine learning approaches to gain deep mechanistic insights into common or different pathways of autoimmunity and identification of immune pathway-specific patient subsets.
- Generation of immune networks from existing tissue banks across autoimmune diseases to connect tissue infiltrates and peripheral signatures using novel technologies and algorithms.
- Short clinical studies across diseases for the identification of immune pathways and networks that associate with response to different classes of immune therapy in different indications.
- Exploration of novel approaches to study processes that may be different between organ-specific versus systemic autoimmunity.
- Exploration of combination therapies across diseases.

Please note that groups with relevant cross-disease area datasets, sample sets and other expertise are strongly encouraged to apply to this RFA.

This RFA is not intended to support pre-clinical/animal studies, creation of novel natural history cohorts, assay optimization, nor single disease specific studies.

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

FUNDING MECHANISMS

All applications must include at least two or more autoimmune disease areas, including at least one of the following autoimmune diseases: Type 1 Diabetes (T1D), Systemic Lupus Erythematosus (SLE) and Multiple Sclerosis (MS). Applications must utilize novel technologies and/or analytical approaches in a multidisciplinary manner. In response to this announcement, LOI's can be submitted under one of the following mechanisms:

Strategic Research Agreement (SRA)

For Strategic Research Agreements, proposed project budgets should not exceed **$750,000 USD** *(including 10% indirect costs)* total costs for up to three years. The level of funding will vary depending on the scope and overall objectives of the proposal. Under the terms of the grant award, written semi-annual reports will be required from the funded investigator as a basis for continued support.

Pilot & Feasibility (PNF)

Pilot & Feasibility projects, with potential to evolve to larger efforts, are encouraged, and should be limited to a total proposed project budget of **$200,000 USD** *(including 10% indirect costs)* total costs for up to two years. Although Pilot & Feasibility proposals have a smaller budget and focus, applicants should follow the same website guidelines as Strategic Research Agreements.

Investigators funded through this RFA will be required to participate in regular meetings of the group and share progress and data under confidentiality.

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

Projects involving parties with complementary expertise are highly encouraged to submit to this RFA. This may include collaborations between research and clinical groups, science groups with technology experts, and public-private partnerships.

There are no citizenship requirements. To assure continued excellence and diversity among applicants and awardees, this RFA 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; 5 page maximum for pilots**] 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.

SUBMISSION INSTRUCTIONS

Applicants must register as an applicant and submit their application in response to this RFA using RMS360, JDRF's grant management system (https://jdrf.smartsimple.us).

PROJECTED TIMELINE

- **RFA Release Date: .....** Wednesday May 29th, 2019

- **Letter of Intent Deadline**…… Monday September 9th, 2019
- **Notification of LOI Outcome**……Friday October 11th, 2019
- **Full Proposal Deadline**……Tuesday December 3rd, 2019
- **Earliest Response to Applicants**…… May 2020
- **Earliest Anticipated Start Date**…… August 2020

SCIENTIFIC REVIEW CRITERIA

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

- Significance
- Relevance
- Approach
- Innovation
- Investigator Experience
- Environment
- Resource sharing plan

Significance: Does the proposal address an important aspect of the RFA?

Relevance: Is the proposed research relevant to the objectives of this RFA?

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 challenge existing paradigms or address an innovative hypothesis, novel target or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools or technologies for this area?

Investigator Experience: Are the lead investigator and collaborators qualified and well-suited to carry out the proposed research?

Environment: Is the research environment appropriate and likely to contribute to the success of the proposed research? Doe the environment foster collaborative arrangements that may support the proposed research activities? Is the research environment compliant with appropriate rules and regulations for study conduct?

Resource Sharing Plan: Does the application make adequate provisions for sharing resource (data and/or samples), stemming from this project, with the wider research community?

PROGRAM CONTACTS

Scientific Inquiries may be addressed to:

Simi Ahmed, Ph.D.
Director, Immunotherapies
JDRF International
☎ 212-479-7679

💻 sahmed@jdrf.org

Administrative Inquiries may be addressed to:

Jami Goodman
Project Manager, International Partnerships
JDRF International
☎ 212-479-7603
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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 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

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ABOUT JDRF INTERNATIONAL:

JDRF is the leading global organization focused on type 1 diabetes (T1D) research. Driven by passionate, grassroots volunteers connected to children, adolescents, and adults with this disease, JDRF is now the largest charitable supporter of T1D research. The goal of JDRF research is to improve the lives of all people affected by T1D by accelerating progress on the most promising opportunities for curing, better treating, and preventing T1D. JDRF collaborates with a wide spectrum of partners who share this goal. For more information, visit www.jdrf.org.

ABOUT LUPUS RESEARCH ALLIANCE:

The Lupus Research Alliance aims to transform treatment while advancing toward a cure by funding the most innovative lupus research in the world. The organization's stringent peer review grant process fosters diverse scientific talent who are driving discovery toward better diagnostics, improved treatments and ultimately a cure for lupus. Because the Lupus Research Alliance's Board of Directors fund all administrative and fundraising costs, 100% of all donations goes to support lupus research programs. For more information, visit lupusresearch.org.

ABOUT NATIONAL MULTIPLE SCLEROSIS SOCIETY:

The Society mobilizes people and resources so that everyone affected by multiple sclerosis can live their best lives as we stop MS in its tracks, restore what has been lost and end MS forever. Last year, the Society invested $35 million in MS research with more than 340 active projects around the world. Through its comprehensive nationwide network of services, the Society is focused on helping people affected by MS connect to the people, information and resources needed to live their best lives. We are united in our collective power to do something about MS now and end this disease forever. Learn more at nationalMSsociety.org. Early and ongoing treatment with an FDA-approved therapy can make a difference for people with multiple sclerosis. Learn about your options by talking to your health care professional and contacting the National MS Society at nationalMSsociety.org or 1-800-344-4867.