ENDIA
environmental determinants of islet autoimmunity

JDRF IMPROVING LIVES. CURING TYPE 1 DIABETES.

Australian Type 1 Diabetes Clinical Research Network

THE LEONA M. AND HARRY B. HELMSLEY CHARITABLE TRUST

Request for Applications

Accelerating Collaborative Research in Type 1 Diabetes Etiology and Pathogenesis using Biosamples from an Observational Clinical Study

Applications Open	6 February 2023
LOI Deadline	7 April 2023
Invitation to Full Proposals^	15 May 2023
Full Proposal Deadline*	11 July 2023
Funding Announcements^	September 2023
Latest Start	December 2023

*Institutional Research Offices are required to submit full proposals in RMS360 and may have an internal closing time which precedes this deadline.
^Subject to change.
Deadlines are at 11:59 pm AEST/AEDT.

Click Here to Apply

1. Purpose

This Request for Applications (RFA) seeks applications for new collaboration with the Environmental Determinants of Islet Autoimmunity (ENDIA) Study Group to support investigative research on the etiology and pathogenesis of type 1 diabetes (T1D) using data and biosamples collected from the ENDIA cohort. This funding opportunity is intended to create collaboration among leading experts around the world to answer important unknowns about disease mechanisms with the long-term aim of T1D prevention. Applications from investigators whose expertise lie outside of T1D are encouraged.

2. Background

The Environmental Determinants of Islet Autoimmunity (ENDIA) is the world's first study from pregnancy to investigate how the environment interacts with an individual's genes to drive the development of islet autoimmunity leading to dysfunction of beta-cells and T1D.

In 2019, ENDIA completed recruitment of 1,473 children born in Australia who have an immediate relative with T1D. In addition to screening for islet autoimmunity, ENDIA has been collecting a rich and diverse set of biosamples and clinical data from the children (see ENDIA Resource Availability and Supplementary Information) starting from the first to third trimester of pregnancy through to early childhood up until 10 years of age.

A nested case-control (NCC) subcohort comprising the first 54 children who developed persistent islet autoimmunity (single or multiple islet autoantibodies) has been established to investigate preliminary associations between environmental and genetic factors that contribute to the development of islet autoantibodies in early childhood. Several investigations are already underway including the analyses of the gut microbiome and metaproteome, gut and respiratory virome, circulatory cytokines, proteome, lipidome, metabolome, glycome and miRNAs, immune cell phenotyping, function, and genomics.

It is projected that most ENDIA children who will develop multiple islet autoantibodies will seroconvert by 2024 (n≈80 multiple autoantibody/T1D, n≈70 single autoantibody). After this time, the full ENDIA cohort will be available for data-driven investigations based on clinical exposures such as growth, diet, and other data collected prospectively via questionnaires. A case-cohort study will be designed for molecular discovery, validation, and hypothesis-driven investigations, including studies based on NCC and other T1D-risk cohort outcomes generated globally.

Accessing biosamples from T1D-related observational studies has been historically challenging. This hinders the study of factors that influence disease pathogenesis by investigators who lack direct access to biosamples and therefore the development of new therapeutic approaches to prevent or delay disease onset. The highly precious resources of ENDIA, spanning pregnancy, birth, and early life, holds tremendous potential to expand investigation into the underlying mechanisms in T1D etiology and pathogenesis ultimately to slow or stop T1D progression.

To that end ENDIA is seeking new collaborations outside of its current network to strengthen prior achievements and to create opportunities to investigate new hypotheses.

The JDRF Australian Type 1 Diabetes Clinical Research Network (T1DCRN) and The Leona M. and Harry B. Helmsley Charitable Trust (Helmsley) have been supporting ENDIA since 2015. The partnership is committed to advancing the development of T1D prevention strategies to positively impact the lives of people with T1D.

3. Objectives of this RFA

The main objective of this RFA is to support collaborations with ENDIA investigators to accelerate understanding of T1D etiology and pathogenesis during gestation and early childhood.

This RFA seeks new collaborators outside of the current network of ENDIA investigators to carry out research using data and biosamples from ENDIA. Relevant proposals led by investigators whose expertise lie outside of the T1D field are also encouraged.

In addition to biosamples, relevant clinical metadata and additional support from ENDIA (e.g., to answer questions around availability of samples, sampling protocols and cohort characteristics) will be provided. Funding will be provided by the JDRF Australia and Helmsley to cover project activities.

Of specific interest are research plans that:

i. Explore novel scientific questions using cutting edge technologies, in areas including but not limited to pancreatic, immune or metabolic research that advance understanding of the early life etiology and pathogenesis of T1D. Applications that demonstrate a strong translational potential to accelerate T1D prevention strategies will be prioritized.

ii. Complement ongoing research approaches and analyses being carried out by ENDIA. Published findings from the ENDIA study are available here. A list of ongoing research projects is provided in the Supplementary Information. Novel investigations that can be integrated with existing studies are encouraged.

iii. Are validated for use with the small sample volumes associated with young children and pregnancy. Merging of resources with other observational cohorts is encouraged.

4. Collaboration and Engagement with ENDIA

Prior to commencing the application process interested parties are strongly encouraged to visit the ENDIA website and consider availability of biosamples and data. Applicants are also encouraged to contact the ENDIA team to discuss their concepts and check their expectations for samples and data prior to submission. Initial contact can be made by emailing to endia@adelaide.edu.au (see Section 11).

ENDIA is a highly collaborative and progressive program with established strong governance and data, resource sharing and publication policies to guide new partnerships. The University of Adelaide is the custodian of the ENDIA biobank and data registry. As such, collaborations formed with ENDIA will need to comply with ENDIA's Governance Policy and the University of Adelaide's Research Data and Primary Materials Policy.

Successful applicants are expected to engage with the ENDIA program in a close collaborative and productive way. This includes working with the relevant members of the ENDIA Steering Committee and participating in ENDIA meetings. Successful applicants are also expected to return unused biosamples and participant-level data generated by their projects to the ENDIA databank/biobank within a pre-agreed time after completion of analysis.

Successful applicants will be required to form a partnership with an ENDIA investigator affiliated with an Australian institution.

5. Application Process

All submissions are to be made using JDRF's online grants management portal RMS360 (http://jdrf.smartsimple.us, see User Guide for details). Applicants are required to login to RMS360 to access supporting documents and templates.

Information submitted are collected, stored and shared in accordance with the JDRF T1DCRN policies on protecting Privacy and managing Conflict of Interest.

The application process will involve two stages.

Stage 1: Submission of LOIs

LOIs can be submitted by investigators based in Australia or internationally.

The following materials are to be included in the LOIs.

i. **A Research Plan** (2 pages maximum) structured as follows:
   a. *Background:* Identify existing evidence and data that justify the proposed study.
   b. *Activities:* Describe proposed project activities. Define risks and outline mitigation strategies.
   c. *Sample requirement:* The sample type (e.g., cells, stool, serum etc.), the minimum volume, approximate numbers and any particular participant characteristics that are required.
   d. *Expected outcomes:* Describe what the research plan aims to produce by the end of the funded project.
   e. *Impact on the field:* How might your proposed project advance knowledge of T1D pathogenesis, above and beyond other studies?
   f. *Project team:* Describe the key members of the project team and any relevant departmental/institutional resources.
   g. *Timeline:* When are key milestones expected to be achieved.

ii. **Bio-sketches** of key members of the project team (using NIH/ JDRF format).

iii. **Indicative Budget**: A high level annual budget for the proposed research.

Stage 2: Full Proposals

Shortlisted LOIs will be invited to submit full proposals. In addition to the materials submitted in the LOI the following information will be required in the full proposal.

i. **Detailed Research Plan,** elaborating on the proposal outlined in the LOI, and addressing limitations identified by ENDIA or external experts.

ii. **Detailed Budget and Justification**: A detailed composite budget for each grant year with clear costing model and justification for use of funds.

iii. **Letters of Institutional Support**.

iv. **Data and Sample Management Plan:** Details of how data/samples from the study will be returned to ENDIA's repositories.

6. Selection Criteria

The ENDIA Steering Committee and external reviewers, where appropriate, will review LOIs and Full Proposals. Proposed research will be assessed based on the criteria below.

i. Feasibility of completion within the proposed time frame and in relation to available ENDIA samples.

ii. Novelty and innovativeness in approach in addressing current knowledge gaps

iii. Significance for understanding the early life factors that initiate and drive the development of islet autoimmunity.

iv. Significance for understanding the processes that drive the progression of disease from autoimmunity to clinical manifestation of T1D.

v. Significance for translation to risk assessment and prevention, and the expected outcomes of the scientific plan.

vi. Expertise and ability of the project team.

vii. Appropriateness of budget.

7. Eligibility

i. Applicants must hold a Ph.D., M.D. or equivalent academic degree.

ii. Any individual with a faculty-level (or equivalent) appointment at an institution performing biomedical research, with the skills, knowledge, and resources (individual and institutional) necessary to carry out the proposed research.

8. Exclusion Criteria

i. LOIs that are not invited for a full proposal.

ii. Full proposals that vary significantly in scope and budget from LOIs.

9. Funding and Contractual Requirements

Applicants may request funding for a maximum of two years, subject to sufficient funding being available and continued satisfactory progress of the study. The level of funding for individual projects will vary depending on the scope of work. Requested funding amounts can range based on activities but should not exceed AUD 800,000 (USD 600,000) over two years.

Funding will be administered by the JDRF Australia T1DCRN. Successful applicants will be required to form a contractual partnership with an Australian administrating institution affiliated with the ENDIA Study Group.

Administrating institutions will be required to sign a Funding Agreement with JDRF Australia that outlines funding and partnership terms of the funders.

Grants awarded through the JDRF Australia T1DCRN are listed on the Australian Competitive Grants Register. As such, indirect costs can be recovered through Research Block Grants funding.

10. Submission Checklist

LOI

☐ Research Plan

☐ Bio-sketches

☐ Indicative Budget

Full Proposal

☐ Detailed Research Plan

☐ Detailed Budget and Justification

☐ Letters of Institutional Support

☐ Data and Sample Management Plan

11. Contacts

For enquires on strategic fit and resource access

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RMS360 related issues

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