TOWARDS EMBEDDING GENOMICS IN TYPE 1 DIABETES

A capacity building JDRF Australia Initiative

Request for Applications: Letters of Intent

Applications Open^	Thursday, 15 June 2023
LOI Deadline	Tuesday, 1 August 2023
Invitation to Full Proposal^	Tuesday, 12 September 2023
Full Proposal Deadline*^	Tuesday, 24 October 2023
Earliest Start^	January 2024

*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.

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1. Introduction and Purpose

JDRF is dedicated to creating a world without Type 1 Diabetes (T1D). Throughout the world, we lead the fight against T1D by funding research to find cures and improve lives for those living with the condition.

The T1D Clinical Research Network (T1DCRN) is a national framework underpinning the most promising T1D clinical research and clinical trials. Focused on patient benefit, it provides a platform to accelerate therapies and amplify research impact. Initiatives under the T1DCRN have supported more than 300 researchers across 70 institutes, connecting approximately 2,500 Australians living with T1D with the latest research, treatments, and technologies. Through the T1DCRN and other key programs, JDRF Australia has built a track record of successful implementation of initiatives aimed at accelerating the pace of translation and embedding outcomes into clinical care.

To understand the pathway towards a more personalised care for T1D patients, from 2021-2023, JDRF Australia embarked upon a four-phased consultation process centred around an expert panel concluding in the release of a White Paper titled*: "Towards precision medicine for Type 1 Diabetes in Australia"*, which will be available through JDRF Australia's website in July 2023. The White Paper presents specific research direction recommendations and priorities that emerged from the consultation process, and outlines JDRF Australia's vision for precision medicine in T1D in Australia.

To be able to realise this vision, we need to tap into existing expertise, leading technology and advanced national infrastructure and align and connect with key global research efforts to deliver a paradigm shift in T1D research.

The **purpose** of the Request for Applications (RFA) "*Towards embedding genomics in T1D"* is to support a capacity building initiative in T1D genomics by harnessing these resources, increasing workforce genomics skill set and capability and broadening the scope of genomic medicine in Australia to address T1D challenges.

2. Goals and Objectives

The **goal** of the "*Towards embedding genomics in T1D"* RFA is to *boost genomics research capacity* in T1D in Australia.

The RFA targets innovative ideas that bring together intersecting, cutting-edge technologies and skills in genomics from within and outside the field of T1D, including machine learning and artificial Intelligence computing, and support this with the recruitment, training and career development of geneticists and bioinformaticians.

The **objectives** of the RFA are:

- To enable the expansion and acceleration of discovery of current efforts in T1D and to support novel genomics research approaches (inclusive of genomics, epigenomics, transcriptomics, phenomics and metabolomics) drawing from established expertise outside the T1D field.
- To promote innovation in identifying clinically relevant cohorts and conduct of meaningful research in functional genomics.

- To support the T1D genomic research community in establishing and fostering national and international collaborations with researchers outside the field of T1D, thereby creating a community dedicated to delivering precision medicine to people living with T1D in Australia.

The RFA will support applications aimed at expanding knowledge onto T1D under the following areas:

1. Prevention of disease onset and progression across all stages of T1D

Submissions in response to this area should focus on prevention of disease onset and progression across all stages of T1D by leveraging and developing local expertise to address critical and clinically relevant research questions. Examples may include but are not limited to:

- All research aimed at increasing the utility of accumulated genomic data to elucidate T1D aetiology and progression such as functional genomics efforts to determine causality, including cellular genomics in specific, clinically relevant cells to connect risk associated T1D SNPs to their function/s.
- Research based on clinical data and observations, leveraging existing screening programs and population registries, including the development of risk models to predict heterogeneity of beta cell decline in T1D.

2. Genomic research interventions

Submissions in response to this area should focus on research that will accelerate the translation of genomic research in earlier access to benefits by all patients, bringing together intersecting, cutting-edge technologies and supporting capacity building, accelerating genomics-driven drug discovery and the development of novel therapeutics, conducting clinical trials and seeking national and international collaborations. Examples may include but are not limited to:

- Studies focused on validation of genomic research data using relevant cohorts.
- Clinical trial secondary analysis to determine underlying mechanisms of the observed varied responses to therapies and technologies.
- Research using a combination of GWAS and cellular genomic approaches to determine diabetes phenotypes in the general population including the Aboriginal and Torres Strait Islanders, particularly in remote and very remote areas, presenting with clinical features that do not fit the classical presentation of T1D.

3. ELIGIBILITY

Researchers, clinicians, geneticists and bioinformaticians with expertise in functional genomics, inclusive of genomics and epigenomics, transcriptomics, proteomics and metabolomics are eligible to apply.

All LOIs submitted in response to this RFA must demonstrate that they meet the following eligibility criteria:

i. Principal Investigators (PI) and Co-PIs must hold Ph.D., M.D. or an equivalent academic degree to be eligible to apply for this Award. PIs must be affiliated with an Australian university, hospital, research institute, or other comparable institutions which may include a for-profit entity. For profit organisations must demonstrate a matching resource commitment to the proposed project that is equal to or greater than the fiscal amount requested from JDRF.

ii. The PI must be affiliated with an Australian institution. Co-PIs and other collaborators may be affiliated with institutions outside of Australia.

iii. **T1D applicants** must conduct research that can be expanded to include functional genomics. Submission by T1D experts must include ***at least one experienced researcher from a field other than T1D***, bringing capacity, skills and knowledge that will benefit the proposed research.

iv. **Non-T1D applicants** who do not have previous track record in T1D must be able to demonstrate expertise in genomics in other diseases and have track record in genomics and clinical application of genomic findings into outcomes for patients. Submissions by non-T1D experts, must include ***at least one T1D expert***.

v. There are no citizenship requirements for this program however, awardees must be eligible to work in Australia for the length of the proposed project. To assure continued excellence and diversity among applicants and awardees, applications are welcomed from individuals with disabilities, and members of minority groups underrepresented in the Australian T1D research landscape.

4. Exclusion Criteria

This RFA limits LOIs to one submission per Principal Investigator or team. The following research areas are excluded from funding:

- Discovery focused solely on genome-wide analysis to screen for new variants associated with T1D.
- Support towards projects focused solely on the establishment of genomic repositories and/or registries.

Submissions will be excluded from further consideration if at any time during the assessment process JDRF or the review panel determines a proposal or parts of it to:

- Be a duplicate (as opposed to expanding) current research (either in Australia or overseas).
- Lack sufficient multidisciplinary collaboration as per the eligibility criteria.
- Lack a clearly articulated hypothesis and clear impact.

5. Overview of the LOI and Full Proposal Application Processes

All submissions are to be made using JDRF's online grants management portal RMS360 (http://jdrf.smartsimple.us). Applicants are required to login to RMS360 to access supporting documents and templates. Please read the User Guide to applicants before commencing your application.

Submitted information is 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 steps: 1. Submission of an LOI to provide a brief overview of their research plan and, 2. Submission of invited applications.

LOI review

The LOI review process consists of two stages: 1. JDRF will screen each LOI for compliance with eligibility (Sections 3 and 4). 2. A review panel of national and international experts will then assess LOIs based on the selection criteria (Section 7).

The reviewers will assess LOIs through a scoring system based on the Selection Criteria outlined in Section 7. Scoring of application is done individually by each expert reviewer, with conflict of interest managed as per our Conflict of Interest policy.

Written critiques from the reviewers will be provided to shortlisted applicants and must be addressed in Full Proposal. Only the highest-quality, highest impact LOIs will be shortlisted and invited to proceed to a Full Proposal. Further information about this process will be provided to applicants who are invited to submit a Full Proposal.

Full proposal review

Full Proposal will also be assessed and scored by a panel of expert reviewers against the selection criteria (Section 7). If recommended for further consideration, applicants may be provided with written critiques from the reviewers and invited to respond in writing. The JDRF Australia Board has the responsibility to approve grants for funding and allocation of the final budget.

Successful awardees will be notified via e-mail, and a Funding Agreement will be executed with the applicant's administrating institution. After a grant is awarded, JDRF monitors the progress of the Project.

6. Submission Requirements

The following materials need to be submitted in RMS360:

Submission of LOIs

i. **Proposal Synopsis** *(1 page maximum, use template)*. Summary outlining the area of research, main objectives of the project, key personnel and institutions, and check for eligibility.

ii. **LOI Research Plan** *(3 pages maximum excluding references, use template)* that provides the following information:

- Significance and translational impact for proposed research.
- Rationale for proposed research including aims.
- Description of research design and methods.
- If applicable, advantages over alternative approaches
- Expertise of the project team and any relevant departmental/institutional resources.
- Timelines of deliverables.

iii. **Bio-sketch** *(4 pages maximum, using NIH/ JDRF template)* of the Principal Investigator (PI) and Co-PIs and other key personnel must be provided.

iv. **Indicative Budget** *(use template)* A high level annual budget for the proposed research.

Submission of Full Proposals

i. **Detailed Research Plan** *(7 pages maximum, use template)***,** elaborating on the proposal outlined in the LOI, and addressing any issues identified by the reviewers.

ii. **Detailed Budget and Justification** *(Use templates)* for each grant year with clear costing models and thorough justification for use of funds.

iii. **Data and Resource Sharing Plan.** With the intention of creating a long-term research legacy, genomic research funded by this RFA will capture valuable research information and invest in secondary analyses of outcomes. Thus, all data generated must be discoverable to external researchers and made available with defined policies and procedures to other ethically approved research programs. In addition, a comprehensive outline of how data and other resources developed during the proposed study will be shared and made available to the broader community within a reasonable timeframe. Please refer to JDRF Australia's Policy on Data and Biosample Sharing.

iv. **Letters of Institutional Support** *(2 pages maximum)* using the official letterhead from all institutions providing cash/in-kind contributions must be provided. Letters of Support must be signed by the Department/School Head (or equivalent) and include the following information:

- The institution's alignment with the proposed research.
- Details of each cash or in-kind contribution (e.g., personnel, training, equipment, resources) including value in AUD where appropriate.
- How will the relationship with the project will be supported beyond this funding period for eventual realisation of its benefit.

7. Selection Criteria

LOIs and Full Proposals will be assessed by an independent expert panel against the following selection criteria:

i. Significance and Impact (25%)

- Significance of the proposed research, its alignment with the goals and broader objectives of the RFA.
- Potential short, mid-, and long-term impact of proposed research.
- Uniqueness of the proposal against national and global efforts in this area, and likelihood of this research to advance the field.

ii. Innovation and Novelty (25%)

- Extent to which the proposed work is original and innovative.
- How the proposed work challenges and seeks to shift current research or clinical practice.
- Scope of novel concepts, approaches or methodologies to be developed or used, and any advantage over existing alternatives.
- Scope of any refinements or improvements of existing concepts, approaches or methodologies.

iii. Study Design and feasibility (25%)

- Quality of the overall strategy, methodology, and analyses to be used to accomplish the specific aims of the project.
- Clarity of how the data will be collected, analysed, and interpreted as well as the scope of resource sharing.
- Foresight of potential problems, alternative strategies and benchmarks of success to achieve the aims.
- Appropriateness of proposed timeline and budget.
- Capability to deliver proposed outcomes.
- Potential and clear plan for future steps including obtaining larger funds from other sources and progressing the research to benefit patients.

iv. Team strength, collaboration and environment (25%)

- Expertise of the PI, Co-PIs and team members (refer to selection criteria)
- Level of collaboration, cross-disciplinary expertise
- Access to institutional resources, infrastructure and other support mechanisms.

8. FUNDING

The "*Towards embedding genomics in T1D"* RFA will fund studies over a maximum of **three years** at up to a total of **$600,000,** 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 and overall objectives of the project. Applicants should propose budgets that are well justified and strongly commensurate with project scope.

Institutions receiving grants awarded by JDRF Australia through the T1DCRN are eligible for recovering indirect costs via Research Block Grants.

More information about the self-assessment system for institutions, which helps determine R&D income category, can be found here.

9. CONTRACTUAL REQUIREMENTS

9.1 Funding Agreement

This funding will be provided by JDRF and administered by the recipient's institution. The award recipient will be required to sign a Funding Agreement (Agreement) with JDRF Australia. A condition of application to this RFA is provision of certification of the PI, Co-PI(s) and their organisations to have read and agree to abide by the terms of the Agreement.

JDRF has no obligation with respect to this RFA, including any funding, unless and until JDRF and the successful applicant(s) have executed the formal Agreement. JDRF expects the Agreement to be executed prior to the grant start date, unless otherwise agreed by JDRF. The Agreement will include, but is not limited to, the following:

i. A payment schedule dependent upon the achievement of project milestones. JDRF will determine such milestones to be included in the Agreement in consultation with the relevant Investigators.
ii. An obligation to comply with all relevant JDRF Policies as further detailed in the Agreement template.
iii. For profit organisations will have additional considerations in their Agreement with JDRF regarding milestone, anticipated funding, intellectual property and royalty issues. Contracts will be negotiated on a case-by-case basis and will be in place before the commencement of funding.

JDRF reserves the right to require changes to the Agreement template to address specific needs and circumstances of an application.

9.2 Consent to Combine Applications

The objectives of this RFA and the T1DCRN is to emphasise collaboration and encourage research that presents the greatest benefit to the T1D community. After the review of the LOIs, shortlisted applications from separate investigators may be invited to combine their applications into a single Full Proposal submission where such collaboration is deemed necessary to maximise benefit and avoid overlap.

In submitting an LOI in response to this RFA, applicants consent to information about their application being shared with other applicants for this purpose and acknowledge they may be asked to combine their application with another applicant as a condition of being invited to submit a Full Proposal. Applicants will be informed about this possibility prior to sharing any information, providing the opportunity for them to withdraw their application if required.

9.3 Consent to Co-funding

JDRF actively seeks co-funding opportunities with other funding bodies and partner institutions. In submitting a proposal in response to this RFA applicants consent to information about their proposal being shared with other funding bodies that are specifically interested in supporting the research and related activities generated through the T1DCRN.

9.4 Data and Resource Sharing

All applicants invited to Full Application will be required to submit a Data Sharing Plan. For more information please refer to the T1DCRN Data and Biosample Sharing Policy.

JDRF acknowledges that resource sharing plans will differ according to the types of data and biosamples collected and does not prescribe the exact content or format. JDRF requests that at a minimum the core elements outlined in the Data Sharing Plan template in Appendix A of the JDRF Australian T1DCRN Data and Biosample Sharing Policy are considered.

9.5 Publications and Open Access

The T1DCRN is committed to the timely publication and dissemination of all information and materials developed under T1DCRN funding and must also comply with the NHMRC Open Access Policy. Recipients of this award must also comply with this policy and must take steps to make available all generated project materials for publication and wider dissemination. The sharing of data will be supported by clear policies and guidelines, as well as mechanisms to satisfy this requirement.

10. Submission Checklist

A submission is complete if:

- All mandatory fields in the online grant management system RMS360 are completed.
- It includes all the documents listed in the submission checklist below.

LOI Checklist

☐ Proposal Synopsis (use template)
☐ LOI Research Plan (use template)
☐ Bio-sketch for each investigator (use template)
☐ Indicative Budget (use template)

Full Proposal Checklist

☐ Detailed Research Plan
☐ Detailed Budget
☐ Budget and Justification
☐ Letters of Institutional Support
☐ Data and Sample Sharing Plan

11. CONTACTS

For enquires on strategic fit, funding or submission requirements please contact:

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12. APPENDIX: ABOUT JDRF AUSTRALIA

Type 1 diabetes (T1D) is a serious, chronic autoimmune condition that affects over 120,000 Australians[1]. T1D is classically characterised by a sudden and pronounced onset in children, adolescents and young adults, requiring immediate and life-long dependence on exogenous insulin due to autoimmune destruction of pancreatic beta cells. It is now recognised that T1D initially progresses through a silent asymptomatic phase characterised by the persistence of circulating islet autoantibodies. This asymptomatic phase can last for months or years, until diagnosis of clinical T1D requiring carefully titrated exogenous insulin therapy[2]. Underlying genetic predisposition or/and delayed trigger factors as well as the role of stressed and sick beta cells in necessitating an immune reactive pathway, are yet to be fully understood. Clinical manifestations and the disease evolving epidemiology of T1D globally remain overwhelming and unresolved.

JDRF is the world's biggest non-profit funder of T1D research with the ultimate goal to find a cure for T1D. Until a cure is found, our focus is on advances that ease the burden for those living with the disease. The key to treating, preventing, and ultimately curing T1D is the swift translation of Australian and global basic science and applied research outcomes into treatments and technologies that work effectively in people. Australian T1D research ranks highly on a global scale[3], but adoption into clinical care remains a challenge[4]. Overcoming this challenge requires an important step out of the laboratory and the translation of research into human trials.

[1] jdrf.org.au
[2] Diabetes Care Oct 2015, 38 (10) 1964-1974.
[3] The Australian Research Impact Analysis
[4] The Australian Type 1 Diabetes Research Resource Map