Breakthrough T1D Request for Applications: Artificial Intelligence Powered Approaches for T1D Cell Therapy

August 2024

Summary

- The goal of this funding opportunity is to accelerate research and development of next generation beta cell replacement therapies for type 1 diabetes (T1D) by leveraging advancements in artificial intelligence and machine learning.
- This initiative will award grants to academic investigators and industry partners of up to $750,000.00 over 3 years.
- Applications of increased scope (time and/or budget) will be considered where there is a strong justification. Interested applicants should discuss with the Breakthrough T1D scientific contact, nmamrak@breakthrought1d.org.

Background

One of Breakthrough T1D's goals is to accelerate the development of therapies capable of restoring metabolic control in type 1 diabetes (T1D) through the transplantation of insulin-producing cells. (Link to Strategy Document Here).

Pancreatic islet transplantation has proven to restore metabolic control, reduce glycemic variability and improve quality of life in T1D patients that experience severe hypoglycemic events and impaired hypoglycemia unawareness. While improvements have been made in donor pancreas procurement and methods to isolate, purify, and preserve islets, major scientific and technical challenges remain that must be addressed before beta cell replacement can be expanded to broader T1D populations. Examples include the adverse side effects from chronic systemic immunosuppression, the limited availability of donor pancreas derived islets, poor cell survival in the post transplantation period, and the lack of biomarkers predictive of transplant health. Breakthrough T1D's role is to enable the scientific community to address these challenges with the ultimate goal of accelerating the development of safe and effective beta cell replacement therapies that are available to all individuals living with T1D.

Funding Opportunity Description

Several critical barriers remain in the pursuit of next generation beta cell replacement therapies for T1D. Among them are considerations of renewable cell sources, immune protection, and engraftment and survival. Through the work of Breakthrough T1D funded researchers and others, the field is making significant progress in each of these areas, exemplified by the development and early clinical testing of human stem cell-derived islets and scaffolds to enhance survival and engraftment. Much of this research utilizes clinical data, single cell biology, genetic screens, or biomaterial formulations, collectively generating a massive amount of data along the way.

Recent advances in artificial intelligence and machine learning (AI/ML) technologies have made it possible to apply these statistical methods to biomedical applications across a range of datasets and data types, ranging from transcriptomics to electronic health records enabling the uncovering of previously hidden patterns and features that can aid in the development of predictive tools and generation of new hypotheses. While these techniques have been applied to T1D research in some capacity, most notably, in generating predictive risk scores of disease progression, they have not been widely applied to the specific barriers of beta cell replacement therapy. This funding opportunity aims to accelerate the pace of scientific progress and catalyze breakthroughs in the development of beta cell replacement therapies for T1D.

Breakthrough T1D is soliciting Letters of Intent (LOI) aimed at addressing one or more of the following gaps in T1D cell therapy research using AI/ML:

- Improving the function and/or survival of renewable sources of insulin-producing cells (e.g., stem cell-derived islets).
- Developing immune protection strategies to prevent rejection of transplanted cells that do not rely on chronic systemic immunosuppression.
- Establishing methods of predicting transplanted cell survival and function prior to decline in c-peptide levels or glycemic control.
- Implications of a specific therapeutic approach (cell type and protection strategy, site of implantation) for efficacy, safety and patient selection.

Proposals coming from multi-disciplinary teams comprised of both data scientists and expert T1D researchers will be prioritized. While applicants to this RFA do not require experience in T1D research, they are encouraged to seek collaborations with T1D experts and provide adequate evidence supporting the feasibility of the approach.

Examples of topics pertinent to this call include but are not limited to:

- Generating and analyzing clinical and/or preclinical datasets to identify signatures of human beta cell stress or immune rejection to better measure and predict graft health/failure prior to decline in beta cell function or recipient's immune status.
- Leveraging single cell datasets from other fields such as solid organ transplant or oncology to identify mechanisms capable of reducing immunogenicity or improving survival (immune checkpoint expression, vascularization, metabolism, etc.).
- Generating and analyzing datasets on foreign body response or oxygenation requirements to understand mechanisms of tissue response at different implant sites and mitigate biomaterial rejection in cell delivery devices.
- Using large multi-well screens of small molecule libraries to identify islet or stem cell-derived islet responses that may improve transplant outcomes.

This RFA is not intended to support other pillars of Breakthrough T1D research strategy such as:

- Development of algorithms calculating risk scores for individuals with presymptomatic or new onset T1D.
- Projects focusing on protecting endogenous beta cell mass from autoimmune destruction during early stages of disease.

Eligibility

Applications may be submitted by domestic and foreign non-profit organization, public and private, such as universities, colleges, hospitals and laboratories, units of state and local governments and eligible agencies of the federal government, for-profit entities, or industry collaborations with academia. Applicants must hold an M.D., D.M.D., D.V.M., Ph.D., or equivalent and have a faculty position or equivalent at a college, university, medical school, or other research facility.

Please note that applications from for-profit entities or industry collaborations with academia may be submitted in response to this RFA. Additional information will be requested from for-profit entities if invited to submit a full proposal.

There are no citizenship requirements for this program. To assure continued excellence and diversity among applicants and awardees, Breakthrough T1D welcomes applications from all

qualified individuals and encourages applications from persons with disabilities, women, and members of minority groups underrepresented in the sciences.

Funding Mechanisms

In response to this announcement, Letters of Intent (LOI) can be submitted under the following mechanism(s):

Strategic Research Agreements (SRAs)

Strategic Research Agreements are intended for support of research activities at non-for-profit entities such as academic institutions. For SRAs, proposed budgets for projects should not exceed $750,000.00 USD (including 10% indirect costs) total costs for up to three (3) years. The level of funding will vary depending on the scope, data available, need to perform additional laboratory assays, access to samples, degree of data analysis to be performed, and overall objectives of the proposal. If your project budget and/or timeline exceeds $750,000.00 and/or 3 years, please discuss with Breakthrough T1D staff (contact information below). For more information on the Strategic Research Agreement (SRA) grant mechanism please refer to our grant handbook.

Industry Discovery and Development Partnerships (IDDPs)

For-profit entities may apply under Breakthrough T1D's Industry Discovery & Development Partnership (IDDP) funding mechanism, which entails additional requirements and typically has a modest royalty payback to Breakthrough T1D. If you would like to submit an Industry Discovery and Development Partnership (IDDP) project LOI to this RFA, please check our grant handbook for additional information and contact Dr. Nicholas Mamrak (nmamrak@BreakthroughT1D.org) to discuss proposed scope and budget prior to submitting an application. Indirect costs are not permitted on IDDP applications.

Letter of Intent

Prospective applicants should submit an LOI, [2 pages maximum] online via RMS360 to be considered for a full proposal request. The LOI template provided on the RMS360 website must be used to complete the application to be considered for a full proposal request. The LOI template provided on the RMS360 website must be used to complete the application.

Proposal

An approved LOI is required prior to the submission of a full proposal. Upon notification of a request for a full proposal, the application must be completed using the templates provided

in RMS360. Proposal section templates in Microsoft Word, [10 pages 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 a 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 section of the grant handbook.

Breakthrough T1D follows the U.S. National Institutes of Health (NIH) guidelines for studies including human subjects, including the Common Rule changes.

Review Criteria

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

- Significance
- Relevance
- Approach
- Innovation
- Environment
- Resource sharing plan including a description of metadata and data collection methods and storage

Informational Webinar and Q&A

Breakthrough T1D will hold an announcement introduction meeting via Zoom on September 10, 2024, from 1-2 pm Eastern Time to which all prospective applicants are invited. Breakthrough T1D scientists will give an overview of the goals of this initiative, explain the application process, and answer initial questions on applications.

Registration for Webinar (please register by September 9, 2024):

https://breakthrought1d-org.zoom.us/webinar/register/WN_A2WAp2i6TLqPwTqEO-AJ2Q

Projected Timeline

Milestone	Date
Information Webinar and Q&A	September 10, 2024, 1-2 PM ET
LOI deadline	September 23, 2024, 5 PM ET
Notification of LOI Outcome	October 8, 2024
Full proposal deadline	November 5, 2024, 5 PM ET
Award notification	April, 2025
Earliest anticipated start	June, 2025

Program Contacts

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