



JDRF/ITN
Partnership in Immune Tolerance

Developing immune tolerance in type 1 diabetes.

Program Information
and
Submission Guidelines

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1. Mission

The JDRF/ITN Partnership in Immune Tolerance Program will encourage and support early stage clinical development of tolerogenic protocols in Type 1 diabetes. The initiative aims to facilitate the development of novel tolerance agents in type 1 diabetes through targeted funding available through a fast-turnaround, streamlined application process administered by the ITN, with JDRF participation.

In particular, this initiative aims to foster the development of partnerships between academia and industry in order to bridge early clinical studies of therapies that have strong preclinical evidence for efficacy by supporting pre-clinical toxicology studies, phase 1 safety trials and small efficacy trials that will provide proof-of-principle in well controlled, safe settings. It is the intent that successful projects emerging from this initiative would then qualify for broader clinical support via the ITN's existing support programs or other funding sources.

Proposals for support from the JDRF/ITN Partnership in Immune Tolerance Program are considered via one of two streams:

Stream 1: Investigator-initiated proposals are accepted via the ITN website utilizing ITN's online Concept Proposal submission system. There are no formal submission deadlines for the initiative – proposals are accepted at all times throughout the year.

Stream 2: Clinical Concept Proposals and/or Full Applications in the area of type 1 diabetes reviewed by the ITN that are deemed by the ITN review panel to be scientifically valid and important, but without sufficient toxicology data to warrant full ITN clinical funding may be considered as candidates for funding from the JDRF/ITN Partnership initiative. In such cases, the ITN may provide a commitment in principle to funding phase II clinical studies should results from the JDRF/ITN initiative be positive.



2. Scope

Total amount of funding available for this initiative is \$3-5 million per year. The size and duration of individual awards will vary depending upon the proposed research and total remaining funds available. Individual project funds will be limited to 10% indirect cost recover rate and can be used for drug development, pre-clinical/toxicology and Phase I safety. All projects funded by this initiative must receive formal approval by appropriate regulatory and safety groups.

Basic Criteria

In general, proposals accepted for review under this initiative must meet the following general criteria:

- projects must exhibit the potential for direct clinical benefit in the treatment of type 1 diabetes.
- there must be appreciable scientific evidence from basic research and small/large animal studies that the proposed intervention has the potential to induce tolerance to the autoimmune response that causes type 1 diabetes.
- proposals aimed at promoting tolerance to islet transplants in type 1 diabetes will be considered providing that the proposed interventions have conceptual underpinnings demonstrating benefits specific to the islet transplantation setting where both auto and alloimmune responses must be controlled.
- support is available to principal investigators or teams of investigators holding positions in academia, industry, government or nonprofit research institutions.

Research that will be considered:

- therapeutic strategies aimed at promoting immune tolerance in new/early onset type 1 diabetes
- therapeutic strategies aimed at promoting immune tolerance in established type 1 diabetes
- interventions aimed at restoring/reconstituting beta cell function without long term immunosuppression
- Therapeutics based on:
 - o monoclonal antibodies
 - o small molecule drugs
 - o cell-based therapies
 - o RNA/DNA-based therapies
 - o other
- Types of studies:
 - o drug development
 - o pre-clinical toxicology studies
 - o phase I safety studies in humans

Research outside the scope of this initiative:

- any animal studies not directly related to toxicology or pharmacodynamics in preparation of human clinical studies
- studies in Type 2 diabetes or gestational diabetes are not eligible for funding.
- type 1 diabetes prevention studies will not be considered – these should be submitted to the ITN or TrialNet as regular Concept Proposals.



3. Preparing and Submitting an Application

3.1 General Instructions

Applications to the JDRF/ITN Partnership in Immune Tolerance Program must be completed and submitted electronically.

Applicants must complete their proposal on the JDRF/ITN Partnership in Immune Tolerance “Application for Support” template form, which is available through the ITN website. Once completed, this form and supplementary information can be submitted via the ITN website for consideration.

3.2 Completing the Forms

Information on completing each of the sections of the proposal forms is below. If you have questions that are not answered here, contact the ITN Office of Scientific Review at osr@immunetolerance.org.

1. Study Title

Enter the title of the proposed study proposal in the space provided. Do not exceed the space provided.

2. Type of Application

Indicate whether you are seeking support for preclinical studies or for a phase I (safety) clinical trial.

3. Principal Investigator

Complete the sections identifying the Principal Investigator (P.I.).

4. Mailing Address

Complete this section with your current contact information. Be sure to double-check your email address for accuracy, as this will be the primary mode of communication regarding your proposal.

5. Collaborators/Co-investigators

If you have identified other investigators who will collaborate on the proposed trial, list them here and provide a brief description of their responsibilities. List only those collaborators or co-investigators who would play (or have played) an integral part in the conceptual framework and planning of the clinical or assay portions of the study – do not provide a list of investigators from all anticipated clinical sites.

6. Project Summary

The Project Summary should provide reviewers with all the information necessary to judge the scientific merits of the proposed research. Provide a short description of the proposed research, including the objectives, scientific basis/rationale and research plan. Describe the planned interventions and provide evidence or rationale for its safety/efficacy. If you are proposing preclinical studies, describe the animal models that will be used. If you are proposing a phase I clinical study, provide details of the proposed clinical protocol and patient population.

NOTE: Do not include figures, charts or tables in this section – these may be attached to your application as appendices, located in separate files.

NOTE: The project summary may be a maximum of two pages of single spaced 10 point font. The ITN will not accept applications that exceed this limit.

7. Significance

Briefly discuss the significance of this proposal with respect to the treatment of type 1 diabetes and provide a brief description of how the proposed research is relevant to immune tolerance. Provide justification why this study meets the goals of the JDRF/ITN Partnership in Immune Tolerance initiative. *Use only the space provided.*



8. Lay Abstract

Provide a description of the proposed work and its relevance to type 1 diabetes using language that can be understood by a non-health professional. This abstract may be released to the public and/or posted on the JDRF/ITN websites if the application is successful. *Use only the space provided.*

9. Reagent Availability

Provide a brief comment on the sources of key reagents/pharmaceuticals for this study. List any possible industrial collaborators and whether you have had discussions regarding drug/reagent supply with them or have received any firm or tentative commitments. If you have a commitment to supply reagents/drugs, attach a letter of support indicating any proposed arrangements in the appendices. *Use only the space provided.*

10. Ethical Considerations

This section only needs to be completed for phase I clinical studies.

This section should briefly discuss compliance with Human Subject Guidelines and summarize any potentially troubling ethical questions raised by the proposed research. The ITN Ethics Review Committee, when considering any such ethical problems, will take into account the likelihood of finding an acceptable resolution for such issues. Questions which should be addressed are:

- Have human subjects been used before? If so, why do they need to be used again? If not, why is it appropriate to use human subjects now?
- What are the risks and benefits involved in the proposed research protocol and will these benefits be directly realized by the subjects involved?
- Are there adequate means to ensure the participation of women, minorities and children? If not, what are the justifications for exclusion?
- Does the proposal raise new or troubling ethical questions for the investigators? If so, please describe in detail.

Use only the space provided.

11. Conflict of Interest Disclosure

The principal investigator and listed collaborators must disclose any professional or financial interests that are related to, or would benefit from the proposed research. Likewise, any personal commercial interests that relate directly to the proposed research should be listed in this section. Please supply information about any potential conflicts of interest you foresee in your research and how you will resolve them. *Use only the space provided.*

12. Appendices

You may list up to five appendices that you wish to attach to your application. During the online submission process, you will be asked to upload these documents with your completed forms; therefore you will need to have electronic files. In the space provided on the application template, list the contents of these appendices in the space provided. Appendices accepted include:

- i) figures, charts and diagrams to accompany the project summary;
- ii) reprints of relevant publications that support your proposal;
- iii) letters of support from collaborators/suppliers.

Figures, charts and diagrams should be provided in a commonly used format. For example, figures supporting the Research Summary may be embedded inside a single MS Word or PowerPoint file and uploaded as a single document.

Publication reprints are preferred as Adobe pdf files; however manuscripts in preparation or in press may be submitted in MS word format.



Letters of support should, likewise, be submitted as Adobe pdf documents scanned from originals. The ITN, at its discretion, may request copies of the original signed letter.

Note that the ITN proposal submission system will accept a maximum of 5 MB uploaded for each proposal (i.e. combined file size). Please ensure your files are below this threshold.

4. Review Criteria

All proposals will be evaluated based upon the following criteria:

- i) **Scientific Basis and Rationale** – Is the proposed research important for the treatment of type 1 diabetes and does it seek to establish immune tolerance? Is the strategy proposed scientifically sound and based on well-established scientific principles? Have basic research studies been completed and to what extent do these studies demonstrate potential for safety and efficacy? Are there novel aspects to the study? Are the animal models/clinical populations proposed appropriate to the goals of the study? Do the studies proposed address important questions and do the studies appropriately address the question asked? Are there more effective methods of addressing the questions/hypotheses proposed?
- ii) **Clinical Implications** – How would the proposed intervention impact type 1 diabetes? Would successful completion of the proposed studies result in sufficient evidence to pursue phase I or II clinical studies?
- iii) **Feasibility** – Are the proposed methods plausible? Are study goals realistic? Are there any obstacles to acquiring the reagents needed for the study and can the Network assist in overcoming these obstacles (e.g. supply or manufacture problems, intellectual property issues, etc)?
- iv) **Reputation and Capabilities of Investigators** – Do the investigators (applicant and collaborators) have a record of achievement in tolerance research and/or type 1 diabetes? Are there potential conflicts of interest in pursuing the proposed trials?

Peer review format

All proposals submitted to the JDRF/ITN Partnership in Immune Tolerance program will be reviewed by both the Juvenile Diabetes Research Foundation and the Immune Tolerance Network. All studies involving human subjects will also undergo a concomitant review by the ITN Ethics Review Committee. In some cases, investigators may be contacted for clarification and/or additional information or to attend a Q&A session with reviewers prior to a final decision on the proposal.

5. Program Administration

Funding Mechanism

The JDRF/ITN Partnership in Immune Tolerance program is funded by the Juvenile Diabetes Research Foundation. The funds will be available to academic, government or industry-based researchers whose proposals have been approved through the review procedures described herein. Funds will be provided to successful applicants through a subcontract with the Immune Tolerance Network's host institution, the University of California San Francisco.

Reporting Requirements

Principal investigators receiving funding via the JDRF/ITN Partnership in Immune Tolerance program are required to submit an annual progress report to the ITN by October 1 of each year the study is active. A final, written report on the research must be submitted to the ITN within 2 months of the conclusion of the study.

In addition, PI's may be required to present final study results to the Network Steering Committee at its first meeting subsequent to study completion.