



# Type 1 Diabetes Research Proposals

*and the Immune Tolerance Network*

## Introduction

The Immune Tolerance Network (ITN) accepts proposals for novel clinical trials of tolerance therapies in type 1 diabetes through its year round, two-stage proposal review system. New applications for research begin as “Concept Proposals,” which are short summaries that provide ITN reviewers with the opportunity to assess the proposal based primarily upon the quality and feasibility of the idea, rather than the logistics of the proposal.

In general, new Concept Proposals are generated from two sources:

- 1) **Independent Investigators** – Investigators in the academic or business sectors are encouraged to bring their ideas for new clinical protocols of tolerance therapies in type 1 diabetes to the ITN through new Concept Proposal submissions. The majority of new clinical trials adopted by the ITN begin as Concept Proposals from independent investigators.
- 2) **ITN Strategic Assessments** – ITN members or a group of external advisors may solicit and develop ideas from the community at large for new Concept Proposals. These proposals may follow the normal application review cycle, or may be evaluated as collaborative ventures with academic or industrial partners and the ITN.

## Immune Tolerance Trials in Type 1 Diabetes

ITN is interested in “tolerance” related trials for prevention of diabetes and loss of C-peptide secretion after diabetes onset as well as innovative assays of the autoimmune process. A large body of evidence indicates that risk of type 1A (immune mediated) diabetes is predictable in man and preventable in animal models. A number of the therapies that prevent type 1 diabetes in animal models relates to therapies that would fit under the umbrella of “tolerance induction”.

To date the ITN has a number of trials in type 1 diabetes in various stages of the pipeline, including but not limited to trials utilizing anti-CD3, anti-thymocyte globulin, IL-2 and Sirolimus, alpha-1 antitrypsin, and insulin vaccination. The ITN also supports studies of islet transplantation where both transplant rejection and autoimmunity are important factors.

The ITN provides a series of core laboratories with direct relevance to type 1 diabetes, including cores that provide screening for various autoantibodies, a cellular immunology core, and gene expression cores.

As trials are reviewed for ITN a number of important questions are usually discussed, and attention to these questions in the Concept Proposal is advised:

- 1) Efficacy data in animal model of type 1 diabetes or relevant human data.
- 2) If the NOD mouse is the animal model studied, efficacy data at later stages of the disease process is appreciated (e.g. 12-16 weeks, new onset, blocking islet transplant destruction).

- 3) Efficacy data with dose response information and utilization of the agents the way they are proposed in man (e.g. in adjuvant, combination of agents).
- 4) Safety data as per FDA requirements and any information concerning safety in man.
- 5) Agent availability.
- 6) Rationale for dose or schedule considered.
- 7) Rationale that the study is evaluating tolerance induction and not simply an immunosuppressive drug administered long-term.
- 8) Good scientific rationale and evidence of some effect in man (e.g. induction of regulatory T cell or suppression of effector T cell response; availability of surrogate markers to speed dose finding studies).
- 9) Phase I and II, and early phase III trials considered.
- 10) Design of clinical trials with standardized entry and endpoint criteria to foster comparison with other trials.
- 11) Utilization of core laboratories of ITN and interesting mechanistic studies.

It is not assumed that all of the above is available and there is the potential for help in developing certain critical information to allow trial development. The ITN strives to create a collaborative, iterative process in helping to test new therapies.

## **Questions:**

If you are interested in submitting a Concept Proposal for a study in type 1 diabetes to the ITN and have questions regarding the process, please contact:

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