Immune Tolerance Network

REQUEST FOR PROPOSALS

Clinical Trials of Immune Tolerance for Protein/Gene-Replacement Therapy

The Immune Tolerance Network (ITN) is an international clinical research consortium founded by the National Institute of Allergy and Infectious Disease of the National Institutes of Health, with the mission to accelerate the clinical development of immune tolerance therapies through a unique collaborative model. Additional support is provided by the NIDDK and JDRF.

The ITN develops, implements, and conducts trials of novel immune tolerance therapeutics in autoimmune diseases, transplantation, and allergy & asthma. ITN trials look beyond the traditional endpoints of safety and efficacy, actively investigating the mechanisms of tolerance induction and maintenance by integrating hypothesis-driven, mechanism-based research into all clinical trials. The goal is to improve our understanding of tolerance in the human clinical setting and to establish new biomarkers of tolerance in human disease. To advance this goal, the ITN is now interested in exploring defined human models of tolerance induction to specific antigens, specifically in clinical settings of tolerance to protein therapeutics.

The ITN is currently inviting proposals for novel clinical trials with the aim of inducing tolerance in patients who receive gene/protein-replacement (e.g. hemophilia, Gaucher's disease) or other exogenous protein therapy, in which the patients are at risk for developing an immune response to the biologic agent. The ideal proposal would meet the following criteria:

1. **The therapeutic strategy should include an antigen or modified antigen and have the potential to be used with an additional immunomodulatory agent(s);**

2. **The proposal should be supported by strong rationale or preclinical data that supports a testable mechanism of action for tolerance induction;**

3. **There must be an appropriate patient population suitable for enrollment with an opportunity to significantly advance clinical practice; and with a plan for risk mitigation in the study design;**

4. **Information is available regarding the molecular details of immune recognition (e.g. T cell epitopes, MHC restriction, B cell epitopes);**

5. **The ITN will commission antigen-specific assays to monitor immune responses in these trials, and priority will be given to proposals with preliminary data on the development of such assays.**

The ideal proposal would have a testable mechanism of tolerance induction and a strategy for assays investigating this mechanism. The ITN will consider phase I safety studies, so long as they are designed to additionally assess mechanistic endpoints. Larger phase II studies, with an efficacy endpoint, would be welcome.

Proposals are welcome from academic, government and industry-based investigators; funding will vary based on the type and scope of the trial. Applicants should submit a 5-page Concept Proposal no later than ***November 30th, 2015***.

The Concept Proposal should include:

- Name, title, and institution of principal investigator (PI), co-investigator and/or key collaborator(s);
- A description of the proposed clinical trial, including the scientific basis and rationale, evidence for tolerance induction, clinical outcome, and potential mechanistic studies and tolerance assays that will accompany the trial;
- A description of the projects feasibility, including an assessment of the patient population, drug availability, projected trial size and estimated number of clinical sites;
- Ethical considerations including compliance with Human Subject Guidelines and discussion of the risk-benefit ratio to the patients and potential ethical concerns raised by the proposed research;
- References to published or preliminary (preclinical and pilot human study) data. Related unpublished data may be submitted as supplemental material.

Please direct all proposal submissions and any questions concerning this RFP to:

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