



REQUEST FOR PROPOSALS

Clinical Trials of Immune Tolerance in Combined Bone Marrow and Solid Organ Transplantation

The Immune Tolerance Network (ITN) is an international clinical research consortium founded by the National Institutes of Health, with additional support from the Juvenile Diabetes Research Foundation, with the mission to accelerate the clinical development of immune tolerance therapies through a unique collaborative model.

The ITN develops, implements, and conducts trials of novel immune tolerance therapeutics in solid organ and islet transplantation, autoimmune diseases, 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 our clinical trials. The goal is to improve our understanding and establish tolerance in the human clinical setting and to develop new biomarkers of tolerance in human disease.

The ITN is currently seeking short “Concept Proposals” (see below) for novel clinical trials designed to induce immune tolerance in combined solid organ plus hematopoietic stem cell transplantation. The proposal should meet the following criteria:

- 1. Combine allogeneic solid organ transplantation (e.g., kidney or liver) with therapeutic cell transfer (e.g., bone marrow or hematopoietic stem cells) to induce donor-specific chimerism in the recipient without GVHD**
- 2. Cross HLA barriers between donor and recipient**
- 3. Utilize tolerance to the solid organ graft (full withdrawal of all immunosuppressive drugs without histologic or clinical evidence of rejection) as a clinical endpoint**

The ideal proposal would have strong preclinical data, with a fully described, testable mechanism of tolerance induction and a strategy for mechanistic assays investigating this mechanism. The ITN is particularly interested in proposals for phase II trials (with approximately 5-30 patients).

The proposal review process will focus on evaluating the conceptual framework of the proposed trial and its significance and suitability for further development; it does not require submission of a detailed clinical protocol (which would be invited only upon acceptance of the Concept Proposal).

Proposals are welcome from academic, government and industry-based investigators and should be submitted no later than August 31st 2011; successful proposals will be discussed at the fall (October) Network Steering Committee Meeting.

For more information about the ITN's portfolio of clinical trials, please visit www.immunetolerance.org.

Proposal Instructions

Proposals should be submitted via our website: (www.immunetolerance.org/submit-a-proposal) and contain the following information on the concept proposal form provided:

- Name, title, and institution of principle investigator (PI), co-investigator and/or key collaborator(s)
- Brief description (no more than two pages in length) of proposed clinical trial, including the scientific basis and rationale, evidence for tolerance induction, clinical implications, feasibility, potential mechanistic studies and tolerance assays that should accompany the trial, and references to published or preliminary data (preliminary data need not be presented in detail)
- Biosketches of PI and co-investigators and collaborators (does not count toward page limit)

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

Philip Bernstein, PhD

Executive Director of Scientific Review

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About the Immune Tolerance Network

The Immune Tolerance Network is a clinical research consortium dedicated to the development of immune tolerance therapies for transplantation, autoimmune diseases, and asthma and allergy. The ITN currently supports over 20 clinical trials, each with integrated investigations of the clinical mechanisms of tolerance. The ITN consortium is led by several institutions, including University of California, San Francisco; Benaroya Research Institute at Virginia Mason, Seattle; Beth Israel Deaconess Medical Center, Boston; and Duke University, Durham, and is sponsored by the National Institute of Allergy and Infectious Diseases, with support from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the Juvenile Diabetes Research Foundation.

www.immunetolerance.org