



REQUEST FOR PROPOSALS

Antigen-Specific Tolerance Assays

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 invites proposals for development and validation of assays that characterize antigen-specific immune responses, suitable for use with human peripheral blood samples derived from subjects in ITN clinical trials.

The ITN makes extensive use of immunological assays and biomarkers to evaluate clinical trial mechanisms of drug action, mechanisms of immunological response, and correlates of prognosis; however in most trials we are still lacking specific immunologic signals that can help guide trial design and mechanistic understanding. Recent advances with antigen-specific and single cell profiling have the potential to open the door to understanding targeted, personalized immunobiology. In order to rapidly exploit this opportunity to apply these tools to ITN clinical trials, we are seeking proposals for assays to measure antigen-specific responses in samples collected from ITN trials. Prior clinical validation is not required; rather, we are seeking exploratory assays that have a strong rationale and some evidence of reproducibility and potential application. We will prioritize assays that envision cross-disciplinary utility; which can be applied to transplantation allo-antigen recognition, autoimmune antigen activation, as well as allergen responses. Any modality of assay is potentially applicable—whether phenotypic, transcriptional, or functional. Direct (e.g., tetramers) and indirect (e.g., antigen-specific functional correlates) assays will both be considered responsive to this request.

The ideal mechanistic assay for cellular tolerance to disease-associated antigens will meet several of the following criteria:

- 1. Identify and enumerates antigen-specific cells;**
- 2. Measure activation of antigen-specific cells;**
- 3. Quantify products secreted in vivo and/or measure other in vivo effects (e.g. cytotoxicity) during antigen-specific responses;**
- 4. Determine lineage commitment of antigen-specific cells;**
- 5. Describe a characteristic phenotype for antigen-specific cells;**
- 6. Priority will be given to assays that measure and characterize antigen-specific CD4 and CD8 effector and regulatory lymphocytes with minimal in vitro manipulation/culture.**



Selected respondents will be provided funding and samples from the ITN biorepository for assay development and validation, analyzed in partnership with ITN scientists.

Proposals are welcome from academic, government and industry-based investigators; funding will vary based on the type and scope of the study. Applicants should submit a 5-page Concept Proposal no later than ***December 1st, 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 assay and supporting data (as enumerated in the above listed criteria);
- References to published or preliminary data. Unpublished data may be submitted as supplemental material.

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

Philip Bernstein, PhD

Executive Director of Strategic Review and Planning

Tel: (240) 235-6132

Email: pbernstein@immunetolerance.org