# The Immune Tolerance Network

**The Immune Tolerance Network (ITN)** is a collaborative network for clinical research focused on the development of therapeutic approaches for asthma and allergy, autoimmune diseases, type 1 diabetes and solid organ transplantation that lead to immune tolerance. These tolerogenic approaches aim to reprogram the immune system so that disease-causing immune responses are stopped while maintaining the immune system's ability to combat pathogen infection. The Network develops, funds and conducts mechanistic, laboratory-based studies in conjunction with clinical trials through collaborations with academic, governmental and industry researchers.

The ITN is funded by a grant awarded to the Benaroya Research Institute at Virginia Mason, the University of California San Francisco and the Massachusetts General Hospital from the National Institute of Allergy and Infectious Disease of the National Institutes of Health.

## ITN by the Numbers

- **19 years of successful clinical trials** – established in 2000
- **75 total clinical trials** – 18 Allergy; 32 Autoimmunity; 25 Transplant
- **250+ clinical sites** and investigators at leading academic hospitals and research institutions worldwide
- **3500+ patients** enrolled in ITN clinical trials
- **579,000 clinical specimens** in the ITN repository

## Selected Highlights

- Demonstrated that high dose immunosuppressive therapy combined with autologous hematopoietic cell transplantation effective for inducing long-term sustained remission of MS through 5 years after transplant [Neurology. 2017]
- Showed that operationally tolerant pediatric liver transplant recipients maintain generally stable allograft histology in spite of apparently active humoral allo-immune responses. [Hepatology. 2017]
- Provided conclusive evidence that early consumption of peanut by high-risk infants prevents the development of peanut allergy even after cessation of consumption [New Engl J Med. 2015; 2016]
- Launched ITN TrialShare (ITNtrialshare.org), a clinical research data portal and analysis platform that permits the sharing of detailed data and analyses from clinical trials. [New Engl J Med. 2013]
- Showed that up to 60% of selected pediatric liver transplant recipients may safely discontinue all immunosuppression, without transplant rejection [JAMA. 2012]
- Established the efficacy of rituximab for ANCA-associated vasculitis, providing justification for FDA approval [New Engl J Med. 2010]
- Discovered a unique genetic signature in transplant patients that may indicate a propensity for tolerance [J Clin Ivest. 2010]
- Established proof-of concept that a novel anti-CD3 drug could preserve beta cell function in recently diagnosed type 1 diabetes patients for over 5 years [Clin Immunol. 2009]
- Demonstrated that combined bone marrow and kidney transplant can induce long-term tolerance with no need for ongoing immunosuppression [New England J Med. 2008]
- Successfully completed the world's first multicenter clinical trial of a standardized protocol for islet cell transplantation for type 1 diabetes [New Engl J Med. 2006]

## Clinical Trial Transparency

The ITN has a major commitment towards improved clinical trial transparency and increased access to clinical trial results. We believe in fostering data sharing – allowing researchers to access participant-level data for ITN trials, over-and-above the data published in the scientific literature. However, the ITN recognizes that technical and operational challenges in the reporting and sharing of highly varied and often complex clinical and translational research data must be addressed for the true benefits of transparency to be realized.

## ITN TrialShare

The ITN TrialShare platform marks a revolutionary step forward in overcoming these barriers and establishing true clinical trial transparency. Developed by the ITN using the open source LabKey Server (www.labkey.org) platform, ITN TrialShare is a clinical research web portal that permits public access to de-identified participant-level clinical trial data, as well as the analysis data and code underlying published findings. Investigators can re-run and validate previously published analyses, interactively perform their own exploratory analyses within the system, and download data and code for further use in their own research.

ITN TrialShare provides a comprehensive set of features and tools opening the door for a new era in clinical trial transparency. ITN TrialShare:

- Enables sharing of complex clinical trial and research assay data in a user friendly interface, allowing custom subset definition and data export in a variety of formats
- Provides access to patient-level data, de-identified for public access
- Allows users to re-run and revise analyses using stored statistical codebases
- Brings interactive advanced visualizations to the desktop with web-based graphical analysis tools
- Enables interactive figures for manuscript publication that give reviewers, editors and readers the ability to delve deeper into the data and accompanying analyses
- Provides access to the ITN specimen repository catalog

At present, ITN TrialShare provides public access to comprehensive de-identified participant-level data for 25 studies, including specialty assay data such as gene expression, flow cytometry, and sequencing T-cell repertoire files. In addition, analysis datasets and code supporting findings are available from 11 ITN publications in the New England Journal of Medicine (NEJM), Journal of Clinical Investigation (JCI) and the Journal of the American Medical Association (JAMA), among others.

### ITN TrialShare Awards and Recognition

- “First Place” in the National Academies Data and Information Challenge in 2014
- “Honorable Mention” at the Bio-IT World’s Best Practices Awards in 2013
- Participant-level data and the new frontier in trial transparency. NEngl J Med. 2013 Aug 1;369(5):468-9. doi: 10.1056/NEJMe1307268
- Clinical trial data access: Opening doors with TrialShare. J Allergy Clinical Immunology, 2016 Sept; 138(3):724-726. doi: 10.1016/j.jaci.2016.05.03
- Looking behind the data curtain. Cell Immunol. 2017 Sep;319:1-2. doi: 10.1016/j.cellimm.2017.07.008