

## **TYPE 1 DIABETES TRIALNET (TrialNet)**

<http://www.diabetestrialnet.org/>

### **Description of project**

- The goal of TrialNet is to create and maintain a national diabetes trial network of clinical research groups whose aim is to recruit patients and support studies that will result in an improved understanding of type 1 diabetes and the prevention of the disease.
- Specific study objectives are:
  - To gain information about the pathogenesis and natural history of diabetes, as part of the TrialNet Natural History Study of the development of Type 1 Diabetes
  - To conduct intervention studies to preserve pancreatic beta cell function in individuals with newly-diagnosed diabetes
  - To conduct intervention studies to prevent type 1 diabetes in individuals at risk for the disease
  - To conduct genetic studies in subjects identified through the Natural History and intervention studies
  - To conduct ancillary mechanistic studies as a part of the Natural History and intervention studies, for improved understanding of the immunologic basis of diabetes.

### **Accomplishments**

- Completion of the DPT-1 Parenteral Insulin Trial of prevention of type 1 diabetes in high-risk subjects; completion of the DPT-1 oral insulin trial in intermediate risk subjects.
- 8 publications based on DPT-1 findings to date, including:
  - Diabetes Prevention Trial - Type 1 Diabetes Study Group. Effects of Insulin in Relatives of Patients with Type 1 Diabetes Mellitus. **New England Journal of Medicine** 2002; 346:1685-1691.
- Establishment of TrialNet committee structure with an Executive Committee, a Steering Committee, a DSMB, 19 sub-committees, and 15 protocol development committees.
- Establishment of policies for protocol development, review and approval; management of dualities of interest; publications and presentations; ancillary studies; and other aspects of network operations.
- Establishment of a main secure study website for conduct of network-wide communications and operations, a public website to assist recruitment and 6 additional websites for use by specific groups, such as potential affiliate sites.
- Addition of 4 international clinical centers (Italy/Germany, Finland, UK and Australia), a Central Biochemistry Laboratory and a Central Virology Laboratory.
- Establishment of a process for entering into a contractual Letter of Agreement (LOA) with up to 350 affiliate sites that will participate in screening and other studies.

- Development of the “*TrialNet Natural History Study of The Development of Type 1 Diabetes*” for the screening of first degree relatives for the presence of autoantibodies; the assessment of risk of diabetes based on number of antibodies present, HLA type and glucose intolerance; and the assessment of the natural history of diabetes onset in autoimmune pre-diabetes.
- Development of the TrialNet “*Clinical Trial of Mycophenolate Mofetil - Daclizumab in New Onset of Type 1 Diabetes*” to assess the effectiveness of MMF alone or in combination with DZB in the preservation of beta cell function in subjects with new onset T1DM. This protocol is in the process of finalization and is expected to begin recruiting soon.
- Six additional protocols are under development for preservation of beta cell function in new onset diabetes, and possibly for prevention in autoimmune pre-diabetes, one for prevention of autoimmune pre-diabetes, and one for prevention of development of autoimmunity in children.
- Continued follow-up of DPT-1 subjects who did not become diabetic during DPT-1.
- Development of procedures for joint collaboration with the Immune Tolerance Network, Autoimmunity Centers of Excellence, and the Type 1 Diabetes Genetics Consortium.

### **Future directions**

- Continuation of Natural History (and screening, risk assessment) Study (see “Accomplishments”).
- Launch of the MMF/DZB study (see “Accomplishments”).
- Launch of additional studies currently under protocol development.

### **Materials to be made available to researchers**

- Materials will be shared via the NIDDK repository which has currently been established. The timing of the sharing is to be determined. For more information on the NIDDK repository, please visit <http://www.niddk.nih.gov/researchprograms/repositories/>.

### **Participants**

Sponsors: National Institute of Diabetes and Digestive and Kidney Diseases  
 National Institute of Allergy and Infectious Diseases  
 National Institute of Child Health and Human Development  
 Juvenile Diabetes Research Foundation International  
 American Diabetes Association

## Participating Institutions

*Chairman's Office*  
University of Miami

*Coordinating Center*  
George Washington University

### *Clinical Centers*

Childrens Hospital Los Angeles  
Stanford University Medical Center  
University of California, San Francisco  
Barbara Davis Center for Childhood Diabetes, University of Colorado-Denver  
University of Florida Health Science Center, Gainesville  
University of Miami School of Medicine  
Riley Hospital for Children, Indiana University - Indianapolis  
Joslin Diabetes Center, Children's Hospital Boston  
University of Minnesota, Minneapolis  
Naomi Berrie Diabetes Center, Columbia University - New York  
Children's Hospital of Pittsburgh  
University of Texas Southwestern Medical Center at Dallas  
Benaroya Research Institute at Virginia Mason, Seattle  
Hospital for Sick Children, Toronto, Canada  
San Raffaele University Hospital and Scientific Institute, Milan, Italy  
University of Turku, Department of Pediatrics, Finland  
University of Bristol, Southmead Hospital, Bristol, U.K.  
Walter and Eliza Hall Institute of Medical Research, Royal Melbourne Hospital Burnet  
Clinical Research Unit, Victoria, Australia

### Steering Committee

<u>Name</u>	<u>Affiliation</u>
Jay Skyler, MD, Chair	University of Miami
Mark Anderson, MD, PhD	University of California, San Francisco
Dorothy Becker, MD	University of Pittsburgh
Christophe Benoist, MD, PhD	Joslin Diabetes Center
Penelope Bingley, MD	University of Bristol, UK
Emanuele Bosi, MD	San Raffaele University, Italy
David Brown, MD	University of Minnesota
H Peter Chase, MD	University of Colorado
Michael Clare-Salzler, MD	University of Florida
Peter Colman, MBBS, PhD	Royal Melbourne Hospital, Australia
George Eisenbarth, MD, PhD	University of Colorado
C. Garrison Fathman, MD	Stanford University
Stephen Gitelman, MD	University of California, San Francisco

Robin Goland, MD	Columbia University
Robert Goldstein, MD	Juvenile Diabetes Research Foundation International
Peter Gottlieb, MD	University of Colorado
Gilman Grave, MD	National Institutes of Health
Carla Greenbaum, MD	Benaroya Research Institute at Virginia Mason
Len Harrison, MBBS, MD, DSc	University of Melbourne, Australia
Bernhard Hering, MD	University of Minnesota
Kevan Herold, MD	Columbia University
Stanley Jordan, MD	Cedars-Sinai Medical Center
Francine Kaufman, MD	Children's Hospital, Los Angeles
Jeffrey Krischer, PhD	Lee Moffitt Cancer Center
John Lachin, ScD	George Washington University
Ellen Leschek, MD	National Institutes of Health
Jeffrey Mahon, MD, MSc	University of Western Ontario, Canada
Jennifer Marks, MD	University of Miami
Kirsti Nanto-Salonen, MD, PhD	University of Turku, Finland
Gerald Nepom, MD, PhD	Benaroya Research Institute at Virginia Mason
Tihamer Orban, MD	Joslin Diabetes Center
Jerry Palmer, MD	University of Washington
Mark Peakman MBBS,BSc,PhD	University of Bristol, UK
Mark Pescovitz, MD	Indiana University
Alberto Pugliese, MD	University of Miami
Philip Raskin, MD	University of Texas
John Ridge, PhD	National Institutes of Health
Henry Rodriguez, MD	Indiana University
Desmond Schatz, MD	University of Florida
Mark Siegelman, MD, PhD	University of Texas
Olli Simell, MD, PhD	University of Turku, Finland
Massimo Trucco, MD	University of Pittsburgh
Diane Wherrett, MD	Hospital for Sick Children, Ontario, Canada
Darrell Wilson, MD	Stanford University
William Winter, MD	University of Florida
Anette Ziegler, MD	Institute for Diabetes, Muenchen, Germany