Type 1 Diabetes Genetics Consortium

IRB# 2007-032
Principal Investigator: Suruchi Bhatia, MD

Synopsis:
Type 1 Diabetes Genetic Consortium (T1DGC) study is an international effort to identify the genes that affect the risk of Type 1 diabetes. This study will establish the “Type 1 Diabetes Genetics Consortium” (T1DGC). The goal of the Consortium is to organize international efforts to identify genes that determine an individual’s risk of type 1 diabetes. Progress towards this goal, worldwide, has been limited by a lack of sufficient clinical and genetic resources. The power of larger collections of families to map type 1 diabetes genes has been demonstrated in a pilot study. The creation of a resource base of well-characterized families from multiple ethnic groups will facilitate the localization and characterization of type 1 diabetes genes that determine disease risk. Statistical genetic analyses will be performed on appropriately powered data sets to identify regions linked to type 1 diabetes and determine how these linked regions act and potentially interact. Building upon these Consortium resources, members and collaborators of the Consortium will undertake positional cloning to identify individual genes that determine susceptibility or protection.

To establish this combined resource of 4800 ASP families and to carry out an appropriately powered search for type 1 diabetes susceptibility genes, a series of specific aims are proposed to fully utilize and update existing materials and to collect new clinical resources. The specific aims will be achieved by the concerted efforts of clinicians, geneticists and genetic epidemiologists. The specific aims of this study are:

1. Ascertain 3000 new families with two or more type 1 diabetic siblings through an established Asia-Pacific Network (200), an European Network (1200), a North American Network (100), and a United Kingdom Network (300).
2. In order to detect the effects of HLA and other candidate regions/genes on the signals from the genome screen, all samples will be genotyped for HLA class I and class II genes (DRB1, DQB1, DPB1, DPA1, A, B, C), INS, and CTLA4 polymorphisms that have previously been implicated in susceptibility to type 1 diabetes.
3. Refine the localization of the 5 most promising regions identified from linkage and association studies.
4. To aid in the confirmation and identification of diabetes susceptibility genes within linked regions, the Consortium will use existing and planned resources of single case families (trios, including an affected child and both biological parents) to carry out detailed disease association analyses.

These collections have been identified through initiatives of individual investigators and the NIDDK/JDRF. The Consortium will facilitate new collections of trio families through its Asia-Pacific Network to obtain diverse disease-associated haplotypes for fine mapping from Asian populations.

The ultimate goal is to provide the fundamental clinical and genetic resources to achieve the necessary sample size and sample availability for gene identification. The Consortium will establish a mechanism to ensure that scientists will work together toward a better understanding of the genetic factors that underlie risk for type 1 diabetes. The Consortium will gain a better understanding of disease mechanisms, with a purpose of altering these mechanisms and pathways in individuals at risk of type 1 diabetes.