RECRUITMENT

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I. INTRODUCTION

The recruitment goal for the Type 1 Diabetes Genetics Consortium (T1DGC) is 2,800 affected sibling pair (ASP) families. In addition, trio families, cases, and controls will be recruited in the Asia-Pacific, European, and North American Networks from populations with a low prevalence of type 1 diabetes. While each network has different strategies for recruiting families, all networks share the same eligibility criteria (see **Chapter IV**, *Eligibility*).

The optimal ASP family structure is two affected siblings, both biological parents and (up to) two unaffected siblings. Up to five affected siblings per family are allowed to participate, but this requires advance notification and permission. The optimal trio family is an affected child and both biological parents. In the North American network, only African American and Mexican American trio families are eligible. In the case-control study, individuals will be recruited and cases and controls will be frequency matched on primary ethnic group, gender, and region.

Recruitment of families requires the parents who provide genetic material be the biological (full) parents of the affected and unaffected siblings, and similarly, the siblings be full (not half-, step-, or adopted) siblings, having the same biological mother and same biological father. Details of study-wide recruitment are provided below.

II. RECRUITMENT GOALS

A. Asia-Pacific Network

The Asia-Pacific Network has a total of 20 clinics and the goal is to recruit 340 ASP families. In addition, the Asia-Pacific Network will recruit trio families from ethnic groups other than Caucasian. In addition to ASP and trio families, cases and controls will be recruited in Cuttack, India.

B. European Network

The European Network has a total of 84 clinics and the goal is to recruit 1,200 ASP families. In addition, trio families, cases, and controls will be recruited in Cameroon.

C. North American Network

The North American Network has 62 clinics and the goal is to recruit 1,100 ASP families. In addition, trio families, cases, and controls will be collected in African American and Mexican American populations.

D. United Kingdom Network

The United Kingdom Network has 48 clinics and the goal is to recruit 160 ASP families. Trio families, cases, and controls will not be collected.

E. Final Enrollment

Recruitment of ASP and trio families was initiated in January 2004 and ended in August 2009. Recruitment of cases and controls in low prevalence populations was initiated in December 2007 and ended in January 2010. Final enrollment by participant type and network are provided in Table 1.

Table 1. T1DGC enrollment, by participant type, network and overall.

Network	ASP Families (Individuals)	Trio Families (Individuals)	Cases	Controls
Asia-Pacific	326 (1,341)	290 (870)	23	77
European	1209 (4,786)	10 (30)	5	2
North American	1140 (4,828)	193 (579)	802	889
United Kingdom	161 (671)	N/A	N/A	N/A
Overall	2836 (11,626)	493 (1,479)	830	968

III. ETHNIC-, RACE-, AND GENDER-SPECIFIC RECRUITMENT

The National Institutes of Health (NIH) is the funding agency for the T1DGC and requires quarterly reporting of enrollment by ethnicity, race and gender. For these purposes, ethnicity is reported as either Hispanic or Latino ***OR*** Not Hispanic or Latino.

Race is reported to the NIH as American Indian/Alaskan Native; Asian; Native Hawaiian or Other Pacific Islander; Black or African American; and/or White. However, race will be collected in network-specific categories. Participants are permitted to report up to three race categories, but must specify a primary category to be reported to the NIH.

Tables 2-5 provide the final enrollment numbers for ASP families, trio families, cases, and controls, respectively, by ethnicity, race and gender, within network and overall.

Table 2. T1DGC ASP Family Enrollment, by NIH Ethnicity and Race Categories and Gender, within T1DGC Network and Overall, February 10, 2011

	NETWORK				
	Asia-Pacific	**European**	**North American**	**United Kingdom**	**Overall**
ETHNIC CATEGORY					
Hispanic or Latino (Females/ Males)	**0**	**0**	**139/118**	**0**	**139/118**
Not Hispanic or Latino (Females/ Males)	**715/626**	**2462/2324**	**2312/2259**	**367/304**	**5856/5513**
Ethnic Category: Total Participants (Females/Males)	**715/626**	**2462/2324**	**2451/2377**	**367/304**	**5995/5631**
RACIAL CATEGORIES					
American Indian/ Alaska Native (Females/Males)	**0**	**0**	**7/6**	**0**	**7/6**
Asian (Females/Males)	**48/49**	**0**	**19/17**	**5/4**	**72/70**
Hawaiian/ Other Pacific Islander (Females/Males)	**9/10**	**0**	**2/7**	**0**	**11/17**
Black or African American (Females/Males)	**9/13**	**6/2**	**55/50**	**2/3**	**72/68**
White (Females/Males)	**649/554**	**2456/2322**	**2368/2297**	**360/297**	**5833/5470**
Racial Categories: Total Participants (Females/Males)	**715/626**	**2462/2324**	**2451/2377**	**367/304**	**5995/5631**

Table 3. T1DGC Trio Family Enrollment, by NIH Ethnicity and Race Categories and Gender, within T1DGC Network and Overall, February 10, 2011

	NETWORK				
	Asia-Pacific	**European**	**North American**	**United Kingdom**	**Overall**
ETHNIC CATEGORY					
Hispanic or Latino (Females/ Males)	**0**	**0**	**162/147**	**--**	**162/147**
Not Hispanic or Latino (Females/ Males)	**449/421**	**12/18**	**145/125**	**--**	**606/564**
Ethnic Category: Total Participants (Females/Males)	**449/421**	**12/18**	**307/272**	**--**	**768/711**
RACIAL CATEGORIES					
American Indian/ Alaska Native (Females/Males)	**0**	**0**	**0**	**--**	**0**
Asian (Females/Males)	**449/421**	**0**	**0**	**--**	**449/421**
Hawaiian/ Other Pacific Islander (Females/Males)	**0**	**0**	**0**	**--**	**0**
Black or African American (Females/Males)	**0**	**12/18**	**149/125**	**--**	**161/143**
White (Females/Males)	**0**	**0**	**158/147**	**--**	**158/147**
Racial Categories: Total Participants (Females/Males)	**449/421**	**12/18**	**307/272**	**--**	**768/711**

Table 4. T1DGC Case Enrollment, by NIH Ethnicity and Race Categories and Gender, within T1DGC Network and Overall, February 10, 2011

	NETWORK				
	Asia-Pacific	**European**	**North American**	**United Kingdom**	**Overall**
ETHNIC CATEGORY					
Hispanic or Latino (Females/ Males)	**0**	**0**	**120/129**	**--**	**120/129**
Not Hispanic or Latino (Females/ Males)	**7/16**	**1/4**	**315/238**	**--**	**323/258**
Ethnic Category: Total Participants (Females/Males)	**7/16**	**1/4**	**435/367**	**--**	**443/387**
RACIAL CATEGORIES					
American Indian/ Alaska Native (Females/Males)	**0**	**0**	**0**	**--**	**0**
Asian (Females/Males)	**7/16**	**0**	**0**	**--**	**7/16**
Hawaiian/ Other Pacific Islander (Females/Males)	**0**	**0**	**0**	**--**	**0**
Black or African American (Females/Males)	**0**	**1/4**	**331/244**	**--**	**1/4**
White (Females/Males)	**0**	**0**	**104/123**	**--**	**435/367**
Racial Categories: Total Participants (Females/Males)	**7/16**	**1/4**	**435/367**	**--**	**443/387**

Table 5. T1DGC Control Enrollment, by NIH Ethnicity and Race Categories and Gender, within T1DGC Network and Overall, February 10, 2011

	NETWORK				
	Asia-Pacific	**European**	**North American**	**United Kingdom**	**Overall**
ETHNIC CATEGORY					
Hispanic or Latino (Females/ Males)	**0**	**0**	**170/66**	**--**	**170/66**
Not Hispanic or Latino (Females/ Males)	**24/53**	**1/1**	**473/180**	**--**	**498/243**
Ethnic Category: Total Participants (Females/Males)	**24/53**	**1/1**	**643/246**	**--**	**668/300**
RACIAL CATEGORIES					
American Indian/ Alaska Native (Females/Males)	**0**	**0**	**0**	**--**	**0**
Asian (Females/Males)	**24/53**	**0**	**0**	**--**	**24/53**
Hawaiian/ Other Pacific Islander (Females/Males)	**0**	**0**	**0**	**--**	**0**
Black or African American (Females/Males)	**0**	**1/1**	**484/185**	**--**	**485/186**
White (Females/Males)	**0**	**0**	**159/61**	**--**	**159/61**
Racial Categories: Total Participants (Females/Males)	**24/53**	**1/1**	**643/246**	**--**	**668/300**

IV. MINIMAL ACCEPTABLE STRUCTURE

A. Affected Sibling Pair (ASP) Families

Recognizing the difficulty in recruiting two affected siblings, both biological parents and two unaffected siblings, the Steering Committee established the following minimum data collection standards that define recruitment of an ASP family (thereby constituting reimbursement): ***completion of data forms (T1DGC ASP Eligibility Form, T1DGC ASP Consent Summary Form, layered portion of the informed consent, T1DGC ASP Exam Form and T1DGC Blood Collection Form) and collection of blood samples for both affected siblings.***

Additional reimbursement is provided for completion of questionnaires and collection of blood samples for each parent, and up to two unaffected siblings. As many as three additional affected siblings per family can also be included if approved by the Regional Network Center.

B. Trio Families

In families where only one affected child is available for participation, the inclusion of both the biological mother and biological father of this child is required. The Steering Committee established the following minimum data collection standards that define recruitment of a trio family (thereby constituting reimbursement): ***completion of data forms (T1DGC Trio Consent Summary Form, layered portion of informed consent, T1DGC Trio Eligibility Form, T1DGC Trio Exam Form, and T1DGC Blood Collection Form) and collection of blood samples for the affected child and both biological parents.*** In the North American Network, the *T1DGC North American Trio Pre-Eligibility Form* must also be completed to meet minimum data collection standards. No reimbursement is provided for any additional family members. Only approved networks and clinics are reimbursed for the collection of trio families.

In the North American Network, a trio family is eligible only if both biological parents are African American or Mexican American. The specific criteria for these low-prevalence trios are:

Mexican American: Defined as any individual of **Mexican** descent living in North America (US or Canada). The proband does not need to be born in North America. While the primary goal of this collection is to ascertain Mexican American individuals, individuals can be recruited and examined if born in Central America: Belize, Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, or Panama.

African American: Defined as any individual of **non-Caucasian of African** descent living in North America (US or Canada). This includes (but is not limited

to) descent from Egypt and Somalia. The proband does not need to be born in North America. No Caucasians of African descent qualify (*e.g.*, white South African) and these individuals cannot be included as trio families due to the sufficient number of Caucasian trios from previous collections.

C. Case-Control Collection

The case-control collection is conducted in low prevalence populations and is in addition to the ASP and trio family collections. Cases are individuals with type 1 diabetes who meet the T1DGC definition will be enrolled. Controls are individuals from the same populations who are unrelated to the cases, do not have any form of diabetes, and do not have any biological relatives (*i.e.*, father, mother, brother(s), sister(s), or children) who have been diagnosed with any form of diabetes. The Steering Committee established the following minimum data collection standards for the case (thereby constituting reimbursement): ***completion of data forms (layered portion of informed consent, T1DGC Consent Record, T1DGC Case Eligibility Form, T1DGC Case Exam Form, and T1DGC Blood Collection Form) and collection of blood samples for the individual.*** The minimum data collection standards for the control (thereby constituting reimbursement) are: ***completion of data forms (layered portion of informed consent, T1DGC Consent Record, T1DGC Control Eligibility Form, and T1DGC Blood Collection Form) and collection of blood samples for the individual.*** No reimbursement is provided for any additional family members. Only approved networks and clinics are reimbursed for the collection of cases and controls.

In the Asia-Pacific Network, only Cuttack, India will participate in the collection of cases and controls. In the European Network, only Cameroon will participate in the collection of cases and controls.

In the North American Network, a case must be a person with type 1 diabetes who is African American or Mexican American. A control must be a person without any type of diabetes who is African American or Mexican American. The specific criteria for these low-prevalence participants are the same as the trio families, described above.

D. Reimbursement

Reimbursement is provided to the clinics to be used for personnel support, supplies, and/or incentives or remuneration for participating family members. Regional Network Centers invoice the Coordinating Center for recruitment on a monthly basis and reimburse the clinics based on family recruitment.

V. RECRUITMENT STRATEGIES

This section describes the planned recruitment strategies for each of the four networks.

A. Asia-Pacific

Network Coordinating Center: Walter and Eliza Hall Institute of Medical Research; Melbourne, Australia
Network Principal Investigators: Grant Morahan, Ph.D. and Peter Colman, M.D.
Network Coordinator: Amanda Loth, R.N.

The Asia-Pacific Network aims to recruit primarily via clinics and patients at collaborating institutions. It is expected that each collaborating clinic develops its own contacts regionally to increase the number of families it is able to recruit. This regional recruitment is the responsibility of each institution.

Regular contact with the clinics is made by the Network Coordinator to facilitate the process of getting blood samples to Melbourne. This is accomplished via regular conference calls and e-mail contact.

Each participating country has identified the anticipated number of families to be recruited. Recruitment goals for this network are 340 ASP families and as many non-Caucasian trios, cases and controls as deemed feasible. A plan has been negotiated with each clinic for timing of recruitment and is monitored by the Network Coordinator.

B. European Network

Network Coordinating Center: Hagedorn Research Institute; Gentofte, Denmark
Network Principal Investigators: Jorn Nerup, M.D., D.M.Sc. and Flemming Pociot, M.D., D.M.Sc.
Network Coordinators: Lotte Albret, B.A.

The recruitment strategy for the European Network follows various approaches. The majority of clinics/regions/countries have registries from which probands can be identified. At least two-thirds of the families are likely to be identified by this approach. The remainder of the families will either be recruited through existing clinical networks for type 1 diabetes (*e.g.,* ENDIT) or by general recruitment strategies. The latter includes announcements at professional meetings, patient organizations' meetings, and advertisements in lay journals.

The European Network contains a number of previously genome-screened families in the Scandinavian countries. In Sweden, there is a registry-based system to ensure that families are not double-ascertained. In Denmark, primary focus is on newly eligible families since the last collection. Because most families collected in Denmark are coordinated from one clinic, it is possible to validate their ascertainment as "new." Participants are queried about previous participation in these studies on the *T1DGC Eligibility Form*.

C. North American Network

Network Coordinating Center: Benaroya Research Institute; Seattle, Washington, USA
Network Principal Investigator: Carla Greenbaum, M.D.
Network Coordinator: Angela Dove, B.A.

The North American Network will recruit 1,100 ASP families. First, approximately half of designated clinics are responsible for collection of approximately 60% of the ASP families (n=660). Second, approximately 30% of families (n=330) are expected to be recruited through interactions with existing clinical networks for Type 1 diabetes (*e.g.,*

TrialNet, EDIC, SEARCH, etc.). Third, 10% of families (n=110) will be recruited through general recruitment strategies. These include announcements at relevant professional meetings (*e.g.,* ADA, CDA, CDE), notices and articles in lay journals directed towards people with Type 1 diabetes (*e.g., Diabetes Forecast, JDRF Countdown*), and directed mailings (*e.g.,* JDRF or ADA members, Certified Diabetes Educators and school nurses). In addition, trios, cases, and controls will be recruited from African American and Mexican American populations.

Recruitment materials include flyers, posters, brochures, small items with TIDGC logos, an 800 phone number, web site, and dedicated e-mail address. Incentive items may include small items such as hats, T-shirts, or similar. Participants and families are compensated for their time and effort to participate in the study.

D. United Kingdom Network

Network Coordinating Center: University of Cambridge; Cambridge, United Kingdom
Network Principal Investigator: John Todd, Ph.D.
Network Coordinator: Heather Withers, BA, MSC

Multiplex families are identified using the existing UK GRID infrastructure, and samples and data are collected using regionally organized, clinic-based recruitment. Affected sibling pairs, unaffected siblings and parents are approached by field workers for DNA and antibody samples. Samples and family histories are collected from parents at the interview. The majority of affected siblings in this network are younger than 16 years.

A number of samples that are suitable for developing cell lines are already available from certain probands and affected siblings. These families will be re-contacted to obtain phenotypic data and other blood samples.

VI. PREVIOUSLY GENOME-SCREENED FAMILIES

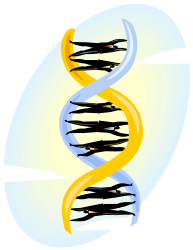
No “double ascertainment” of families is permitted. These may include participants in the United States, United Kingdom, and Scandinavian countries (*e.g.,* HBDI, BDA/Warren I, and SCAND). Individuals also are ineligible if a member of their family has previously participated in the Type 1 Diabetes Genetics Consortium. Attempts to identify such individuals are made by asking a question about participation in genetic studies as part of the eligibility screening process on the *T1DGC Eligibility Form*.

VII. RECRUITMENT MATERIALS

Each network can assist the clinics in developing clinic-specific recruitment materials. However, local Internal Review Board (IRB) or Ethics Committee (EC) approval must be obtained to use such materials. Regional Network Centers may require copies of approved recruitment materials from each clinic. Examples of recruitment flyers and brochures for ASP families are available in Appendix A.

APPENDIX A

EXAMPLES OF RECRUITMENT MATERIALS



Type 1 Diabetes Study

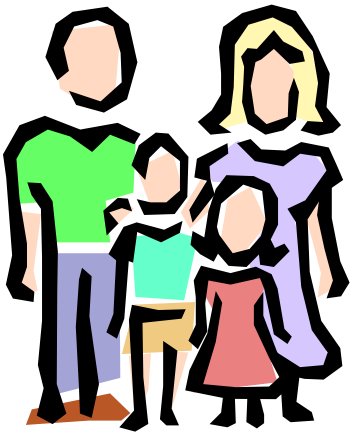
Type 1 Diabetes Genetics Consortium

In your family, are there two siblings (brothers or sisters) **with Type 1 diabetes?**

If so, your family may be eligible to help researchers understand the genetic causes of Type 1 diabetes.

If eligible, some members of your family will have a **small** amount of blood collected and will be asked questions about their health. There is no cost to you.

If you are interested in participating or would like to learn more about this study, please contact:



Name of Clinic Coordinator
Name of Clinic
Contact Information

Or get more information on our web site:
http://www.t1dgc.org

National Institute of Diabetes and Digestive and Kidney Diseases
Juvenile Diabetes Research Foundation
National Institute of Allergy and Infectious Diseases
National Human Genome Research Institute

What is the Type 1 diabetes genetic consortium?

The consortium is a group of diabetes researchers from around the world who have come together to collect samples and information from families with Type 1 diabetes.

What is the consortium trying to do?

We are trying to discover how differences in the genes that we inherit from our parents contribute to the risk for development of Type 1 diabetes. Genes are the 'blue prints' in our bodies which we get from our parents at birth, that decide our characteristics like the color of our hair, our eyes and the shape of our bodies. Some genes are also involved in whether you have diabetes or not. If we find out more about these genes, we may be able to prevent diabetes in the future.

Who can participate?

We are looking for families in which there are at least two siblings (brothers or sisters) with Type 1 diabetes. In these families, we would like the participation of the people with diabetes, other siblings without diabetes, and their parents.

What you will need to do:

If you want to help us, we will take some blood and ask you some questions about your diabetes and your health.

What is being done with my blood?

The blood will go to XXXXX where scientists will study the genes in the cells of the blood. The blood will be prepared in such a way that you do not need to come back in the future.

What do I do next?

After you have read this brochure, think about it and talk with other family members. If you have any more questions or want more information, please ask XXXXXXXXX or visit our web site at http://www.t1dgc.org. If interested, you will receive more information and an appointment will be scheduled. If you have e-mail, you can send your questions to the Clinic Coordinator in XXXXXXX at the address given.

Contact Information

Clinic Coordinator:

Phone:

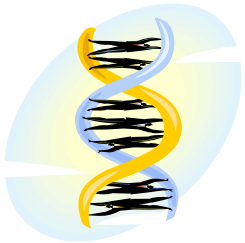
e-mail:

XXXXXX Network:

Network Principal Investigator:

Network Coordinator:

The Type 1 Diabetes Genetic Consortium



National Institute of Diabetes and Digestive and Kidney Diseases
Juvenile Diabetes Research Foundation
National Institute of Allergy and Infectious Diseases
National Human Genome Research Institute

Enter local hospital details