Strong Heart Family Study

Analyses of data from the Strong Heart Study indicate that rates of cardiovascular disease (CVD) are now higher in American Indians than in other US populations and appear to be increasing (Howard et al., 1999). The continuing health disparities that exist between American Indians and the general U.S. population are a serious problem that must be addressed. Moreover, studies in American Indian populations, which are enriched for diabetes, obesity, and other cardiovascular risk factors, provide a unique opportunity to identify genes that increase susceptibility.

A component of the Strong Heart Study is the Strong Heart Family Study (SHFS), with its goal being to assess the genetic contributions to CVD. The SHFS is the only large, genetic study of cardiovascular disease risk factors in American Indians. This is a collaborative project involving investigators at the Southwest Foundation for Biomedical Research, the University of North Carolina, Medstar Research Institute, the University of Oklahoma Health Sciences Center, Missouri Breaks Industries Research, Inc, and Cornell Medical Center with the cooperation of the Indian Health Service and the tribes in the three geographical areas. The long-term goals of the SHFS are to map and identify genes that contribute to CVD risk in American Indians.

In 1996 (the beginning of Strong Heart Study Phase III), a pilot family study was initiated in which more than 300 members of 9-12 extended families were recruited and examined in each of the three centers in Arizona, South Dakota, and Oklahoma. In Phase IV, more than 900 additional family members were recruited in each center. Another examination of the Family Study participants is ongoing in the Strong Heart Study Phase V. Risk factors for CVD and diabetes were measured in the three rounds of examinations in all three field centers. By the end of recruitment in Phase IV, we had examined more than 3,800 members of extended families, with the goal of localizing genes that influence risk factors for clinical and subclinical CVD, diabetes, and obesity and their progression over time.

We clearly have ample raw material to use in our efforts to map genes that increase CVD risk in American Indians, and also map those that are protective. We have found substantial heritabilities for many cardiovascular disease risk factors, meaning that these risk factors have a genetic (inherited) component. We generated a 10 cM map using genotypes for about 400 short tandem repeat markers in each of the 3,800 enrolled family members. Using linkage analysis and the information from the 10 cM map, we have conducted a preliminary search for regions of the genome that harbor genes that affect CVD risk factors. Examples of our findings include evidence for a gene influencing weight and body mass index on chromosome 4q, a gene influencing insulin and lean body mass on chromosome 2p, and evidence that variation in a region of chromosome 17 influences blood pressure differently between men and women. We are also exploring whether genes have an important effect on individual lifetime CVD risk. The family data from Phases III, IV, and V of the Strong Heart Study will enable us to address this issue in American Indians. We anticipate that we will be able to map other genes that influence cardiovascular disease risk in American Indians. We hope that ultimately we will be able to identify people who, on the basis of the genes they carry, will benefit the most from specific therapies or lifestyle changes.

Genetic Marker Data:
SHFS genetic marker data includes both microsatellite genotypes and SNP genotypes. Approximately 400 microsatellite genotypes were generated in more than 3,800 participants using primer pairs of the ABI PRISM Linkage Mapping Set-MD10 version 2.5 (Applied Biosystems, Foster City, CA). SNP genotyping is being used to fine map QTLs and perform
association analyses. For this reason, SNP genotyping is conducted in both the full SHFS dataset as well as appropriate subsets of participants. Since SNP genotyping efforts are ongoing, questions surrounding markers that have been typed should be addressed to the SHFS using the contact information below.

Collaborations:
The Strong Heart Family Study welcomes collaborations with outside investigators that further the goals of the study and are respectful of the participants’ wishes and contributions. For questions about collaborations and ancillary studies utilizing the available genetic data, please contact Dr. Shelley Cole or Dr. Jean MacCluer at the Southwest Foundation for Biomedical Research in San Antonio, Texas:

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