DIGS Version 3.0/Study 42 (SZ)

Study 42 Description (adapted from CRISP entry)

The long-term objective of this study is to elucidate the genetic heterogeneity of schizophrenia by identifying genes associated with susceptibility. We will conduct dense SNP genotyping using both family-based and population based analyses in four candidate chromosomal regions in order to detect SSL. Regions on chromosomes 6p21, 8p21, 12q32 and 22q11 have been identified based on replicated linkage analyses or confirmed associations. Case-control and linkage disequilibrium studies in a unique genetically homogeneous community (Ashkenazi Jews) will be conducted using state-of-the-art high throughput, robust, and cost-effective SNP BeadArray technology developed by Illumina. DNA and clinical assessments of 418 individuals with schizophrenia are already available (parental DNAs are available for 281 of the subjects). An ethnically matched screened control sample of Ashkenazi DNAs will be available for case/control analyses. In order to confirm any detected risk loci, the proposed study will ascertain 1) a new clinical sample of 300 Ashkenazi Jewish individuals who have a DSM-IV diagnosis of schizophrenia or schizoaffective disorder and; 2) an additional 300 ethnically-matched screened controls. A verification strategy will use DNAs from this replication sample in follow-up case/control analyses. The laboratory plan consists of a 1) a dense search of four candidate regions at an average 25 Kb density using innovative family-based and case/control statistical methods to detect risk haplotypes; 2) evaluation and sequencing of identified positional candidate genes; 3) a staged follow-up and verification strategy in an idependent sample.

Ascertainment: non-systematic

Nonsystematically ascertained subjects with a diagnosis of schizophrenia or schizoaffective disorder were recruited nationwide through advertisements in newspapers and Jewish newsletters; letters and/or talks to community organizations, leaders of the Jewish community, and service providers; and a study Web site hosted by the Johns Hopkins Epidemiology-Genetics Program in Psychiatry. The 256 subjects were recruited from 23 states (including Canadian provinces); the 5 largest concentrations were as follows: NY (34%); FL (13%); MI (6%); MD (4%); PA (3%). Pedigrees were sequentially extended through first-degree relatives of probands and affected (psychotic or Bipolar I disorder) relatives.

309 control subjects were similarly recruited through advertisements at conventions, talks at religious congregations, as well as at talks given to smaller gatherings (e.g. Elderhostel meetings:
see http://www.roadscholar.org/). Approximately 85% of the 309 controls came from Elderhostel courses, which in turn are based on national recruitment.

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