Genome Scan Reveals Areas Linked to Alcoholism

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The most extensive analysis of genetic variations more common in people with alcohol dependence than in healthy controls has identified 51 small chromosomal regions spread across the genome that hold genes with various important functions, reported Catherine Johnson of the National Institute on Drug Abuse and her associates.

Previous research has shown that a substantial portion of the regions where these genes are located have been associated with alcohol and other addictive phenotypes, according to Ms. Johnson and her colleagues.

The researchers identified and pooled together samples from 120 unrelated alcohol-dependent individuals and then pooled a separate group of samples from 160 unrelated, unaffected controls who self-reported European American ethnicities. Most of the healthy control participants had married into the pedigrees, which were collected as part of the Collaborative Study on the Genetics of Alcoholism (Am. J. Med. Genet. B Neuropsychiatr. Genet. Epub ahead of print 2006;DOI:10.1002/ajmg.b.30346).

Using a new kind of SNP microarray chip, the investigators assessed a set of 104,268 SNPs that were localized to the autosomal chromosomes. In each of the sample pools, alleles with frequencies of 2% or higher could be identified, allowing the study of many more SNP markers for more unrelated individuals than were previously available.

From these 104,268 SNPs, the investigators narrowed their analysis down to 188 SNPs that lay in 51 clustering loci in people with alcohol dependence.

This provides the first genome-wide, association-based assessment for genomic loci likely to contain variants that contribute to alcoholism.

Of the 26 candidate genes that were identified within these clusters, 10 also had been identified in the results of other association and linkage studies of addictions in European American, African American, and Japanese individuals who were dependent on at least one substance.

“This level of replication is especially remarkable, since these convergences were sought for samples from different ethnic backgrounds and different addictions,” Ms. Johnson and her associates said.

The candidate genes that were identified in the study involve a potassium channel, intra- and intercell–signaling molecules, enzymes that convert propeptides to biologically active peptides, phospholipid-signaling pathways, regulatory and developmental genes that could alter brain development and/or adult form and function, cell adhesion molecules and their possible ligands, as well as those that encode proteins with unknown function, they noted.

“The data provide strong support that additional research in this area will result in the identification of genes that influence alcohol dependence risk,” the researchers said.

However, this investigation represents a step forward in the area of identifying genetic pathways to addiction. “As we identify more and more of the allelic variants that contribute to abuse of alcohol and other substances, we will be better able to understand addiction itself,” they said.