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Variation in bitter-taste receptor gene increases risk for alcoholism

A team of researchers, led by investigators at Washington University School of Medicine in St. Louis, has found that a gene variant for a bitter-taste receptor on the tongue is associated with an increased risk for alcohol dependence. The research team studied DNA samples from 262 families, all of which have at least three alcoholic individuals. The families are participating in a national study called the Collaborative Study of the Genetics of Alcoholism (COGA). COGA investigators report in the January issue of the American Journal of Human Genetics on the variation in a taste receptor gene on chromosome 7 called TAS2R16.

"In earlier work, we had identified chromosome 7 as a region where there was likely to be a gene influencing alcoholism risk," says principal investigator Alison M. Goate, D. Phil., the Samuel and Mae S. Ludwig Professor of Genetics in Psychiatry at Washington University. "There's a cluster of bitter-taste receptor genes on that chromosome, and there have been several papers suggesting drinking behaviors might be influenced by variations within taste receptors. So we decided to look closely at these taste receptor genes."

Because taste receptors tend to vary a lot in the general population, Goate and colleagues had the opportunity to look at a large number of differences in genetic sequences and determine whether certain sequences might influence risk. In this study, they concentrated on TAS2R16, which helps regulate the response to bitter tastes.

They found a single base variation in the TAS2R16 receptor gene that seemed to put people at an increased risk for alcoholism. In cell culture experiments, Goate found that the variant receptor produced by this gene was less responsive to bitter compounds.

"The more common variant is more sensitive to bitter tastes, and people with that variant had a lower risk of being alcohol dependent," Goate says.

Goate hopes to replicate these findings in human taste tests, to verify that individuals with this variant also tend to be less sensitive to bitter tastes as suggested by the cell culture experiments.

As part of this investigation, Goate's team took advantage of available genome sequence databases to speed work in identifying and studying genes on chromosome 7. She says data from the Human Genome Project allowed the investigators to more quickly recognize individual variations in genes, called polymorphisms, that can influence how a gene product or protein functions.

As part of this study, Goate's team sequenced the TAS2R16 receptor gene in a number of individuals, but they didn't identify genetic variants they hadn't found already in the public databases.

The variant that increases risk of alcohol dependence was common in African Americans -- where about 45 percent of those studied carried this variation in the TAS2R16 receptor gene -- but rare in Caucasians -- where only 0.6 percent had this variation. Although the increased incidence of the variant means a larger percentage of African Americans are at risk because of this genetic factor, the variant in the TAS2R16 receptor also significantly increased risk in those Caucasians who carried the genetic variation.

The fact that this particular genetic variation is more common in African Americans does not necessarily mean African Americans will have a higher incidence of alcoholism. The difference in the TAS2R16 gene is only one of several genetic and environmental factors involved in risk for alcoholism, according to Goate.

"I don't think our result has any implications for the levels of alcoholism within different populations," Goate says. "We know that this polymorphism is more common in African Americans than in Caucasians, but the frequency of alcoholism still can be similar between the two groups because many genes and environmental factors influence risk."

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