MedicalXpress

Gene hunters fine-tune marker for common obesity gene

March 12 2008

Genomics researchers, seeking to replicate another group's discovery of an important gene associated with obesity, have further refined the signal to a particular variant in DNA that may be more helpful in identifying this gene's role in obesity in various human populations worldwide. The finding suggests that the gene variant, identified in DNA from African American children, may be a tag of an ancient mutation that first arose in Africa, where humans originated.

The research team, led by Struan Grant, Ph.D., and Hakon Hakonarson, M.D., Ph.D., both of the Center for Applied Genomics of The Children's Hospital of Philadelphia, was studying the FTO gene, identified by a British group in 2007 as raising the risk of adult and childhood obesity. Although environmental influences are certainly important, family studies have indicated that obesity has a genetic component as well.

The research team, from Children's Hospital and the University of Pennsylvania School of Medicine, reported its findings in the March 12 issue of the journal *Public Library of Science One*.

The 2007 British group had originally found the FTO gene variant among obese Caucasians. Using samples from Caucasian and African American children, who were either obese or not, the Children's Hospital group used a genetic screening technique to replicate the previous finding. They found the same gene variant among Caucasian children, but not among the African American children.

Instead, a second variant, found in both Caucasians and African Americans, was the only marker significantly linked to obesity among the African American children. Both variants were changes to a single chemical base along the DNA strand, which geneticists call single nucleotide polymorphisms, or SNPs.

For genomics researchers, said Grant, the findings mean that if other investigators look only for the first SNP in subjects with African ancestry, they would find no association with obesity. The second SNP may have deep roots in evolutionary history. Scientists have multiple lines of evidence indicating that humans originated in Africa, and this SNP may be related to an original mutation in the distant past that initiated a human predisposition to obesity.

The fact that mutations in the FTO gene carry a comparable risk of obesity in both children and adults, said Grant, suggests that the gene may be primarily associated with obesity that begins in childhood. Future medical treatments may benefit patients by targeting the FTO gene pathway, added Grant, although such treatments await a better understanding of the underlying biology of obesity.

Source: Children's Hospital of Philadelphia