Researchers identify common gene variant linked to high blood pressure

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Researchers at the University of Maryland School of Medicine have identified a common gene variant that appears to influence people's risk of developing high blood pressure, according to the results of a study being published online Dec. 29, 2008 in the *Proceedings of the National Academy of Sciences* (*PNAS*).

The STK39 gene is the first hypertension susceptibility gene to be uncovered through a new technique called a genome-wide association study and confirmed by data from several independent studies. Located on chromosome 2, the gene produces a protein that helps to regulate how the kidneys process salt, which plays a key role in determining blood pressure.

"This discovery has great potential for enhancing our ability to tailor treatments to the individual - what we call personalized medicine - and to more effectively manage patients with hypertension. We hope that it will lead to new therapies to combat this serious public health problem worldwide," says the senior author, Yen-Pei Christy Chang, Ph.D., an assistant professor of medicine and of epidemiology and preventive medicine at the University of Maryland School of Medicine.

But, Dr. Chang says, more research is needed. "Hypertension is a very complex condition, with numerous other genetic, environmental and lifestyle factors involved. The STK39 gene is only one important piece of the puzzle," she says. "We want to determine how people with different variations of this gene respond to diuretics and other

medications, or to lifestyle changes, such as reducing the amount of salt in their diet. This information might help us discover the most effective way to control an individual patient's blood pressure."

One in four Americans has elevated blood pressure, or hypertension, which can lead to death or result in complications, such as cardiovascular disease, stroke and end-stage kidney disease. Doctors consider the ideal systolic and diastolic blood pressure to be less than 120/80. (The numbers reflect the pressure of the blood against the arteries when the heart beats and is at rest.) When blood pressure is elevated, doctors recommend lifestyle changes or prescribe medications, such as diuretics, which force the kidneys to remove water from the body, in order to treat the condition.

However, patients respond differently to treatments and finding the best treatment among all the possible ones for specific patients is still a "try and see" process, according to Dr. Chang.

Scientists believe multiple genes are involved in the most common form of high blood pressure called essential hypertension. But, because so many factors affect blood pressure, including diet, exercise and stress levels, it has been difficult to pinpoint a specific gene or group of genes, says the lead author, Ying Wang, Ph.D., a researcher at the University of Maryland School of Medicine.

The University of Maryland researchers identified the link between the STK39 gene and
blood pressure by analyzing the DNA of 542 members of the Old Order Amish community in
Lancaster County, Pa., scanning approximately 100,000 genetic markers across the entire
genome for variants known as single nucleotide polymorphisms, or SNPs, associated with systolic and diastolic blood pressure. The

researchers found strong association "signals" with common variants of the serine/threonine kinase gene, or STK39, and confirmed their findings in another group of Amish people and in four other groups of Caucasians in the United States and Europe.

People with one particular variant showed slight increases in blood pressure compared to those with a more common form of the gene and were more likely to develop hypertension, researchers found. The researchers estimate that about 20 percent of Caucasians in the general population have this variant of the STK39 gene.

"With this new 'scanning' approach - the genome-wide association study - we are able to uncover genes that have previously eluded us. The field of complex disease genetics has undergone a revolution in terms of discovering new genes and understanding the genetic basis of common adult-onset diseases," says co-author Alan R. Shuldiner, M.D., professor of medicine; head of the Division of Endocrinology, Diabetes and Nutrition; and director of the Program in Genetics and Genomic Medicine at the University of Maryland School of Medicine.

The study being published online in *PNAS* is titled, "Whole-genome association study identifies STK39 as a novel hypertension susceptibility gene." It will appear in the print edition of *PNAS* early next month.

The Amish are ideal for such studies because they are a genetically homogeneous people whose forefathers came to Pennsylvania from Europe in the mid-1700s and share a similar diet and rural lifestyle. Because many in the Amish community don't have regular medical check-ups, they often don't know they have high blood pressure or take medications for it, according to Dr. Chang. The Amish appear to have as much hypertension as other Caucasians. As a result of the study, some of the participants learned that they had hypertension and were able to start treatment.

The research, which was funded by the National Institutes of Health, is a spin-off project of another University of Maryland study - the Amish Family Diabetes study - looking for
genes that may cause type 2 diabetes. Researchers at the School of Medicine already have
identified a number of genes that may play a role in the development of this type of diabetes.

Source: University of Maryland