Coriell Institute, NHGRI Report New Genetic Findings Linked to Hypertension in African Americans

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One of the largest clinical trials conducted to study the genetic underpinnings of hypertension in African Americans may eventually lead to the development of personalized drugs and diagnostics in this subpopulation.

According to Michael Christman, CEO of the Coriell Institute for Medical Research and a co-author of the study published in PLoS Genetics this week, the genome variations identified in the project may lead to the development of new treatments and prevention strategies for hypertension.

In the genome-wide association study conducted with samples from more than 1,000 African Americans, researchers from CIMR and the National Human Genome Research Institute looked for genetic variations linked to blood pressure levels. The study participants were recruited from the Howard University Family Study, a multigenerational study of families from the Washington, DC, area who identified themselves as African American. Half of the study participants had hypertension and half did not.

Using Affymetrix arrays, researchers analyzed the samples against a panel of 800,000 SNPs and identified multiple SNPs around five genes that were linked to systolic blood pressure: PMS1, SLC24A4, YWHA7, IPO7, and CACANA1H.

"Two of these genes, SLC24A4 (a sodium/potassium/calcium exchanger) and CACNA1H (a voltage-dependent calcium channel), are potential candidate genes for blood pressure regulation and the latter is a drug target for a class of calcium channel blockers," the study authors said in the paper's abstract. The researchers did not find
any variants that reached genome-wide significance for association with diastolic blood pressure or with hypertension as a binary trait.

The most significant variants from this study, funded by a $500,000 grant from the W.W. Smith Charitable Trust, were replicated in 980 samples from West Africans with and without hypertension.

This study also gives credence to the approach used by researchers to try to look for variants around certain gene regions thought to be linked to blood pressure.

"Pathway analysis revealed that genes harboring top-scoring variants cluster in pathways and networks of biologic relevance to hypertension and BP regulation," the abstract states.

"The findings suggest that, in addition to or in lieu of relying solely on replicated variants of moderate-to-large effect reaching genome-wide significance, pathway and network approaches may be useful in identifying and prioritizing candidate genes/loci for further experiments," the researchers concluded in the study.

This is the first GWAS for hypertension and blood pressure in an African American population, according to the researchers.

"This type of study is few and far between," Christman told Pharmacogenomics Reporter this week. "There is a huge need for more types of studies like this, because the frequencies of the predisposing risk factors in different ethnic populations may be indeed very different."

Christman noted that most of the genetic research on hypertension has been done on Caucasian populations. "We have sort of a biased view of the genetic factors that influence hypertension, because most of those studies have been done in populations of Western European ancestry. Virtually nothing has been done on other ethnic groups, including African Americans."

According to the CDC's National Center for Health Statistics, around 30 percent of adults in the US have hypertension. In the African American population, around 40 percent develop hypertension. While diet, physical activity and obesity affect one's risk of hypertension, this study shows that genetics plays a significant role in the development of the disease.

**Discrimination Risk?**

Although pharmacogenomics research in ethnic groups can uncover genetic risk factors allowing for more effective treatments in these subpopulations, healthcare regulators have cautioned that such research could stigmatize these groups and result in the denial of healthcare.

Even though the Genetic Information Nondiscrimination Act is now law, making it illegal for insurers and employers to make coverage and employment decisions based on genetic risk information, much of these worries are not laid to rest.

"GINA provides pretty good protection against discrimination from a medical insurer," Christman said.
However, there are some gaps in the law. Health insurers, for instance can deny coverage for manifest diseases that have a genetic basis. Certain pharmacogenomic data for manifest diseases would not be protected under the law. GINA also limits an individual’s ability to sue employers or health insurers for allegedly misusing genetic information.

The law also does not protect against genetic discrimination in getting life insurance or disability insurance.

"This is not a big issue," Christman said. "This will be market driven. Life insurance is already very personal. If I want life insurance, they want to know my age, cholesterol level, my weight, what did my parents die from, what diseases do I have. And they'll use that personal information to decide whether they will cover me and what rate they will give me.

"Genetic information will add just a bit more to that," Christman continued. "If you have an insurer that comes along and makes incorrect decisions by denying people based on a risk factor, another insurer will come along and try to capture that market."

According to Christman the CIMR is looking to do similar studies on other ethnic populations where genomic research is sparse. The institute is in the early stage of planning a PGx drug response study in Arab populations. He did not provide further details on this effort.

Given the success of the hypertension trial in African Americans, Christman hopes that "similar successes will come of studies, such as the Coriell Personalized Medicine Collaborative, that delve into determining how personal genomic information can be useful in improving healthcare and treatment options of not only African Americans, but of all populations."