'Rare' gene is common in African descendants and may contribute to risk of heart disease

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Researchers at Weill Cornell Medical College have found that a genetic variation that is linked to increased levels of triglycerides—fats in the blood associated with disorders such as heart disease, type 2 diabetes, obesity and stroke—is far more common than previously believed and disproportionally affects people of African ancestry. Investigators say their discovery, reported in the *American Journal of Cardiology*, reinforces the need to screen this population for high levels of triglycerides to stave off disease.

The finding offers a clue as to why Africans and people of African descent have an increased risk of cardiovascular disease and type 2 diabetes compared to many other populations, says the study's senior author, Dr. Ronald G. Crystal, chairman of genetic medicine at Weill Cornell. African Americans with the variant had, on average, 52 percent higher triglyceride levels compared with blacks in the study who did not have the variant.

"The prevalence of the ApoE mutation may put large numbers of Africans and African descendants worldwide at risk for a triglyceride—linked disorder," Dr. Crystal says. "But we don't yet know the extent of that risk or its health consequences.

"Inheriting this genetic variant does not mean a person is going to get heart disease and other diseases. It increases their risk, and screening for

fats in the blood—both cholesterol and triglycerides—as well as maintaining a healthy lifestyle is important," Dr. Crystal says. "There are many factors at work in these diseases. This may be one player."

The number of Africans and African descendants who may have this gene variant is significant, Dr. Crystal says. "Based on our findings, we estimate that there could be 1.7 million African Americans in the United States and 36 million sub-Saharan Africans worldwide with the variant, which increases risk of the lipid disorder and, to some unknown extent, the diseases associated with it," he says.

So Rare No One Paid Attention

The study began in Qatar, at Weill Cornell Medical College in Doha.

The gene variant the scientists studied is a single point mutation—a replacement of one of DNA amino acid with another—in the ApoE gene, which carries fats and other molecules through the blood.

Scientists have believed that more than 95 percent of the world's population has one of three common ApoE variants—2, 3, or 4. The rest have one of 38 rare ApoE mutations, among them the R145C variant studied in this research. In the three decades since the variant's discovery, only 32 instances of it have been reported in the scientific literature, Dr. Crystal says.

"This ApoE variant was believed to be so extremely rare that no one paid much attention to it," he says.

Weill Cornell researchers in Qatar decided to investigate the mutation in their work evaluating the genetics of Qatari natives—people who have lived in the country for three generations or more. That population is made up of three genetic subpopulations: Arab, Persian, and sub-Saharan

African. The researchers were able to look at the genomes of 228 Qatari participants.

To their surprise, investigators found that 17 percent of the African-derived genetic subgroup had the rare ApoE variant. None of the Arab or Persian participants had the mutation.

The team then expanded their study. They looked at participants in the worldwide 1000 Genomes Project (1000G), and found that while the R145C variant is rare to non-existent in populations that are not African or of African descent, it is common (occurring 5 to 12 percent of the time) among African-derived populations, especially those from sub-Sahara.

Weill Cornell Medical College researchers then looked for the variant in New York—area participants taking part in a study on smoking—related lung health. They found that R145C was rare (occurring 0.1 percent of the time) in the 1,012 Caucasians they studied, but common in the 1,266 African-American participants, 4 percent of whom carried the variant.

"This research is a good example of how studying a small population can give you insights that are very relevant to the rest of the world," Dr. Cyrstal says.

Provided by Weill Cornell Medical College