Researchers find five novel gene mutations linked to platelet counts in African Americans

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Researchers, led by scientists from Johns Hopkins, have found five previously unknown gene mutations believed to be associated with elevated blood platelet counts in African-Americans, findings they say could someday lead to the development of new drugs to help prevent coronary artery disease.

The study is believed to be the first of its size to focus on platelet genetics in African Americans, who have a higher risk of stroke than other racial groups. They also have relatively higher platelet counts and average platelet volume, and worse outcomes than whites after a heart attack.

"Improving our understanding of the biology and genetics of platelets and how they function will aid us in developing better treatments and more individualized treatments to reduce risk of heart disease associated with platelets," says study leader Rehan Qayyum, M.D., an assistant professor in the division of general internal medicine at the Johns Hopkins University School of Medicine.

Qayyum cautions that there are believed to be many more genes involved in platelet function that remain unknown.

Platelets are cells produced in bone marrow, smaller than red or white blood cells, which foster blood clotting. While clotting is critical to stop

bleeding after injuries, it can also cause harm by allowing clumps of blood cells to clog blood vessels leading to the heart, brain and other organs, cutting off blood flow.

Studies have shown that the greater the platelet volume or count in the blood, and the larger platelets are, the greater the risk of dangerous clot formation. Qayyum notes that the number of platelets in a given amount of blood (platelet count) and the size of these platelets (measured as average platelet count) vary from person to person in much the way that height, weight and eye color traits differ. Thus, he said, the search for genes that control this variation is a potentially fruitful line of scientific inquiry.

Qayyum and his colleagues, publishing in the online journal PLoS Genetics, report that they conducted a meta-analysis and genomewide association study, looking at genetic data from 16,000 African-American participants from seven separate studies. They compared information from each study, tracking 2.5 million single possible changes in the human genetic code to see which genes stood out across the entire group as significantly associated with increased or decreased platelet counts.

The researchers found five such alterations, involving the addition or deletion of a single piece of genetic code, across the studied genomes that had not been identified in other populations. When they checked their findings against data from Caucasian and Hispanic groups, they found three of the novel gene mutations in those populations, too. Four of the previously unknown gene mutations were later found in the genetic code of platelet cells, but one was not. That one, however, was found close to a gene that is known to be essential in the formation of normal platelets. The exact role played by each of these mutations still needs to be determined, Qayyum says.

Qayyum says one goal of their research is to identify new targets for

drugs that decrease platelet aggregation in the arteries and prevent clot formation. Blood thinners, including aspirin, clopidogrel and warfarin, are widely used antiplatelet medications. But some people can't tolerate the side effects, which include bleeding, bruising and gastrointestinal upset.

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