Study identifies genetic predeterminants for diabetes in African-Americans

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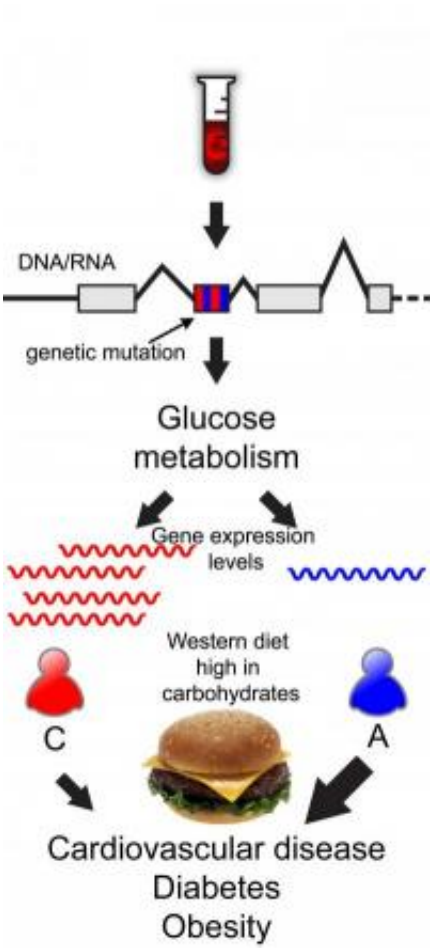

Blood samples were analyzed for differences (mutations) in DNA and RNA that affect the level of gene expression. The result of these mutations would cause the individual to be less able to metabolize carbohydrates. Credit: UNC McAllister Heart Institute

For years, scientists have tried to determine the basis for discrepancies between race and the predisposition for development of diseases such as type II diabetes and cardiovascular disease. Could factors such as differences in lifestyle or access to health care play a role, or is there something else in play?

Researchers at the University of North Carolina at Chapel Hill School of Medicine believe the latter may be true, in part, due to a recent discovery that suggests inherited genetic variations exist between whites and blacks living in the U.S., leading to less efficient metabolism of glucose and predisposition to diabetes in the blacks.

"We found gene expression profiles that suggest that carbohydrate metabolism should be different in the African-Americans in our population compared to Caucasians," said Cam Patterson, M.D., chief of cardiology and director of the McAllister Heart Institute at UNC.

The researchers made the discovery while performing RNA and DNA analyses of blood samples taken from patients undergoing treatment in the cardiac catheterization lab at UNC. "We didn't set out to look at differences in genetics or gene expression based on race or ethnicity. We were looking at the major factors that were contributing to differences in gene expression across all the patients we were studying," Patterson says.

The findings from this novel study will be published Wednesday, Dec. 9 in the journal PLoS One. The lead author is Jonathan C. Schisler, Ph.D., a postdoctoral research fellow at the McAllister Heart Institute.

Comparing blood samples taken from black and white patients led to two striking findings, said Patterson. "First, it was apparent that there was a subset of patients in the study whose RNA profile included specific inhibition of some genes known to be involved in glucose metabolism. Secondly, and surprisingly, when the race of these patients with inhibited

glucose metabolizing genes was revealed, it was apparent that the majority of these patients were of African-American descent."

Knowing, however, that genetic changes often don't equate with physiological implications, the researchers continued their genetic comparison between patients to determine if there was any indication that the variation in glucose metabolizing genes might lead to health-related differences in these racially distinct patient groups. "We tested that functionally by looking at markers known to be related to diabetes, and we found indeed that there was more disregulation of blood glucose levels in the African-Americans in our study," Patterson said.

Importantly, these findings held up to scrutiny when the researchers also looked at data from an independent database, the International HapMap Project, which characterizes genetic differences in human populations from Europe, Asia, and Africa. When comparing HAP-MAP data on whites of European ancestry and African-Americans, the genetic variations found in the UNC patients held up, with inhibition of glucose metabolizing genes being found in the African-American dataset.

What is the meaning of this difference between how whites and blacks metabolize sugars (carbohydrates)? Why do these differences exist? The answer may lie far back in history, in a time when these races were not living in the same country or environment.

The researchers suggest that the apparent inhibition of glucose metabolism in blacks may be a reflection of an environment where food was scarce or that the diet was significantly different to that consumed by whites. "In essence, although African populations moved geographically as they came to the United States, their genes retained a pattern more suited to their ancestor's home, becoming maladaptive as African populations adopted a Western diet," Patterson explained.

Although the finding may be controversial, it's not the first time that researchers have found that geographic ancestry predicts genetic variations, he adds. "For example, G6PD deficiency, an inherited disorder that affects red blood cells and is most common in African-American males, is believed to have evolved in some populations as a protection against malaria."

"This study raises the question, are there other examples of groups of gene changes that might be protective under some environments or nutritional scenarios, and maladaptive under others? The practical value of this is providing a tool for looking for these sorts of things. If we really are going to be serious about personalized medicine, we can't ignore the value of this type of knowledge," Patterson said.

Source: University of North Carolina School of Medicine (news : web)