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Researchers find gene mutation to lower heart disease

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Singapore: By scouring the DNA of thousands of patients, researchers at Broad Institute, Massachusetts General Hospital, have discovered four rare gene mutations that lower the levels of triglycerides, a type of fat in the blood and also significantly reduce a person's risk of coronary heart disease, dropping it by 40 percent.

The mutations all cripple the same gene, called APOC3, suggests a powerful strategy in developing new drugs against heart disease.

"The combination of our genetic results, together with recent clinical trials of drugs that raised HDL levels but failed to prevent heart disease, are turning decades of conventional wisdom on its head," said Sekar Kathiresan, Broad associate member and director of preventive cardiology at Massachusetts General Hospital. "HDL and triglycerides are both correlated with heart attack, and have an inverse relationship with one another, the lower the HDL, the higher the triglycerides. It has long been presumed that low HDL is the causal factor in heart disease, and triglycerides are along for the ride. But our genetic data indicate that the true causal factor may not be HDL after all, but triglycerides."

Coronary artery disease, the most common form of heart disease, is the leading cause of death in the United States and a major cause of death worldwide. Fats circulating in the blood have long been associated with risk of the disease. These fats, or lipids, come in several forms, and include low-density lipoproteins (LDL cholesterol), high-density lipoproteins (HDL cholesterol), and triglycerides.

While the causal link between LDL or the bad cholesterol, and heart disease is well known, LDL is the target of the blockbuster drugs known as statins, the relationship between HDL, triglycerides, and heart disease has been murky. It is clear both are predictive of future heart disease in observational studies, but it wasn't clear if heart attack rates would be altered by changing levels of HDL, triglycerides, neither or both.

The researchers sequenced the exomes of nearly 4,000 people, searching for genetic variants associated with blood triglyceride levels. They discovered four distinct mutations, all within the gene APOC3, that are tied to lower blood triglycerides. Remarkably, individuals carrying a single APOC3 mutation had almost 40 percent lower blood triglyceride levels.