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# Research explains link between cholesterol and heart disease

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Cholesterol contributes to atherosclerosis – a condition that greatly increases the risk of heart attack and stroke – by suppressing the activity of a key protein that protects the heart and blood vessels, researchers at the Saint Louis University School of Medicine have found.

Their findings could lead to new therapies to treat or prevent heart disease – the leading cause of death in the United States – as well as answer key questions about other diseases associated with high cholesterol levels, including some types of cancer.

The study is published in an early online edition of the *Journal of Cell Science* (http://jcs.biologists.org).

“We believe these findings represent a significant and novel breakthrough in cardiovascular research,” said Jung San Huang, Ph.D., professor of biochemistry and molecular biology at the Saint Louis University School of Medicine and the study’s lead researcher.

“This study gives us new insight into how cholesterol promotes atherosclerosis – and in turn, how it leads to heart attack and stroke,” Dr. Huang added. “This could give us important new tools in the fight against heart disease.”

It has long been known that high blood cholesterol is a key risk factor for developing atherosclerosis – sometimes called hardening of the arteries. The condition causes the arteries of the heart and other tissues

to become damaged and narrowed, preventing blood from pumping through as it should and increasing the risk of heart attack and stroke.

Until now, however, the process by which cholesterol contributes to atherosclerosis has not been well understood.

Using an animal model, Chun-Lin Chen, a senior graduate student on Dr. Huang's research team, found that cholesterol limits the activity of a key protective protein called transforming growth factor-beta (TGF-beta). TGF-beta serves many important functions in the body; in the heart, it protects the aorta and other vessels from damage caused by a variety of factors, including hypertension and high blood cholesterol levels.

Cholesterol, however, suppresses the responsiveness of cardiovascular cells to TGF-beta and its protective qualities – thus allowing atherosclerosis to develop. Similarly, the research found that statins, drugs that lower cholesterol levels, enhance the responsiveness of cardiovascular cells to the protective actions of TGF-beta, thus helping prevent the development of atherosclerosis and heart disease.

Dr. Huang believes that this research could lead to the development of novel and effective therapies to treat or prevent atherosclerosis.

For example, drugs that enhance or promote the protective activity of TGF-beta in cardiovascular cells should be effective in treating or preventing atherosclerosis, alone or in combination with other cholesterol-lowering agents.

In addition, the findings also suggest answers to questions about other diseases associated with high blood cholesterol levels, including cancer. For example, why are patients with high cholesterol also prone to develop cancer" And why does drug therapy to lower blood cholesterol correlate with a lower incidence of some cancers, as has been previously

reported"

TGF-beta, it turns out, is a well-known tumor suppressor, and loss of TGF-beta's protective effects – caused by high blood cholesterol – could thus increase formation of these cancers, the findings suggest.

"We believe the effects of our research could be far-reaching and of great interest to the pharmaceutical, academic and clinical communities," Dr. Huang said.

Source: Saint Louis University