Researchers closer to understanding actions of cells involved in atherosclerosis

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Researchers at St. Michael's Hospital are one step closer to understanding why plaque bursts in coronary arteries and causes heart attacks.

The clue might be something called microRNA-145. MicroRNAs are short chains of bossy molecules that scientists are increasingly coming to realize control a wide variety of biological processes.

Dr. Subodh Verma, a cardiac surgeon at St. Michael's, published a paper in the journal *Circulation* today, describing for the first time how microRNA-145 gene therapy can drastically reduce the severity and progression of atherosclerosis in mice.

In addition this approach appeared to make the atherosclerotic plaque more stable and less prone to burst.

Atherosclerosis, commonly called hardening of the arteries, is a condition in which fat, cholesterol and other substances build up in the walls of arteries and form hard structures called plaques. It is the leading cause of death in Canada.

Dr. Verma said most heart attacks occur when plaques rupture like a broken eggshell and release their contents into the artery. Researchers are therefore looking for ways to reduce the size of plaques and make them more stable.

One of the key questions is what causes the outer layer of the plaque to finally burst – a layer of smooth muscle cells known as the fibrous cap. These cells undergo "phenotypic transformation" in response to various stressful environments and cardiovascular risk factors, making them more likely to rupture and cause heart attacks.

MicroRNA-145 is one of the factors that appear to play a critical role in preventing the transformation of vascular smooth muscle cells into rupture-prone cells.

In atherosclerosis-prone animals, microRNA-145-based gene therapy reduced the plaque size by approximately 50 per cent and increased the collagen content of the plaque and fibrous cap area by 40 to 50 per cent, indicating that this therapy can reduce plaque buildup and also make it less prone to rupture, the inciting event of heart attacks.

The researchers also found that in human atherosclerotic plaques, the amount of microRNA-145 was reduced compared to normal arteries that were free of plaque, providing supporting human insights to the animal study.

"Atherosclerosis continues to be the number one killer in modern societies and finding new ways to treat this problem are needed," said Dr. Verma.

Dr. Fina Lovren, a senior research associate at St Michael's Hospital, carried out the experimental work on this project under the direction of Dr. Verma.

Provided by St. Michael's Hospital