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Failure to bridle inflammation spurs atherosclerosis

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When a person develops a sore or a boil, it erupts, drawing to it immune system cells that fight the infection. Then it resolves and flattens into the skin, often leaving behind a mark or a scar.

A similar scenario plays out in the blood vessels. However, when there is a defect in the resolution response – the ability of blood vessels to recover from inflammation – atherosclerosis or hardening of the arteries can result, said researchers at Baylor College of Medicine in Houston and Harvard Medical School in Boston in a report that appears online today in The *Journal of the Federation of American Societies for Experimental Biology*. The major factor in this disease is a deficiency in the chemical signals that encourage resolution (pro-resolution signals). These signals are produced in the blood vessel where the inflammation occurs, the researchers said.

Chronic inflammation of the artery wall can cause atherosclerosis, a major risk factor for heart disease and heart attack. However, said Dr. Lawrence C.B. Chan, professor of medicine and molecular and cellular biology and chief of the division of division of diabetes, endocrinology and metabolism at BCM, in many instances, the lesions or little sores inside the artery arise and then resolve, often from a very young age. The mystery is why some lesions do not heal.

What he and his colleagues from BCM and Harvard found was that genetically increasing the production of the pro-resolution signals would cool down the inflammation and give the "sores" a chance to heal or the

atherosclerosis to slow down. However, genetically clamping down on these signals would fan the fire of inflammation and speed up the progression of atherosclerosis.

"Inflammation is a two-edged sword. If resolution fails and the response gets out of hand there is a never ending civil war in the body," said Dr. Aksam J. Merched, assistant professor of molecular and cellular biology at BCM and lead author of the study. "Continued inflammation draws more macrophages (potent immune system cells) to the site of the inflammation. They produce molecules that turn this into a vicious cycle."

Dr. Charles Serhan of Brigham and Women's Hospital and Harvard Medical School in Boston, a key collaborator who first discovered many of the chemical mediators, provided special expertise in understanding the role of the mediators as well as performed analyses that allowed us to measure them accurately, said Chan.

"Resolution is not a passive process," said Chan, who is also the Betty Rutherford Chair for Diabetes Research at BCM. "It is active and produces specific anti-inflammatory mediators that 'cool down' the inflammatory process.

Some natural mediators that 'cool' this inflammation are derived from omega-3 polyunsaturated fatty acids, which are plentiful in fish and are frequently cited for their beneficial effects on the heart. Another kind of mediator is triggered by the anti-inflammation drug aspirin, said Chan.

"The specific chemical mediators that naturally cool down the inflammatory process identified in this study represent a new drug target for anti-atherosclerosis therapy," said Merched.

Source: Baylor College of Medicine