Research shows why certain arterial plaques can turn deadly

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A common misconception about arterial plaque is that it inevitably leads to a heart attack or a stroke. New research at Columbia University Medical Center, however, sheds light on why so few plaques in any given individual actually cause a problem. Furthermore, the research has identified a key protein that may promote the conversion from benign to dangerous plaques.

While a vast majority of atherosclerotic lesions are relatively harmless, the rest - some two percent of all plaques - eventually lead to an acute blood clot and to heart attack, sudden death or stroke. What separates the average blood vessel plaque from those that are at high risk for triggering the development of dangerous - even fatal - blood clots, is the "billion dollar question," says Columbia University Medical Center's Ira Tabas, M.D., Ph.D., whose findings are presented in the cover story of the May issue of Cell Metabolism.

Dr. Tabas believes that the real danger from the fatty deposits lies not with their size, but with what lies underneath the surface of the deposit. Like magma underneath a volcano, rumblings in the core of a deposit, which contains dead cells, can break open the plaques. Once the plaque ruptures, a blood clot in the lumen of the artery can form. "It is this sudden clotting that restricts blood flow and can cause a heart attack, stroke, or sudden cardiac death," Dr. Tabas says.

"Just about everybody in our society has atherosclerosis by the time we reach 20," Dr. Tabas added. "So the wave of the future in treating

atherosclerosis will be in preventing harmless lesions in young people from becoming dangerous ones, or soothing dangerous plaques so they don't rupture as we age."

The best way to do that is unclear at the moment. Volatile plaques are complicated, and there are likely many things that lead to instability and rupture. But a graveyard - or necrotic core - of dead cells inside the plaque undoubtedly contributes, Dr. Tabas says, because substances released by the dead cells tend to weaken the cap covering the lesion and thereby trigger clot formation.

The research by Dr. Tabas' lab found that when a specific gene was deleted in two separate strains of atherosclerosis-prone mice, the dangerous plaques were much smaller. The gene encodes a protein that is part of a cell stress reaction that can lead to cell death. The work raises the possibility that drugs designed to quiet this form of cellular stress might be useful in treating heart disease, which is the number one killer in the United States and becoming more prevalent.

Cholesterol-lowering drugs can reduce the amount of plaque stuck to our arteries, but it's a tall order. Fatty streaks start appearing in our arteries by the time we're in our teens, and atherosclerotic plaques continue to develop from then onward. "A therapy that prevents the deaths of these cells may be able to reduce the number of vulnerable plaques and prevent heart attacks and strokes in the 70 percent of people who aren't protected from cholesterol-lowering drugs," Dr. Tabas says.

Though relieving this stress, or preventing cell death, could soothe volatile plaques and be an effective way to reduce heart attacks and strokes, it may take years before such a therapy is available. On the other hand, it may be possible to bypass the problem of cell death by coaxing other cells in plaques to rapidly capture and clean up the dead cells before they do damage.

In the meantime, the best way to quiet volatile plaques is probably one that you've already heard of: "Our understanding of atherosclerosis may be changing, but the old standbys, diet, exercise, and keeping your risk factors like cholesterol and blood pressure in check, still remain the best option," Dr. Tabas says.

Source: Columbia University Medical Center (news : web)