A new drug target in atherosclerosis: The anaphylatoxin C5a

January 4 2011

For decades, doctors have looked at fitness levels, weight, and overall health risk factors for heart disease and stroke. Now, they may soon add a new risk factor to the list: activation of the complement system. The complement system is usually implicated in immune responses, but now there's a role for it in cardiovascular disease. In a new research report appearing in the January 2011 print issue of the *FASEB Journal*, scientists from Europe and the United States show that anaphylatoxin C5a, a protein released when complement is activated, contributes to atherosclerotic disease. C5a causes plaques to break free from where they would be anchored to ultimately cause blockages elsewhere in the body. This new discovery not only shows that C5a is a new marker for identifying risk for heart attack and stroke, but it also establishes C5a as a new therapeutic target for preventing these problems.

"Given the huge impact of cardiovascular disease in general, and atherosclerosis in particular, on public health, we feel that unraveling mechanisms involved in the development and progression of the disease are of utmost importance," said Johann Wojta, Ph.D., a researcher involved in the work from the University of Vienna in Austria. "Our findings have identified a particular component possibly involved in the development of atherosclerosis as a target for future therapies."

To make this discovery, Wojta and colleagues treated white blood cells with the C5a. In turn, these cells responded with the production of specific enzymes capable of dissolving the inner wall of atherosclerotic plaques in coronary or brain vessels. This causes the plaques to rupture,

break free from where they are anchored, and ultimately create a blockage of the vessels, leading to the development of more serious problems such as heart attacks or strokes. The researchers also showed that C5a was present in blood vessels of patients with myocardial infarction, but not in cardiac patients without infarct. This suggests that inhibiting C5a might provide a therapeutic tool in the prevention or treatment of atherosclerosis, as well as other diseases with immune system participation such as arthritis.

"Up to now, anaphylatoxin C5a has been mainly implicated in immunologic diseases such as asthma, rheumatoid arthritis or lupus," said Gerald Weissmann, M.D., Editor-in-Chief of the FASEB Journal. "But now, this study shows that C5a, a product of an activated complement system may be responsible for the devastating effects of atherosclerosis."

More information: Walter S. Speidl, Stefan P. Kastl, Randolph Hutter, Katharina M. Katsaros, Christoph Kaun, Gerhard Bauriedel, Gerald Maurer, Kurt Huber, Juan J. Badimon, and Johann Wojta The complement component C5a is present in human coronary lesions in vivo and induces the expression of MMP-1 and MMP-9 in human macrophages in vitro *FASEB J* January 2011 25:35-44; doi:10.1096/fj.10-156083

Provided by Federation of American Societies for Experimental Biology