Researchers prove direct link between immunoglobulin E and atherogenesis

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There is an observed correlation between Immunoglobulin E (IgE) levels atherosclerosis, with twice amount of IgE present in patients with acute myocardial infarction as in patients with stable angina or without coronary heart disease (CHD). Guo-Ping Shi, ScD, Jing Wang, MD, PhD, and colleagues in the Department of Medicine at Brigham and Women's Hospital (BWH), have demonstrated the direct participation of IgE in atherogenesis in a mouse model. These findings appear in the August 8, 2011 issue of *Journal of Clinical Investigation*.

Mechanistic studies demonstrated that IgE contributes to atherogenesis by stimulating macrophage and vascular smooth muscle cell and endothelial cell apoptosis and inflammatory molecule expression. Using IgE receptor FcR1alpha KO mice, the researchers demonstrated that inactivation of IgE activity reduced atherosclerotic lesions by 50% in aortic arches and >70% in thoracic-abdominal aortas.

The researchers first discovered that IgE activities require a complex formation between IgE receptor FcR1 and TLR4. Lack of any one of these receptors abolished completely IgE activities. These novel discoveries are important in any IgE-associated human disease study.

They also found that IgE induces macrophage apoptosis by activating a proton pump molecule NHE-1 (Na-H+ exchanger-1), thereby reducing extracellular pH. Both human and mouse macrophages undergo apoptosis in acidic pH. Absence or pharmacological inactivation of

NHE-1 abolished IgE-induced macrophage apoptosis and inflammatory molecule expression. Indeed, in human atherosclerotic lesions, areas rich in IgE and macrophages are acidic and filled with apoptotic cells.

Further studies may investigate how Anti-IgE monoclonal antibodies may become a novel therapy for atherosclerosis.

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