Inflammatory Biomarkers Update: Overview of Recent Research

The sequence of events that leads to atherosclerosis and plaque rupture remains a fruitful area of cardiology research. "We now have growing evidence that there is heterogeneity in monocytes that plays a role in the inflammatory pathways of disease," commented Peter Libby, MD, Brigham and Women's Hospital and Harvard University, Boston, MA, in a lecture on recent developments in inflammation research. Monocytes contribute to the atherosclerotic process as precursors of foam cells in the atherosclerotic plaque. The mouse monocyte Ly-C6^{hi} subset appears in experimentally-induced inflammatory sites. Swirksi and Libby's other colleagues (*J Clin Invest* 2007) analyzed circulating monocytes in both apoE$^{+/+}$ and apoE$^{-/-}$ mice that consumed either a high fat or regular chow diet. "When one commences an atherogenic diet there is a profound shift in the blood monocytes," commented Dr. Libby. "You see an enormous accumulation of the inflammatory subset."

In humans, mast cells paly a role in allergic responses, wound healing, and immunologic defense. In a recent publication, Sun et al (*Nature Medicine* and *J Clin Invest* 2007) provide genetic evidence that mast cells may be involved in atherothrombosis in mice. Mast cell-deficient atherosclerotic-prone mice developed less lesion formation than those with mast cells. In another study, both wild-type mice received, a chemical injury–induced abdominal aortic aneurysm. Examination of the aortas post-injury indicated that mast cell-deficient mice had less aortic expansion and less medical elastin degradation 6 weeks after the injury than did wild-type mice (both $p<0.001$). "I would like to caution you however, that mast cells may play a different role in mice than their human counterparts," said Dr. Libby.

Amir Lerman, MD, Mayo Clinic, Rochester, MN, gave an update on lipoprotein-associated phospholipase A_2 (Lp-PLA_2) and its role as a marker of inflammation. Inflammatory cells such as T-lymphocytes, mast cells, and macrophages generate the protein Lp-PLA_2. In a recently published study, Lavi et al (*Circulation* 2007) collected blood samples from the left main coronary artery and coronary sinus to measure the transcardiac gradient of Lp-PLA_2, lysophosphatidylcholine (produced by Lp-PLA_2), and C-reactive protein (CRP) in patients with mild atherosclerosis and control patients (n=30). Correlating these results to different hemodynamic measurements of the coronary tree, including blood flow, flow reserve, endothelial function, and findings from intravascular ultrasonography, the study revealed significantly higher levels of Lp-PLA_2 in the coronary circulation of patients with mild atherosclerosis compared with controls ($p=0.001$). Additionally, elevated levels of lysophosphatidylcholine correlated well with endothelial dysfunction ($r=0.5$, $p=0.005$). No significant differences emerged between the 2 groups in the levels of CRP, cholesterol, and arterial Lp-PLA_2, or in hemodynamic measures (Lavi et al. *Circulation* 2007), leading the authors to conclude that levels of Lp-PLA_2 correlate with the degree of coronary atherosclerotic plaque. "We need to translate the evidence from basic science…and actually demonstrate that the risk factor can also serve as a risk marker," concluded Dr. Lerman. Additional work aims to more clearly define the inflammatory mechanisms associated with heart disease.

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