GENE EXPRESSION PATTERNS IN THE UNSTABLE PLAQUE

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The atherosclerotic lesion, the plaque, is present in the wall of large and medium size arteries and in late stages may trigger clotting and thrombosis and therefore be responsible of severe, life-threatening, injuries. Atherosclerotic lesions may be found in young persons, even in infants, and from the beginning these lesions show an inflammatory infiltrate with monocytes and lymphocytes. A deposition of lipoproteins in the intima of arteries, the so called "fatty streak" lesion, is found before the formation of the plaque, but these lesions do not evolve to be plaques necessarily. Many data suggest that accumulation of lipids is not the only cause of atherogenesis. Over the years, several reports, both experimental and clinical, performed either on humans or in animal models, have clearly demonstrated that atherosclerosis is an inflammatory disease characterized by endothelial malfunction, production of vasoactive factors, cytokines and chemokine, growth factors. Macrophages and T cells (both CD4 and CD8) are found in the lesion at every stage of its development and play a critical role in determining the fate of the lesion. The rupture of the plaque is responsible of acute coronary syndromes which are life-threatening conditions with poor prognosis. The complex phenomena underlying the instability and the rupture of the atherosclerotic plaques are not yet understood, several papers in the last years have used a genomic approach to further investigate this issue. Microarrays are high-throughput genomic tools that allow the comparison of global expression changes in thousands of genes between normal and diseased cells/tissues. Using this approach, several papers have tried to address the differences between unstable and stable atherosclerotic lesions both in animal models and in humans. Due to technical issues, most of the work done on humans has been performed using carotid plaques. However, all the data clearly indicate that genes regulating lipid metabolism, coagulation and immune activation seem to be critical in atherosclerosis. Here, we will briefly review the genes that appear to be more important in determining the instability and the rupture of the plaque and we will present some more insight on the function of some immune-related genes in the process.