A chronic inflammatory process, initiated by lipoprotein extravasation and oxidation in the intimal space, builds up atherosclerotic plaques in the arterial wall.

Cytokines are fundamental actors of inflammation as they exert autocrine and paracrine effects and allow intercellular communication between effector and target cells. More than fifty cytokines have been identified by now. Shortly after their discovery, novel and unexpected biological actions of cytokines are brought to light by cross-disciplinary studies.

Thus, the intersection between the cardiovascular and the immunology research fields has prompted an increasing number of studies focusing on the identification of either proatherogenic or antiatherogenic effects of cytokines (please see Tedgui and Mallat [1] for extensive review).

Blumberg et al [2] have used a bioinformatics algorithm designed to identify helical cytokines, which has allowed them to discover a novel cytokine, interleukin (IL)-20. The authors determined that its heterodimeric receptor is structurally related to the IL-10 receptor and therefore assigned IL-20 to the IL-10 subfamily within class II cytokines. Nevertheless, concurrently with its discovery, Blumberg et al have demonstrated that the biological activity of IL-20 in skin and its role in psoriasis is opposite to that of IL-10 [2].

In this issue of Arteriosclerosis, Thrombosis, and Vascular Biology, Chen et al show that IL-20 and its receptors are expressed in human and experimental atherosclerotic plaques. More importantly, the authors demonstrate that systemic delivery of IL-20 accelerates atherogenesis in the apolipoprotein E–knockout mouse model [3].

Thus, as in the case of psoriasis, the role of IL-20 appears to be opposite to that of the structurally related IL-10 in atherosclerosis [4,5].

Of note, at variance with the antiangiogenic action of IL-10 [6], it has recently been described that IL-20 [7] has both direct and indirect angiogenic effects. Such angiogenic potential has consequently been explored by the authors as an important putative proatherogenic mechanism. Indeed, plaque growth in the intimal space is inevitably accompanied by the development of an hypoxic condition within the atherosclerotic wall. As a consequence, hypoxia-induced proangiogenic factors are released and drive local neovascularization. The intraplaque neovessels are immature and hence prone to rupture. The subsequent intraplaque hemorrhage and accumulation of cholesterol from erythrocyte membranes in the necrotic core accelerates plaque growth and atherosclerotic complications [8,9].

Therefore, the recent burst of enthusiasm and research focused around angiogenic strategies as therapeutic tools for the treatment of ischemic atherosclerotic diseases [10] shall be carefully considered against the potential proatherogenic “side effects” of such approaches. Experimental studies have already shown that proangiogenic bone marrow–derived cells accelerate experimental atherosclerosis [11], whereas antiangiogenic treatment reduces disease extent [12]. The present finding that IL-20 exerts proangiogenic and proatherogenic effects adds to the growing evidence for a deleterious role of systemic treatments aimed at promoting angiogenesis in atherosclerotic disease.

As the field of cytokine research progresses, a considerable number of cytokines (tumor necrosis factor [TNF]–α, IL-1, IL-2, IL-3, IL-6, IL-8, IL-12, IL-18, IFN–γ . . .) has already been identified as contributing to the building up of the atherosclerotic plaques [1]. Although the proatherogenic role for most of them results from the accumulation of cellular and extracellular components in the arterial wall (Figure), the work by Chen et al indicates that the proangiogenic IL-20 might as well add another brick in the wall.

Disclosures

None.

References


IL-20 and Atherosclerosis: Another Brick In the Wall
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