Editorial

Update on Inflammatory Targets Modulating Atherogenesis

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In the last decades, inflammatory processes characterizing atherogenesis have been widely investigated, leading to improvement of knowledge on disease pathophysiology as well as development of novel and promising anti-inflammatory treatments already tested in clinical trials [1]. A recent update by Libby and co-workers emphasized the role of inflammation as a major determinant of plaque maturation, vulnerability and final rupture, underlying acute ischemic events within the heart and brain [2]. From the "classical" concept of intraplaque inflammation triggered by endothelial activation in response to oxidized low-density lipoprotein (LDL) and followed by leukocyte recruitment, the pathophysiology of atherogenesis is now seen as a complex network including both "systemic" and "local" processes, mediated by several resident cell subsets, such as dendritic cells, osteoclast-like cells, B cells and neutrophils [3-5]. The relevance of inflammatory cell infiltration within atherosclerotic plaques has also been weakened by the demonstration that these cells can differentiate and proliferate within intimal lesions, favoring adverse plaque remodeling till rupture [6]. Moreover, the role of inflammatory pathways is not limited to atheroprogression, but also involves acute thrombosis of ruptured plaques as well as ischemic injury within the myocardial and cerebral tissues downstream the arterial occlusion [2, 7-10]. In this Special Issue, we updated knowledge on these molecular and cellular processes underlying atherosclerotic plaque initiation, maturation till final rupture. Conserved cylindromatosis (CYLD), a cornerstone of the inflammatory response in several diseases, was discussed as a potential new target for reducing inflammation in atherogenesis and cardiovascular (CV) diseases. Although additional studies are required, CYLD was indicated as a promising mechanism regulating vascular smooth muscle cell pathophysiology through the modulation of defined intracellular pathways. Furthermore, our Issue updated knowledge about the role of adipokines (from traditional adiponectin and leptin till the more recently discovered vaspin, and myostatin) in atheroprogression. A special attention was paid to discuss the controversial role of such molecules as potential biomarkers of CV risk. Steffens and Pacher nicely presented evidence for the activated endocannabinoid system as both active and protective mediator in atherosclerosis. By summarizing the activities of the two distinct transmembrane receptors CB1 and CB2, the authors discussed how the selective regulation of endocannabinoid-mediated mechanisms might be a promising target for novel anti-atherosclerotic treatments.

On the other hand, Satta and Vuilleumier updated evidence on the active and controversial role of auto-immunity in myocardial ischemic syndromes. The authors commented and discussed the pathophysiological features of different auto-antibodies, defining them as "pro-atherogenic" (antiphospholipid, anti-Heat Shock Protein, and anti-apolipoprotein A-I antibodies), "controversially associated with atherogenesis" (anti-oxidized LDL antibodies) or "anti-atherogenic" (anti-phosphorylcholine auto-antibodies). Dr. Madonna and De Caterina focused on sodium-hydrogen exchangers (NHEs) and aquaporins (AQPs), which are the main determinants of cell volume and homeostasis. These molecules were indicated as promising therapeutic and pathophysiological targets against diabetic atherosclerosis. The research group of Dr. Ameri provided an overview about the role of indoxyl sulfate as a pharmacological modulator of atherogenesis in chronic kidney disease, typically associated with an increased CV risk and accelerated atherosclerosis. Finally, the authors updated evidence on the critical role of neutrophils, macrophages and dendritic cells in atherogenesis and plaque vulnerability. Recent clinical evidence on the potential therapeutic role of neutrophil inhibition to reduce acute cardiovascular events was particularly discussed. This Issue provided an overview of novel pathophysiological aspect of atherogenesis in 2014. We hope that the reader will find a number of inputs for updating knowledge and suggestions for researches.

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