Innate Immunity in Atherosclerosis

Atherosclerosis is a chronic inflammatory disease of the arteries that is the underlying cause of most cardiovascular diseases, including myocardial infarction and stroke. Innate immunity plays an important role in the atherosclerotic disease process, starting from the earliest events of endothelial cell expression of adhesion molecules, chemokine release and monocyte recruitment to the complex cellular interactions in the mature lesion [1–3]. Pattern recognition receptors, including Toll-like receptors and scavenger receptors, have been shown to play pivotal roles in the development of the disease [4–7]. Although the precise etiology of atherosclerosis remains to be fully elucidated, it is likely that endogenous molecules formed during hyperlipidemia, lipid accumulation and oxidative modification of lipids retained in the vessel wall can act as danger signals that activate innate immune responses. In addition to endogenous molecules, exogenous microbes can amplify, accelerate and modulate the atherosclerotic disease process by activation of innate immune receptors.

This issue of *Journal of Innate Immunity* consists of five articles addressing the role of atherosclerosis in innate immunity. In the first article, Ionita et al. [8] present an overview of endogenous ligands activating innate immune responses and their role in atherosclerosis.

Great advances have been made in understanding the contribution of various immune cells to atherosclerosis development within the last years. The second article, by Braun et al. [9], is a review of the role of NK T cells in atherosclerosis. These cells have the ability to quickly secrete large amounts of inflammatory cytokine mediators upon

recognition of lipid and glycolipid antigens by CD1d. The finding that CD1d-activating lipids may accumulate in hyperlipidemic subjects supports a role for NK T cells in bridging hyperlipidemia and inflammation [10].

Another immune cell, the Th17 cell producing IL-17, and its role in atherosclerosis has been much debated due to recent apparently conflicting data [11–13]. In the third article, Chen et al. [14] give their view on the controversy and review recent advances in understanding the role of Th17 cells in atherosclerosis.

In the fourth article, Hayashi et al. [15] show that mice infected with the oral pathogen *Porphyromonas gingivalis* display accelerated atherosclerosis development, highlighting how exogenous microbes can modulate the atherosclerotic disease process.

Studies have shown that disruption of many inflammatory mediators and deletion of key innate immune components can reduce atherosclerosis burden [16]. In the last contribution to this special topic section, van Olfen et al. [17] show that over-expression of CD70 on B cells leads to a phenotype consisting of increased numbers of IFN γ -producing effector T cells, reduced numbers of B cells and increased inflammatory Ly-6C^{high} monocytes in ApoE*3-Leiden mice. Although these phenotypic changes could be expected to increase atherosclerosis, CD70 transgenic mice are protected against it. The explanation may be an increased apoptotic rate in the monocyte population, reinforcing the strong relationship between monocyte numbers and atherosclerosis development that has emerged recently [18, 19].

The use of therapies intervening against risk factors, such as hyperlipidemia and hypertension, has significantly reduced cardiovascular mortality over the last couple of decades. However, experience from randomized clinical trials suggests that it is difficult to lower cardiovascular risk by more than 40% by risk factor intervention alone. To achieve further risk reduction, novel

therapies directly targeting the disease process in the arterial wall must be developed. Elucidating the role of innate immunity in atherosclerotic plaque inflammation will help to identify such novel drug targets.

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