Fakultät für Medizin

Dokumenttyp: journal article

Autor(en) des Beitrags:
Manthey, HD; Cochain, C; Barnsteiner, S; Karshovska, E; Pelisek, J; Koch, M; Chaudhari, SM; Busch, M; Eckstein, HH; Weber, C; Koenen, RR; Zernecke, A

Titel des Beitrags: CCR6 selectively promotes monocyte mediated inflammation and atherogenesis in mice.

Abstract:
The chemokine receptor CCR6 is expressed by various cell subsets implicated in atherogenesis, such as monocytes, Th17 and regulatory T cells. In order to further define the role of CCR6 in atherosclerosis, CCR6-deficient (Ccr6-/-) mice were crossed with low-density lipoprotein receptor-deficient (Ldlr-/-) mice to generate atherosclerosis-prone mice deficient in CCR6. Compared to Ldlr-/- controls, atherosclerotic burden in the aortic sinus and aorta were reduced in Ccr6-/-Ldlr-/- mice fed a high fat diet, associated with a profound depression in lesional macrophage accumulation. Local and systemic distributions of T cells, including frequencies of Th1, Th17 and regulatory T cells were unaltered. In contrast, circulating counts of both Gr-1high and Gr1low monocytes were reduced in Ccr6-/-Ldlr-/- mice. Moreover, CCR6 was revealed to promote monocyte adhesion to inflamed endothelium in vitro and leukocyte adhesion to carotid arteries in vivo. Finally, CCR6 selectively recruited monocytes but not T cells in an acute inflammatory air pouch model. We here show that CCR6 functions on multiple levels and regulates the mobilisation, adhesion and recruitment of monocytes/macrophages to the inflamed vessel, thereby promoting atherosclerosis, but is dispensable for hypercholesterolaemia-associated adaptive immune priming. Targeting
CCR6 or its ligand CCL20 may therefore be a promising therapeutic strategy to alleviate atherosclerosis.