Protective Role for Myeloid Specific KLF2 in Atherosclerosis

Iftach Shaked, Klaus Ley

In this issue of Circulation Research, Lingrel and colleagues3 describe the phenotype of myeloid-specific Klf2 knockout mice. Although this transcription factor has long been known to be involved in protection from atherosclerosis, the cell type responsible was not clear.

Kruppel-like factor (Klf)-2 belongs to the zinc finger family of DNA-binding transcription factors. Klf family members have been recognized as playing key roles in controlling cellular processes in many different cell types; however, the best-established role is KLF2 in endothelial cells.4 KLF2 has been shown to be a potent inhibitor of cytokine-mediated induction of endothelial NO synthase and thrombomodulin in a KLF2-deficient mouse. This mouse will be instrumental for future work in the atherosclerosis field.

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Lingrel et al describe a 22% increase in aortic root lesion size in myeloid-specific Klf2 knockout mice on the Lalir−/− background (a standard model of atherosclerosis), with no change in blood lipids. Although monocyte polarization to M1 (IL-6, NOS2) and M2 (Fizz1) was slightly reduced, the authors attribute enhanced atherosclerosis to increased adhesion of peritoneal macrophages and neutrophils to an endothelial cell line. Such static adhesion assays do not predict recruitment under flow conditions, but increased numbers of macrophages and neutrophils in atherosclerotic lesions of the aortic root suggest that myeloid-specific ablation of Klf2 might enhance recruitment of these cells, associated with increased detection of myeloperoxidase, chlorotyrosine, and nitrotyrosine in the tissue. Other mechanisms could include reduced egress or reduced apoptosis of myeloid cells. Because neutrophil viability in Klf2-deficient is actually slightly reduced, the latter seem less likely.

The present report does not identify the mechanism by which absence of Klf2 in myeloid cells enhances atherosclerosis, but it describes an important new tool, the myeloid-specific Klf2 knockout mouse. This mouse will be instrumental for future work in the atherosclerosis field.

Disclosures

None.

References


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