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Oral Sessions

MRTF-A regulates proliferation and survival properties of pro-atherogenic macrophages

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Atherosclerosis often results in high incidence of vascular occlusion and has been recognized as the major cause of coronary artery disease. We had previously reported that promoter polymorphism of myocardin-related transcription factor A (MRTF-A) is associated with coronary atherosclerosis. However, the contribution of MRTF-A to the development of atherosclerosis remains unclear. Macrophages are known to be important mediators of atherosclerosis. In this study, we found that MRTF-A was highly expressed in lesional macrophages in human carotid atherosclerotic plaque. To investigate the role of macrophagic MRTF-A in the pathogenesis of atherosclerosis, we generated ApoE null MRTF-A transgenic mice (ApoE^{-/-}/MRTF-A^{tg/+}), in which human MRTF-A was specifically overexpressed in monocytes/macrophages. We found that ApoE^{-/-}/MRTF-A^{tg/+} aggravated atherosclerosis and accumulated prominent lesional macrophages in the aortic sinus. We also found that MRTF-A promoted proliferation of macrophages and mitigated apoptosis both *in vitro* and *in vivo* due to downregulation of the expression of cyclin-dependent kinase inhibitors. Taken together, our data indicated that MRTF-A contributes to the development of atherosclerosis by modulating functional properties of pro-atherogenic macrophages.