CHOP protein promotes vascular smooth muscle cell proliferation in atherosclerosis, report Zhou et al.

Atherosclerotic plaques are characterized by high levels of inflammation, macrophage infiltration, and abnormal smooth muscle cell proliferation. Moreover, both human and mouse plaques exhibit symptoms of chronic endoplasmic reticulum (ER) stress, including prolonged increase in the expression of C/EBP homologous protein (CHOP). Chronically elevated levels of CHOP promote macrophage apoptosis and associated plaque necrosis. However, it is not clear whether CHOP affects the other major cellular component of plaques—vascular smooth muscle cells (VSMCs). Therefore to test the role of CHOP in smooth muscle cells, Zhou and colleagues specifically deleted CHOP from VSMCs in atherosclerosis-prone mice. They found that in these mice, plaques were approximately 30 percent smaller and that the number of VSMCs were significantly reduced—even after correcting for decreased plaque size. They also found that CHOP-deficient VSMCs expressed greater levels of the protein KLF4—an inhibitor of VSMC proliferation. KLF4 expression was increased both by transcriptional upregulation and by reduced degradation of the protein itself. These findings suggest that CHOP promotes the progression of atherosclerosis in at least two ways—macrophage apoptosis and VSMC proliferation—making it a potential target for future anti-atherosclerotic therapies.

Climent et al discover that smooth muscle cells control endothelial cell function via microRNA transfer.

MicroRNAs (miRs) are short, non-coding RNAs that bind and inhibit expression of target miRNAs. Recent evidence has also revealed that miRs can act as communication signals, being released by cells to exert effects on their neighbors. In vascular smooth muscle cells (VSMCs), the two miRs, miR143 and miR145, are critical controllers of both differentiation and switching of phenotype to a proliferative state. Climent and colleagues have now examined whether these SMC-derived miRs might also effect neighboring endothelial cells (ECs). In agreement with previous suggestions, they found that the miRs are transferred from SMCs to ECs in co-culture—most likely via membrane protrusions called tunneling nanotubes. The transferred miRs suppressed angiogenic potential of the ECs, impairing the ability of these cells to form capillary-like structures in culture. The team also showed that the transfer of miR143 and 145 was induced by TGFβ—which promotes VSMC differentiation and vessel stabilization. Finally, they confirmed that SMC-to-EC transfer of the miRs also occurred in live mice. Together the results highlight the role of miR143 and 145 as important anti-angiogenic signals that could be useful targets for future pro- or anti-angiogenic therapies.

Blooms of arterial endothelial cells emerge from the heart’s endocardium after an infarction, according to research by Miquerol et al.

Revascularization is an important prerequisite for ischemic tissue to survive after myocardial infarction. However, innate revascularization ability is limited. Strategies to therapeutically boost revascularization are thus the focus of intense research, but so far have met only limited success. To learn more about this process, Miquerol and colleagues turned their attention to the endocardium because recent evidence suggests that during embryogenesis, coronary vessels originate from this tissue. They found that after myocardial infarction, the endocardium provided a source of new vesSEL endothelial cells in adult mice. Three to seven days after the infarction, bursts of new arterial endothelial cells, which formed structures described by the authors as endocardial flowers, were apparent within the endocardium. Analyses revealed that these structures described by the authors as endocardial flowers, were apparent within the endocardium. Analyses revealed that these endocardial flowers were indeed endocardial in origin, and colleagues turned their attention to the endocardium because recent evidence suggests that during embryogenesis, coronary vessels originate from this tissue. They found that after myocardial infarction, the endocardium provided a source of new vessel endothelial cells in adult mice. Three to seven days after the infarction, bursts of new arterial endothelial cells, which formed structures described by the authors as endocardial flowers, were apparent within the endocardium. Analyses revealed that these flowers were indeed endocardial in origin, and were connected to coronary artery fistulae (or stems) and gradually acquired the expression of endothelial markers. Determining the molecular mechanisms that control the endocardial to endothelial fate switch will likely be important for optimizing therapeutic revascularization strategies, say the authors.