Anti-miR33 Improves Plaque Regression in Diabetes (p 759)

Distel et al suggest an additional therapy for treating atherosclerosis in people with diabetes.

Statins are the most widely prescribed drugs for reducing cholesterol in individuals with high cardiovascular disease risk. However, in diabetics the risk of cardiovascular disease remains high even with statin treatment. Why diabetes worsens atherosclerosis is not clear, but part of the problem may be that hyperglycemia represses the activities of the transporters ABCA1 and ABCG1, which remove cholesterol from macrophages and which also suppress monocyte/macrophage production. The levels of these proteins are regulated by miR33, which represses their mRNAs. Hence inhibition of miR33 in atherosclerosis-prone mice upregulates these proteins promoting plaque regression. Distel and colleagues now show that inhibition of miR33 also reduces atherosclerotic plaques in diabetic mice. The team induced diabetes in atherosclerosis-prone mice and then lowered bad cholesterol (LDL) to mimic the effect of statin treatment. They found that in this model inhibition of miR33 increased ABCA1 and ABCG1 mRNA levels and suppressed the production of circulating monocytes as well as the number of macrophages in atherosclerotic plaques. The improved plaque regression with anti-miR33 treatment suggests this might be a useful adjunct to statins in patients with diabetes.

Tbx1 Role in the Posterior Second Heart Field (p 790)

Tbx1 sends second heart field cells to both poles of the developing heart, report Rana et al.

The second heart field (SHF), discovered a little over a decade ago, is a cell population in the early embryo that contributes to the development of the heart. The transcription factor Tbx1 regulates proliferation and differentiation of SHF cells and is also thought to drive migration of SHF cells to the arterial pole of the developing heart, including what will later become the outflow tract. Indeed, Rana and colleagues discovered that, unlike wild type mouse embryos, Tbx1−/− embryos lacked labeled SHF-derived cells in their developing outflow tracts. However, at stages E14.5 to E18.5 the Tbx1−/− embryos also exhibited atrioventricular septal defects, which are indicative of problems arising from the venous pole of the heart. Genetic tracing experiments revealed that unlike in wild-type embryos, in the Tbx1−/− embryos the SHF cells failed to contribute to venous pole structures—suggesting that Tbx1 regulates the migration of progenitor cells to this region. These results provide new information about the origin of heart cells as well as the underlying mechanisms that control their ultimate destinations, information that is important for understanding the etiology of congenital heart malformations and for developing potential preventive strategies.

Activin A Induces SMC Differentiation of ASC (p 800)

Cell-based revascularization therapies may benefit from a boost in activin A, say Merfeld-Clauss et al.

Cell therapies that combine endothelial cells (ECs) and adipose stromal cells (ASCs) have been suggested as potential treatments to promote the growth of new blood vessels in ischemic tissue. The ability of these two cells to form vascular networks in vitro is associated with the induction of smooth muscle actin (αSMA)—a marker of vascular smooth muscle cells (VSMCs)—in ASCs following their contact with ECs. Merfeld-Clauss and colleagues have now shown that this EC-ASC contact is in fact essential for the differentiation of ASC into VSMCs and for the development of vascular networks. Indeed, when separated from ECs, ASCs cultured in the same dish do not differentiate. Investigating the underlying mechanism, the team found that when ASCs come in contact with ECs, their activin A, which induces αSMA expression, is increased. These cells also secrete activin A, which induces αSMA expression, is increased. These cells also secrete activin A, which enables nearby ASCs (not in contact with ECs) to differentiate. Given that activin A appears to be a master regulator of VSMC differentiation, the authors suggest that modulating activin A activity could enhance the outcomes of cell therapies comprising ECs and ASCs.