Glut1, Myelopoiesis, and Atherosclerosis (p 1062)

Inhibiting extramedullary hematopoietic activity may halt progression of atherosclerosis, say Sarrazy et al.

To proliferate and differentiate hematopoietic stem and progenitor cells (HSPCs) in the bone marrow increase their glucose uptake to meet the rising metabolic demand. Indeed PET-CT imaging can identify increased metabolic activity in HSPCs by the uptake of glucose (or rather its radiolabeled analogue) during bone marrow and extramedullary hematopoietic activity. Cell proliferation dependent glucose uptake has been observed in atherosclerotic plaques as well as the spleen. Overproduction of hematopoietic cells, including neutrophils and monocytes, could both contribute to atherosclerosis onset and exacerbate plaque growth. To study extramedullary hematopoiesis more closely, Sarrazy and colleagues examined atherosclerosis-prone mice. They found that glucose uptake was increased in the aortic arch, spleens and bone marrow of these animals, which correlated with increased expression of the glucose transporter Glut1 in their HSPCs. Furthermore, suppression of Glut1 activity reduced not only HSPC proliferation and differentiation—specifically myelopoiesis—but also the progression of atherosclerosis. The authors propose that preventing glucose uptake by HSPCs with an appropriately targeted Glut1 inhibitor could be a potential treatment strategy for atherosclerosis.

Long-Term Effects of Cardiac Progenitor Cells (p 1091)

The benefits of cardiac progenitor cell therapy lasts at least a year in rats, report Tang et al.

Several studies show that the therapeutic use of cardiac progenitor cells (CPCs) can promote repair and improve function of damaged hearts in animals after myocardial infarction. However, long-term effects of CPC therapy remain unknown as most studies have examined the potential benefits for only four-to-six weeks. Therefore, Tang and colleagues studied the outcome of CPC therapy for myocardial infarction in rats, one year after CPC transplant. They found that while the overall survival rate was no different between control and CPC-treated animals, the treated group exhibited less hypertrophy, smaller scars, increased left ventricle wall thickness, and evidence of less fibrosis. Significantly, CPC treatment did not result in tumor formation. The team used male CPCs and female recipients to enable identification of the cells—by the Y chromosome—and this approach revealed that while a small number of the cells were still present even after 1 year, the transplanted cells had not differentiated into mature cardiomyocytes, although increased proliferation of endogenous CPCs was observed. Together these results indicate that CPC therapy is safe, and that it provides long-term benefits, and induces endogenous CPCs to proliferate and promote repair. The study paves the way for long-term studies evaluating the clinical efficacy of stem cells, say the authors.

GRK2 and Prognosis in Heart Failure (p 1116)

Rengo et al assess the usefulness of a possible new biomarker for heart failure.

Heart failure (HF) is a leading cause of death worldwide, and about five million people in the United States suffer from the condition. A major characteristic of HF is chronic sympathetic nervous system (SNS) hyperactivity, which while compensatory in the initial stages of disease becomes deleterious in the long run. Indeed, chronic SNS hyperactivity boosts cardiac levels of G-protein coupled receptor (GPCR) kinase 2 (GRK2), which in turn leads to dysfunctional β-adrenergic signaling—a key factor contributing to the progress of HF pathology. Importantly, the levels of GRK2 in peripheral lymphocytes correlate with those in the failing heart. Rengo and colleagues studied levels of lymphocyte GRK2 in 257 HF patients and found that they accurately reflect disease severity. Patients at low risk of death has lower levels of GRK2, while high levels of protein were identified in high risk individuals. Currently, left ventricle ejection fraction and levels of NT-proBNP are used as biomarkers for HF; however, the team suggests that GRK2 could offer independent and additional prognostic value over and above current approaches. The authors therefore suggest that further larger-scale clinical investigations are warranted to assess the value of the prognostic value of GRK2 in heart failure patients.