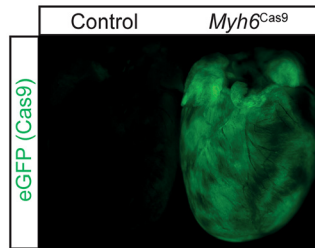


Monocyte PKC δ Deletion Accelerated Atherosclerosis (p 1153)

Li et al uncover an unexpected effect of protein kinase C deletion on atherosclerosis.

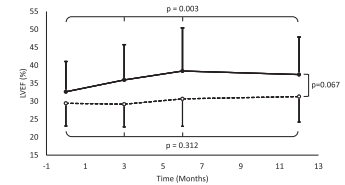
Excess lipids in the blood can activate monocytes and enhance their uptake into artery walls, thus promoting the development of atherosclerotic plaques. This lipid-induced activation of monocytes involves the signal transduction factor protein kinase C (PKC); but PKC has a number of isoforms, so exactly which enzyme is involved in the process, and how, remains unclear. To find out, Li and colleagues examined rats with hyperlipidemia. They showed that PKC levels were indeed increased in the animals' monocytes, and that most of this was accounted for by an increase in PKC δ . To determine the physiological significance of this increase, the team generated transgenic atherosclerosis-prone mice with macrophages lacking PKC δ . To their surprise, the researchers found that mice lacking PKC δ in macrophages exhibited accelerated atherosclerosis compared with controls, their plaques were larger, and contained more macrophages. Further investigations revealed that the numbers of plaque macrophages increased due to reduced apoptosis and increased proliferation of these cells, as well as to increased phosphorylation of pro-survival factors. The authors conclude that specific activation of the δ isoform of PKC in monocytes may be a way to limit atherosclerosis progression.



CRISPR/Cas9 Postnatal Cardiac Gene Editing (p 1168)

Gene editing of mouse hearts is not yet a reliable approach for functional genetic analyses, say Johansen et al.

Engineering mice to possess specific genetic deletions is a powerful tool for studying gene function. But generating transgenic mice is time-consuming, expensive, and requires large numbers of animals. Gene editing is a successful approach for studying gene functions in cultured cells and has been used in live animals to correct genetic defects. So Johansen and colleagues considered that it might be a cheaper, quicker, and less animal-intensive approach for studying gene functions in vivo. The team introduced gene-editing vectors targeting 3 genes of known function (*Myh6*, *Tbx20*, and *Sav1*) into the hearts of newborn mice. However, only 1 of the genes (*Myh6*) resulted in the expected phenotype. Further examinations revealed that only 5% to 15% of gene copies had been disrupted by the editing, resulting in a mosaic of edited and nonedited cells, which, in the case of *Sav1* and *Tbx20*, was clearly insufficient to produce a phenotype. While the team could boost the editing efficiency of *Sav1* by targeting 2 sites in the gene simultaneously, the authors conclude that considerable technical improvements would be necessary for in vivo gene editing to be a reliable tool for gene function studies.



Umbilical Cord MSCs for Heart Failure (p 1192)

Umbilical cord stem cells could be a promising therapy for heart failure, say Bartolucci et al.

Stem cell treatment for heart failure has shown promise in animal models of the disease, but in clinical trials, the benefits have been moderate, at best. Most clinical trials have used bone marrow-derived mononuclear cells or mesenchymal stem cells (BM-MSCs), but MSCs derived from human umbilical cords offer several advantages over their bone marrow counterparts, say Bartolucci and colleagues. For one thing, these cells have more proliferative and differentiation potential than adult cells, and they are very easy to obtain. The team now reports on a first-of-its-kind randomized placebo-controlled trial of umbilical cord MSCs (UM-MSCs) for heart failure. Fifteen patients aged between 18 and 75 received intravenous injections of UC-MSCs, while another 15 received a placebo. None of the UC-MSC recipients suffered adverse effects as a result of the treatment. In comparison with control patients, the treatment recipients exhibited a significant and sustained improvement in heart function—including increased left ventricle ejection fraction—and an improved quality of life. These encouraging results now pave the way for further larger-scale trials of UC-MSCs to examine how dosage, administration methods, and other factors might further improve outcomes.

Written by Ruth Williams
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