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Amniotic Membrane-Derived Stem Cells (p 1613)

The best bet for fixing a broken heart might be amniotic stem cells, say Tsuji et al.

Several types of stem cell have been investigated for their potential to differentiate into cardiac muscle and repair damaged hearts. Bone marrow-derived mesenchymal stem cells have been a recent favorite because they are naturally immunoprivileged (tolerated by the host’s immune system). Concerned that bone marrow cells might have low cardiac muscle differentiation efficiency, however, Tsuji et al looked for an alternative. Human amniotic membrane-derived mesenchymal stem cells (AMCs), the team showed, differentiate into cardiac muscle with high efficiency both in vitro and in vivo. These cells also improved rat heart function following myocardial infarction. Because amniotic material is tolerated by the mother’s immune system during pregnancy, the team reasoned, AMCs should show strong immunoprivilege. And they did: AMCs were still present in the rat hearts 80 days after transfer. Immunoprivilege in the AMCs came down to their secretion of a molecule called HLA-G. Treating AMCs with cytokine IL-10 boosted HLA-G secretion and thus the cells’ tolerability. As a surprising added bonus, however, IL-10 treatment also improved the AMC’s differentiation efficiency.

IL-17A Is Essential for Dilated Cardiomyopathy (p 1646)

Inhibiting cytokine IL-17A might save inflamed hearts from failure, report Baldeviano et al.

Inflammation of the heart (myocarditis) is caused by infection and/or autoimmunity and can often lead to heart muscle deterioration and death. Indeed, myocarditis-induced dilated cardiomyopathy (DCM) is a major cause of sudden death in young adults. Baldeviano et al show that in a mouse model of autoimmune myocarditis, IL-17A-secreting cells (Th 17 cells) turn up at the battleground, suggesting that IL-17A might be a molecular provocateur of pathology. To the team’s surprise, autoimmune myocarditis raged on in mice that genetically lacked IL-17A as well as in mice where IL-17A activity was blocked with neutralizing antibodies. However, there was one important difference. In mice lacking IL-17A, autoimmune myocarditis never led to the potentially fatal DCM. This is likely to be because enzymes that regulate heart remodeling and fibrosis (processes involved in DCM) were diminished. Patients with DCM have also been reported to have high levels of IL-17A in their blood, suggesting that a similar mechanism is at work in humans and that a similar therapeutic strategy, if given early enough, might save lives.

Cheng et al have uncovered how an enzyme that promotes cell survival can also help protect transplanted blood vessels from rejection.

Transplanted tissues and organs are susceptible to attack from the host’s immune system. The instigators of the attack are dendritic cells, which display antigens from the grafted tissues (in combination with MHC class II molecules) to host lymphocytes, inciting them to strike. In the blood vessels of transplanted tissue, the continuous immune attack leads to progressive arteriosclerosis (blood vessel scarring). This is a common cause of failure in heart transplantation. In rats, it was reported that tissue graft survival could be prolonged if heme oxygenase 1 (HO-1) levels were increased. HO-1 is known to be cell protective and has antioxidant, anti-apoptotic, and immune-modulatory activities. How exactly this enzyme might protect grafts from rejection, however, was unclear. Cheng et al have now shown in mice that if host dendritic cells lack HO-1, they mount a far more pronounced immune attack against blood vessel grafts. Investigations revealed that HO-1 normally suppresses key factors in the MHC class II antigen presentation pathway.
In This Issue

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