Vascular Inflammation, T cells, and Hypertension (p 263)

T cells do not instigate hypertension but they make it a whole lot worse, Marvar et al suggest.

The team had previously found in mice that T cells are essential mediators of angiotensin II-induced hypertension. Their next question was: How does angiotensin II activate the T cells? Angiotensin II is known to work on the brain, and it has been shown that lesions in the anteroventral third cerebral ventricle prevent angiotensin’s hypertensive action. The team found that such lesions also prevented angiotensin-induced T-cell activation. However, the brain lesions did not prevent hypertension and T-cell activation in mice treated with norepinephrine, which works directly on the blood vessels. Together, these results suggest that angiotensin’s effect on T cells might be the result of the hypertension itself. The team gave hydralazine—a smooth muscle relaxant and antihypertensive agent—to normal mice treated with angiotensin. Sure enough, T-cell activation was inhibited. Given that T cells not only promote hypertension but also, as shown here, are activated by hypertension, the team suggests a feed forward mechanism whereby T cells add fuel to the growing blood pressure fire.

Cardiomyocyte Renewal in Humans (p 305)

Kajstura et al reveal the rates of heart cell regeneration.

Until a few years ago, the prevailing view of heart cells was that they were postmitotic and irreplaceable. The discovery of cardiac stem cells challenged that presumption. However, it remains unclear exactly which cells were regenerated, how often, and to what extent. Kajstura et al came up with the original idea of looking at the hearts of cancer patients that had been treated with iododeoxyuridine (IdU). This thymidine analog is given as part of radiotherapy; it incorporates into DNA during replication, making cycling cells (such as cancer cells) sensitive to radiation damage. Other cycling cells pick up IdU, too, and pass it on to their progeny. The team thus looked to see how many and what type of IdU-positive cells were present in the hearts of patients who died. They found IdU-labeled cardiomyocytes, endothelial cells, and fibroblasts. By counting the number of cells and dividing it by the time between IdU treatment and death, they calculated that cardiomyocytes regenerated at a rate of approximately 22% per year, fibroblasts at 20%, and endothelial cells at 13%. These rates are much higher than previously estimated and are sufficient, says the team, for the entire heart to be replaced several times over a lifetime.

MRTF-A Promotes Cardiac Fibrosis (p 294)

Small et al suggest a strategy to stop hearts from scarring and, thus, to save lives.

Ironically, the healing process after a heart attack is itself a danger to the health of the heart. The scarring (fibrosis) can lead to reduced contractility, reduced vascularization, arrhythmias, and ultimately heart failure. Understanding the process of fibrosis is the first step toward suppressing its dangerous effects. Parts of the process are known. For example, it is thought that myofibroblasts are key regulators of fibrosis and that a protein kinase called ROCK is required for myofibroblast activation. Small et al looked downstream of ROCK to see if they could identify additional components of the fibrosis pathway. MRTF-A is a mediator of ROCK signaling, and the team showed that MRTF-A prompted a myofibroblast phenotype in cultured heart fibroblasts, including the production and secretion of collagen, the major component of the extracellular matrix. More importantly, they also showed that mice that lacked MRTF-A were protected from fibrosis after suffering a heart attack. MRTF-A could thus be a promising target for therapy.
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