Intramyocardial Stem Cell Injections in Patients (p 792)

Preliminary clinical trial data suggest that bone marrow cells can fix damaged hearts, report Williams et al.

After a heart attack, scarring to the cardiac muscle reduces its contractility and can lead to heart enlargement (hypertrophy) and failure. Recent research has focused on attempts to repair such damage by cell replacement therapy. A number of different cell types have been tried, and bone marrow-derived progenitors are a favorite due to their relative accessibility and differentiation capacity. However, injections of bone marrow progenitors into patients’ hearts have shown only modest improvements in the ejection fraction of the heart. Williams et al now report that ejection fraction might not be the best parameter to measure functional improvement. Using state of the art imaging technology to assess different parameters, they found that bone marrow-derived progenitors work better than thought. Eight patients’ hearts were injected with progenitor cells derived from their own bone marrow, and after just 3 months, improvements were observed in infarct size and contractility. By 6 months, improvements in the chamber dimensions of the hearts were also seen, suggesting that reverse remodeling had occurred. This reduction in chamber volumes might, in part, account for the apparently modest improvement in the ejection fraction, say the authors. Encouragingly, these results pave an optimistic path for future bone marrow progenitor trials.

Cardiac Stem Cells and End-Stage Heart Failure (p 857)

Tiny heart biopsies can provide useful numbers of functionally competent cardiac stem cells, say D’Amario et al. In the human heart, two types of cardiac stem cells (CSCs) have been identified: myogenic CSCs, which give rise to cardiomyocytes, and vascular CSCs, which give rise to vascular endothelial and smooth muscle cells. These CSCs do not intrinsically make a significant contribution to repair after infarction because, it is thought, they do not exist in large numbers in the adult heart. Hence, it is thought that if sufficient numbers of CSCs could be isolated, expanded, and transferred back to damaged hearts, they might significantly boost repair. D’Amario et al decided to test the first two steps in this process—isoaltion and expansion—to see if such an approach would be feasible. When heart failure patients were undergoing surgery, tiny heart tissue biopsies, estimated to contain just 100 CSCs, were taken. Cells from these biopsies were dissociated, expanded, and sorted to isolate CSCs. After 30–40 days in culture, 5 × 10^6 mCSCs and vCSCs were obtained. These CSCs could differentiate into muscle or vascular cells, confirming their functionality. Although the remaining step—transferring cells back to the patient will be the proof of the pudding, this important study attests to the feasibility of obtaining sufficient CSCs for clinical trial.

Arcuate Leptin Receptor and Sympathetic Traffic (p 808)

Harlan et al pinpoint the brain site at which the fat hormone leptin controls blood pressure.

Leptin, released from body fat, regulates several physiologic responses, including the suppression of appetite, increase in brown adipose tissue (BAT) metabolic activity, and increase in blood pressure. Interestingly, while the ability of leptin to suppress appetite is dampened in obese individuals, its ability to elevate blood pressure and BAT metabolism is not. The main center for leptin activity in the brain is a region of the hypothalamus called the arcuate nucleus. This nucleus contains a high concentration of leptin receptors and has been shown to be responsible for appetite suppression. However, leptin receptors are found elsewhere in the brain and so it has been proposed that the blood pressure and BAT activity might be controlled remotely. Harlan et al have now found that this is not the case. The team selectively deleted leptin receptors in the arcuate nucleus and found that sympathetic nerve responses in BAT and kidney (site of blood pressure control) were abrogated. Furthermore, in obese mice, high blood pressure was resolved by arcuate-specific removal of the leptin receptor. The question of why some but not other responses to leptin are dampened in obesity remains, of course, but Harlan et al have certainly narrowed the search for the answer.