Imaging Granzyme B Activity in Myocarditis (p 502)

Konishi et al develop a fluorescent probe for monitoring myocarditis in vivo.

Current methods for monitoring the extent and progression of inflammatory changes in conditions such as myocarditis include repeated tissue biopsies and imaging of inflammation-homing radioactive tracers. But, biopsies are invasive and at risk of sampling errors; and imaging provides little information about the cells and pathological changes associated with the inflammation. Konishi and colleagues therefore developed a fluorescent probe for in vivo visualization of granzyme B activity—a protease released by antigen-specific T cells that attack the cardiomyocytes. To test their probe, they used a mouse model of autoimmune myocarditis, in which the animals express ovalbumin protein in their hearts and receive a transfer of ovalbumin-specific T cells. The resulting inflammation was then monitored both ex vivo and in vivo. The team found that the probe—a substrate for granzyme B—fluoresced 3.7 times brighter when cleaved by the enzyme, and provided a good correlation between signal brightness and myocarditis severity. These results indicate that such probes could be used to quantitatively and non-invasively monitor myocarditis as well as the efficacy of new treatments.

Renal Nerves and Inflammation (p 547)

Sympathetic nerves promote renal inflammation and hypertension, report Xiao et al.

Renal inflammation is a critical contributor to high blood pressure. Mice that genetically lack lymphocytes, for example, are resistant to hypertension induced by angiotensin II and other hormones, and transfer of donor lymphocytes into such mice restores their hypertensive response. Evidence suggests that this inflammation is regulated by the central nervous system: blocking renal sympathetic neurons reduces T cell activation and hypertension in mice, while activating these neurons has the opposite effect. Furthermore, surgical renal sympathectomy reduces blood pressure in humans with hypertension. But exactly how immune responses are linked to the nervous system is still largely unknown. To find out, Xiao and colleagues denervated mouse kidneys and then treated the animals with angiotensin II. They found that this procedure reduced both leukocyte accumulation in the kidneys and hypertension. They went on to show that in normal kidneys angiotensin II boosted the activation of dendritic cells—stimulators of T cell activity—and that transfer of angiotensin II-activated dendritic cells from normal mice restored hypertension in mice with denervated kidneys. These results support the findings from previous clinical trials of denervation and suggest that sympathetic stimulation of dendritic cells could be a target pathway for hypertensive therapies.

Meta-Analysis of Bone Marrow Cell Therapy (p 558)

Bone marrow cell therapy improves heart function and survival in patients with ischemic heart disease, say Afzal et al.

In recent years, the use of adult bone marrow cells to repair damaged heart tissue has emerged as an attractive and promising experimental treatment. But clinical trials have produced mixed results with some trials failing to document any benefit. To clear things up, Afzal and colleagues have performed a systematic meta-analysis of published results from 48 randomized and controlled clinical trials of the treatment. Altogether the analysis, which looked at the outcomes for 2602 patients with ischemic heart disease, revealed that bone marrow cell therapy did indeed improve left ventricle ejection fraction and reduce infarct scar size. Importantly, the approach was associated with a significantly lower chance of adverse outcomes, such as death, recurrent myocardial infarction, arrhythmia and heart failure. The analysis also suggests that for the best chance of success, patients should receive a dose of more than 50 million cells within the first 48 hours after myocardial infarction. The findings of this analysis provide a firm foundation on which to develop new, large-scale randomized controlled trials, say the authors.

Written by Ruth Williams
(Circ Res. 2015;117:483. DOI: 10.1161/RES.0000000000000071.)
© 2015 American Heart Association, Inc.
Circulation Research is available at http://circres.ahajournals.org

DOI: 10.1161/RES.0000000000000071
