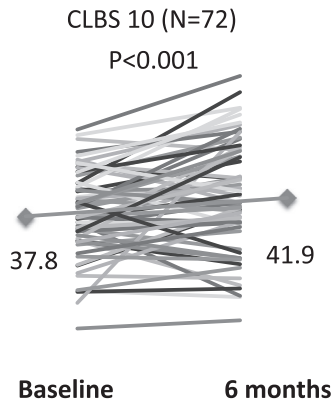


SMC Reprogramming to Resident Progenitor Cells (p 296)

Majesky et al discover an unexpected origin of vascular progenitor cells.

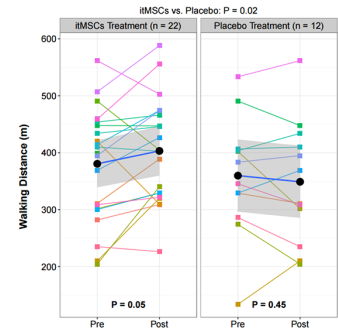
The adventitia, which forms the outer layer of blood vessels, is a collagen-rich tissue that has been traditionally thought to provide only structural support to the vessel. But recent research has shown that the adventitia contains a variety of dynamic cell types, such as the vascular progenitor cells. The origin of these progenitors was unclear, but Majesky and colleagues have now discovered, quite by accident, the source of at least a subpopulation of these cells in mice. The team was studying how, after injury, the smooth muscle cells (SMCs) within the medial layer of blood vessels dedifferentiate and migrate to the innermost intimal layer. Unexpectedly, the team observed that SMCs also migrate to the adventitia, where they lost their SMC characteristics and gained stem cell markers. Further fate-mapping experiments confirmed that SMCs do indeed give rise to a subpopulation of adventitia-residing progenitors. These SMC-derived progenitors were multipotent, giving rise to several cell types in vitro and in matrigel implants in mice. The team also found that the transition from SMC to progenitor was regulated by the transcription factor Klf4. Further studies are required to assess how these SMC-derived progenitors contribute to vascular homeostasis and pathology and how these cells could be targeted to treat vascular diseases, say the authors.



CD34+ Cells for Post STEMI LV Dysfunction (p 324)

Quyumi et al report the results of a phase II stem cell trial for treating myocardial infarction.

Nearly 20% of patients aged 45 and over who suffer a heart attack die within a year. Treatments to improve outcomes are desperately needed, and one possible therapeutic approach that has received much recent attention is coronary infusion of bone marrow-derived cells. Indeed, over 2600 patients have received autologous bone marrow cells in a variety of trials, but the outcomes have been inconsistent. It has been suggested that such unpredictable results may be due to variable bone marrow cell constituents, and that enriching for cells that express the stem cell marker CD34 may provide cell populations with greater clinical benefit. Indeed, a phase I trial of treatment with autologous CD34-positive bone marrow cells improved outcomes in heart attack victims. Now, Quyumi and colleagues report that some patients enrolled in a randomized, double-blind phase II trial of CD34 cells also fared better than control subjects—with improved ejection fractions and reduced infarct sizes after 6 months. Improvement was seen in patients who were given a high-dose of cells (over 20 million), but low-dose recipients were indistinguishable from controls. The results confirm the safety of autologous CD34+ cell infusions and suggest that high doses of these cells may have some clinical benefit. Based on these results, the authors suggest that further randomized controlled trials should be performed to examine the efficacy of bone marrow-derived CD34+ cells.



Mesenchymal Stem Cells for Heart Failure (p 332)

Butler et al present the results of an intravenous stem cell therapy trial for nonischemic cardiomyopathy.

Nonischemic cardiomyopathy is a contractile dysfunction not caused by coronary artery disease (CAD) or myocardial infarction (MI). Nevertheless, as with CAD- or MI-induced heart failure, patients with nonischemic cardiomyopathy could potentially benefit from stem cell therapy. To date, cell therapies for any form of heart failure have been administered directly to the heart—because cell engraftment was considered necessary for clinical effect. However, some effects may derive from secreted factors, such as the anti-inflammatory factors produced by mesenchymal stem cells (MSCs). Butler and colleagues have, therefore, performed the first trial of intravenously administered stem cells for heart failure, giving 22 patients with nonischemic cardiomyopathy infusions of allogenic MSCs. While the team noted no difference in the occurrence of death or hospitalization between test and control subjects, patients receiving the MSCs had reduced systemic inflammation and could walk greater distances after 3 months. An inverse association between inflammation and left ventricle ejection fraction was also noted. These promising early results now pave the way for further follow up trials, say the authors.

Circulation Research

JOURNAL OF THE AMERICAN HEART ASSOCIATION



In This Issue Ruth Williams

Circ Res. 2017;120:245

doi: 10.1161/RES.000000000000134

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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Print ISSN: 0009-7330. Online ISSN: 1524-4571

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