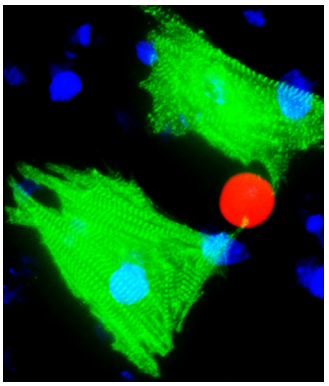
IN THIS ISSUE

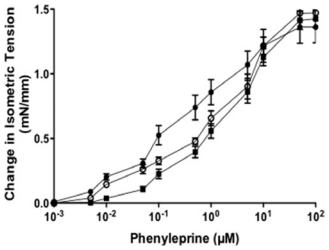
Circulation Research ■ Vol. 120 ■ No. 11 ■ May 26, 2017



Therapeutic Potential of Synthetic Stem Cells (p 1768)

***Luo* et al generate synthetic stem cells for cardiac therapies.**

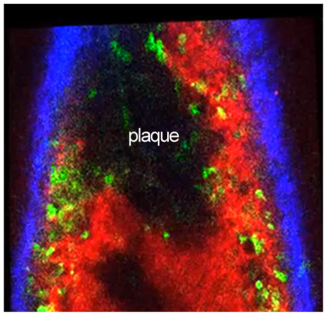
Evidence indicates that the administration of stem cells, such as mesenchymal stem cells (MSCs), to patients with damaged hearts can improve myocardial function. It is currently believed that such reparative effects of MSCs are largely due to secreted factors. However, treating patients directly with such factors has been unsuccessful—possibly because the effects of the factors could not be sustained. Luo and colleagues reasoned that if such factors were enclosed in protective packaging, they might prove more effective. To find out, the team loaded MSC secretome proteins onto particles of poly(lactic-co-glycolic acid)—a biocompatible polymer that protects cytokines from degradation—and coated these particles with MSC membranes. Like regular MSCs, the repackaged synthetic MSCs (synMSCs), when cocultured with neonatal rat cardiac myocytes, synMSCs induced proliferation and contractility. And when given to mice with myocardial infarction, the reduced infarct size increased ventricle wall thickness and increased blood vessel density. Given these similar results, unpackaging and repackaging MSCs may seem unnecessary, but the defined composition of the synMSCs should provide a more uniform and predictable medication than cell-based approaches. Furthermore, the synMSCs exhibited superior stability to MSCs—suggesting synMSCs may be useful as an off-the-shelf treatment option.



20-HETE–GPR75 Pairing and Hypertension (p 1776)

***Garcia* et al identify a receptor for the potent inducer of hypertension 20-HETE.**

Hypertension is the leading cause of stroke and cardiovascular diseases, but because many different environmental and genetic factors contribute to the disorder, the underlying pathology is difficult to define. The complex etiology of hypertension could explain why, despite a range of treatment options, many patients have uncontrolled blood pressure (resistant hypertension). Among several hypertension-inducing factors is 20-hydroxyeicosatetraenoic acid (20-HETE)—a lipid produced by arachidonic acid hydrolysis. 20-HETE promotes vascular dysfunction—including inflammation and remodeling—and elevated blood levels of 20-HETE have been linked with hypertension, stroke, myocardial infarction, and vascular disease. To shed light on the mode of action of 20-HETE, Garcia and colleagues have now identified a 20-HETE receptor on endothelial and smooth muscle cells called G-protein receptor 75 (GPR75), which associates with G-protein–coupled receptor kinase interactor 1 (GIT1). The team showed that both GPR75 and GIT1 are required for 20-HETE-induced signaling activity. Moreover, genetic knockdown of GPR75 in mice prevented 20-HETE-dependent vascular dysfunction and hypertension. These findings open potential new avenues for developing treatments for resistant hypertension.



Monocyte Patrolling in Arteries (p 1789)

***Quintar* et al investigate monocyte patrolling behavior in arteries.**

Unlike classical inflammatory monocytes, nonclassical monocytes patrol blood vessel endothelium scavenging dead cells and debris. These patrolling cells were discovered in the microcirculation, and all subsequent studies have focused on these vessels. As a result, with the exception of monocyte recruitment to atherosclerotic plaques in arteries, little is known about monocyte-endothelial interactions in large vessels. Using a recently developed imaging technology, called intravital live cell triggered imaging system (ILTIS), Quintar and colleagues have now been able to monitor nonclassical monocytes in the arteries of healthy, hyperlipidemic, and atherosclerotic mice. They found that monocytes patrol healthy arteries—with each patrolling session lasting 5 to 10 minutes. In 2 different mouse models of hyperlipidemia, the patrolling behavior of these cells was increased by 8- to 9-fold. In atherogenic mice, patrolling increased by 22-fold, with each patrol lasting longer and proceeding more slowly. The number of patrolling cells directly correlated with the extent of endothelial damage, and mice with deficient patrolling monocytes exhibited greater atherosclerotic lesions. Together, the results suggest that the patrolling cells have a protective role in arteries and raise the possibility that therapeutically increasing monocyte patrolling behavior could help in reducing atherogenesis.

Written by Ruth Williams

(*Circ Res*. 2017;120:1687. DOI: 10.1161/RES.0000000000000156.)

Circulation Research
JOURNAL OF THE AMERICAN HEART ASSOCIATION

In This Issue

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Circ Res. 2017;120:1687
doi: 10.1161/RES.0000000000000156
Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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