Fibroblast Behavior Upon Injury (p 625)

Ali et al report that birthplace does not influence future potential—at least for cardiac fibroblasts.

Myocardial infarction or pressure-overload leads to the accumulation of fibrotic scar tissue that hinders the function of the cardiac muscle. Hence, minimizing fibrosis could prevent negative remodeling of the heart and improve cardiac function after injury. However, in the heart, scar formation is driven by fibroblasts, which are a heterogeneous mixture of cells of different origins and it is unclear which of these contribute to injury-induced fibrosis. Therefore, Ali and colleagues performed lineage tracing experiments to track fibroblasts from different origins. They showed that the vast majority of fibroblasts in the adult mouse heart are derived from the epicardium, while a significant proportion comes from the endothelium. A small number of fibroblast also arise from the neural crest. While these different origins influenced the ultimate location of the cells in the heart, there was no difference in their behavior. Regardless of origin, the cells proliferated at similar rates and exhibited similar gene expression patterns both in vitro and in the hearts of mice subjected to pressure-overload. Thus, therapies aimed at reducing fibrosis in the heart should target pathways common to all fibroblasts, say the authors.

VSMC Plasticity in Atherosclerosis (p 662)

In atherosclerotic plaques, most macrophages come from muscle, say Feil et al.

Atherosclerosis is a chronic inflammatory condition in which the walls of the blood vessels develop plaques filled with fatty deposits and immune cells. Upon plaque rupture, blood flow is interrupted by an occlusive thrombus, which can result in a heart attack or stroke. Indeed, atherosclerosis is a leading cause of death in the developed world. Besides immune cells, smooth muscle cells (SMCs) in the blood vessel walls can also expand and contribute to plaque formation. Interestingly, recent research showed that some cells in plaques show characteristics of both SMCs and macrophages, leading Feil and colleagues to investigate how such cells arise. The team labeled adult differentiated SMCs in mice that are prone to developing atherosclerosis and then tracked the progeny of the labeled cells as lesions developed. They observed that by clonal expansion SMCs contribute to the formation of new plaques and start to express macrophage markers. They found that such SMC-derived macrophages account for the majority of macrophages in the lesions. Based on these findings, the authors say that the extent of SMC plasticity and their contribution to lesion formation may have been vastly underestimated, and that targeting transdifferentiation of SMCs to macrophages could be an important future strategy for slowing the progression of atherosclerotic lesions.

IncRNAs and Myocardial Infarction (p 668)

Vausort et al investigate blood levels of long non-coding RNAs after myocardial infarctions.

Although 80 percent of the human genome is transcribed into RNA only two percent is translated into proteins. In scratching the surface of what the remaining 78 percent might do, scientists have discovered that microRNAs are important regulators of gene expression. They have also recently discovered that long non-coding RNAs (IncRNAs)—greater than 200 nucleotides—may play important regulatory roles. Recent studies have shown that IncRNA regulate a variety of physiological functions and they have also been implicated in cardiac disease processes, such as heart failure, hypertrophy and infarction. In addition, levels of IncRNA could also be used as biomarkers of disease risk, progression, or outcomes. Vausort and colleagues therefore analyzed levels of such RNAs in the blood of 414 myocardial infarction patients. Of the five RNAs they investigated—MALAT1, MIAT, aHIF, ANRIL and KCNQ1OT1—they have also recently discovered that microRNAs are important regulators of gene expression. In scratching the surface of what the remaining 78 percent might do, scientists...
In This Issue
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Circ Res. 2014;115:601
doi: 10.1161/RES.0000000000000034
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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