IN THIS ISSUE

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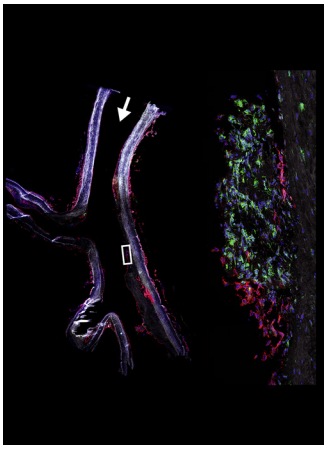
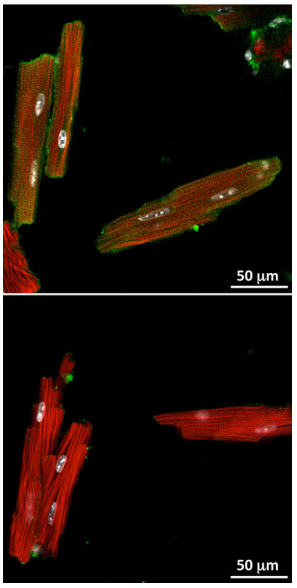


PAD4 in Atherosclerosis and Arterial Injury (p 33)

Neutrophil extracellular traps exacerbate thrombosis in atherosclerosis, say Franck et al.

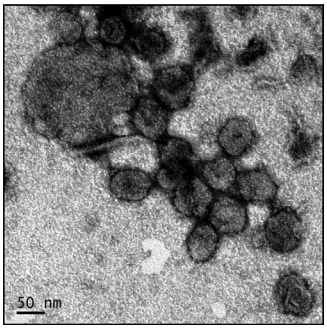
Thrombus formation, secondary to plaque rupture or erosion, can lead to vessel occlusion and tissue ischemia, resulting in myocardial infarction or stroke. Although the development of a thrombus is mediated by platelets, it has been suggested that the process is also influenced by neutrophils, which by releasing neutrophil extracellular traps (NETs)—stringy bits of genomic DNA—cause the additional accumulation of clotting factors and debris. To investigate the role of NETS in atherosclerosis-associated thrombosis, Frank and colleagues examined atherosclerosis-prone mice in which the enzyme PAD4—essential for NET formation—was genetically deleted in hematopoietic cells. They found that even though the development and stability of the plaques themselves were unaffected by PAD4, deletion, arterial injury, and thrombus formation were reduced. By administering DNase I—an enzyme that degrades NETs—to mice with normal levels of PAD4, the team could recapitulate the beneficial effects of PAD4 deletion. These findings suggest that preventing or degrading NETS may reduce the possibility of thrombus development in patients with at-risk plaques.



Cardiac c-Kit Biology Revealed by Transgenesis (p 57)

Expression of the stem cell marker c-kit is more widespread in the heart than once thought, say Gude et al.

C-kit is the best-known marker of cardiac stem cells. While it is accepted that c-kit–expressing cells participate in myocardial development and injury response, the full range of functions performed by these cells remains unclear. One of the difficulties in studying c-kit cell function is that the marker is in fact not strictly limited to stem and progenitor cells. Indeed, Gude and colleagues have now found that c-kit is expressed in certain adult mouse cardiomyocytes. The team generated transgenic mice in which cells with active c-kit production could be identified via expression of a green fluorescent protein. They showed that not only did some nonmyocytes, which include stem cells, glow green, but some myocytes did, too. Furthermore, following myocardial injury, the numbers of both c-kit–positive nonmyocytes and myocytes increased, suggesting that both populations of cells may be involved in the myocardial injury response. Taken together, these results provide supporting evidence that c-kit is not solely a stem cell marker, and suggest that investigating the roles of c-kit in different cell types may provide novel insights into the processes of cardiac repair and regeneration.



Endogenous Cardiac EVs and Myocardial Infarction (p 100)

Loyer et al investigate the role of extracellular vesicles in myocardial infarction.

Myocardial infarction leads to widespread inflammatory changes in the heart, characterized by an influx of inflammatory cells and increased cytokine production. Although several different types of cells orchestrate this response, inflammation is also thought to be regulated by extracellular vesicles—small membrane-bound packages released from cells believed to be involved in cell-to-cell communication. Loyer and colleagues now report that the release of extracellular vesicles from cardiac tissue is dramatically increased after experimental myocardial infarction in mice. They found that the majority of these vesicles were released from cardiomyocytes, and were preferentially taken up by monocytes infiltrating the myocardium. In vitro, extracellular vesicles isolated from infarcted hearts prompted proinflammatory cytokine release from monocytes, while vesicles isolated from control hearts had no such effect. The team went on to show that patients undergoing aortic valve replacement surgery had similar types of vesicles present in their myocardium, suggesting that the findings in mice might also have clinical relevance.

Written by Ruth Williams
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