IN THIS ISSUE

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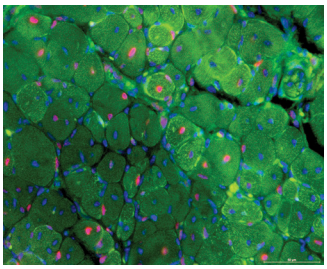
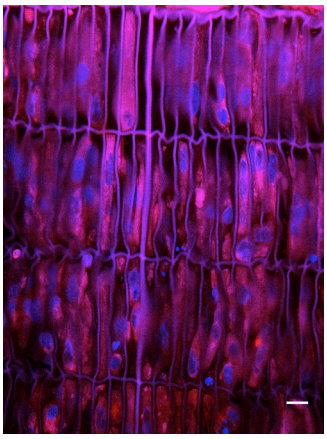


miRNA Mimics for Cardiac Regeneration (p 1298)

Lesizza et al inject microRNAs into the heart to boost cardiac regeneration.

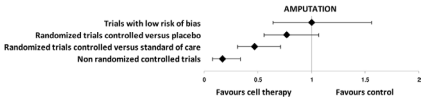
MicroRNAs (miRs) regulate all manner of cellular and physiological processes, including practically every aspect of cardiovascular biology. For example, at least 40 miRs have been found to promote various steps in cardiomyocyte proliferation. Two of these proliferation-promoting miRs—miR-5903p and miR-199a-3p—when packaged into viral vectors and injected into mouse hearts have been shown to contribute to tissue regeneration after myocardial infarction. While these results were encouraging, the use of viral vectors to deliver miRs has inherent safety and efficacy concerns that hinder the chances of such treatments reaching the clinic. With this in mind, Lesizza and colleagues examined whether a more desirable delivery method could also provide pro-proliferative effects in mice. The team injected miR-199a-3p or miR-5903p combined with lipid-based transfection reagents into the hearts of mice that had been subjected to experimental myocardial infarction. They found that while left ventricle ejection fraction steadily deteriorated in control mice, it was better preserved in animals that received the miRs. MiR recipients also had reduced infarct sizes and evidence of increased cardiomyocyte proliferation. These results suggest that in vivo lipid-based transfection of miRs is a therapeutic strategy ripe for further optimization.



3D-Printed Scaffolds for Engineered Myocardium (p 1318)

Gao et al use cutting-edge 3D printing technology to create artificial matrices for myocardial patches.

Cardiac cells derived from human-induced pluripotent stem cells (iPSCs), when injected into the hearts of large animals, have been shown to improve recovery from myocardial infarction. Because cell engraftment is not optimal, however, researchers are also using iPSCs to create embeddable tissue patches. Such engineered tissues may be enhanced by incorporating an extracellular matrix (ECM)-like scaffold to which the cells can adhere. To this end, Gao and colleagues turned to state-of-the-art printing—specifically multiphoton-excited 3D printing, which can produce features smaller than a micron. Using a mouse myocardial ECM as the template, the team printed their artificial version using a gelatin polymer, and on to it seeded human iPSC-derived cardiac cells. After just 1 day of culture, the cells were beating synchronously, and after a week the tissue patch exhibited both functional electrophysiology and cell-to-cell communication. Incorporating the patches into the hearts of mice that had suffered myocardial infarctions led to improved heart function, reduced infarct size, increased vasculogenesis, and reduced apoptosis, compared with control animals. Although it is not yet clear whether the tissue patches electromechanically integrate with the heart, the results encourage further development of this potential therapeutic technique.



Meta-Analysis of Cell Therapy for PAD (p 1326)

A meta-analysis suggests autologous cell therapy can improve prognosis of chronic limb ischemia, say *Rigato* et al.

Peripheral artery disease (PAD), in which the blood vessels narrow due to build-up of calcium or fatty deposits, is a common complication of atherosclerosis and is estimated to affect ≈10% of people aged 40 and over. For some PAD sufferers, the condition may develop into chronic limb ischemia (CLI), and while some CLI patients may be treated with revascularization procedures, many face amputation. Cell therapies aimed at promoting vasculogenesis in such patients have been extensively investigated, but trials have drawn inconsistent conclusions. Rigato and colleagues, therefore, conducted a meta-analysis of autologous cell therapy trials for CLI. Their investigation included nonrandomized and uncontrolled trials, but their most important findings focused on randomized controlled trials (RCTs), which accounted for more than a third of the patients treated. Within these RCTs, the team discovered that intra-muscular or intra-arterial cell injection reduced the risk of amputation by 37%, improved amputation-free survival by 18%, and improved wound healing by 59%. The authors suggest that further trials are warranted, but also argue that, since amputation may be the only option for patients enrolled in such trials, clinical equipoise may not be appropriate.

Written by Ruth Williams

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