# IN THIS ISSUE

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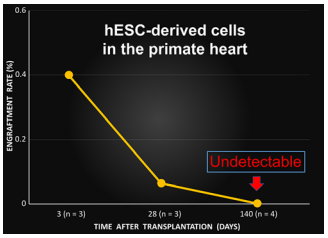
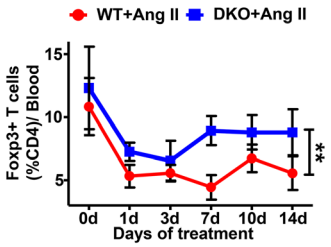



## Lack of Cardiac Remuscularization by ESCs in Primates (p 958)

### Human stem cell–derived cardiovascular progenitors do not remuscularize the infarcted hearts of nonhuman primates, say Zhu et al.

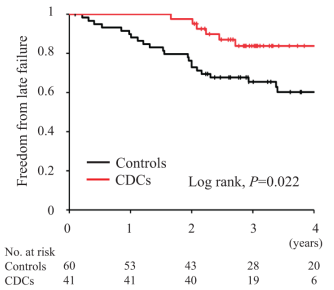
Human pluripotent stem cells (hPSCs) are under investigation for their potential to serve as regenerative treatments after myocardial infarction (MI). Indeed, several studies indicate that hPSC-derived cardiovascular progenitors (hPSC-CVPCs) improve recovery from MI in model organisms. Nevertheless, the mechanisms by which human cells promote myocardial recovery after infarction remain unclear. Such mechanisms can be tested by transplanting human cells in nonhuman primates, but such xenotransplant studies are limited by immune rejection of the cells, which prevents their long-term engraftment. Now, Zhu and colleagues have tested the effectiveness of 2 immunosuppression regimens—cyclosporine alone and cyclosporine plus methylprednisolone and basiliximab—for their ability to improve hPSC-CVPC engraftment in 32 cynomolgus monkeys after MI. Compared with the single-drug treatment, the team found that the combination regimen increased cell retention, reduced apoptosis, and improved heart function after 1 month. By 140 days, however, no cells remained in the hearts of animals in either treatment group. Direct remuscularization by the cells can, therefore, be excluded as the mechanism of functional improvement, say the authors.




## C3aR/C5aR in Tregs Regulates Hypertension (p 970)

### Lack of the complement receptors C3aR and C5aR protect mice against hypertension, report Chen et al.

Hypertension is a leading risk factor for coronary artery disease, stroke, and heart failure. To study the condition in mice, researchers experimentally induce hypertension with either angiotensin II or a combination of deoxycorticosterone acetate and salt. Such induced hypertension has been shown to depend on the presence of T-effector cells. Immunosuppressive T-regulatory cells (Tregs), by contrast, are protective against high-blood pressure. Secreted immune proteins of the complement system—C3a and C5a—have been shown to downregulate Tregs, leading Chen and colleagues to predict that absence of the C3a and C5a receptors would protect against hypertension. They found that treatment with Ang II failed to induce hypertension in mice with a double knockout of the C3a and C5a receptors. Furthermore, adoptive transfer of Tregs lacking the receptors to wild-type mice provided greater protection against Ang II–induced hypertension than that conferred by wild-type Tregs. Importantly, the authors found that humans with hypertension have increased expression of the C5a receptor on their Tregs, suggesting the findings of the study may be of relevance to future drug development.




## Outcomes After Cell Therapy in Single Ventricles (p 994)

### Sano et al report improved outcomes for patients with single ventricle heart defects after cardiac stem cell treatment.

Children born with single ventricle hearts have a high risk of heart failure and premature death. The treatment for such congenital heart defects is either a heart transplant or a series of 3 reconstructive surgeries, called staged palliation, during infancy and childhood. In adults with heart failure, stem cell therapies to enhance myocardial function have shown some promise, but whether such therapy could enhance recovery and heart function in single-ventricle patients after surgery is largely unknown. Sano and colleagues compared 41 patients enrolled in either the TICAP or PERSEUS trials—in which patients received intracoronary infusions of autologous cardiosphere-derived cells (CDCs) shortly after stage 2 or 3 surgeries—with 60 patients who underwent staged palliation only. The authors found that at 2 years of follow up, patients who received CDCs had improved ventricular function as well as fewer late failures and adverse events compared with controls. Improved survival rates were also observed in a subset of patients suffering heart failure with reduced ejection fraction. Together, these results serve as a foundation for longer-term follow-up studies and larger-scale trials.



**Written by Ruth Williams**
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# In This Issue

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