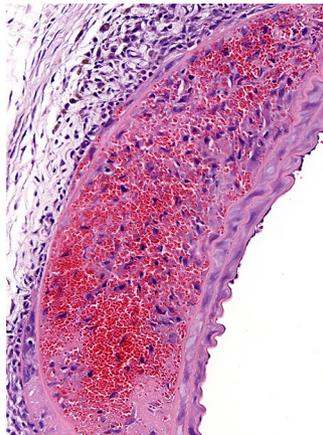


**Cardiac Myocyte Maturation In Vivo (p 1874)**

**Guo et al create a CRISPR system for analyzing gene function during cardiomyocyte maturation.**

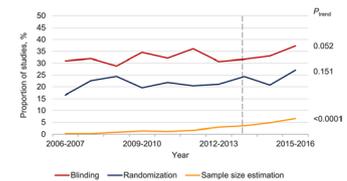
The ability to differentiate stem cells into cardiomyocytes opens an array of research possibilities from disease modeling to regenerative therapies. However, the process is not optimal, in part because the cardiomyocytes generated by the process do not reach full maturity. To examine factors that control full post-natal maturation of myocytes, and how these could be leveraged to improve stem cell differentiation, Guo and colleagues developed a CRISPR/Cas 9–based system for mutating genes of interest in the hearts cells of newborn mice. They attached fluorescent tags to mutated cells, allowing them to follow resulting phenotypic changes in the context of the developing heart. Using this system, they targeted 9 genes with potential roles in the development of transverse tubules (T-tubules), which are essential for excitation–contraction coupling and are hallmarks of fully matured cardiomyocytes. They found that 1 gene (*Jph2*), previously implicated in T-tubule development, was actually minimally involved in the process, instead playing a role in T-tubule stabilization, while another (*Ryr2*) was critical for T-tubule formation. The new system should improve gene function analyses not only during cardiomyocyte maturation but other aspects of cardiomyocyte biology too.



**Nampt and Thoracic Aortic Degeneration (p 1889)**

**Nampt is critical for aortic smooth muscle health, report Watson et al.**

Although built to withstand continuous hydrodynamic stress, the aorta, like all tissues, degenerates over time. Chronic diseases such as atherosclerosis and hypertension quicken this degeneration, and, if severely weakened, the aorta can dilate leading to the formation of an aneurysm or even rupture. Smooth muscle cells (SMCs) that surround the aorta effectively fix minor damage, but this ability dwindles with cell age. It has been found that the enzyme Nampt—which produces the cell metabolism and vitality factor nicotinamide adenine dinucleotide (NAD<sup>+</sup>)—can extend the life of SMCs in vitro and that levels of the enzyme decline as SMCs senesce. Now, Watson and colleagues show that Nampt is essential for maintaining SMC health and aortic integrity in vivo as well. They found that mice genetically engineered to lack Nampt specifically in their SMCs were more prone to hypertension-induced aortic dilation and rupture, and that their SMCs were more prone to senescence and DNA damage. Furthermore, the team showed that patients with dilated ascending aortopathy had lower levels of Nampt, and correspondingly increased DNA damage in their aortic SMCs. The Nampt gene promoter region was also epigenetically repressed in these cells. Together, these results show Nampt is critical for aortic health and suggest that the enzyme may be involved in the pathogenesis of aortic aneurysms.



**Methodological Rigor in Preclinical Research (p 1916)**

**Methodological rigor in preclinical research has not improved, say Ramirez et al.**

Irreproducible scientific results raise particular concerns for translating preclinical research into human studies. To improve pre-clinical methodology, and therefore the chances of reproducibility, the National Institute of Neurological Disorders and Stroke (NINDS), in 2012, published guidelines that outlined the following minimal reporting requirements: randomization of animals, blinding of investigators, sample size estimation (the computation of the appropriate sample size for the study), as well as data handling. The American Heart Association (AHA) journals unanimously agreed to comply with these guidelines, but whether this has led to an improvement of standards is unknown. To find out, Ramirez and colleagues reviewed preclinical cardiovascular studies in AHA journals from 2006 to 2016. They found that just 21.8% of studies reported randomization, 32.7% reported blinding, and just 2.3% reported sample size estimation. Significantly, with the exception of the journal *Stroke*, there had been no increases in these percentages over the 10 years, or since the NINDS report. Moreover, papers that did adhere to the guidelines were no more highly cited than those that did not. The findings highlight that methodological shortcomings are common, that such shortcomings do not affect the impact of research, and that improvements are thus urgently needed.

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## In This Issue Ruth Williams

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