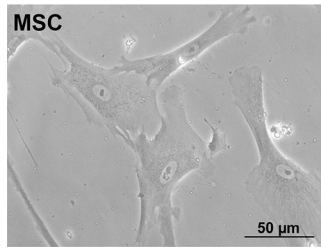


EZH1 Promotes Heart Regeneration (p 106)

Epigenetic factor EZH1 promotes myocardial regeneration, report Ai et al.

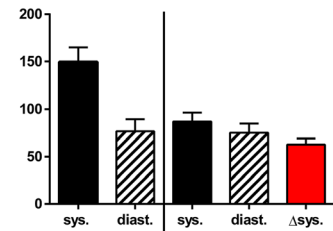
Adult myocardium has limited regenerative potential, such that injuries to the heart result in scarring and reduced function. The hearts of newborn mice, by contrast, have incredible regenerative power, though this ability dwindles rapidly after the first few days of life. This loss of regenerative potential is accompanied by alterations to the epigenetic landscape of the cardiomyocytes. It has been shown, for example, that levels of the 2 catalytic subunits of a major chromatin silencing factor—polycomb repressor complex 2 (PRC2)—decrease in cardiomyocytes coincident with decreasing regenerative potential. Ai and colleagues examined the roles of these 2 subunits—called EZH1 and EZH2—in mouse heart regeneration and showed that genetic deletion of *Ezh1*, but not *Ezh2*, in cardiomyocytes prevented heart regeneration after injury in newborn mice. Furthermore, over-expression of EZH1, but not EZH2, could prolong the neonatal regeneration period, as myocardial infarction at postnatal day 10 was still repairable. This prolongation of regenerative potential was accompanied by increased expression of genes involved in cardiac growth and development, the team showed. Together, the results suggest that manipulations of EZH1 in adult cardiomyocytes may restore the regenerative capacity of these cells to a more youthful setting.



Concurrent Isolation of Human Cardiac Stem Cells (p 113)

Monsanto et al devise a straightforward protocol for isolating key stem cell types from human heart tissue.

Although the adult human heart largely consists of nonreplicating cells, there is growing evidence that resident stem cells can contribute to cell replacement throughout life and to tissue repair, albeit minimally. To boost the reparative potential of endogenous stem cells, or to determine the best cells, or combination of cells, to use for therapies, researchers first need a better understanding of these cells' properties and characteristics. To that end, Monsanto and colleagues have developed a straightforward protocol for isolating the 3 main groups of cardiac stem cells—mesenchymal stem cells (MSCs), endothelial progenitor cells (EPCs), and cardiac progenitor cells (CPCs)—from tissue biopsies obtained during open-heart surgery. The protocol is robust and reproducible, say the authors, and consistently produces MSCs, EPCs, and CPCs that display their expected and distinct morphologies, growth kinetics, gene expression profiles, and propensities for particular fates. The approach will, therefore, allow researchers to study the 3 cell types either individually or in combination, to determine how each contributes to heart regeneration, and to devise ways to best promote such regeneration in patients after heart injuries.



Role of STIM1 in Contractile Dysfunction (p 125)

Troupes et al identify a potential therapeutic target for the treatment of heart failure.

Cardiac hypertrophy—the enlargement of the heart and its cells—is associated with aberrant calcium handling in cardiomyocytes, which increases a patient's risk of arrhythmia and heart failure. Stromal interaction molecule 1 (STIM1) is a protein that, in nonexcitable cells, mediates calcium influx via channel protein Orai. In cardiomyocytes, calcium influx largely occurs via L-type calcium channels, so the role for STIM1 and Orai, which are also expressed in these cells, is unclear. STIM1–Orai activity is increased during hypertrophy, however, which prompted Troupes and colleagues to examine the contribution of these factors to the condition. Using a large animal model (cats), they showed that during cardiac hypertrophy, STIM1 expression and activity was increased and calcium handling was altered (calcium sparks were more numerous and action potentials were longer). Furthermore, over-expressing STIM1 in normal cat cardiomyocytes recapitulated these problems, while blocking Orai activity prevented them. Together, the results indicate that increased calcium influx mediated by increased STIM1–Orai activity directly contributes to the pathology of hypertrophy and that targeting STIM1–Orai could be a potential strategy for reducing the risk of arrhythmia and heart failure in hypertrophy patients.

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