Cardiac Reporter iPS Cell Lines (p 340)

Good news: induced pluripotent stem (iPS) cells and embryonic stem (ES) cells make virtually identical cardiac progenitor cells, report van Laake et al.

Reproducible results are everything in science, which is why it is so important to limit one’s experimental variables. Reports of variance between ES and IPS cell lines have, thus, raised concerns regarding the ability to compare results from one line with the next. What was not known, however, was whether the heterogeneity seen in undifferentiated ES and IPS lines persists as the cells differentiate into specific cell types. To address this issue, van Laake and colleagues compared ES and IPS cell lines from mice that contained a cardiac-specific fluorescent reporter transgene. The reporter allowed for the detection and sorting of cells that had differentiated to become cardiac progenitors. Microarray comparison of ES- and IPS-derived fluorescent cardiac progenitors revealed that from 28,853 transcripts, only 195 were significantly different—less than 0.7%. The team also found that variation between individual IPS cell lines was far less than expected.

Hypoxia and PKCe Gene Repression (p 365)

Patterson et al reveal how lack of oxygen to the fetus represses a cardioprotective gene for life.

It is known that stress to the developing fetus can lead to increased risk of ischemic heart disease later in life. One major cause of intrauterine stress is hypoxia, which can be caused by, among other things, anemia, placental insufficiency, and preeclampsia. It has been shown that hypoxic treatment of pregnant rats causes vulnerability to cardiac ischemia in male offspring. It has also been shown that such male offspring have lower levels of a cardioprotective protein (PKCe) in their hearts. Patterson et al now show that low PKCe in fetuses and offspring is due to methylation of transcription factor binding sites in the PKCe gene’s promoter region. Interestingly, this methylation and the resulting downregulation of PKCe expression are more pronounced in males than females. It is not clear why there is this sex-dependent difference, although the team did observe that in the hearts of female fetuses, the PKCe transcription factor binding sites associated with estrogen receptors. The team suggests that this association somehow protects against methylation of the chromatin.

Dilated Myopathy in Newborns (p 429)

Cardiac stem cells are busy after birth, say Urbanek et al. The team’s findings refute previous suggestions that myogenesis is minimal after embryogenesis.

Immediately after birth, the mammalian heart undergoes a rapid increase in size to accommodate the increased demand of the circulatory system. It was thought that this growth was almost entirely due to hypertrophy of existing cardiomyocytes—a process of cellular expansion without division. This group of researchers recently identified the existence of cardiac stem cells (CSCs) in the hearts of adult mice. They thought it likely that such cells were also present in the newborn heart and wondered whether CSCs might contribute to the rapid neonatal heart growth. CSCs were indeed present, and the majority expressed the receptor for Notch1—a transmembrane protein that regulates cell fate decisions in various developmental settings. Overexpression of Notch1 pushed the CSCs into a proliferative state, whereas blocking Notch1 prevented myogenesis. Without Notch1, newborn hearts did not grow as they should and mice suffered dilated cardiomyopathy and increased mortality. Cardiomyogenesis, thus, not only occurs in the newborn, but also is absolutely essential.
In This Issue

Circ Res. 2010;107:317
doi: 10.1161/RES.0b013e3181f1af78

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2010 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/107/3/317

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/