Impulse Propagation of Cardiac Monolayers (p 1556)

Lee et al make monolayers of iPS-derived cardiomyocytes and monitor their electrophysiology.

The derivation of human-induced pluripotent stem (iPS) cells from patients with heart disorders and the subsequent differentiation of these cells into cardiomyocytes provide an excellent renewable resource of cells for studying disease mechanisms and for testing potential therapies. To investigate disease mechanisms, researchers need accurate ways to assess the physiology, including electrophysiology, of these cells in culture. So far, such assessments have been possible in single cells or small groups of cells only. In the heart, however, cardiomyocytes beat together as a syncytium. Thus, it would be desirable to study how iPS-derived cardiomyocytes behave as a tissue. Lee et al now describe a method for assessing the electrophysiology of human iPS-derived cardiomyocytes grown in large monolayers. They grew the cells on elastic membranes to allow for contractions and viewed calcium waves and voltage propagation through the monolayers simultaneously—using fluorescent reporter molecules for both. Importantly, they showed that the spontaneous beating rate of the monolayers resembled that of normal resting human hearts. The new technique will be especially helpful for studying mechanisms underlying genetic cardiomyopathies and arrhythmias, say the authors.

miR-181c Regulates Mitochondrial Genome (p 1596)

Das et al discover a microRNA that regulates a mitochondrial gene in heart cells.

MicroRNAs (miRs), which are known to play important roles in cardiovascular physiology and pathogenesis, are small noncoding RNAs that bind to and suppress the expression of target mRNAs. MiRs normally suppress gene expression in the cytosol, where they and their target mRNAs associate with silencing complexes. Recently, however, miRs have also been detected in the mitochondria of a handful of cell types. Das et al now add heart cells to that list. The team isolated RNA from cardiomyocyte mitochondria and found a number of miRs that were highly expressed. Chief among them was miR-181, which was 2-fold more abundant in mitochondrial RNA than total heart RNA. MiR-181 bound to and suppressed the expression of the mitochondrial mRNA, mt-COX1, which encodes a key component of the energy-producing electron transport chain. Furthermore, overexpression of miR-181 disturbed mitochondrial function, leading to an increase in oxygen consumption and overproduction of damaging reactive oxygen species. Given the energy demands of heart muscle cells, optimal mitochondrial function is essential; therefore, Das et al suggest that the action of miR-181 could have important implications for heart health.

AT1 Receptors on T Cells and Hypertensive Injury (p 1604)

Angiotensin II receptors on T cells play an unexpected role in hypertension, say Zhang et al.

The hormone angiotensin II promotes increases in blood pressure via interaction with its receptor in blood vessels and various organs. Drugs that block the angiotensin receptor have been shown to lower blood pressure, but they do not halt or reverse the kidney damage that is often associated with hypertension. Zhang et al have now discovered why this happens. The team was investigating the effect of angiotensin II on immune cells—namely T lymphocytes—both because these cells were found to express angiotensin II receptors and because some reports indicated T cells might be activated by the hormone. It turns out that the opposite is true, however. In hypertensive mice, a T-cell–specific knockout of the receptor prompted the cells to mount a proinflammatory response, caused more T cells to accumulate in the kidneys, and exacerbated the damage they caused there. Angiotensin, thus, appears to protect the kidneys and other organs by suppressing the inflammatory response of T cells. The authors suggest that if angiotensin II receptor blockers are used to treat hypertension, it would be worthwhile to develop a parallel strategy to prevent the blockage of the receptor in T cells and, thus, decrease the chances of kidney damage.
In This Issue

Circ Res. 2012;110:1539
doi: 10.1161/RES.0b013e3182601cf2
Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 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/110/12/1539

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/