**IN THIS ISSUE**

_Circulation Research_ Vol. 117 No. 5 August 14, 2015

---

**Optogenetic Voltage Sensing in Cardiac Myocytes (p 401)**

_Liao et al_ measure electrical activity of heart cells and whole hearts with a fluorescent reporter.

Monitoring electrical activity of the heart or cardiomycocytes in culture provides important information about normal and pathological cardiac physiology. But each recording method has limitations. Extracellular electrodes are non-invasive but have poor resolution. Intracellular recordings provide good resolution but are time-consuming, invasive and resource-intensive. Genetically-encoded voltage indicators (GEVI), however, may provide the best of both. They have been used to non-invasively measure electrical activity in brain cells of the mouse and fly, and now Liao and colleagues have tested one GEVI—called VSFP2.3—in whole mouse hearts and heart cells. Similar to VSFP2.3’s behavior in neurons, the protein’s fluorescent signal altered upon heart cell membrane depolarization: yellow emission increased and cyan decreased. This measurable change in fluorescence enabled the team to perform optical cardiograms on whole ex vivo mouse hearts, and on live mice—via optical fibers inserted into the animals’ chests. Lastly, the team used VSFP2.3 to monitor electrical activity of induced pluripotent stem cell-derived cardiomycocytes in vitro. Together the results provide a proof of principle that the use of GEVIs can provide high resolution monitoring of cardiovascular activity in vitro and in vivo.

---

**Methods to Study Cardiac Myocyte Epigenomics (p 413)**

_Preissl et al_ investigate the epigenetic code and transcription profile of cardiomycocyte nuclei.

The identity of a cell does not just come down to the proteins it expresses but to the genetic and epigenetic mechanisms that regulate protein expression. A thorough understanding of the epigenetic landscape of cardiomycocytes and how that landscape changes during development and disease could thus offer valuable insights into heart physiology. To gain such an understanding, Preissl and colleagues first devised a method for isolating highly pure cardiomycocyte nuclei, which relied on cold conditions and avoided enzymatic digestion to preserve the structural integrity of the nuclei and chromatin therein. The team separated cardiomycocyte nuclei from those of other heart cell types on the basis of expression of a specific marker protein—PCM1—and then analyzed nuclear mRNA expression, cellular mRNA expression and a number of epigenetic marks. Their study revealed that the pattern of epigenetic marks correlated more closely with nuclear mRNA expression than cellular mRNA, confirming that the former is a more accurate reflection of the transcription activity of cells. The procedure described in this paper serves as a springboard for further epigenetic analyses of cardiomycocytes from different stages of development or under different pathological conditions, say the authors.

---

**Role of miR-34a Post-MI (p 470)**

_MicroRNA-34a impairs heart regeneration after myocardial infarction, report Yang et al._

The hearts of newborn mice can almost entirely recover from injury, but by one week of age this regenerative capacity diminishes and remains lost throughout adulthood. If researchers could understand what makes regeneration possible in young mice they might be able to recapitulate regeneration in human hearts after myocardial infarctions. To this end, Yang et al have now investigated the role of microRNA miR34a in mouse heart regeneration. Mir34a is a suppressor of cell proliferation known to increase in expression in the heart with age. Furthermore, suppression of miR34a reduces age-associated cardiomycocyte death. The team showed that levels of miR34a are low in the newborn mouse heart and rise to adult levels within a week of birth.

Over-expression of miR34a in the newborn mice prevented heart regeneration, whereas inhibition of miR34a in the adult heart improved cardiac function after infarction. Lastly, the team identified direct targets of miR34a repression—Sirt1, cyclinD1, and Bcl2—which are known to be involved in cell aging, proliferation and survival. Inhibition of miR34a in adult hearts led to the upregulation of these genes. Together the results suggest that inhibiting miR34a, or boosting its targets, may offer therapeutic routes to improve heart recovery after myocardial infarction.
In This Issue

_Circ Res._ 2015;117:389
doi: 10.1161/RES.0000000000000070
_Circulation Research_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2015 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/117/5/389

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/