**IN THIS ISSUE ...**
*Circulation Research*  Vol. 113  No. 3  July 19, 2013

*Leung et al discover an Angiotensin II–controlled, long non-coding RNA that carries two microRNAs.*

Angiotensin II (Ang II) is a hormone that promotes vasoconstriction and hypertension, as well as inflammation, fibrosis and the growth of vascular smooth muscle cells (VSMCs). A number of genes and microRNAs (miRs) have been identified in VSMCs that respond to Ang II treatment, controlling proliferative, inflammatory, and fibrosis pathways. But, recent findings have indicated that longer non-coding RNAs can also regulate cell responses. This led Leung and colleagues to investigate whether other forms of RNA are regulated by Ang II. Comparing the transcriptionomes of Ang II–treated and non-treated rat VSMCs, they discovered 491 differentially expressed transcripts including 24 novel long non-coding RNAs and 14 novel protein-coding transcripts. Upon further examination, the team found many of the non-coding RNAs were located in close proximity to other Ang II–regulated transcripts. The expression of one particular RNA called Lnc-Ang362 closely resembled that of two miRs previously implicated in Ang II–induced VSMC proliferation. In fact, Lnc-Ang362 actually contained the two miRs. Furthermore, suppressing Lnc-Ang362 also suppressed VSMC proliferation. Lnc-Ang362 and the other novel transcripts could be targets for therapy in hypertension and other Ang II–related disorders, the authors suggest.

*PDH2 Silencing Improves Stem Cell Survival (p 288)*

Silencing PDH2 protein in stem cells could improve their ability to mend hearts, say Wang et al.

Stem cell therapy remains a promising technique for improving cardiac function after myocardial infarction. Thus far, however, the majority of experimental stem cell transfers have produced only marginal recovery. Part of the problem is that the engrafted cells do not survive in their new environment for very long. The protein PDH2 is a negative regulator of two different survival factors—HIF-1α and NF-κB—leading Wang et al to investigate whether suppressing PDH2 activity in stem cells might improve their survival in the heart. The team used RNA interference to inhibit PDH2 in human adipose-derived stem cells and compared the heart-mending capability of these cells with non-treated cells in mice that had suffered myocardial infarctions. Four weeks after transferring the cells, mice that had received PDH2-silenced stem cells showed better left ventricle function, including improved ejection fraction, less fibrosis, and a smaller infarcted area. In vitro studies revealed that the PDH2-silenced cells secreted increased levels of an anti-apoptotic factor and the growth factor IGF-1, which might explain the improved performance of these cells. Thus, PDH2 silencing could prove a successful strategy for enhancing the efficacy of current stem cell therapy.

*Matsumoto et al discover potential microRNA biomarkers for predicting heart failure.*

Because of advances in medical therapy, more patients now survive heart attacks than before, but the number of those that go on to develop life-threatening heart failure is on the rise. Biomarkers for predicting which patients are at risk of heart failure would therefore be extremely beneficial. It was discovered recently that microRNAs (miRs) can be secreted from a variety of tissues and can circulate stably in the blood—protected inside tiny membrane-bound vesicles called exosomes. Matsumoto and colleagues investigated whether the levels of any circulating miRs in patients with myocardial infarction are predictive of future heart failure. They collected blood from patients between two and three weeks after myocardial infarction and documented the expression levels of multiple miRs. One in particular, miR-192, was expressed more highly in those patients that went on to develop heart failure within a year. miR-192 is regulated by the tumor suppressor protein p53, and the team discovered that two additional p53-regulated miRs, miR194 and miR34a, were also highly expressed in the patients that would later develop heart failure. These three miRs might therefore be useful for predicting, monitoring, and treating heart failure.

*Matsumoto et al discover potential microRNA biomarkers for predicting heart failure.*

Because of advances in medical therapy, more patients now survive heart attacks than before, but the number of those that go on to develop life-threatening heart failure is on the rise. Biomarkers for predicting which patients are at risk of heart failure would therefore be extremely beneficial. It was discovered recently that microRNAs (miRs) can be secreted from a variety of tissues and can circulate stably in the blood—protected inside tiny membrane-bound vesicles called exosomes. Matsumoto and colleagues investigated whether the levels of any circulating miRs in patients with myocardial infarction are predictive of future heart failure. They collected blood from patients between two and three weeks after myocardial infarction and documented the expression levels of multiple miRs. One in particular, miR-192, was expressed more highly in those patients that went on to develop heart failure within a year. miR-192 is regulated by the tumor suppressor protein p53, and the team discovered that two additional p53-regulated miRs, miR194 and miR34a, were also highly expressed in the patients that would later develop heart failure. These three miRs might therefore be useful for predicting, monitoring, and treating heart failure.

Written by Ruth Williams
(Circ Res. 2013;113:239.)
© 2013 American Heart Association, Inc.
*Circulation Research* is available at http://circres.ahajournals.org

DOI: 10.1161/RES.0b013e3182a2ab85

239
In This Issue

_Circ Res._ 2013;113;239
doi: 10.1161/RES.0b013e3182a2ab85

_Circulation Research_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2013 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/113/3/239

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/