**cGMP Sensor Mice (p 365)**

*Thunemann et al* generate transgenic mice for live imaging of cyclic GMP.

Cyclic GMP (cGMP) is an important signaling molecule that controls a number of cardiovascular processes. Indeed, dysfunctional cGMP signaling has been linked to arterial hypertension, angina and more. But investigating the role of cGMP in cardiovascular physiology is an arduous task because the molecule is difficult to monitor in live cells and tissues. To circumvent this problem, Thunemann and colleagues developed a mouse that expresses a fluorescent biosensor of cGMP: This sensor consists of a cGMP-binding peptide flanked by two fluorescent proteins—one cyan, one yellow. When not bound to cGMP, excitation of the sensor’s cyan protein leads to a transfer of energy to the yellow protein, making it fluoresce brightly. Binding to cGMP, however, reduces energy transfer, by forcing the two fluorescent proteins further apart, which enhances the cyan and reduces the yellow fluorescence. To test this probe, the team treated smooth muscle cells from the mice with vasodilators to induce relaxation, a process known to be controlled by cGMP. Sure enough, they found the cyan signals increased and yellow signals diminished indicating an increase in cGMP levels. Equivalent experiments looking at whole blood vessels in live mice also showed the vasodilator-induced increase in cGMP, confirming the usefulness of these animals for studying cGMP dynamics in vivo.

**HCN4, Dynamic Marker of First Heart Field and CCS (p 399)**

*Liang et al* discover a useful marker for tagging cells of the first heart field.

During embryogenesis, the heart develops from two cell populations called the first and second heart fields. Cells of the first heart field give rise to the early heart tube, and later, to most of the left ventricle as well as parts of the left and right atria. The second heart field by contrast contributes to the right ventricle and outflow tract, and the majority of the two atria. While the transcription factor Is11 is a useful marker of the second heart field, no such marker was identified for the first heart field—until now. The channel protein HCN4 is associated with adult pacemaker cells, but studies of its expression during early development hinted at a first field-like pattern. Liang and colleagues therefore engineered mice to express easily visualized reporters from the HCN4 locus to track HCN4-expressing cells in embryos. They found that HCN4 did indeed mark the first field cells, labeling the early heart tube and left ventricle as expected. They also found that HCN4 is expressed in distinct precursors of the cardiac conduction system and marks the entire system by late fetal stages. Determining the cellular origins of the conduction system will help researchers understand how and why it sometimes fails causing cardiac arrhythmia.

**Endothelial PKCβ2 Promotes Atherosclerosis (p 418)**

*Inhibiting PKCβ2 may reduce the risk of atherosclerosis in patients with diabetes, say Li et al.*

Patients with diabetes are at an increased risk for cardiovascular complications, including atherosclerosis. Likewise, diabetic mice prone to atherosclerosis develop more severe atherosclerotic lesions than non-diabetic mice. The molecular details explaining why diabetes worsens atherosclerosis are still being deciphered, but part of the problem seems to be that during diabetes insulin-resistant endothelial cells fail to increase the production of the vasodilator nitric oxide and to suppress production of VCAM-1, which promotes immune cell adherence to vessel walls. Activation of protein kinase C (PKC) β in endothelial cells of patients with diabetes has been shown to inhibit insulin signaling, and now Li and colleagues have investigated the involvement of PKCβ2 more closely. They found that even in the absence of diabetes, overexpression of PKCβ2 in the endothelium of atherosclerosis-prone mice decreased the activation of endothelial nitric oxide synthase in response to insulin and prevented insulin-induced downregulation of VCAM-1. PKCβ2 overexpression also increased production of the vasoconstrictor endothelin-1, thus further antagonizing insulin action. As a result, these mice exhibited larger atherosclerotic lesions in their aortas. Altogether, the results suggest that inhibiting PKCβ2 may be a potential treatment for reducing atherosclerosis in patients with diabetes.
In This Issue

Circ Res. 2013;113:349
doi: 10.1161/RES.0b013e3182a4edbe

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

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