Zhang et al. suggest that blocking the receptor EP3 could prevent injury-induced restenosis.

Coronary angioplasty, whereby doctors mechanically widen narrowed blood vessels can restore blood flow to the heart and improve symptoms of coronary heart disease. However, the procedure can also injure the vessel wall, which promotes the migration and proliferation of vascular smooth muscle cells (VSMCs) and restenosis. Such injury, induced by angioplasty causes the release of inflammatory signals such as prostaglandins, and it has been shown that blocking the activity of prostaglandin E2 (PGE2) or the enzyme COX2, that blocking the activity of prostaglandin E2 (PGE2) or the enzyme COX2, which synthesizes PGE2, attenuates

prostaglandins, and it has been shown that blocking the activity of prostaglandin E2 (PGE2) or the enzyme COX2, which synthesizes PGE2, attenuates VSMC hyperplasia after vascular injury. Zhang and colleagues now confirm this finding, showing that such VSMC growth is reduced in COX2-knockout mice. But simply blocking COX2 activity in angioplasty patients is not a viable option for therapy, say the authors, because the enzyme also synthesizes prostacyclin, which has cardioprotective effects. The good news is the team also identified the receptor EP3 on VSMCs as the target for PGE2, EP3 antagonists prevented VSMCs from migrating in response to PGE2, suggesting that targeting EP3 might be a good option for preventing angioplasty-induced restenosis in patients.

Deficiency of the protein UPC2 in pulmonary artery cells mimics hypoxia to promote pulmonary hypertension, report Dromparis et al.

When the body experiences acute hypoxia, arteries and arterioles of the lungs constrict, while in chronic hypoxia these vessels undergo remodeling that involves overt proliferation of endothelial and smooth muscle cells and this can cause chronic pulmonary hypertension. Within the vessel wall cells themselves, hypoxia directly inhibits glucose oxidation, but glucose oxidation can also be indirectly inhibited by stress signals from the endoplasmic reticulum (ER), limiting the transfer of calcium to mitochondria, causing the dysfunction of several respiratory enzymes. The protein UPC2 transfers calcium from the ER to mitochondria, and now Dromparis and colleagues have found that UPC2 deficiency leads to pulmonary artery remodeling and pulmonary hypertension in mice, even in the absence of hypoxia. Within the pulmonary artery smooth muscle cells, loss of UPC2 caused reduced mitochondrial calcium levels, respiratory enzyme dysfunction, and induction of the transcription factor hypoxia-inducible factor 1α. Thus at both the tissue and cell level, UPC2 deficiency closely mimics hypoxia. For this reason, UPC2-lacking mice could serve as a useful model for future investigations into the pathological pathways that cause pulmonary hypertension in humans, say the authors.

Inhibiting CETP activity may help diabetes patients as well as those with atherosclerosis, say Siebel et al.

Cholesterylester transfer protein (CETP) is a plasma protein that decreases plasma HDL levels. Therefore CETP inhibition may be one approach for increasing HDL levels in the plasma. Indeed, several on-going clinical trials are investigating the use of CETP inhibition to raise HDL levels and attenuate atherosclerosis. Although the results to date have not been encouraging, circumstantial evidence from these trials with this class of drugs indicates that they might be beneficial by improving glucose homeostasis in patients with type 2 diabetes. To examine the potential anti-diabetic effects of CETP inhibition, Siebel and colleagues have performed a small placebo-controlled trial in 25 healthy males to investigate whether CETP inhibition could increase insulin secretion. They found that after 14 daily doses of a CETP inhibitor, post-breakfast insulin levels in the subjects were raised. Furthermore, mouse pancreatic β cells incubated with plasma from the study subjects who received the CETP inhibitor secreted greater amounts of insulin than those incubated with plasma from the placebo-control subjects. These findings suggest that independent of their potential anti-atherosclerotic effect, CETP inhibitors could be an effective treatment for type 2 diabetes, but larger trials are needed to explore this potential therapeutic use.
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