Medical Xpress

Scientists discover a new way our bodies control blood pressure: the P450-EET system

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If you are one of the millions of Americans with high blood pressure, more help is on the way. That's because a new research study published in the October 2010 print issue of The *FASEB Journal* shows that a protein, called P450, metabolizes arachidonic acid in our blood vessel walls to create a tiny molecule with a big name—epoxyeicosatrienoic acid (EET)—which in mice, turns off genes responsible for vascular inflammation and ultimately relaxes blood vessels to lower blood pressure. This protein and genes are also present in humans.

"We hope these results will help advance the development of new blood pressure lowering agents that increase EETs," said Craig R. Lee, M.D., from the National Institutes of Health's National Institute of Environmental Health Sciences in Research Triangle Park, N.C. "In particular, we hope that targeted-use of these new therapies in individuals with a poorly functioning P450-EET system will ultimately prove to be an effective treatment for patients with high blood pressure."

Lee and colleagues discovered this new protein using genetically modified mice with human P450 present in the cells lining the blood vessels, and using normal mice as a control group. The scientists found that the P450 caused the mice to produce EETs, which in turn caused the relaxation of blood vessels and lower blood pressure. When the mice were exposed to substances that increased blood pressure, the P450 mice had lower blood pressure and less damage to the kidneys than the normal mice. These results show that the P450-EET pathway is a target for the development of new blood pressure medications, and these findings may

influence drug development for other diseases, such as coronary artery disease, stroke, and cancer.

"Whether you're a Type A personality, overweight and out of shape, or genetically wired to have high blood pressure, this research offers real hope," said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal "Having discovered a pivotal role for the P450-EET system, scientists can now develop a new class of drugs not only for lowering blood pressure, but also for preventing strokes and heart attacks."

More information: Craig R. Lee, et al. Endothelial expression of human cytochrome P450 epoxygenases lowers blood pressure and attenuates hypertension-induced renal injury in mice. *FASEB J.* 2010 24: 3770-3781. DOI: 10.1096/fj.10-160119

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