

Researchers find potential new target for hypertension treatment

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Huijing Xia, PhD, a postdoctoral research associate in the lab of Eric Lazartigues, PhD, Assistant Professor of Pharmacology at LSU Health Sciences Center New Orleans, is the lead author on a paper reporting that a recently identified enzyme in the brain plays a critically important role in the central regulation of blood pressure.

The LSUHSC research team showed that Angiotensin-converting enzyme 2 (ACE2) helps preserve the function of a key spontaneous reflex involved in blood pressure regulation and confirms its potential as a target for the prevention or treatment of High Blood Pressure. The research is published in the February 1, 2009 issue of the peer reviewed journal, *Hypertension*, and the cover of the issue features images of ACE2 expression from the Lazartigues laboratory at LSU Health Sciences Center New Orleans.

The LSUHSC researchers had previously identified ACE2 in the mouse brain in areas involved in the central regulation of cardiovascular function. In this study, they wanted to clarify the role it plays.

Beat-to-beat short term regulation of blood pressure is provided by a spontaneous reflex called the baroreceptor reflex. Receptors in the arteries sense blood pressure and relay the information to the central nervous system where a network of brain stem cells adjust vascular resistance and heart rate. Action of a hypertensive hormone - Angiotensin II - is known to interfere with that process.

First, the researchers demonstrated that chronically hypertensive mice showed dramatically decreased baroreceptor reflex sensitivity and ACE2 activity. Following treatment with compounds to block both Angiotensin II receptors, the researchers found that by blocking one of these receptors - AT1Rs - ACE2 activity increased. In order to determine the relationship between

AT1Rs blockade and ACE2, as well as the significance of ACE2, the LSUHSC researchers generated a triple-transgenic mouse model with increased ACE2 on a background of chronic hypertension. In this model, they observed that the impaired baroreceptor reflex and other critical functions normalized, as did blood pressure.

"We now have evidence that brain ACE2 plays a critical role in baroreceptor reflex function and , consequently, in the prevention of hypertension," says Dr. Xia.

"Blood pressure" is the force of blood pushing against the walls of the arteries as the heart pumps out blood. If this pressure rises and stays high over time, it can damage the body in many ways. According to the National Institutes of Health, in the United States, about 72 million people have hypertension or High Blood Pressure (HBP). This is about 1 in 3 adults. HBP itself usually has no symptoms. Rarely, headaches may occur. Some people only learn that they have HBP after it causes health problems, such as coronary heart disease, stroke, or kidney failure.

"Beyond our discovery of ACE2, we have now confirmed its potential as a target for the treatment of hypertension and other cardiovascular diseases," concludes Dr. Lazartigues.

Source: Louisiana State University

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