Research reveals kidney enzyme as a new target for treatment of high blood pressure

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Persistent high blood pressure—or hypertension—can increase the risk of a number of serious and potentially life-threatening health conditions, such as heart disease, heart attacks and strokes.

The team of researchers were investigating the kidney—the key organ

responsible for the development of high blood pressure. The study benefitted from access to the world's largest collection of human kidney samples collected after surgery or kidney biopsy conducted before transplantation, known as the Human Kidney Tissue Resource, at The University of Manchester.

The research team had access to almost 800 kidney samples from this resource and from other research studies.

They extracted both DNA and RNA from each sample and connected information from their analysis, together with data from previous large-scale analyses of blood pressure (called genome-wide association studies), using sophisticated computational methods.

They identified hundreds of kidney genes responsible for changes in blood pressure and found an enzyme called glutamyl aminopeptidase, or ENPEP, to be one of the strongest and most persuasive genes associated with blood pressure.

ENPEP is an integral part of the hormonal system within the body that is essential for regulation of blood pressure. This means the enzyme is an attractive target for developing new medications to treat high blood pressure.

It had been believed reducing levels of ENPEP in the brain could lower blood pressure. However, a recent clinical trial which tested a new drug called Firibastat, the FRESH study, failed to show a significant reduction in blood pressure in patients with hypertension.

The Manchester-led research team instead found that increasing levels of ENPEP in the kidney could have the desired effect of lowering blood pressure.

Study principal investigator and integrative cardiovascular medicine theme co-lead at Manchester BRC, Professor Maciej Tomaszewski, announced the results at the European Society of Cardiology (ESC) Congress in Amsterdam on Sunday 27 August 2023, as part of the Basic and Translational Late-Breaking Science session.

Professor Tomaszewski, who is also chair of cardiovascular medicine at The University of Manchester, and an Honorary Consultant Physician at Manchester University NHS Foundation Trust, said, "We need more choices of blood pressure lowering medications for our hypertensive patients.

"While we have several classes of effective medications available, the last new medication approved for management of high blood pressure in the U.K. and many other countries was direct renin inhibitor (aliskiren), and this was approximately 15 years ago. In contrast, patients with other complex cardiometabolic conditions, such as diabetes or coronary artery disease, continue benefiting from new excellent life-saving drugs constantly entering the therapeutic arena.

"Our results show that through a robust connection to blood pressure emerging from our study and a high 'druggability' potential (its ability to be therapeutically modulated by medicines), kidney ENPEP is a new promising target for development of new blood pressure lowering medications."

Provided by University of Manchester