UNIVERSITÉ DE GENÈVE

PRESS RELEASE

Geneva 29 April 2025

A Renal Protein Reveals a New Mechanism in Hypertension

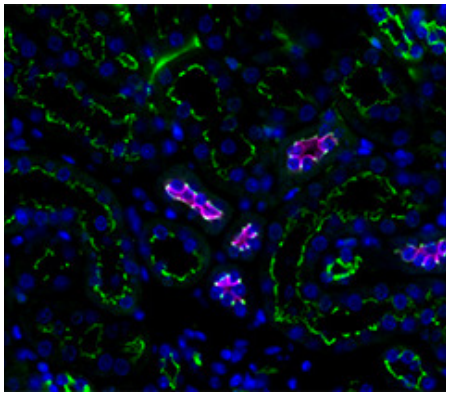
UNIGE scientists discovered a new mechanism involved in blood pressure regulation, opening the door to novel therapeutic approaches.

Hypertension affects nearly one in three adults worldwide and is one of the major risk factors for cardiovascular disease. Previous studies suggest that the junctional protein paracingulin plays a role in the development of hypertension, but the underlying mechanisms remain poorly understood. Scientists from the University of Geneva (UNIGE) developed a mouse model of hypertension to understand the mechanisms through which the loss of paracingulin attenuates the development of hypertension. The team now confirms its essential role in the development of hypertension and provides an in-depth analysis of this mechanism. The results have been published in the *American Journal of Physiology, Renal Physiology*.

Blood pressure refers to the force exerted by the blood as it flows through the blood vessels. It is regulated by several factors, including the kidneys. By filtering blood, the kidneys control the amount of salt and water excreted in urine, which directly affects blood volume and, consequently, blood pressure. In addition, hormones such as angiotensin II and aldosterone stimulate the body to retain sodium and constrict blood vessels. This regulatory system keeps blood pressure within an optimal range but can become dysregulated, leading to hypertension—a major cardiovascular health risk.

The Dahl Rat Model for Studying Hypertension

A well-known animal model, the Dahl rat (named after the American researcher who developed it), has been used for decades to study hypertension. This rat strain spontaneously develops high blood pressure when fed a high-salt diet. However, it was previously reported that in the absence of a cell junction protein called paracingulin (CGNL1), these rats do not develop hypertension, even on a high-salt diet.



Localisation of paracingulin (green) and sodium and chloride ion cotransporter (red) by immunofluorescence on a mouse kidney section. Cell nuclei are shown in blue.

High resolution pictures

Sandra Citi, Associate Professor in the Department of Molecular and Cellular Biology at the UNIGE Faculty of Science, is a specialist in cell-cell junctions. These protein-based “locks” connect neighboring cells to maintain tissue integrity and control the passage of ions and nutrients across tissue compartments. In collaboration with Eric Feraille, Full Professor in the Department of Cell Physiology and Metabolism at the UNIGE Faculty of Medicine and a specialist in kidney physiology, Sandra Citi’s team investigated the role of paracingulin in hypertension. After creating a knock-out of CGNL1 in mice, they observed that the loss of paracingulin protects against angiotensin II-induced hypertension.

A Kidney-Specific Effect

Angiotensin II-induced hypertension involves the activation of sodium transporters in the kidneys. The researchers thus analyzed the levels of activated transporters in the kidneys lacking paracingulin. “We did not observe activation of the transporters. Our results suggest that the protection against hypertension is linked to kidney function, not blood vessel constriction,” explains Florian Rouaud, Senior Research Assistant in the Department of Molecular and Cellular Biology at UNIGE and first author of the study. “In the absence of CGNL1, angiotensin II can no longer activate certain sodium transporters in the renal tubules, which prevents the body from retaining salt and water, and therefore from increasing blood pressure.”

A Novel Therapeutic Avenue

This study identifies paracingulin for the first time as a key player in the renal signaling of angiotensin II— a pathway where junctional proteins were not known to be implicated. It could eventually lead to the development of new therapeutic strategies targeting this protein, as a complement to current treatments, which are often based on inhibitors of the renin-angiotensin system.

contact

Sandra Citi
Associate Professor
Department of Molecular and Cellular Biology
Faculty of Science
UNIGE
+41 22 379 61 82
Sandra.Citi@unige.ch

DOI: 10.1152/ajprenal.00271.2024

UNIVERSITÉ DE GENÈVE
Communication Department
24 rue du Général-Dufour
CH-1211 Geneva 4

Tel. +41 22 379 77 17

media@unige.ch
www.unige.ch