Medical Xpress

Genetic defect disturbs salt handling and pushes up blood pressure levels

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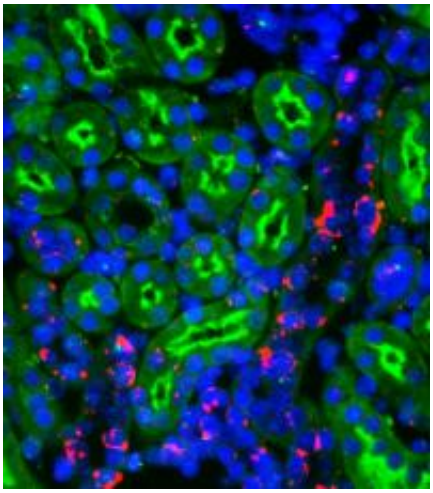

Microscopic cross section of a kidney. The image shows the organs filtration tubes, the so-called tubules. The cell walls of the tubules contain proteins, which are active as water transporter (green) and sodium transporters (red). The cell nuclei are highlighted in blue. © MPI for Heart and Lung Research

(Medical Xpress) -- Hypertension is an endemic condition with far-reaching consequences. For instance, high blood pressure is the main cause of heart attacks and strokes. Other organs are also damaged by the chronic condition. Hypertension is attributed to a high salt intake and a genetic predisposition. Scientists from the Max Planck Institute for Heart and Lung Research in Bad Nauheim have now discovered that even a normal salt intake can cause hypertension in people suffering from a sodium dysregulation. Researchers have managed to identify the

responsible gene.

The regulation of blood pressure is highly complex. The blood pressure level is first and foremost determined by the blood volume. The more blood is circulated in the body, the higher the blood pressure. The 'control centre' is located in the kidneys: Here, blood volume and, in turn, blood pressure, are regulated by renal excretion of water and sodium. To do this, the kidneys receive information from arterial pressure receptors, the autonomic nervous system and different hormones.

The research group headed by Thomas Böttger from the Max Planck Institute for Heart and Lung Research in Bad Nauheim has looked closer at the gene SLC4A5. This gene encodes a protein that transports certain ions (salt compounds), thereby preventing an excessive concentration of salt in the blood. The scientists were able to prove that a defect in this particular gene causes excessive renal retention of sodium and water. This leads to an abnormal increase in blood pressure. "Through studies of large series of patients, many genes have been identified that could be associated with hypertension. However, their specific roles were often not clear", Böttger says.

The scientists in Bad Nauheimer managed to corner the gene when studying mutant mice in which the gene had been specifically inactivated. The so-called "knockout mice" suffered from hypertension. Although various compensatory mechanisms had been activated in the mice, the sodium concentration and blood pressure remained permanently high in these mice. "This shows that we have indeed discovered an important gene for blood pressure regulation in SLC4A5", Böttger says. The study of the knockout mice largely contributed to the result. It actually enabled the scientists to closely investigate the mechanisms that cause high blood pressure. In previous studies of human genetics, SLC4A5 was only known as one of many candidate

genes.

The Max Planck scientists hope that they have found a new approach to treating hypertension more effectively. “First, we must investigate in which percentage of patients hypertension is caused by the SLC4A5 gene”, Böttger says. Any potential treatment depends on this. “If it is possible to re-establish the regulation of sodium in these patients, we could bring the blood pressure back to normal levels.”

More information: Nicole Gröger, Helga Vitzthum, Henning Fröhlich, Marcus Krüger, Heimo Ehmke, Thomas Braun, Thomas Böttger, Targeted mutation of SLC4A5 induces arterial hypertension and renal metabolic acidosis, *Hum. Mol. Genet.* (2011); doi:10.1093/hmg/ddr533 , advance online publication, 14 November 2011

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