New insights into salt transport in the kidney

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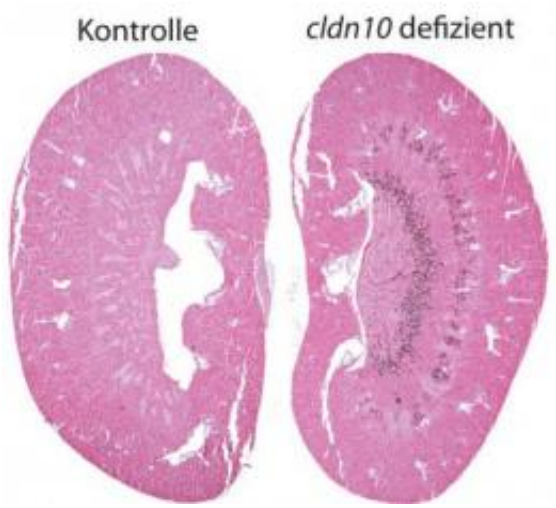

The photo shows sections of a kidney from a claudin-10-deficient mouse and from a control mouse. Black staining (right) shows calcium deposits in the renal medulla, which are characteristic for nephrocalcinosis, a serious disease characterized by calcium deposits in the kidney.Credit: Photo: Tilman Breiderhoff/ Copyright: MDC

Sodium chloride, better known as salt, is vital for the organism, and the kidneys play a crucial role in the regulation of sodium balance. However, the underlying mechanisms of sodium balance are not yet completely understood. Researchers of the Max Delbrück Center for Molecular Medicine (MDC) Berlin-Buch, Charité – Universitätsmedizin Berlin and the University of Kiel have now deciphered the function of a gene in the kidney and have thus gained new insights into this complex regulation process.

In humans, the kidneys filter around 1700 liters of blood every day, of which 180 liters are collected as primary urine and ultimately one to two liters of urine are excreted. The kidneys thus wash toxic waste products out of the body, but retain some useful substances and reintroduce them into the body, thus simultaneously regulating the salt and water balance.

Molecular velcro

In the study just published by Dr. Tilman Breiderhoff, Prof. Thomas Willnow (both MDC), as well as Dr. Nina Himmerkus and Prof. Markus Bleich (both of the University of Kiel) and Dr. Dominik Müller (Charité) the focus is on the claudin-10 gene, which is expressed in a specific segment of the kidney, in Henle's loop. In the thick ascending limb of this loop, , a large part of the filtered sodium chloride, as well as calcium and magnesium are reabsorbed. The gene product under investigation, the claudin 10 protein, belongs to a family of proteins that connect the epithelial cells which cover the inner and outer surfaces of the body and stick them together like velcro. Claudins, however, also form pores, through which ions and substances are transported between the cells.

"If these transport processes are disturbed, this can lead to serious loss of function of the kidneys," Dr. Breiderhoff explained. As example he cited various human hereditary diseases in which either absorption of table salt (Bartter syndrome) or of calcium and magnesium (familial hypomagnesemia with hypercalciuria and nephrocalcinosis – FHHNC) is disturbed. The second disease is characterized by a lack of magnesium in the blood and an excess of calcium in the urine, which leads to calcification of the kidneys. It is caused by mutations in one of two genes (claudin 16 or claudin 19), which also belong to the gene family of the claudins.

The researchers have now demonstrated in mice that the claudin-10 gene

is involved in the reabsorption of salt in the kidney. If the gene in the kidney is deactivated, the reabsorption of sodium is impaired, but the reabsorption of calcium and magnesium is increased. The consequence is that the mice have elevated magnesium levels in the blood, and excess calcium is deposited in the kidney. Simultaneously, the urine volume is increased because the kidneys of the mice cannot reabsorb enough water, a sign that the recovery of salt is disturbed.

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