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Titel des Beitrags:
Standardized, systemic phenotypic analysis of Slc12a1I299F mutant mice.

Abstract:
Type I Bartter syndrome is a recessive human nephropathy caused by loss-of-function mutations in the SLC12A1 gene coding for the Na+-K+-2Cl- cotransporter NKCC2. We recently established the mutant mouse line Slc12a1I299F exhibiting kidney defects highly similar to the late-onset manifestation of this hereditary human disease. Besides the kidney defects, low blood pressure and osteopenia were revealed in the homozygous mutant mice which were also described in humans. Beside its strong expression in the kidney, NKCC2 has been also shown to be expressed in other tissues in rodents i.e. the gastrointestinal tract, pancreatic beta cells, and specific compartments of the ear, nasal tissue and eye. To examine if, besides kidney defects, further organ systems and/or metabolic pathways are affected by the Slc12a1I299F mutation as primary or secondary effects, we describe a standardized, systemic phenotypic analysis of the mutant mouse line Slc12a1I299F in the German Mouse Clinic. Slc12a1I299F homozygous mutant mice and Slc12a1I299F heterozygous mutant littersmates as controls were tested at the age of 4-6
months. Beside the already published changes in blood pressure and bone metabolism, a significantly lower body weight and fat content were found as new phenotypes for Slc12a1I299F homozygous mutant mice. Small additional effects included a mild erythrogenic anemia in homozygous mutant males as well as a slight hyperalgesia in homozygous mutant females. For other functions, such as immunology, lung function and neurology, no distinct alterations were observed. In this systemic analysis no clear primary effects of the Slc12a1I299F mutation appeared for the organs other than the kidneys where Slc12a1 expression has been described. On the other hand, long-term effects additional and/or secondary to the kidney lesions might also appear in humans harboring SLC12A1 mutations.