CALCIUM OXALATE (CaOx) CRYSTAL ADHESION/AGGLOMERATION DEPENDENCE OF CLC-5 EXPRESSION IN RENAL EPITHELIAL CELLS

Dent disease I is a rare X-linked recessive chronic kidney disorder caused by mutations of the CLCN5 gene, which encodes the electrogenic Cl-/H+ exchanger (transporter) ClC-5. Clinical manifestations of patients with Dent disease include low molecular weight proteinuria (LMWP), hypercalciuria, nephrocalcinosis, nephrolithiasis, bone disease (rickets), and often progressive renal failure. The etiology of the nephrocalcinosis and kidney stones often observed in Dent disease patients is not known. Therefore we investigated the effects of several CLC-5 mutations identified in Dent disease patients by the Mayo Clinic Rare Kidney Stone Consortium (RKSC), on cellular processing of calcium oxalate (CaOx) crystals. Our findings support the hypothesis that mutated CLC-5 proteins alter the apical surface of epithelial nephron cells and encourage CaOx aggregation/adhesion. Further investigation into the impact of specific CLC-5 mutation of protein structure and function, including protein-protein interactions, is needed.

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