Growth hormone and Klotho

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Acromegaly is characterized by excessively high GH and IGF1 levels. Recent data suggest that soluble Klotho (sKlotho) is also elevated in patients with active acromegaly. sKlotho decreases towards normal following removal of the GH-producing pituitary adenoma. The Klotho gene was identified in mice following its accidental disruption by ectopic DNA. It is an ageing suppressor gene of restricted expression (mainly in kidneys, brain, and parathyroid and pituitary glands) encoding a transmembrane protein, mKlotho. mKlotho serves as a co-receptor in fibroblast growth factor 23 (FGF23) signalling. FGF23 promotes urinary phosphate excretion and inhibits the synthesis of calcitriol. The ectodomain of mKlotho is enzymatically released to result in a humoral factor, sKlotho, which exerts systemic effects (on ion channels and signalling pathways), possibly by working as an enzyme that modifies glycans of cell surface glycoproteins. GH enhances renal phosphate reabsorption and calcitriol production, i.e. exerts effects in the proximal tubule opposing those attributed to mKlotho, and attenuates calciuria in the distal tubule similar to sKlotho. sKlotho can be measured in extracellular fluids (serum, urine and cerebrospinal fluid (CSF)) by an ELISA. In line with predominant expression of Klotho in kidneys and choroid plexus, concentrations of sKlotho are particularly high in urine and CSF. Determination of sKlotho in serum and urine (both presumably reflecting GH action on the kidneys) could be used as a supplementary tool in the diagnosis and follow-up of patients with acromegaly. The question arises whether GH exerts selected actions via modifying activities of Klotho.