High Phosphate diet affects the regulation of endocrine FGFs functions.

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The endocrine FGFs require the Klotho family as co-receptors for high affinity binding to their cognate FGFRs. FGF23 requires alphaKlotho to bind to FGFRs and functions as a phosphaturic hormone and as a counter-regulatory hormone of Vitamin D_3. In response to increased dietary intake of phosphate, FGF23 is secreted from the bone. FGF23 acts on the kidney to suppress phosphate re-absorption and Vitamin D_3 synthesis. Identification of the FGF23-alphjaKlotho endocrine axis has substantially advanced our knowledge of phosphorus metabolism and transformed our view of the role of phosphate.

Recent clinical studies demonstrated that, in addition to FGF23, plasma FGF21 levels were significantly increased with the progression of early- to end-stage chronic kidney disease (CKD) . In the present study, we investigated the effect of a high phosphorus diet on the endocrine FGFs and found that the HP diet induced up-regulation of FGF23 and FGF21 mRNA expression in the bone and the liver, respectively. On the other hand, the HP diet also induced remarkable down-regulation of FGF15 mRNA expression in the ileum. FGF21 and FGF15 require betaKlotho to bind to their cognate FGFRs, FGFR1c and FGFR4, respectively. These findings indicate that phosphate overload induces the cross-talk between the FGF-Klotho endocrine axes and potentially contributes to pathophysiology of CKD.