



## PTH deletion ameliorates the anomalies of Fgf23-deficient mice by suppressing elevated Vitamin D and calcium levels

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**F**ibroblast Growth Factor 23 (FGF23) is a key regulator of calcium and phosphate homeostasis. Fgf23-deficient mice exhibit an elevated serum level of 1,25 dihydroxyvitamin D (1,25(OH)<sub>2</sub>D), calcium, phosphate and a decreased PTH level. As PTH is known to increase 1,25(OH)<sub>2</sub>D and calcium level, the authors of a recent study [1] hypothesized that PTH deletion in a Fgf23 deficient background could suppress these vitamin D, ion and PTH abnormal levels, and could ameliorate their negative effects on soft tissue atrophies and skeletal abnormalities.

They indeed show a marked reduction of 1,25(OH)<sub>2</sub>D level in the depleted PTH and Fgf23 double knockout background, associated with lower serum calcium level. This lower concentration level partially rescues soft tissues and skeleton abnormalities, and ameliorates the general health of these mice. On the other hand, administration of a large amount of PTH in Fgf23-depleted mice result in very high serum concentrations of 1,25(OH)<sub>2</sub>D and calcium, leading to a marked reduction of trabecular bone volume.

This work highlights the role of PTH in the absence of FGF23 by controlling serum vitamin D and calcium levels.

1. Yuan Q et al. *Endocrinology*. 2011;doi:10.1210/en.2011-1113.

### PTH deletion ameliorates the anomalies of Fgf23-deficient mice by suppressing the elevated vitamin D and calcium levels

FGF23 specifically binds to the canonical FGF receptor 1c (FGFR1c) and Klotho complex. Through this binding, FGF23 targets the parathyroid gland to decrease PTH secretion and acts on the kidney to lower 1,25(OH)<sub>2</sub>D production, leading to decreased intestinal calcium absorption. On the contrary, PTH increases vitamin D and calcium serum level. In Fgf23-depleted mice, high levels of vitamin D and calcium are responsible of kidney and spleen alterations, major skeletal alterations and affect mass, size and physical activity (1). The authors showed that depletion of PTH in a Fgf23 depleted background reduces the vitamin D and calcium levels. These changes partially rescued soft tissue atrophy, skeletal abnormalities, and the general health of double knockout mice (2). On the other hand, the infusion of PTH in a Fgf23-depleted background increased vitamin D and calcium serum level and worsened the general phenotype of treated mice. In particular, these mice present a decrease of the trabecular bone volume when compared with Fgf23-depleted mice (3).

