FGF23 AND X-LINKED HYPOPHOSPHATEMIC RICKETS

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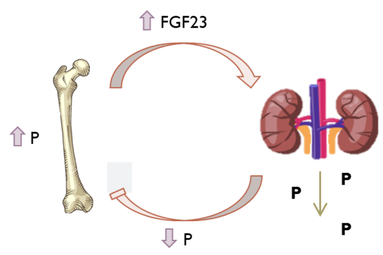
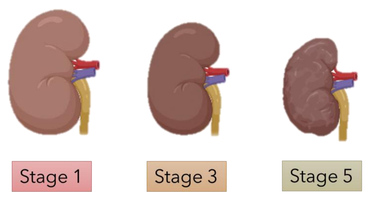
INTRODUCTION

Fibroblast growth factor number 23 (FGF23) is a hormone synthesized in bone, specifically in mature osteoblasts and osteocytes. In the kidney, its main function is the elimination of phosphorus in the urine, which is why it plays an essential role in the maintenance of mineral metabolism in the organism. High levels of FGF23 are related to various pathologies, such as the progression of chronic kidney disease, bone alterations, left ventricular hypertrophy and cognitive impairment, among others.

X-linked hypophosphatemic rickets is an inherited disorder due to a mutation in the X-linked PHEX gene. PHEX encodes an enzyme that locally degrades proteins such as FGF23, so a mutation in PHEX will cause a high increase in plasma FGF23 levels. Therefore, it is hypothesized that an increase in FGF23 levels in mutant mice with X-linked hypophosphatemic rickets will cause an increased excretion of phosphorus and calcium.



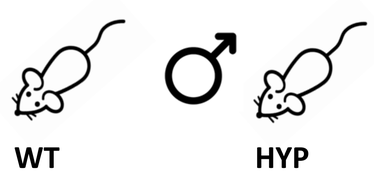


OBJECTIVES

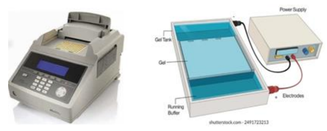
- To identify the presence or absence of the PHEX gene in mice, as a molecular marker to determine its implication in the development of the disease.
- To evaluate the differences in phosphorus and calcium excretion between mice carrying the mutation and those without genetic alterations, in order to analyze its impact on mineral metabolism.

MATERIALS AND METHODS

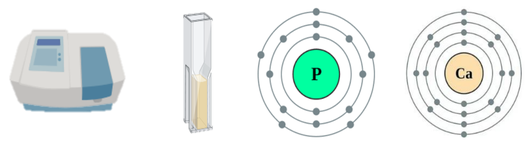
1. Genotyping of mice



2. Agarose gel electrophoresis



3. Evaluation of phosphorus and calcium in urine using specific analysis kits



RESULTS

Figure 1. Parameters for genotyping between WT and HYP mice. A) Genotyping of mice. Mice 2 and 4 show banding for alleles 6 and 22 of the PHEX gene, indicating that they are WT. Mice 1 and 3 present band for 6 and absence of allele 22, indicating that they are HYP. B) Determination of intact FGF23. Previous results of the group show how HYP mice present a significant increase of FGF23 ($p<0.05$ *) in plasma.

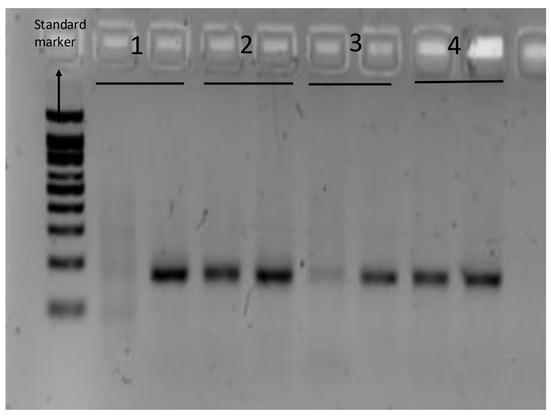


Figure 2. Analysis for the determination of phosphorus and calcium concentration in urine. A) Phosphate regression line. The analysis shows a value of $R^2 = 0.99$. **B) Calcium regression line.** The analysis shows a value of $R^2 = 0.99$.

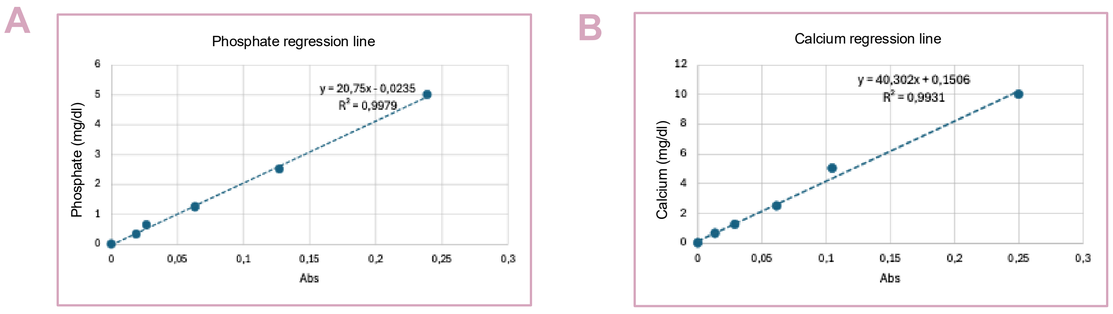
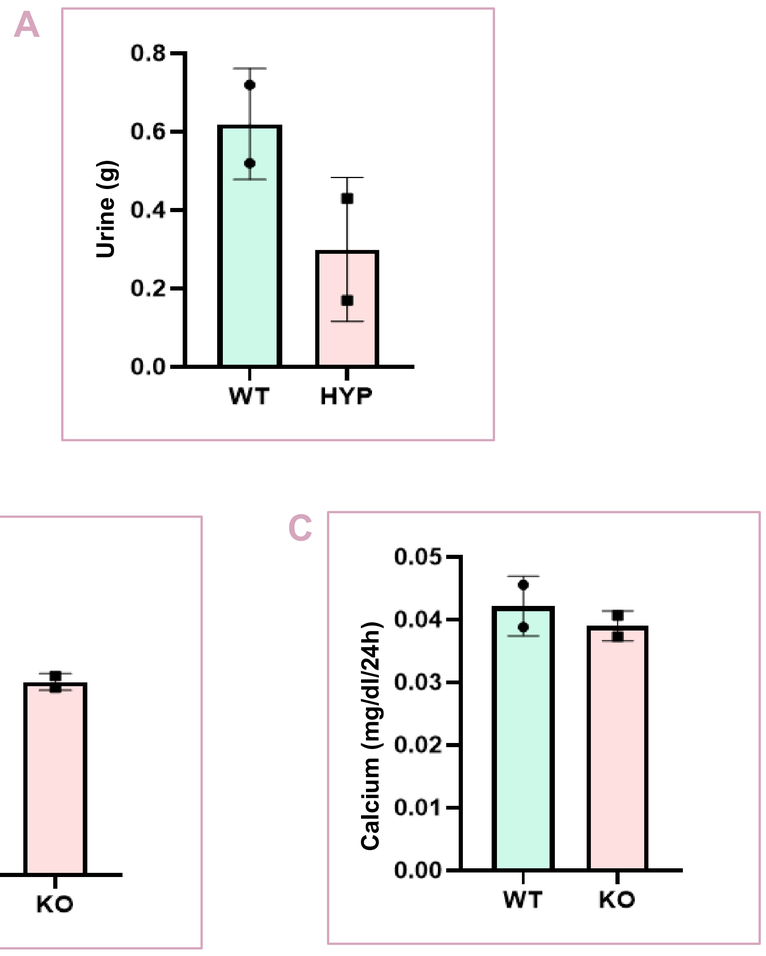


Figure 3. Analysis of urine mineral metabolism parameters. A) Urine volume between WT and HYP mice. Comparison of concentrations in both groups. **B) Phosphorus in urine.** Determination of phosphorus concentration in 24h. **C) Calcium in urine.** Determination of calcium concentration in 24h.



CONCLUSIONS

It has been determined that, after only 10 weeks of life, no significant differences can be observed in the concentration of phosphorus and calcium in the urine of WT and HYP mice. However, according to the results of previous studies, it has been shown that at 10 weeks HYP mice already show an increase in FGF23 levels, so there are changes in mineral metabolism, but they have not yet affected the composition of urine.

REFERENCIES

Sánchez-González, M. C., Salanova, L., & Ruano, P. (2011). "FGF-23: ¿solo regulador del metabolismo del fósforo o algo más?", Reumatología Clínica, 7 (S2), 5-7. 2. Rodelo-Haad, C., Santamaria, R., Muñoz-Castañeda, J. R., Pendón-Ruiz de Mier, M. V., Martin-Malo, A., & Rodríguez, M. (2019). FGF23, Biomarker or Target?. Toxins, 11(3), 175. 3. Hruska, K. A., Rifas, L., Cheng, S. L., Gupta, A., Halstead, L., & Avioli, L. (1995). X-linked hypophosphatemic rickets and the murine Hyp homologue. The American journal of physiology, 268(3 Pt 2), F357–F362.

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