A NEW MUTATION OF *PHEX* GENE IN A PATIENT WITH HYPERPHOSPHATURIA AND HYPERCALCIURIA

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The most common form of familial hyposphatemic rickets (FHR), a group of disorders with similar clinical and biochemical features [hypophosphatemia, hyperphosphaturia, normal levels of $1,25(OH)_2D_3$ and PTH, skeletal deformities, short stature, osteomalacia, dental abscesses bone pain], is represented by the dominant X-linked hyposphatemic rickets (XLH). Individuals with FHR phenotype and a negative familial history in 60-80% of cases are carriers of mutations in *PHEX* gene, on chromosome Xp22.2-p22.1. The mice phenotypical analogue of the human XLH is represented by Hyp strand, in which a 3' deletion of *Phex* removes its COOH-terminal domain. The clinical consequences of PHEX inactivating mutations indicate that its encoded product, an endopeptidase member M13Zn-metallopeptidases family expressed at the skeletal level by osteoblasts, osteocytes, and odontoblasts, is involved in phosphate regulation and mineral homeostasis. *PHEX* inactivating mutations widespread along the gene cause XLH. exons 3-4-11-12-14-15-17-20-22 represent the regions with the higher rate of mutation; such mutations could enable the accumulation of phosphaturic factors and/or mineralization inhibitors. A 26 years old male patient (height 176cm, weight 65 kg) referred to our Centre exhibiting a clear hyperphosphaturia (>2000 mg/24h), hypophosphatemia, hypercalciuria (>600 mg/24h), hypocalcemia (8,1 mg/die), PTH circulating levels at the upper values of the normal range and normal values of 25(OH)D; other symptoms were: deep asthenia, muscle pain and spasms, abundant diuresis (2,5 lt/die). After obtaining the signed informed consent we performed a blood sampling from which genomic DNA has been prepared to analysed *PHEX* gene. The 22 exons and the intron-exon boundaries of PHEX gene have been investigated by a PCR/Sequencing protocol (ABI-Prism 3100). It has been determined the presence of a hemizygous missense mutation of *PHEX* gene in codon 401 (CCT/CTT) causing a Pro/Leu substitution in the extracellular domain closely a cysteine residue highly conserved in exon 11. Nearly future functional studies will be helpful to characterize the molecular mechanisms underlying this mutation.