THE SPECTRUM OF MOLECULAR DEFECTS IN 64 PATIENTS WITH HYPOPHOSPHATEMIC RICKETS IDENTIFIED BY TARGETED NEXT-GENERATION SEQUENCING.

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Introduction and objectives: To assess the value of targeted next-generation sequencing (NGS) used for molecular analysis of candidate genes of Hypophosphatemic rickets (HR).

Patients: n= 64 patients with HR aged 3 months to 45 years

Methods:
1. Custom Ion AmpliSeq™ "Calcium Disorders" gene panel:
   - 22 genes (ALPL, ATP6V0A4, ATP6V1B1, CASR, CLCN5, CLCNKB, CYP24A1, CYP27B1, CYP2R1, DMP1, ENPP1, FGF23, GALNT3, KL, LRP5, PHEX, PTHR1, SLC2A2, SLC34A1, SLC34A3, SLC9A3R1, VDR);
   - ~83 kb, 409 amplicons, coverage 98.5%.
2. PGM semiconductor sequencer (Ion Torrent, Life Technologies).
3. Bioinformatics: Torrent Suite 4.6 (Ion Torrent, Life Technologies), ANNOVAR¹, version 2013 Feb21 (annovar.openbioinformatics.org).

Results: Mutations were identified in 100% of familial and 88.5% of sporadic cases.

Conclusions:
- The study confirmed predominance of PHEX mutations among the patients with HR.
- The large size and complexity of PHEX gene makes the targeted NGS a feasible tool for diagnostics of HR.

References:

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