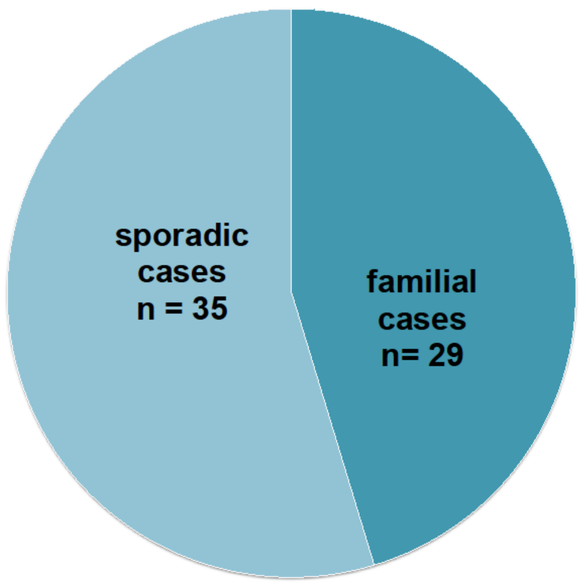
THE SPECTRUM OF MOLECULAR DEFECTS IN 64 PATIENTS WITH HYPOPHOSPHATEMIC RICKETS IDENTIFIED BY TARGETED NEXT-GENERATION SEQUENCING.

Kristina Kulikova[1], Anna Kolodkina[1], Evgenij Vasiliev[1], Vasilij Petrov[1], Fedor Gofman[2], Anatoly Horkin[2], Vladimir Kenis[3], Mikhail Petrov[4], Anatoly Tiulpakov[1]

[1]Endocrinology Research Centre, Moscow, of Ministry of Healthcare, the Russian Federation
[2]Federal State Budgetary Institution “Russian Ilizarov Scientific Center "Restorative Traumatology and Orthopaedics" of Ministry of Healthcare, the Russian Federation
[3]Federal State Budgetary Institution The Turner Scientific Research Institute for Childrend′s Orthopedics, of Ministry of Healthcare, the Russian Federation
[4]V.E.Morozovsky Children′s Hospital, Moscow

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

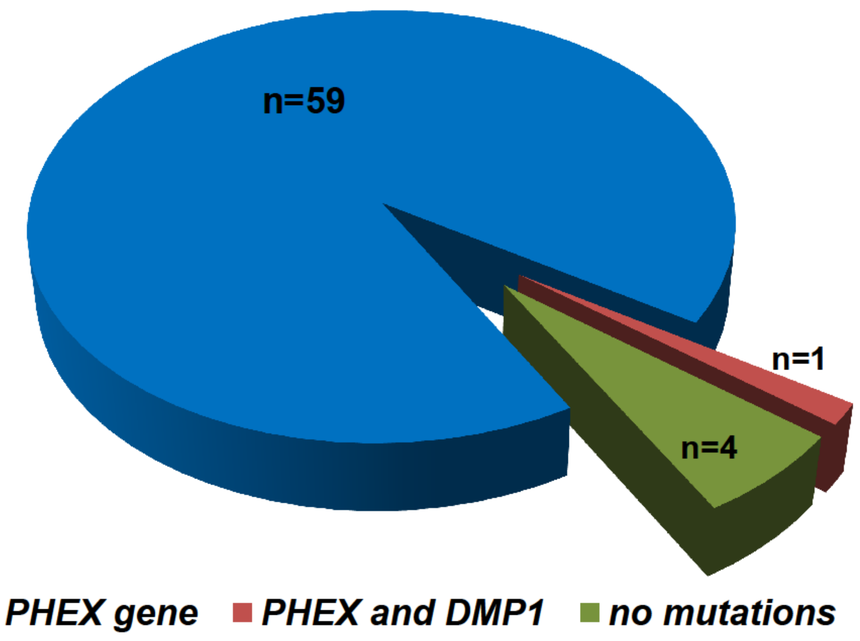


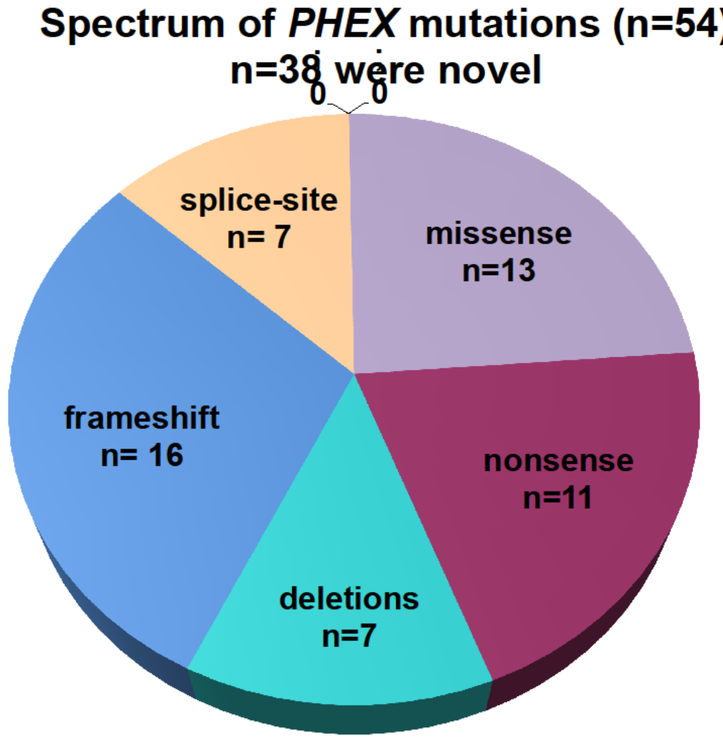
Methods:

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), ANNOVAR[1], version 2013 Feb21 (annovar.openbioinformatics.org).

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

n=64 patients





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 :
1. Wang K., Li M., Hakonarson H. ANNOVAR: functional annotation of genetic variants from high-throughput sequencing data. *Nucleic Acids Research*, 38:e164, 2010

Financial support

LIFE LINE FUND TO SUPPORT SERIOUSLY SICK CHILDREN

Альфа-Эндо