Clinical and genetic profiles of 168 Russian patients with hypophosphatemic rickets.

Kristina Kulikova[1], Anna Kolodkina[1], Evgeny Vasiliev[1], Vasilij Petrov[1], Vladimir Kenis[2], Michel Petrov[3], Anatoly Korkin[4], Fedor Gofman[4], Anatoly Tiulpakov[1]

1 Endocrinology Research Centre, Moscow, Russian Federation
2 The Turner Scientific and Research Institute for Children's Orthopedics, Moscow, Russian Federation
3 Russian pediatric university hospital, Moscow, Russian Federation
4 Federal State Budgetary Institution “Russian Ilizarov Scientific Center "Restorative Traumatology and Orthopaedics", Moscow, Russian Federation

Introduction: The aim of this study was to clinically characterize and perform genetic analysis of 168 cases with HR.

Patients:

- n= 168 patients with the diagnosis of HR
- age, from 1 months to 56 years
- female n=111, male n=57
- 52 familial and 116 sporadic cases from 137 families

Methods:

1. Custom Ion AmpliSeq™ «Rickets panel» 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%.

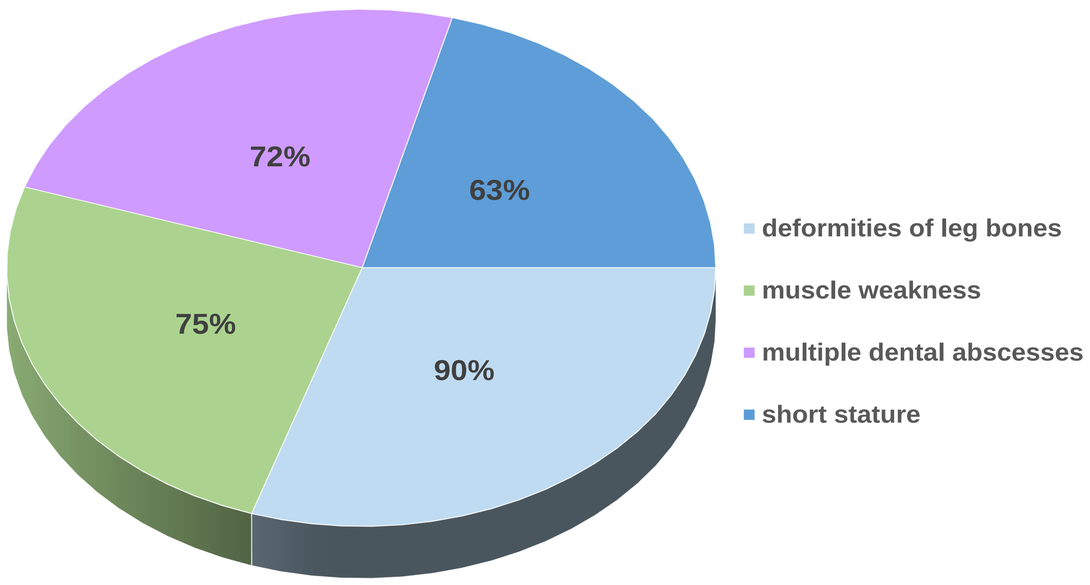
2. PGM semiconductor sequencer (Ion Torrent, Life Technologies).

3. Bioinformatics: Torrent Suite (Ion Torrent, Life Technologies), ANNOVAR version 2013 Feb21 (annovar.openbioinformatics.org)

Results:

- The mean age at diagnosis was 7.5 years (aged from 2 month to 17 years).

Clinical symptoms of HR



- The mean height SDS, -2.3±1,8
- The mean RSS= 4.5 points (range: 1.5-10)

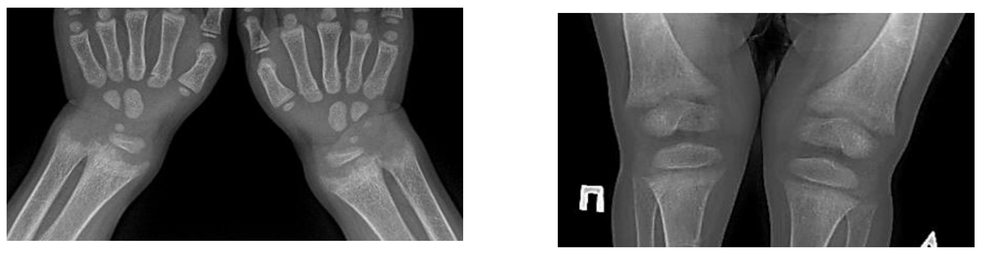
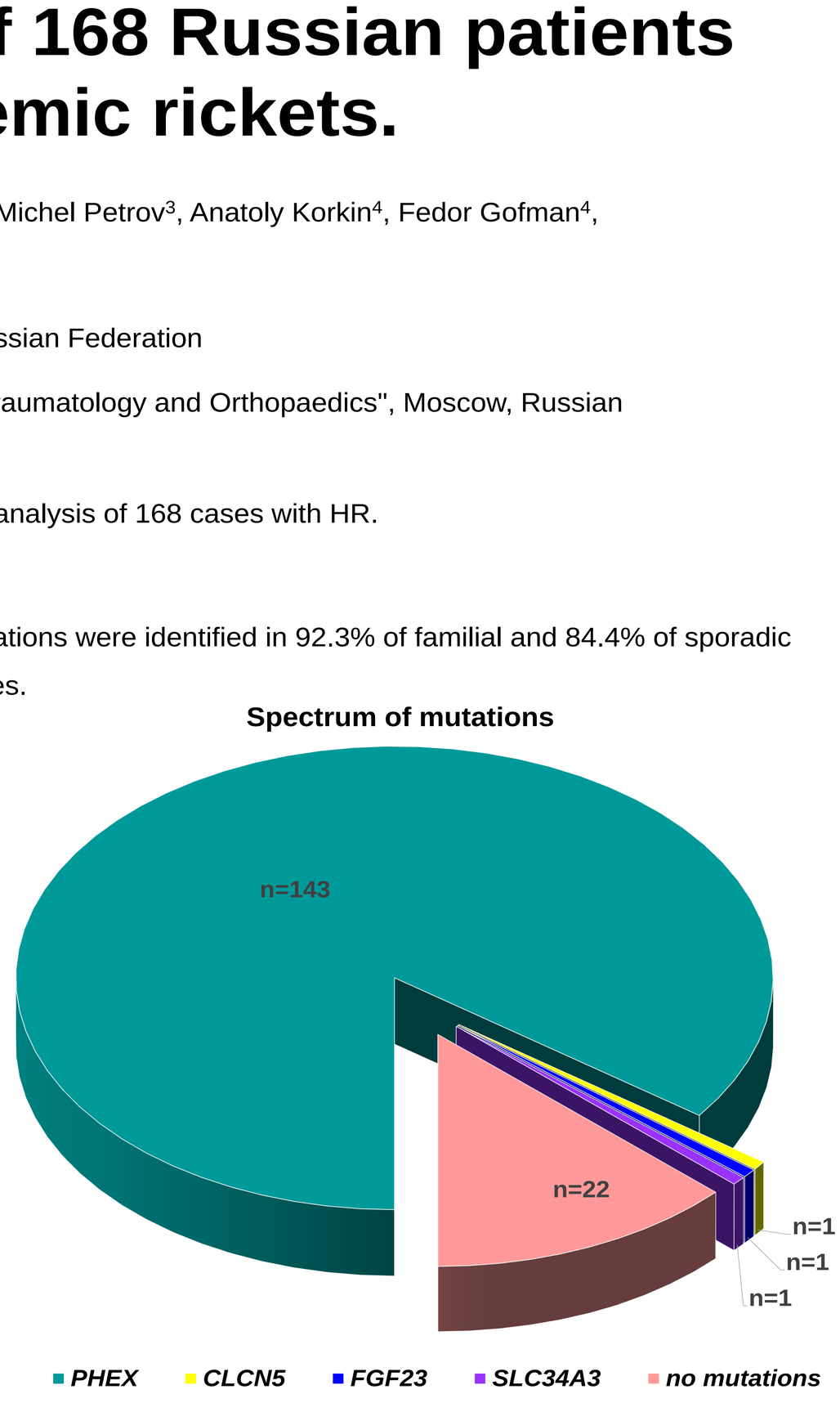


Figure 1. Radiographs of wrists and knees of a 3-year-old male with severe rickets (RSS = 10 points).

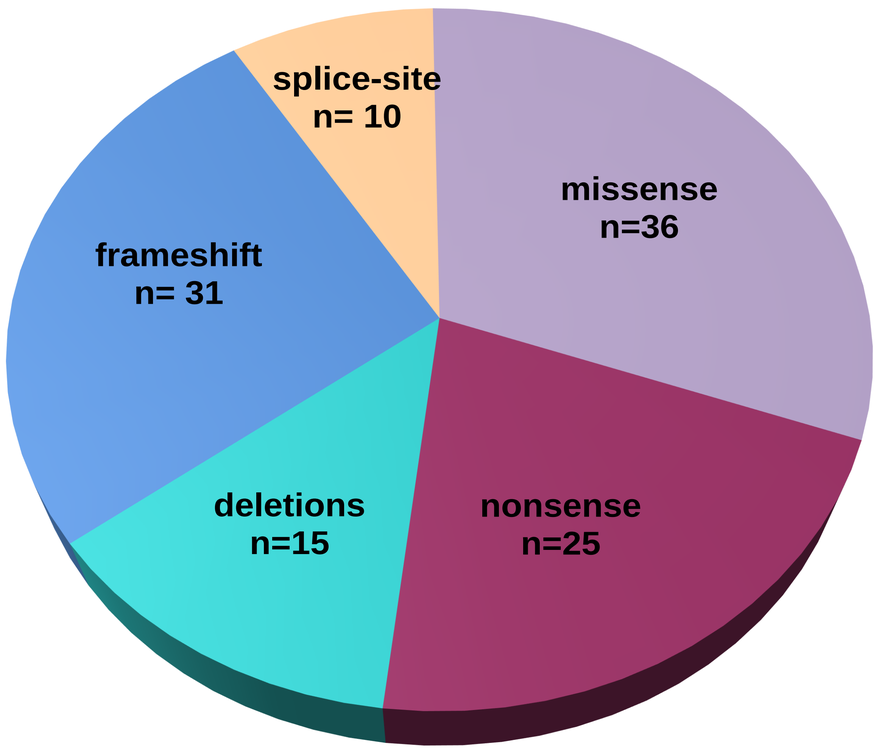
- Mutations were identified in 92.3% of familial and 84.4% of sporadic cases.

Spectrum of mutations



- In 143 probands mutations were detected in *PHEX*, 70 of which were novel.

Spectrum of *PHEX* mutations (n=117)



Conclusion:

- This study showed the predominance of *PHEX* mutations among the patients with HR in Russia.
- We identified 117 *PHEX* mutations, including 70 unreported ones.
- Earlier diagnostic and treatment can result in less severe complications and improve the quality of life of patients with HR.

Financial support

LIFE LINE FUND TO SUPPORT SERIOUSLY SICK CHILDREN

Альфа-Эндо