The prevalence of different subtypes of maturity-onset diabetes of the young in Russian Federation as defined by targeted next-generation sequencing

Zubkova N.A.[1], Gioeva O.A.[1], Tikhonovich Y.V.[1], Vasilyev E.V.[1], Petrov V.M.[1], Malievsky O.A.[2], Kiyaev A.V.[3], Timofeev A.V.[4], Tiulpakov A.N.[1]

[1] Endocrinology Research Centre, Moscow; [2] Republican Children's Clinical Hospital, Ufa; [3] Ural State Medical University, Ekaterinburg; [4] I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation

Objective: to evaluate the frequency of different subtypes of MODY in the Russian population using a targeted next generation sequencing (NGS)

Criteria of inclusion:

- diabetes or intermediate hyperglycemia;
- absence of β-cell autoimmunity (ICA, GAD, IA2, IAA antibodies);
- preserved C-peptide secretion

Subjects:

224 subjects (0.3-25 yrs)
males=118, females=106

Methods:

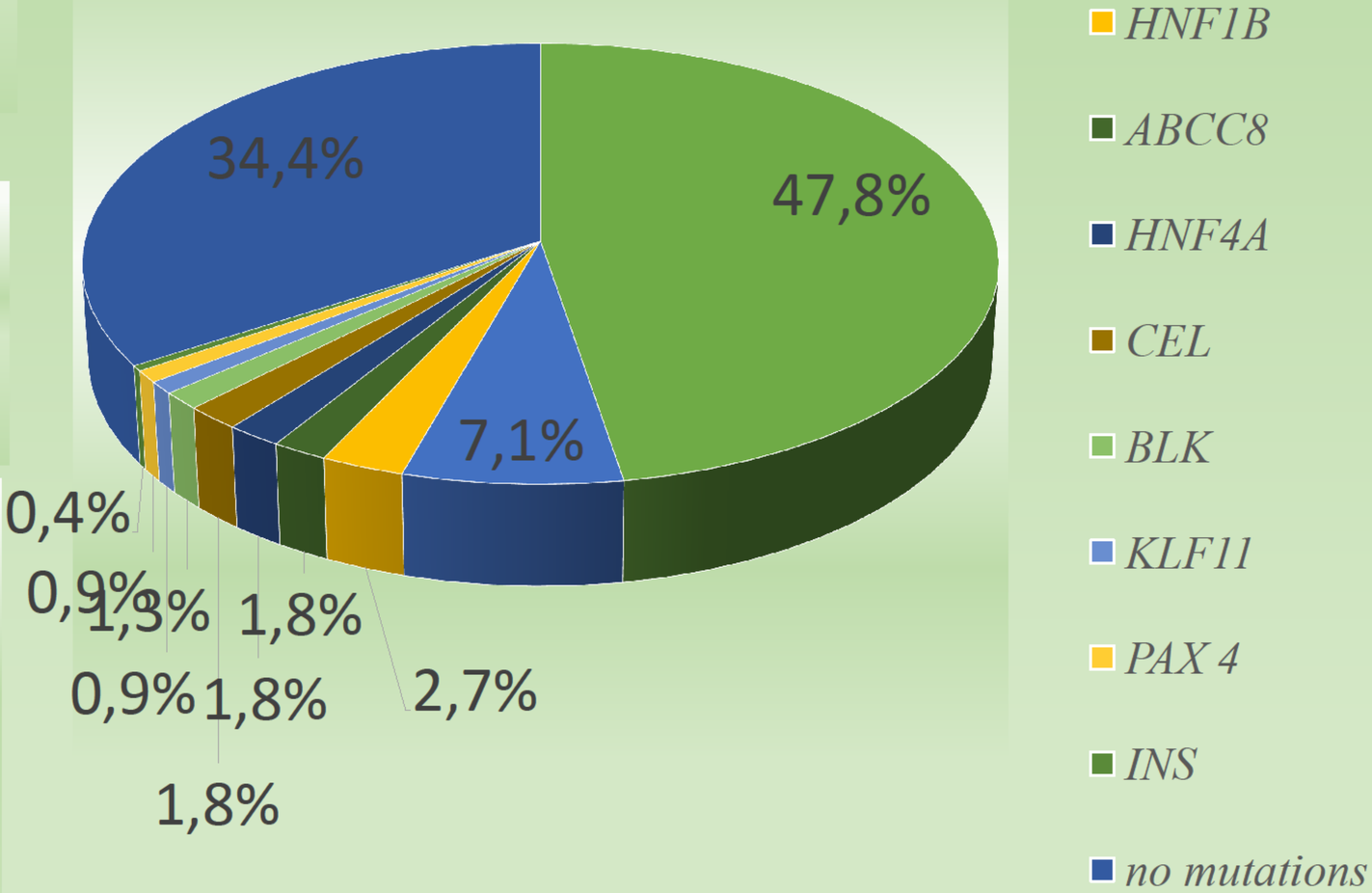
- PGM semiconductor sequencer (Ion Torrent, Life Technologies);
- Custom Ion AmpliSeq™ 'Diabetes panel': *ABCC8, AKT2, BLK, CEL, EIF2AK3, FOXP3, GCG, GCGR, GCK, GLIS3, HNF1A, HNF1B, HNF4A, SLC16A1, KLF11, INS, INSR, KCNJ11, PAX4, PPARG, PDX1, PTF1A, NEUROD1, RFX6, GLUD1, WFS1, ZFP57, SCHAD* **(28 genes, 488 amplicons);**
- Bioinformatic analysis: Torrent Suite (Ion Torrent, Life Technologies) and ANNOVAR* (annovar.openbioinformatics.org) software packages;
- Non-synonymous sequence variants were rated as "probably pathogenic" if they had minor allele frequency <1% and pathogenic ljb database scores

*Wang K, Li M, Hakonarson H. ANNOVAR: Functional annotation of genetic variants from next-generation sequencing data Nucleic Acids Research, 38:e164, 2010

Results:

- 65.6 % of patients - 129 pathogenic or "probably pathogenic" mutations;
- 5 patients - digenic mutations

Spectrum of mutations identified



Patient	Digenic mutations
1	*HNF1B+CEL*
2	*HNF1B+GCK*
3	*HNF1A+GLIS 3*
4	*HNF1A+INSR*
5	*ABCC8+GLUD1*

Conclusion:

- MODY2 is the most prevalent in the studied population
- NGS is useful in identifying rare subtypes of MODY;
- Some cases of MODY may be associated with digenic mutations

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