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

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**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

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

**Spectrum of mutations identified**

<table>
<thead>
<tr>
<th>DNA</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>GCK</td>
<td>47.8%</td>
</tr>
<tr>
<td>HNF1A</td>
<td>34.4%</td>
</tr>
<tr>
<td>HNF1B</td>
<td>7.1%</td>
</tr>
<tr>
<td>ABCC8</td>
<td>0.4%</td>
</tr>
<tr>
<td>HNF4A</td>
<td>0.4%</td>
</tr>
<tr>
<td>CEL</td>
<td>0.9%</td>
</tr>
<tr>
<td>BLK</td>
<td>1.8%</td>
</tr>
<tr>
<td>KLF11</td>
<td>1.8%</td>
</tr>
<tr>
<td>PAX4</td>
<td>0.9%</td>
</tr>
<tr>
<td>INS</td>
<td>1.8%</td>
</tr>
<tr>
<td>no mutations</td>
<td>2.7%</td>
</tr>
</tbody>
</table>

**Patient** | **Digenic mutations**
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1 | HNF1B + CEL
2 | HNF1B + GCK
3 | HNF1A + GLIS3
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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