7. Results

All analyses are to be run with the ID gene panel selected.

7.1 De novo analysis

RAI1:c.3253G>C heterozygous.
The de novo analysis as shown in the demo already shows this variant.
Clinical features: Delayed psychomotor development, Speech delay, Mild intellectual disability, Macrocephaly, Autism. Prader-Willi Syndrome, usually caused by deletions. Heterozygous, but dominant inheritance.

7.2 X-linked recessive analysis

An X-linked disorder is discarded judging from the pedigree.

7.3 Recessive analysis

HADHB:c.209+1G>C and HADHB:c.980T>C compound heterozygous.
Clinical features: Polyneuropathy (associated with Hereditary Motor Sensory Neuropathy (HMSN)), Delayed psychomotor development, Hypotonic.

The analysis returns 11 variants. Besides the two HADHB variants, 9 variants remain. Six can easily be discarded; the ZSWIM6 variant has no reads supporting the variant in the index and is an artefact of the variant caller; the CDKN1C/SLC22A18AS variants and one CCDC40 variant have very low conservation scores and a neutral effect prediction; the other CCDC40 variant and the PEX5 variant are homozygous in one of the parents. The X-chromosomal SHROOM4 variant is discarded looking at the pedigree and also doesn't look too probable to be damaging - the conservation scores aren't very high and the Grantham score is rather low. The DOCK6 variants can not easily be discarded given the information in LOVD$^+$, however its frequencies in GnomAD are rather high (in one case there are homozygotes found) and several prediction programs state the variants are likely to be benign.

7.4 Imprinted analysis

MAGEL2:c.1996dupC heterozygous.
Note that this variant can only be found when the EVS filter is turned off, as the variant has a frequency there of 0.35%.
Clinical features: Multiple affected family members (see family tree), Delayed psychomotor development, Intellectual disability, Short stature.

The analysis, with the EVS filter removed, returns 2 variants. Besides the MAGEL2 variant, 1 other variant remains. The CDKN1C/SLC22A18AS variant, the same as found in the recessive analysis, has a very low conservation score and a neutral effect prediction, and is therefore easily discarded.