**Supplementary Table 1: *TCF20* frameshift and nonsense variants (n=4) deposited in the ExAC database.**

Three of the four frameshift and nonsense variants in the ExAC database are classified as disputable (highlighted in gray and column “Flags”). These variants have i) a QualByDepth (QD) below 2 and therefore are considered “bad” (Van der Auwera et al., 2014) and ii) are located in a homopolymer run of seven G nucleotides and thus are most likely a sequencing artifact. In addition, the pipeline LOFTEE (Loss-Of-Function Transcript Effect Estimator) classified the two variants at chr22: 42,564,715 as “low-confidence” LOF variants since they are very close to the N-terminus of the protein and affect only one isoform. Only the nonsense variant at chr22: 42,609,973 which is predicted to lead to a premature stop at position 447 may be valid. This variant with a minor allele frequency of 0.00082% is present in only one heterozygous individual. However, ExAC variants are not confirmed by independent methods. Since the ExAC consortium excludes individuals affected by severe pediatric diseases, the variant carrier should be a “healthy control person”*.* Thus, this finding could indicate that at least some *TCF20* LOF variants may indeed not be completely penetrant as has been shown for other, well-established intellectual disability genes such as *ASXL1* and *ARID1B* 1. However, given the number of only one healthy carrier with a single unverified LOF variant, no final conclusions regarding a potentially incomplete penetrance should be drawn.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Chr: Position (hg19)** | **Reference** | **Alternate** | **Transcript**  **Consequence** | **Protein**  **Consequence** | **Annotation** | **Allele**  **Number** | **Allele**  **Count** | **MAF [%]** | **QD** | **Flags** |
| chr22: 42,610,947 | T | TG | c.364dupC | p.(Gln122ProfsTer12) | frameshift | 121230 | 1 | 0.00082 | 0.38 | QD, homopolymer |
| chr22: 42,609,973 | G | A | c.1339C>T | p.(Arg447Ter) | stop gained | 121408 | 1 | 0.00082 | 11.07 |  |
| chr22: 42,564,715 | A | AG | c.5826dupC | p.(Gln1944AlafsTer39) | frameshift | 97734 | 13 | 0.01330 | 0.38 | QD, homopolymer, LC LoF |
| chr22: 42,564,715 | AG | A | c.5826delC | p. (Leu1943CysfsTer118) | frameshift | 97734 | 1 | 0.00102 | 0.38 | QD, homopolymer, LC LoF |

QD: QualByDepth, LC LoF: low-confidence” LOF variant according to LOFTEE, MAF: minor allele frequency

1. Ropers HH, Wienker T. Penetrance of Pathogenic Mutations in Haploinsufficient Genes for Intellectual Disability and Related Disorders. *Eur J Med Genet* 2015; **58**: 715-718.