Supplementary Information

NAA10 mutation causing a novel intellectual disability syndrome with Long QT due to N-terminal acetyltransferase impairment

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Table S1. Rare or novel X-specific variants identified by whole exome sequencing in patient III:1.

Gene	Transcript	cDNA alteration	Protein alteration	dbSNP ID	MAF (%)	Implicated in DD/ID	Variant segregates
SHROOM2	NM_001649.2	c.4274C>T	p.(Ser1425Leu)	rs149373874	0.81	no	-
SHROOM4	NM_020717.3	c.1879C>T	p.(Pro627Ser)	rs150861758	0.29	yes	no
IL13RA1	NM_001560.2	c.597_599delAAC	p.(Gln199del)	novel	-	no	-
ZCCHC12	NM_173798.2	c.722G>C	p.(Arg241Thr)	rs140976011	0.06	yes	no
GPR112	NM_153834.3	c.6217C>A	p.(Pro2073Thr)	rs371661996	0.01	no	-
SPANXD	NM_032417.2	c.220A>G	p.(Lys74Glu)	rs2983592	unknown	no	-
MAGEA4	NM_001011550.1	c.122C>T	p.(Ser41Phe)	rs41302158	0.46	no	-
NAA10	NM_001256120.1	c.128A>C	p.(Tyr43Ser)	novel	-	yes	yes

Variant prioritisation identified eight hemzygous coding variants on the X chromosome of patient III:1 which were novel or had a minor allele frequency (MAF) less than 1% in control databases and Irish controls. Three of the eight genes have previously been implicated in developmental delay (DD) or intellectual disability (ID). Only one of those three remaining candidates segregated with the phenotype in this family.

Table S2. Whole exome sequencing variant prioritisation strategy

Criteria	Number of Variants
Variants identified	203,992
+ absent or present with a frequency <1% in dbSNP130, NHLBI EVS and 1000G	27,486
+ Nonsense, missense, splice site or indel	1,260
+ X Chromosome	27
+ hemizygous and X-specific	11
+ absent or present with a frequency <1% in 60 Irish control exomes	7
+ previously implicated in developmental delay or intellectual disability	3
+ segregates with the phenotype	1

Rare or novel hemizygous variants in genes on the X chromosome implicated in developmental delay or intellectual disability were prioritised. Of the three candidate variants, only one variant segregated with the phenotype; a novel missense variant (c.128A>C; p.(Tyr43Ser)) in the *NAA10* gene.

Table S3. Primer sequences for PCR.

Gene	Exon number	Forward primer 5'-3'	Reverse primer 5'-3'	Size (bp)	Annealing temperature
SHROOM4	Exon 4	CACAGCAGCCACAAAGGG	TGAAGAGCTTGTCTCTGGGG	613	60°
ZCCHC12	Exon 4	CAAACCGGACTCGCTTGCAG	CCTGGGCCTTGTCACTCTCG	597	60°
NAA10	Exon 3	ACTCGTCCAGTTTGTGTCCC	ACAGAGGCATCCACCAGAC	192	60°

PCR primer sequences were designed using the Exon Primer programme available in the UCSC Genome Browser.