

Supplementary methods

Whole exome sequencing

Whole exome sequencing was performed for the proband and his parents by Genotek Ltd. Genomic DNA from peripheral blood samples was isolated using QIAamp DNA Mini Kit (Qiagen, Hilden, Germany) according to the manufacturer's protocol. DNA libraries were then prepared using QIAseq FX DNA Library Kit (Qiagen, Hilden, Germany) according to the manufacturer's protocols. Samples were enriched with SureSelect XT2 kit (Agilent Technologies, Santa Clara, CA, USA) and then sequenced by HiSeq 2500 sequencer (Illumina, San Diego, CA, USA), generating 2×100 bp reads. An additional table file shows all genes and exons that have been sequenced. After sequencing, we trimmed 3'-nucleotides with read quality below 10 using Cutadapt.¹ Raw reads were aligned to reference genome hg19 (GRCh37.p13) using BWA MEM.² FastQC was used for data quality control. We called short variants using GATK HaplotypeCaller according to GATK Best Practices DNA-seq.^{3,4,5} The effect of each mutation was assessed using snpEff.⁶ To assess pathogenicity and conservatism, the data was extracted from the dbNSFP, Clinvar, OMIM database and HGMD, as well as using the SIFT and PolyPhen-2 utilities to predict the pathogenicity of the mutation. Information on the frequency of mutations was taken from 1000Genomes project, ExAC) and Genotek frequency data. Description of mutations and their pathogenicity were predicted according to the Standards and Guidelines developed by ACMG (American College of Medical Genetics and Genomics), AMP (Association for Molecular Pathology) and CAP (College of American Pathologists).^{7,8,9,10,11,12} Sanger sequencing confirmed all variants identified by exome sequencing.

This variant was classified as a "likely pathogenic" variant according to the variant interpretation guidelines of ACMG (PM1, PM2, PM5, PP2, PP3, PP5). The variant was classified as a "pathogenic" according to the predictive programs SIFT and PolyPhen2 (PolyPhen2 HumDiv score 1,00; PolyPhen2 Hum Var score 0,96; SIFT score 0,00).

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8. Ng PC, Henikoff S. SIFT: Predicting amino acid changes that affect protein function. *Nucleic Acids Res* 2003;31:3812–3814.
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10. Auton A *et al.* A global reference for human genetic variation. *Nature* 2015;526:68–74.
11. Lek ML *et al.* Analysis of protein-coding genetic variation in 60,706 humans. *Nature* 2016;536.
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Gene	Transcript	Sequenced exons
AGRN	NM_198576	All
TNFRSF4	NM_003327	All
TAS1R3	NM_152228	All
MRPL20	NM_017971	All
GABRD	NM_000815	All
SKI	NM_003036	All
PEX10	NM_153818	All
MMEL1	NM_033467	All
PRDM16	NM_022114	All
TP73	NM_005427	All
NPHP4	NM_015102	All
KCNAB2	NM_001199862	All
TNFRSF25	NM_148965	All
PLEKHG5	NM_001265593	All
TAS1R1	NM_138697	All
CAMTA1	NM_015215	All
PER3	NM_016831	All
UTS2	NM_021995	All
PARK7	NM_007262	All
ENO1	NM_001428	All
CA6	NM_001270500	All
SLC2A5	NM_003039	All
H6PD	NM_004285	All
PIK3CD	NM_005026	All
KIF1B	NM_015074	All
PGD	NM_002631	All
PEX14	NM_004565	All
MASP2	NM_006610	All
MTOR	NM_004958	All
UBIAD1	NM_013319	All
MTHFR	NM_005957	All
NPPA	NM_006172	All
NPPB	NM_002521	All
PLOD1	NM_000302	All
MFN2	NM_001127660	All
MIIP	NM_021933	All
TNFRSF1B	NM_001066	All
DHRS3	NM_004753	All
CTRC	NM_007272	All
CASP9	NM_001229	All
RSC1A1	NM_006511	All

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HSPB7	NM_014424	All
EPHA2	NM_004431	All
SPATA21	NM_198546	All
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SDHB	NM_003000	All
PAX7	NM_002584	All
TAS1R2	NM_152232	All
ALDH4A1	NM_003748	All
EMC1	NM_015047	All
HTR6	NM_000871	All
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PLA2G5	NM_000929	All
PLA2G2D	NM_012400	All
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DDOST	NM_005216	All
KIF17	NM_020816	All
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ALPL	NM_000478	All
HSPG2	NM_005529	All
WNT4	NM_030761	All
ZBTB40	NM_014870	All
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C1QC	NM_001114101	All
C1QB	NM_000491	All
EPHB2	NM_004442	All
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RPL11	NM_000975	All
GALE	NM_001127621	All
HMGCL	NM_000191	All
FUCA1	NM_000147	All
CNR2	NM_001841	All
GRHL3	NM_198174	All
RUNX3	NM_004350	All
LDLRAP1	NM_015627	All
STMN1	NM_001145454	All
SLC30A2	NM_001004434	All
TRIM63	NM_032588	All
CNKSR1	NM_006314	All
CATSPER4	NM_198137	All
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PIGV	NM_017837	All

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TEKT2	NM_014466	All
COL8A2	NM_005202	All
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GRIK3	NM_000831	All
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EXO5	NM_022774	All
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USP24	NM_015306	All
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ADAM17	NM_003183	All
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APOB	NM_000384	All
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ADCY3	NM_004036	All
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OTOF	NM_194248	All
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KHK	NM_006488	All
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IFT172	NM_015662	All
GCKR	NM_001486	All
PCARE	NM_001029883	All
ALK	NM_004304	All
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CRIM1	NM_016441	All
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CYP1B1	NM_000104	All
SOS1	NM_005633	All
SLC8A1	NM_021097	All
THADA	NM_022065	All
ABCG5	NM_022436	All
ABCG8	NM_022437	All
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LHCGR	NM_000233	All
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GFER	NM_005262	All
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FUT6	NM_001040701	All
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GLUD2	NM_012084	All
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