

Supplementary Table 2. Population frequencies and *in silico* pathogenicity predictions for *GGPS1* variants reported in this study

Gene	<i>GGPS1</i>	<i>GGPS1</i>	<i>GGPS1</i>	<i>GGPS1</i>	<i>GGPS1</i>
Variant	c.269A>G p.(Asn90Ser)	c.439A>G p.(Met147Val)	c.196A>C p.(I1166Leu)	c.545T>C p.(Leu182Pro)	c.770T>G p.(Phe257Cys)
Transcript	NM_004837.4	NM_004837.4	NM_004837.4	NM_004837.4	NM_004837.4
Rs-ID	rs1012843795	rs1237799550	Absent	Absent	Absent
gnomAD	Absent	1 heterozygous allele out of 251328	Absent	Absent	Absent
Iranome and GME	Absent	Absent	Absent	Absent	Absent
UK Biobank	Absent	2 heterozygous alleles out of 537358	Absent	6 heterozygous alleles out of 537358	Absent
Queen Square Genome database (23 000 exomes)	Absent	Absent	Absent	Absent	Absent
Centogene database	1 heterozygous allele Centogene AF ~5.6 x 10 ⁽⁻⁶⁾	2 heterozygous alleles	Absent	Absent	Absent
TOPMed	1 heterozygous allele	1 heterozygous allele	Absent	Absent	Absent
ClinVar	Not reported	Not reported	Not reported	Not reported	Not reported
CADD PHRED score	26.4	25.8	25	26	27.3
GERP	6.17	6.17	5.05	6.17	6.17
SIFT score	0.02 (Deleterious)	0.00 (Deleterious)	0.01 (Deleterious)	0.00 (Deleterious)	0.00 (Deleterious)
PolyPhen score	0.964 (Probably damaging)	0.946 (Probably damaging)	1 (Probably damaging)	0.999 (Probably damaging)	0.994 (Probably damaging)
PROVEAN	-5.0 (Damaging)	-3.73 (Damaging)	-1.88 (Neutral)	-6.55 (Damaging)	-6.98 (Damaging)
FATHMM PRED	Tolerated	Tolerated	Tolerated	Tolerated	Damaging
LRT PRED	Deleterious	Deleterious	Deleterious	Deleterious	Deleterious
MetaLR score	0.5429 (Damaging)	0.5090 (Damaging)	0.4605 (Tolerated)	0.6008 (Damaging)	0.5524 (Damaging)
MutPred score	0.859	0.728	0.776	0.734	0.751

MutationAssessor score	3.42 (High functional impact)	3.765 (High functional impact)	2.845 (Medium functional impact)	3.19 (Medium functional impact)	3.38 (Medium functional impact)
REVEL score	0.624	0.570	0.50	0.7039	0.7179
ACMG	PS4, PP1 (moderate), PM2, PP3 Likely pathogenic	PS4, PP1 (moderate), PM2, PP3 Likely pathogenic	PM2, PP3, PP4 VUS	PM2, PP3 VUS	PM2, PP3 VUS