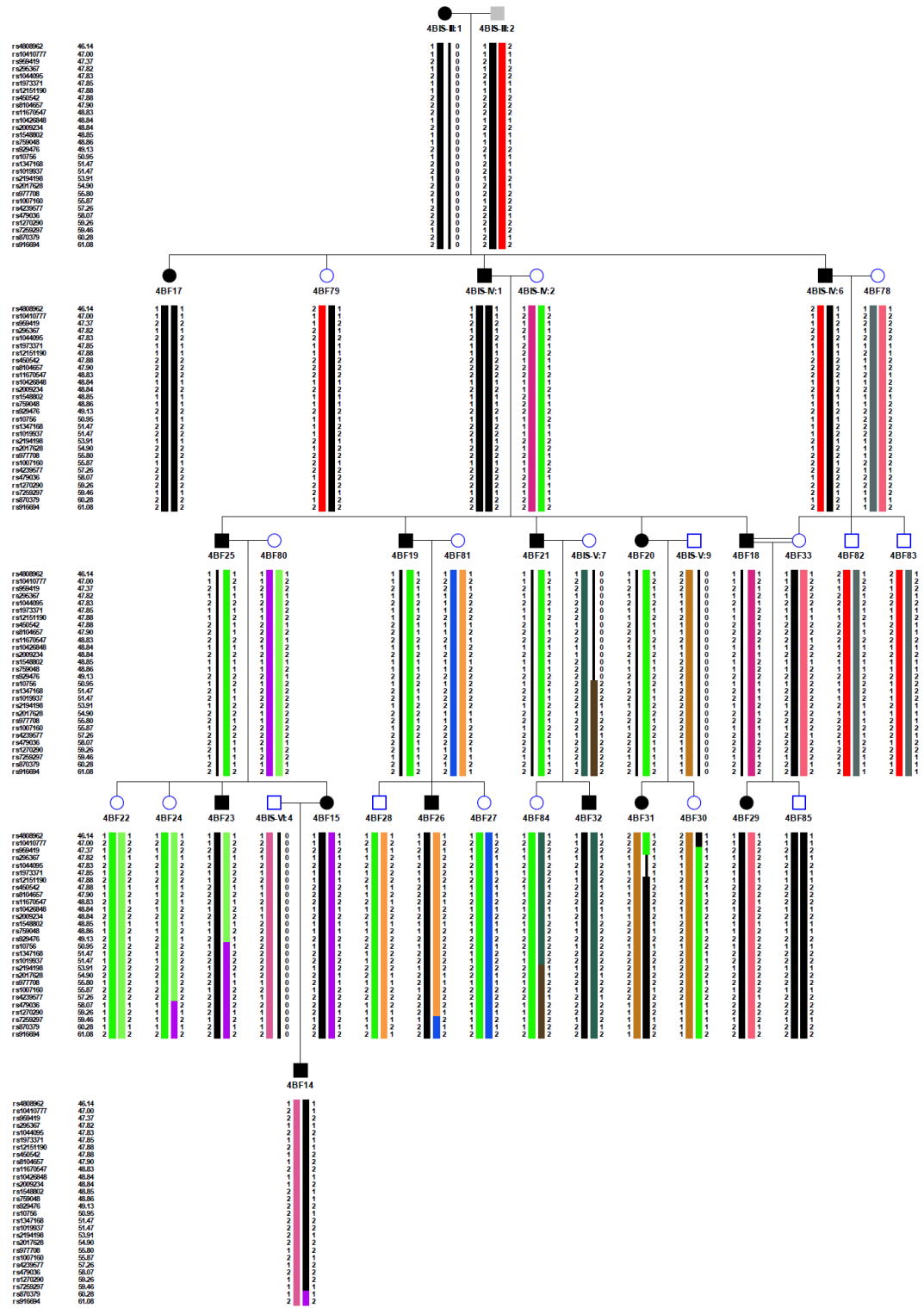


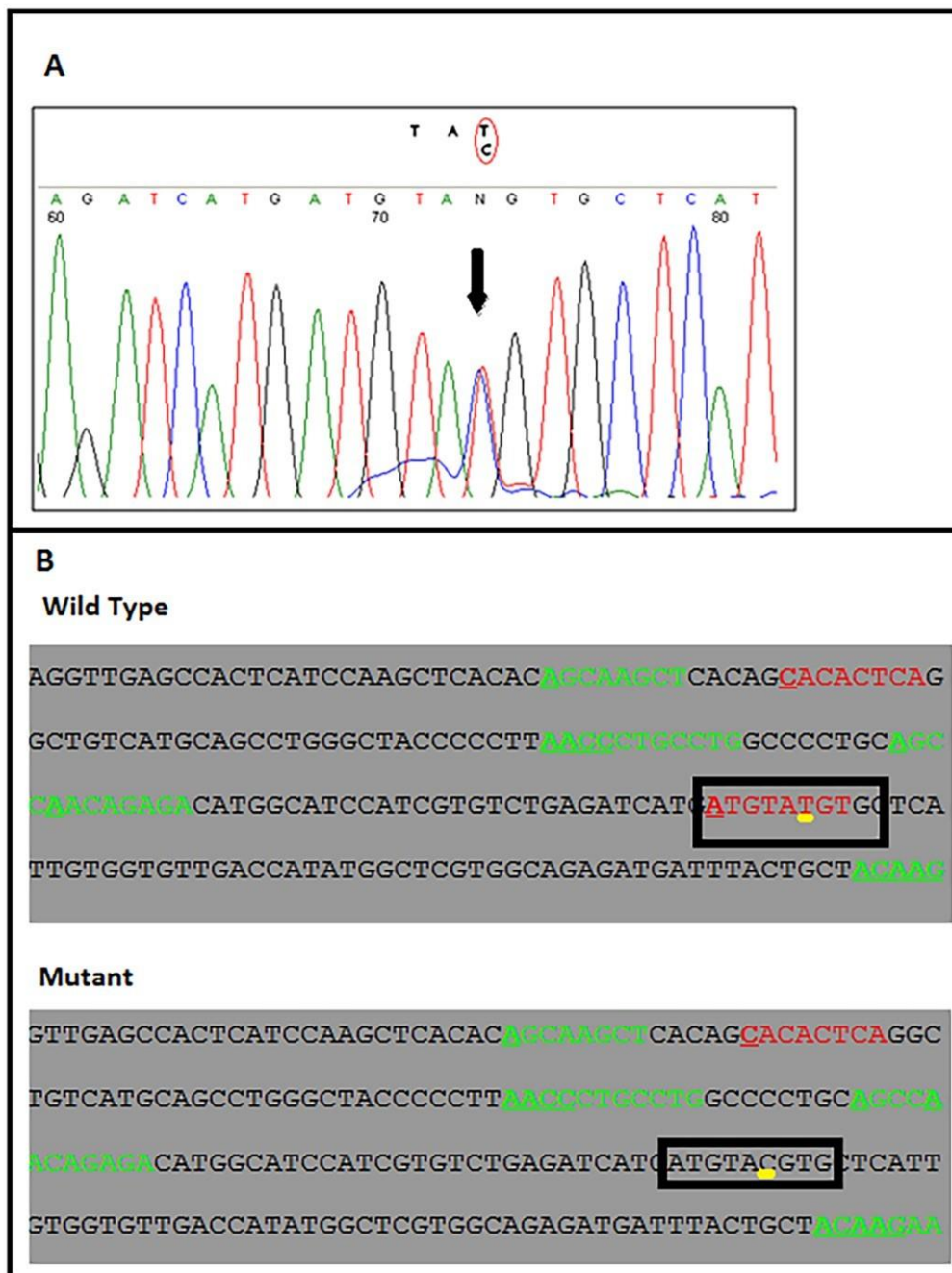
**Figure 1:** Genome-wide Linkage analysis result of the BFIS family.

(A) Whole genome linkage results obtained from Allegro module with AD inheritance and 70% penetrance model. (B) Linkage analysis result of SimWalk module with AD inheritance and 70% inheritance model focusing on chromosome 19 linkage region.

### Family 4BFIS

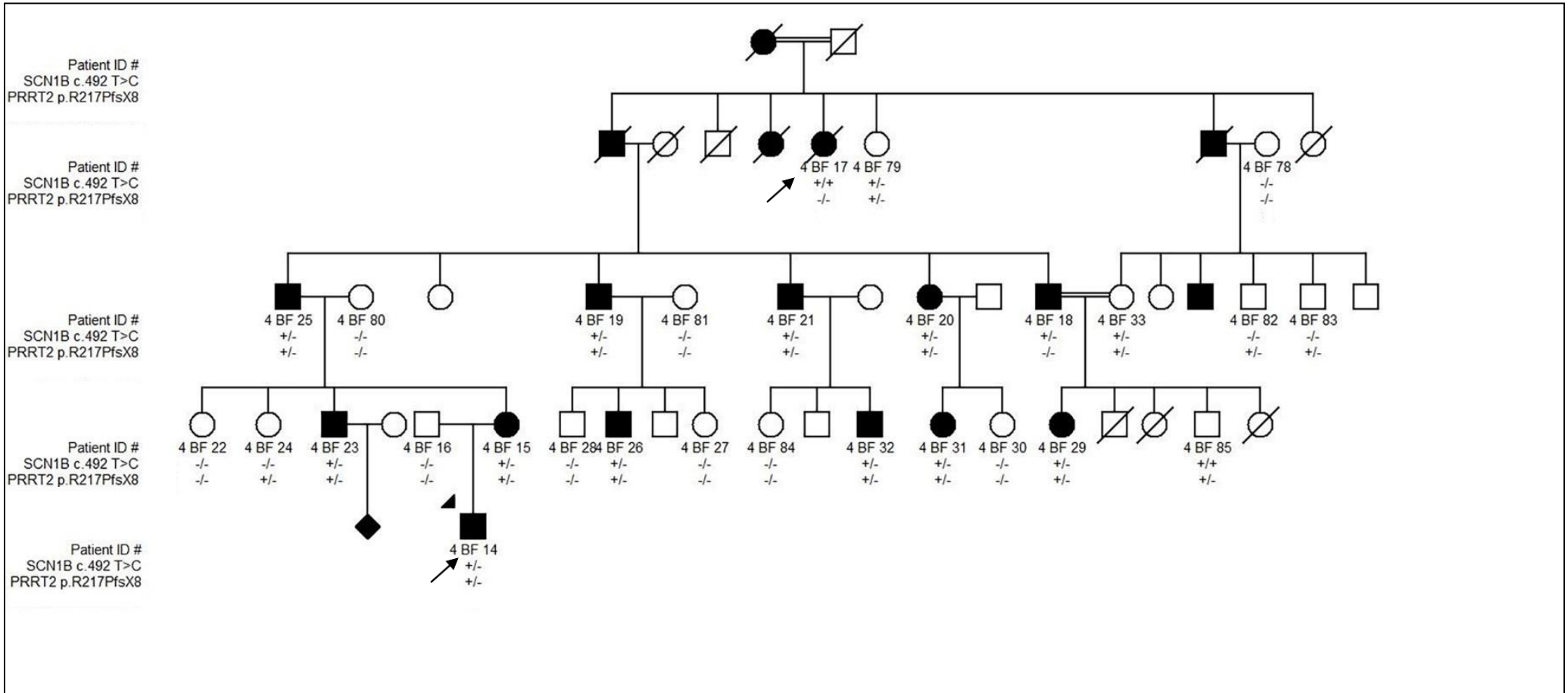


**Figure 2:** Haplotypes at the linkage region. Co-segregating risk haplotype is shown as black bar. Individuals with a sample ID are actually genotyped.



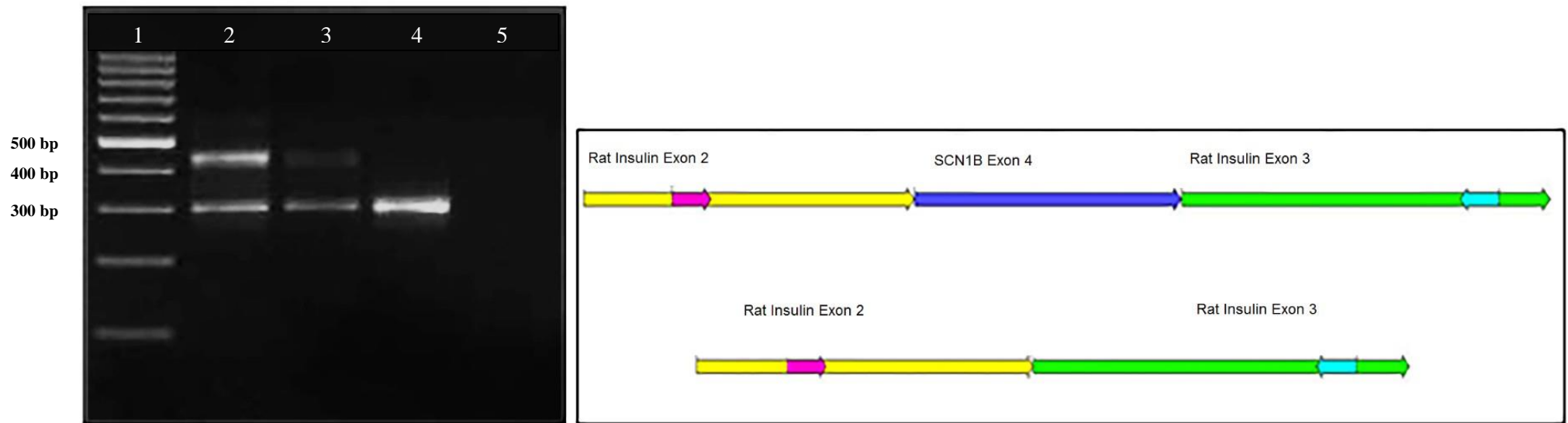
**Figure 3:** The synonymous variant in the *SCN1B* gene.

(A) NM\_001037.3, c492T>C transition in the index patient (4BF14). Arrow indicates the presence of the variant in heterozygous state (T/C). (B) PESX analysis. Red sequences show splicing silencers and green sequences show splicing enhancers. Upper panel shows the wild type sequence, lower panel shows the sequence with altered nucleotide which is underlined with yellow line.



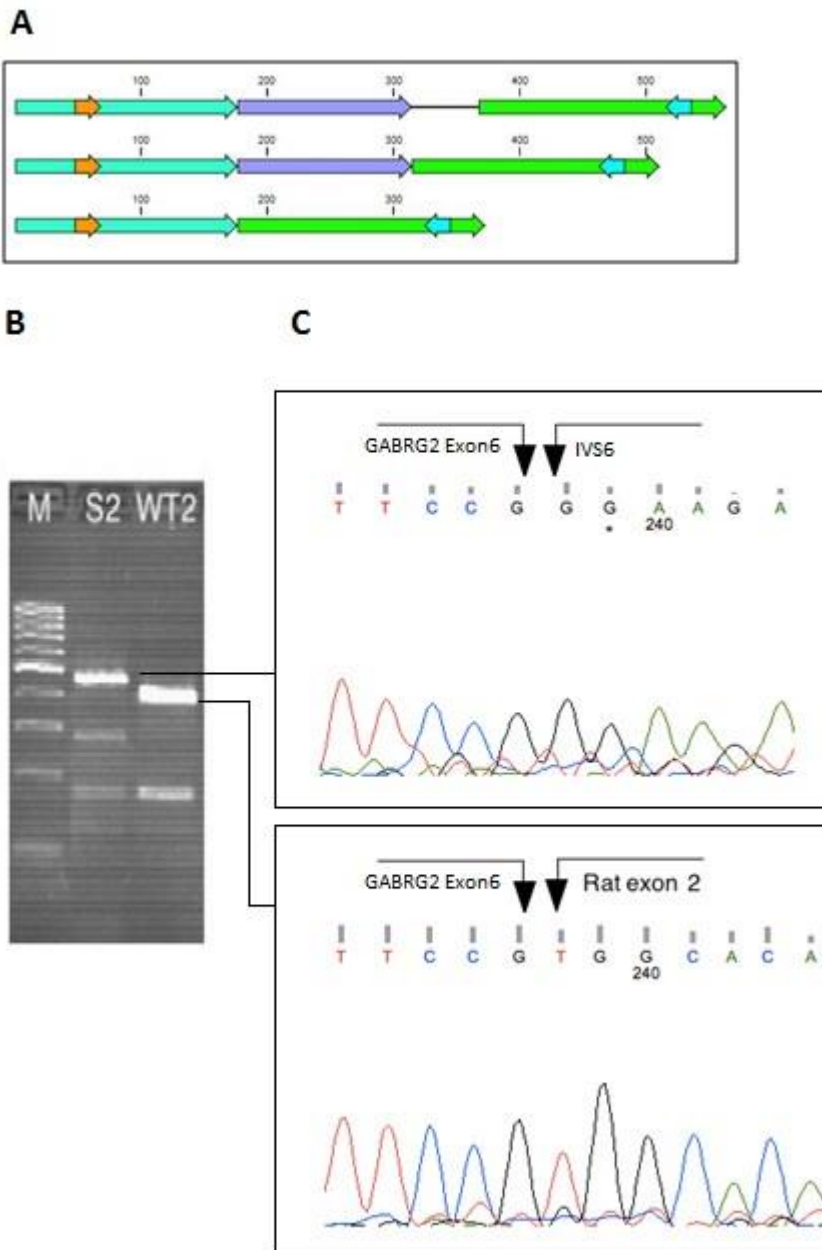
**Figure 4:** The family pedigree.

The family pedigree shows the segregation of *SCN1B* c.492T>C/p.Tyr164Tyr and *PRRT2* c.649dupC/p.Arg217Profs\*8 variations. The two individuals analyzed by WES are shown by an arrow. 4BF14 was the index patient. Phenotype information was not available for individuals marked in gray.



**Figure 5:** The minigene assay for the *SCN1B* c.492T>C/p.Tyr164Tyr variation.

Left panel shows the agarose gel picture. cDNA amplification of mRNA isolated from Shsy-5y cells transfected by pSpliceExpress plasmid with *SCN1B* exon 4 with c.492T>C/p.Tyr164Tyr mutation (lane 2), wild type *SCN1B* exon 4 (lane 3) and 300 bp empty vector with the two rat exons (lane 4). Lane 1 shows 100 bp ladder (Fermentas) and lane 5 shows no plasmid control. Right panel shows the schematic representation of the plasmid with the insert and the empty vector alone. Yellow and green arrows represent Rat Insulin 2 gene exon 3 and exon 2, respectively. Blue arrow represents human *SCN1B* gene exon 4. Pink and light blue arrows represent primer locations for PCR amplification.



**Supplementary Figure 1:**(A) Expected fragments: top sequence rat insulin exons with *GABRG2* exon 6 and intron retention, middle sequence rat insulin exons with *GABRG2* exon 6, and bottom sequence rat insulin exons only. Orange and blue arrows represent RT-PCR primer binding sites. (B) RT-PCR products on 2 per cent agarose gel: M: 100 bp DNA length marker, S2: variant created by site directed mutagenesis, WT2: wild type 2. (C) Sanger sequencing results for mutant (upper panel) and wild type (bottom panel) of *GABRG2* exon6.

**Supplementary Table 1:** Variants validated by Sanger sequencing and included in segregation analysis.

dbSNP ID	MAF	Locus (GRCh37)	Gene ID	Gene	Amino acid Change	Change Biotype	LOD Score
rs60235724	0.3770/1888	19:34304262	79047	KCTD15	XP_011525598.1:p.Tyr297Leufs	Frameshift	2,02
rs200278064	T=0.0198/99	19:35448919	126375	ZNF792	NP_787068.3:p.Ala614Thr	Non-synonymous	3,01
rs201800628	G=0.0198/99	19:35448945	126375	ZNF792	NP_787068.3:p.Ser605Thr	Non-synonymous	3,01
rs558298045	T=0.0018/9	19:35500319	57655	GRAMD1A	NM_020895.3:c.220-8C>T	-8 nucleotide from splice site	3,01
rs535042320	C=0.0014/7	19:35530064	6324	SCN1B	NP_001028.1:p.Tyr164Tyr	Synonymous	3,01
rs730882071	NA	16:29813703	112476	PRRT2	NP_001243371.1:p.Arg217Glufs	Frameshift	1,08
rs137852776	C=0.0018/9	6:52317597	114327	EFHC1	NP_060570.2:p.Phe229Leu	Non-synonymous	0
rs115466046	T=0.0044/22	1: 160012270	3766	KCNJ10	NP_002232.2:p.Arg18Gln	Non-synonymous	0