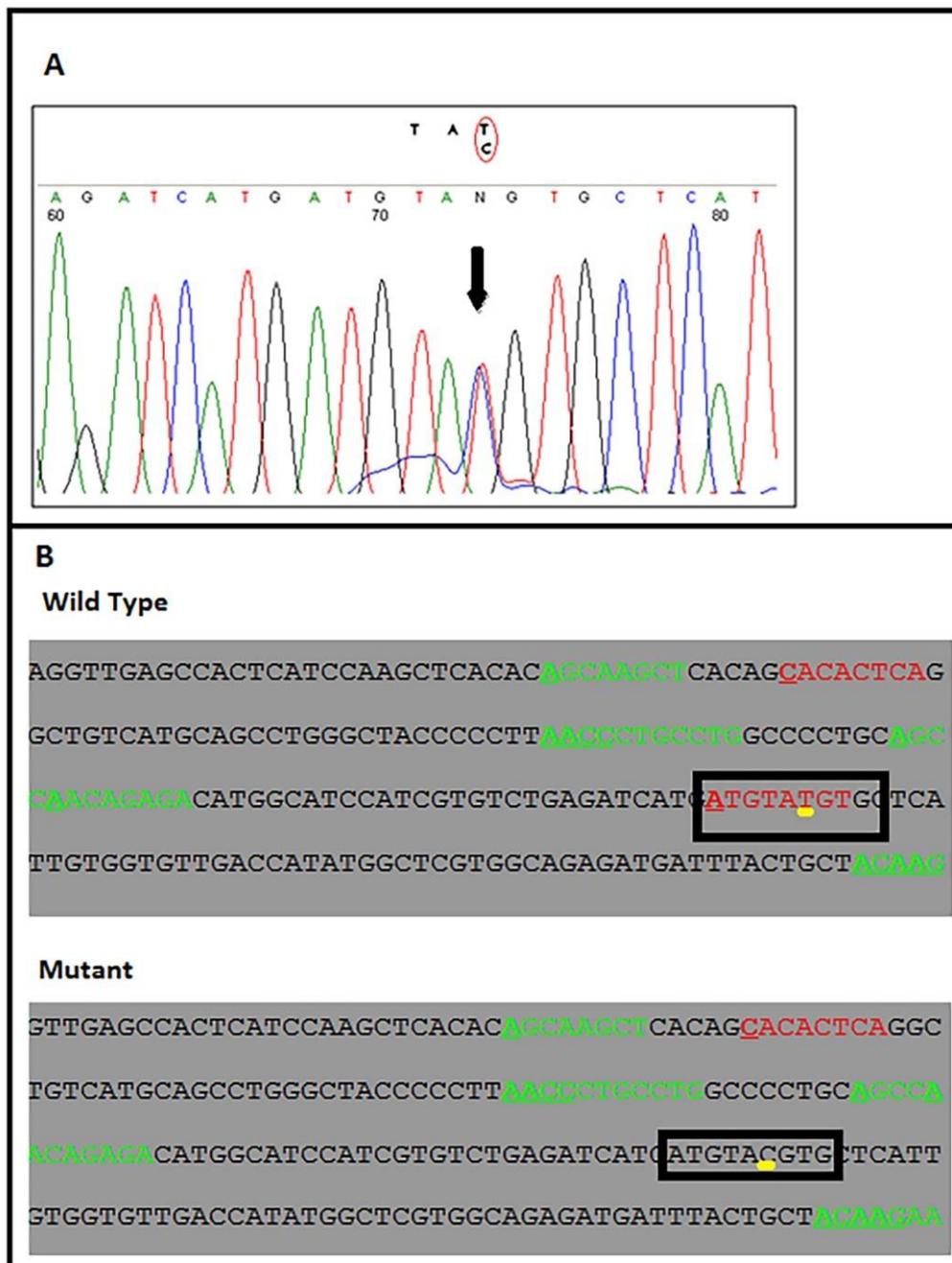


**Figure 1:** Genome-wide Linkage analysis result of the BFIS family.

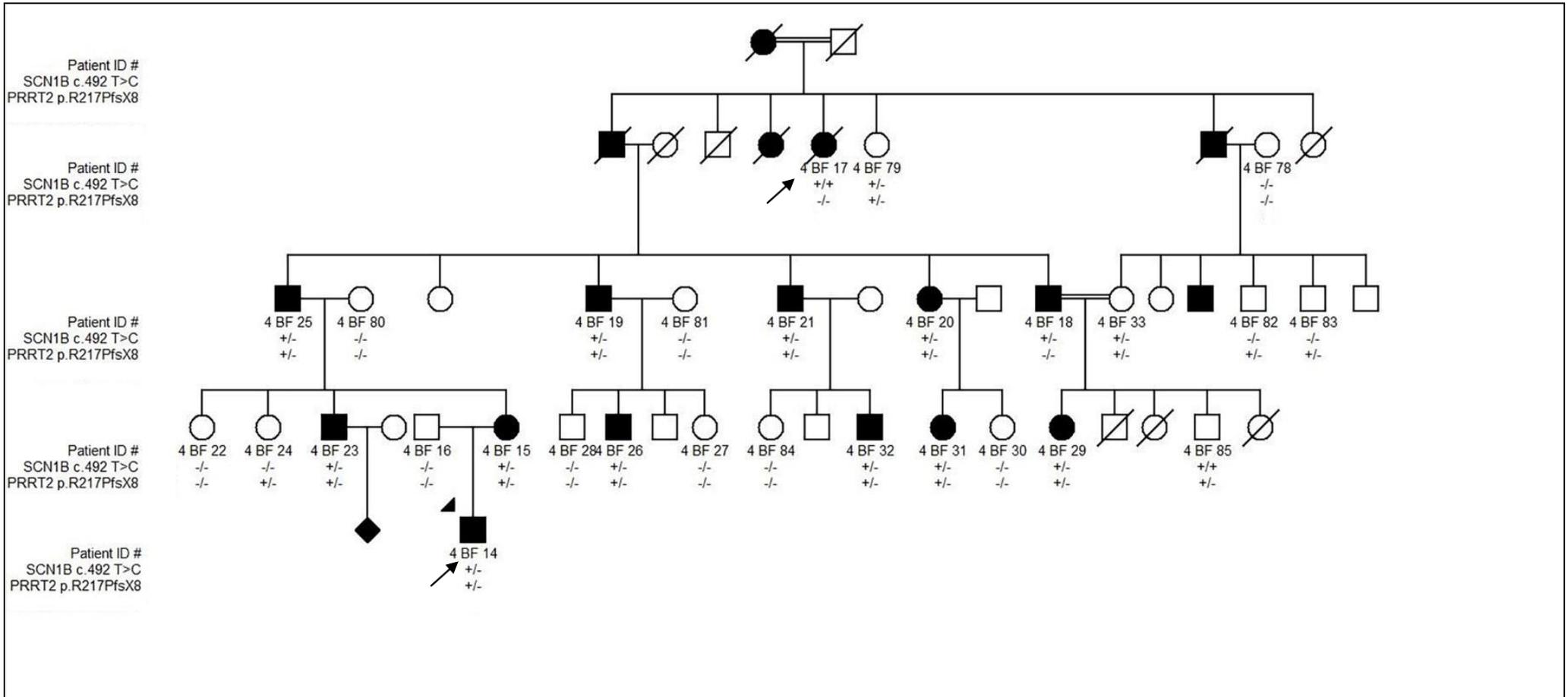
(A) Whole genome linkage results obtained from Allegro module with AD inheritance and 70% penetrance model. (B) Linkage analysis result of SimWalk module with AD inheritance and 70% inheritance model focusing on chromosome 19 linkage region.





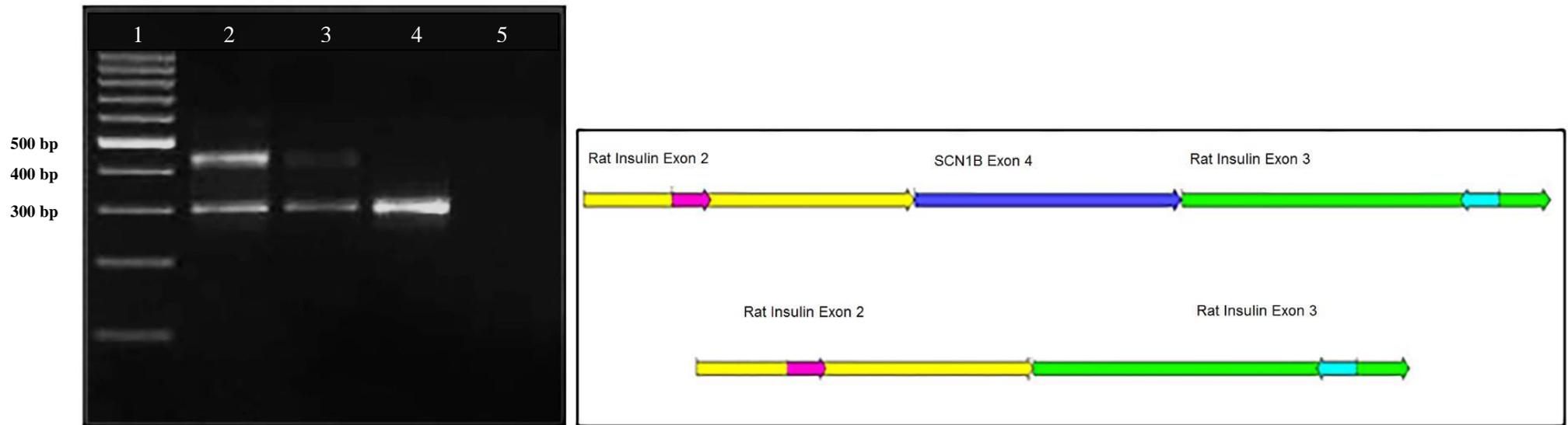
**Figure 3:** The synonymous variant in the *SCN1B* gene.

(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.



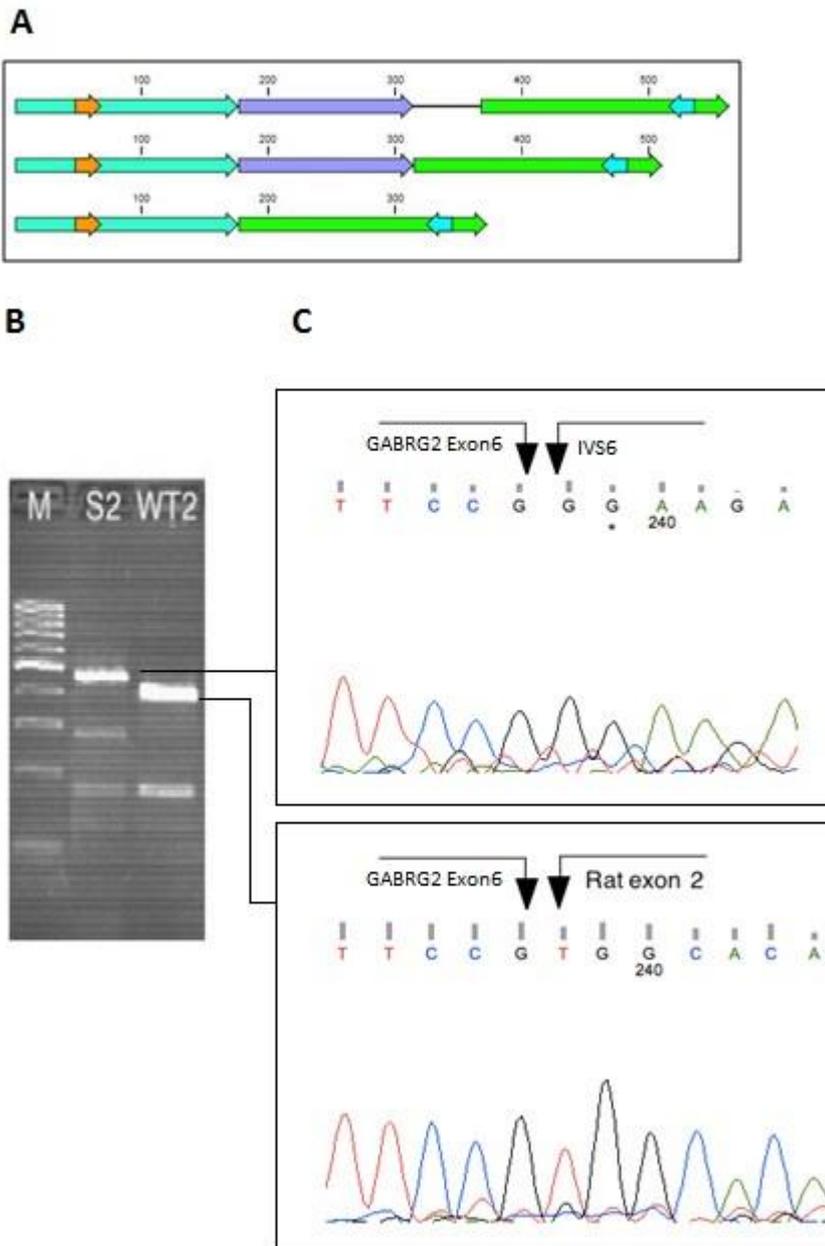
**Figure 4:** The family pedigree.

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         |