**Supplemental Methods**

A trio whole-exome sequencing was performed using a SureSelect Human All Exon V5 (Agilent Technologies, Santa Clara, CA, USA) on a HiSeq 2500 platform (Illumina, San Diego, CA, USA). DNA was obtained from peripheral blood samples of the patient and the parents after written informed consent was obtained from the parents. The reads in the FASTQ files were aligned to the human reference genome using Novoalign version 3.0 (http://www.novocraft.com/). Trio-based genomic variation information was detected by the Genome Analysis Toolkit software version 3.4-46 (1). Subsequently, *de novo*, homozygous, heterozygous, and X-linked variations were extracted and annotated by the ANNOVAR software (2). This process excluded variants with allele frequencies >0.5% in any of the Exome Aggregation Consortium (ExAC) (http://exac.broadinstitute.org/), NHLBI GO Exome Sequencing Project (http://evs.gs.washington.edu/EVS/), Human Genetic Variation Database (http://www.hgvd.genome.med.kyoto-u.ac.jp), or the 1KJPN database of Tohoku Medical Megabank (http://www.dist.megabank.tohoku.ac.jp). Heterozygous variations sharing the same GENCODE v19 genes were also extracted to detect compound heterozygous mutations. The mutation was confirmed via Sanger sequencing.

**Reference**

1. McKenna A, Hanna M, Banks E, Sivachenko A, Cibulskis K, Kernytsky A, Garimella K, Altshuler D, Gabriel S, Daly M, DePristo MA. The Genome Analysis Toolkit: a MapReduce framework for analyzing next-generation DNA sequencing data. *Genome Res.* 2010;**20**:1297–1303.

**2.** Wang K, Li M, Hakonarson H. ANNOVAR: functional annotation of genetic variants from high-throughput sequencing data. *Nucleic Acids Res*. 2010;**38**: e164.

Supplemental Table 1. Candidate pathogenic variants in the patient.

| Gene | Locus | Inheritance pattern | Transcript ID | Mutation | | | Allele frequency[a] | Number of homozygotes[a] | Predicted Pathogenesity | | Associated diseases |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Annotaiton | cDNA | Protein | | | SIFT[b] | PolyPhen-2[c] | |
| *PKN2* | 1p22.2 | AR | ENST00000370505.3 | missense | c.2455G>C | p.Asp819His | 0 | - | 0.001 (D) | 0.998 (D) | Unknown |
| *ROBO1* | 3p12.3 | AR | ENST00000464233.5 | splice site | c.1342+1G>A | p.Asn391fs*1 | 0 | - | - | - | PSIS (AD), Axonal guidance disorder (AR) |
| *CCDC91* | 12p11 | AR | ENST00000539107.1 | missense | c.585T>A | p.His195Glu | 0 | - | 0.015 (D) | 0.555 (P) | Unknown |
| *CYP1A2* | 15q24.1 | AR | ENST00000343932.4 | missense | c.130G>A | p.Glu44Lys | 0.00001688 | 0 | 0.001 (D) | 0.118 (B) | Unknown |
| *TTLL12* | 22q13.2 | AR | ENST00000343932.5 | missense | c.1508A>G | p.Asn503Ser | 0.0000167 | 0 | 0.056 (T) | 0.042 (B) | Unknown |

[a] data from the Exome Aggregation Consortium (ExAC) database. AR, autosomal recessive; AD, autosomal dominant; PSIS, pituitary stalk interruption syndrome.

[b] SIFT (http://sift.jcvi.org/); D: detleterious (≦0.05), T: tolerated (>0.05). [c] PolyPhen-2 (http://genetics.bwh.harvard.edu/pph2/); D: Probably damaging (≧0.957), P: possibly damaging (0.453 ≦, ≦0.956); B: benign (≦0.452)