■ Supplementary data ■

Supplementary Table 1. Exome Sequencing Statistics

Total number of sequenced reads	121,404,828
Total number of mapped reads	107,365,053 (88.4%)
Total bases uniquely mapped	10,628,649,847
Total bases mapping to targets	6,301,863,802
% targets with 10x coverage	89.20%
Mean target coverage	101.5X

Exome Sequencing

With parental informed consent, genomic DNA (gDNA) was extracted from peripheral blood leukocytes using the Wizard Genomic DNA purification kit according to the manufacturer's instructions (Promega, Madison, WI, USA), and subjected to exome capture by using TruSeq Exome Enrichment kit (Illumina, San Diego, CA, USA). For captured library construction, one microgram of gDNA was fragmented by nebulization, and Illumina adapters were then ligated to the fragments. A 350–400 base pair product was selected and amplified by polymerase chain reaction (PCR). The final product was validated using the Agilent Bioanalyzer (Santa Clara, CA, USA). The pooled DNA libraries were mixed with capture probes of targeted regions and subjected to three cycles of hybridization-elution steps for library enrichment.

For clustering and sequencing of DNA library, a flow cell containing millions of unique clusters was loaded into the HiSeq 2000 (Illumina, San Diego, CA, USA) for automated cycles of extension and imaging. Paired-end sequences produced by HiSeq2000 were mapped to the human genome, where the reference sequence was UCSC assembly hg19 (NCBI build 37), without unordered sequences or alternate haplotypes, using the mapping program BWA (version 0.5.9rc1). Uniquely mapped reads were only included for the latter steps. After making a consensus sequence by creating a pileup file from BAM file, variant calling process was run using SAMtools (version 0.1.12a), at which stage SNP and short indels candidates were detected at nucleotide resolution. Then those variants were annotated by ANNOVAR (version 2011 Jun 18) to filter SNPs from dbSNP for the version of 131 and 132, and SNPs from the 1000-genomes project (http://1000genomes.org).

Sanger Sequencing

SERPINF1 exons and their flanking introns were amplified using primer sets designed by the authors (available upon request). The PCR was performed with a thermal cycler (Verti, Applied Biosystems, Foster City, CA) as follows: 32 cycles of denaturation at 94°C for 30 sec, annealing at 60°C for 30 sec, and extension at 72°C for 30 sec. After treatment of the amplicon (5 µL) with 10 U shrimp alkaline phosphatase and 2 U exonuclease I (USB Corp., Cleveland, OH), direct sequencing was performed with the BigDye Terminator Cycle Sequencing Ready Reaction kit (Applied Biosystems) on the ABI Prism 3730xl genetic analyzer (Applied Biosystems). To describe sequence variations, we followed the guidelines from the Human Genome Nomenclature Committee (HGVS); so "A" of the ATG translation start site was numbered +1 for DNA sequence and the first methionine was numbered +1 for protein sequence.

Supplementary Fig. 1A

Supplementary Fig. 1B