**Supplementary text**

**A:** Whole-exome sequencing was done by an Illumina HiSeq 4000 platform (Illumina). For sequence alignment and variant calling, the human reference genome UCSC NCBI37/hg19 was used. All exonic, exonic splice site, and splice site variants were selected and synonymous variants removed after preliminary filtering. Afterward, variants with a minor allele frequency (MAF) more than 0.001 in public exome/genome databases (Supplementary text; B) and in Iranome database (http://iranome.com/), or found in in-house exome data of more than100 unrelated Iranians affected with non-neurological, were removed. Subsequently, due to dominant pattern of the disease, heterozygous variants were considered. After that, the remaining sequence variants were compared to more than 1900 genes that involved in HSP and other neurodegenerative diseases such as ataxia, neuropathies, Parkinson’s disease (PD), ALS, and neurodegeneration with brain iron accumulation (NBIA). Variants with a minor allele frequency (MAF) more than 0.001 in the 1000 Genomes database (www.1000genomes.org), the Greater Middle East Variome Project (http://igm.ucsd.edu/gme/), the NHLBI Exome Sequencing Project (http://evs.gs.washington.edu/EVS/), the Exome Aggregation Consortium database (http://exac.broadinstitute.org/), ABraOM: Brazilian genomic variants (http://abraom.ib.usp.br/), the Genome Aggregation Database (http://genomad. broadinstitute.org/), the Healthy Exomes database (https://www.alzforum.org/exomes/hex), and Iranome database (http://iranome.com/), or found in in-house exome data of more than100 unrelated Iranians affected with non-neurological, were removed.

**B:** PANTHER (http://www.pantherdb.org/tools/csnpScoreForm.jsp), PROVEAN (<http://provean.jcvi.org/seq_submit.php>), Polyphen2-HVAR and Polyphen2-HDIV (<http://genetics.bwh.harvard.edu/pph2/>), SIFT (<https://sift.bii.a-star.edu.sg/www/Extended_SIFT_chr_coords_submit.html>), Mutation Taster (<http://www.mutationtaster.org/>), Mutation Assessor (<http://mutationassessor.org>), FATHMM (<http://fathmm.biocompute.org.uk/>), SNAP (<http://www.rostlab.org/services/SNAP/>), LRT (<http://www.genetics.wustl.edu/jflab/lrt_query.html>) , PhyloP (<http://hgdownload.cse.ucsc.edu/goldenPath/hg18/phyloP44way>), GERP (<http://mendel.stanford.edu/sidowlab/downloads/gerp/index.html>), and CADD webserver (<http://cadd.gs.washington.edu>).