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Supplemental Data

THOC2 Mutations Implicate mRNA-Export Pathway in X-Linked Intellectual Disability

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Figure S1

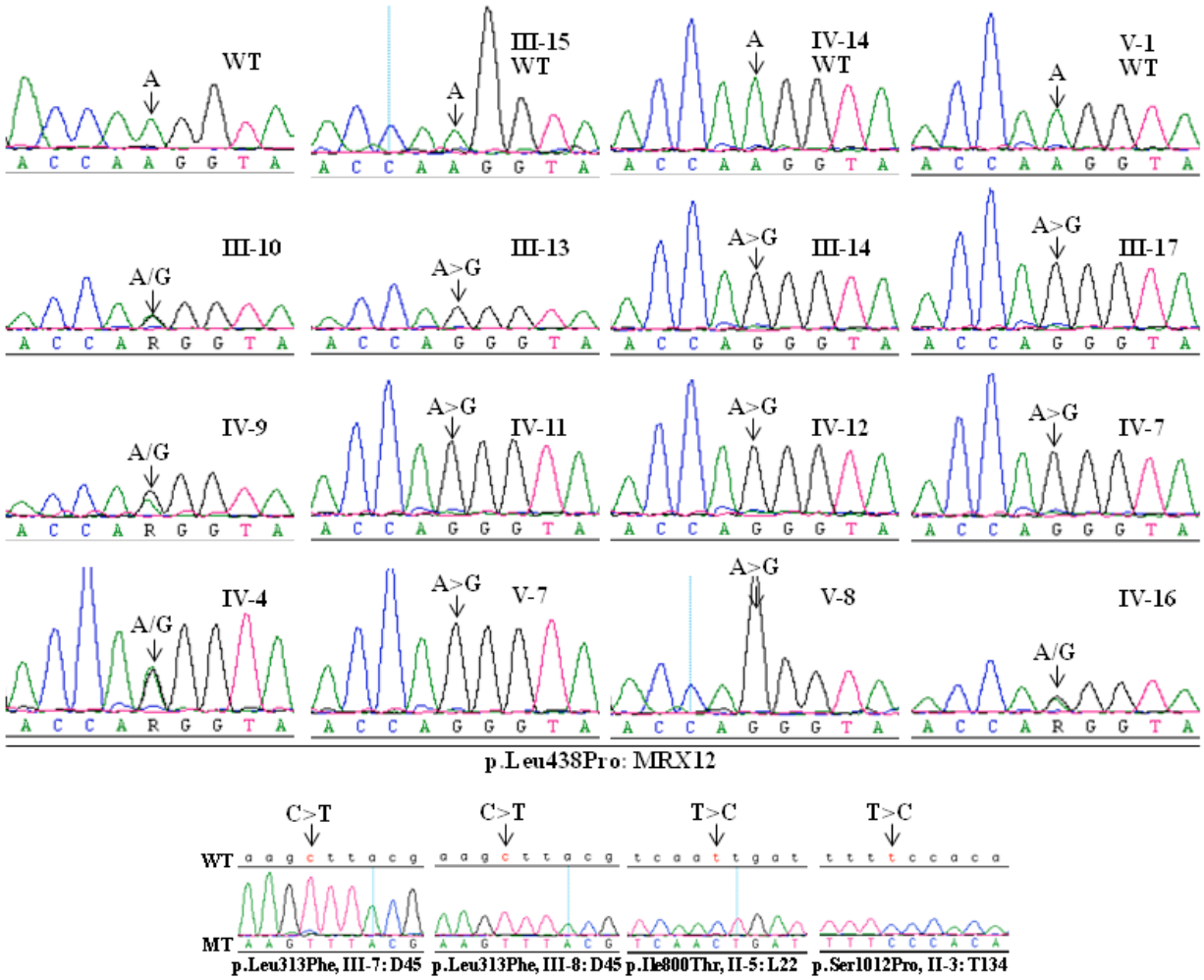

Figure S1. Sanger sequencing chromatograms of representative affected individuals from each family are shown. Top panel. MRX12 family sequence chromatograms of the complementary strand of *THOC2* are shown. Bottom panel. Representative chromatograms are shown from two individuals from family D45 and one each from families L22 and T134, respectively. WT = wild type allele. Primers used for PCR and sequencing are listed in Table S3.

Figure S2

Figure S2. Mutated THOC2 amino acid residues are highly conserved. Amino acid sequence alignments flanking the mutated residues (red) at the conserved positions (green) among different orthologs are shown. Sequence alignment of variant amino acids across different species was performed using EBI CLUSTALW server.

Figure S3

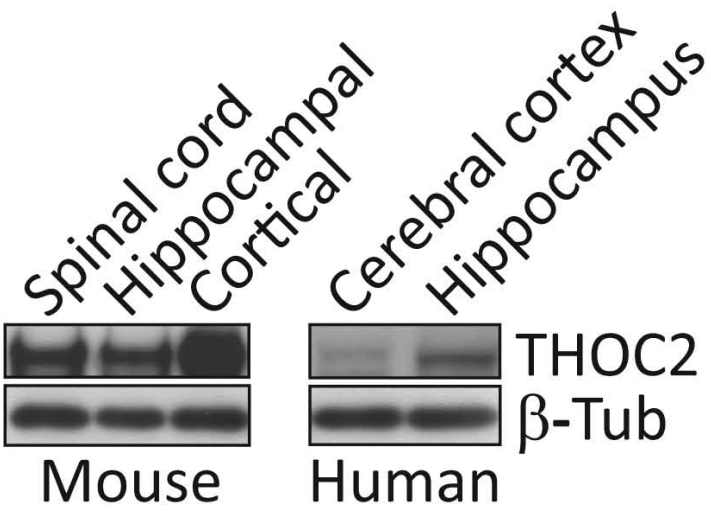

Figure S3. THOC2 expression in mouse hippocampal and cortical neurons and human cerebral cortex and hippocampus.

Figure S4

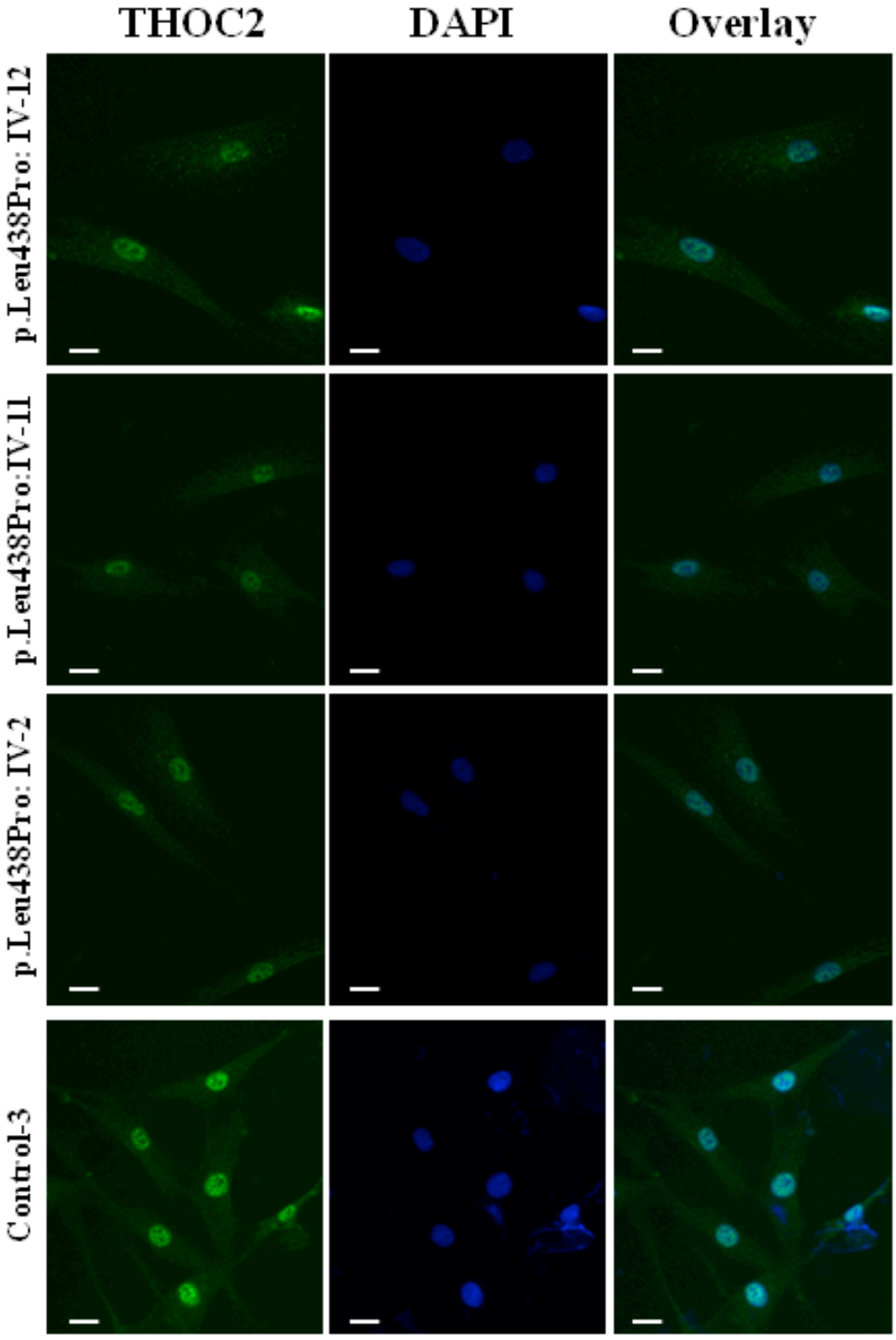

Figure S4. THOC2 immunofluorescence staining is significantly reduced in fibroblasts with the THOC2 p.Leu438Pro mutation compared with a bright speckled staining in the control fibroblasts. Scale bars = 20 μm. Linked to Figure 3.

Figure S5

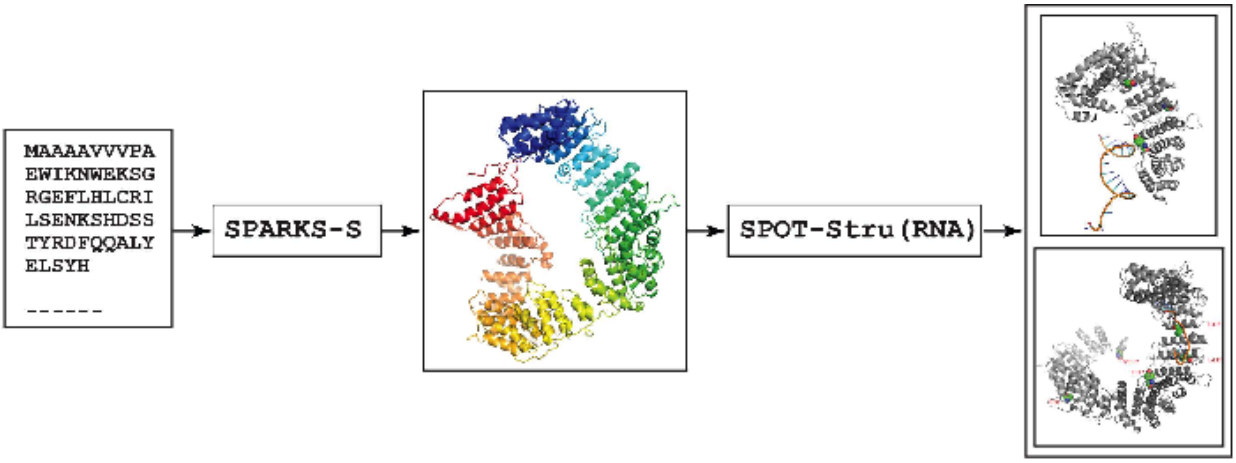

Figure S5. The workflow used for predicting the THOC2-RNA interaction. The 3-dimensional THOC2 structure was predicted from the protein sequence using SPARKS-X (ref 25 of the manuscript) that employs experimentally determined protein structure as templates to build structural models. Whole Protein Data Bank (PDB) was considered as a template library and scanned by matching sequence profiles and structural profiles of query and known structure proteins. Here, the sequence profiles include the information generated from multiple sequence alignment. The structural profiles include actual properties for templates and predicted properties for query protein. The structural properties contain secondary structure, solvent accessible surface area, and main-chain dihedral angles.

Supplementary Tables

Table S1. Pathogenicity predictions by different methods

Table S2. Summary of clinical features

Table S3. Primer sequences and Taqman probes.