

## Description of Additional Supplementary Files

**Supplementary Data 1** | 21 genes with extreme divergence in regional nonsense constraint (OE95 >90th centile) and basewise conservation (median phyloP <90th centile) scores.

**Supplementary Data 2** | Longlist of candidate disease genes which have no association with an autosomal dominant phenotype in OMIM, and carry at least 3 *de novo* nonsense or frameshift variants in a constrained NMD region in 27,762 rare disease trios.

**Supplementary Data 3** | Regional nonsense constraint annotations and summary statistics.