FIGURE LEGENDS

Figure 1. Review of SLC25A38 Mutation Types and Genotypes. A. Mutation types. **B.** Genotypic combinations by mutation type. **C.** Genotypic combination zygosity. **D.** Genotypic combination by function. Cmpd, Het, Compound Heterozygous; EXT, Extension; FS, Frameshift; Hom, Homozygous; SPL, Splicing; X, Premature stop.

Figure 2. Distribution of SLC25A38 mutations in relation to structural and genetic features. Vertical bars depict the number of independent occurrences of missense (green), stop-gained (red), frameshift (yellow), splicing (blue), and stop-loss (purple) pathogenic SLC25A38 mutations at that codon. Horizontal bars: transmembrane (TM) segments are indicated in black. The relative frequency of loss-of-function (LOF: stop-gained, frameshift, and splicing) and missense (MS) variants in gnomAD are depicted in red and green heat maps. Absolute conservation of amino acid in 16 SLC25A38 orthologues from 15 diverse species (Table 2) and 53 *H. sapiens* SLC25 protein family members in magenta and blue heat maps. Short tandem (aqua) and direct (light green) repeats and CpG dinucleotides (navy blue) are indicated, demonstrating clustering of disease-associated mutations at these sequences. The first 23 amino acids, approximately corresponding to the mitochondrial targeting sequence, are not shown; no pathogenic mutations are found in this region. Each block of sequences corresponds to one mitochondrial carrier family repeat unit containing two TM domains.