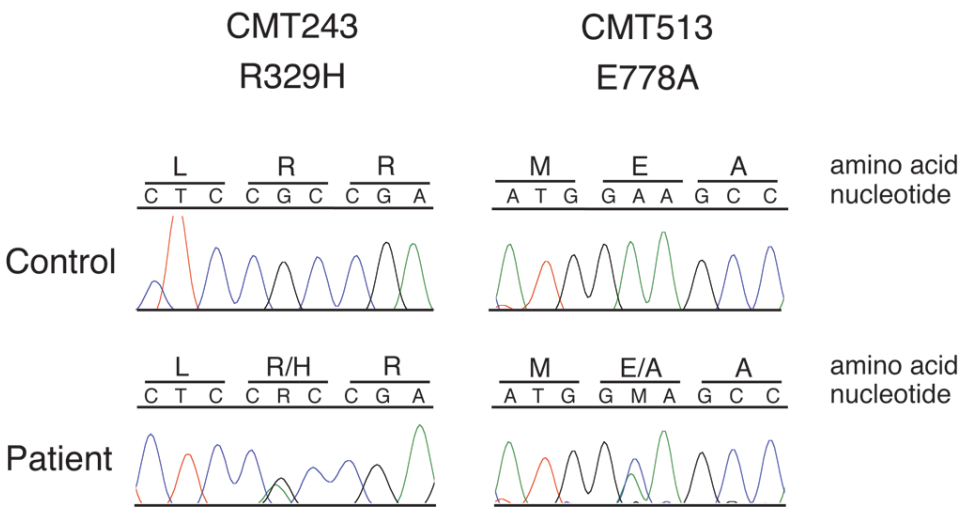
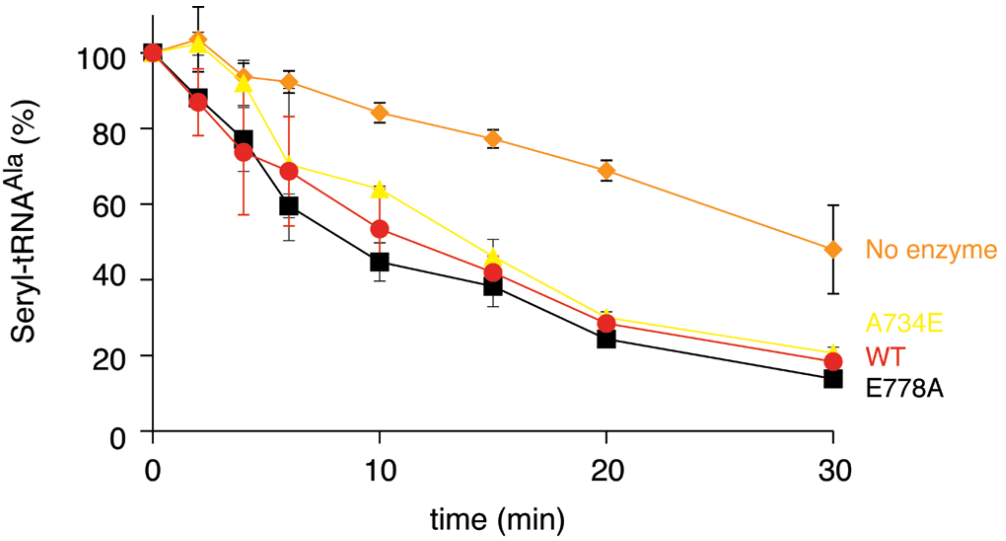
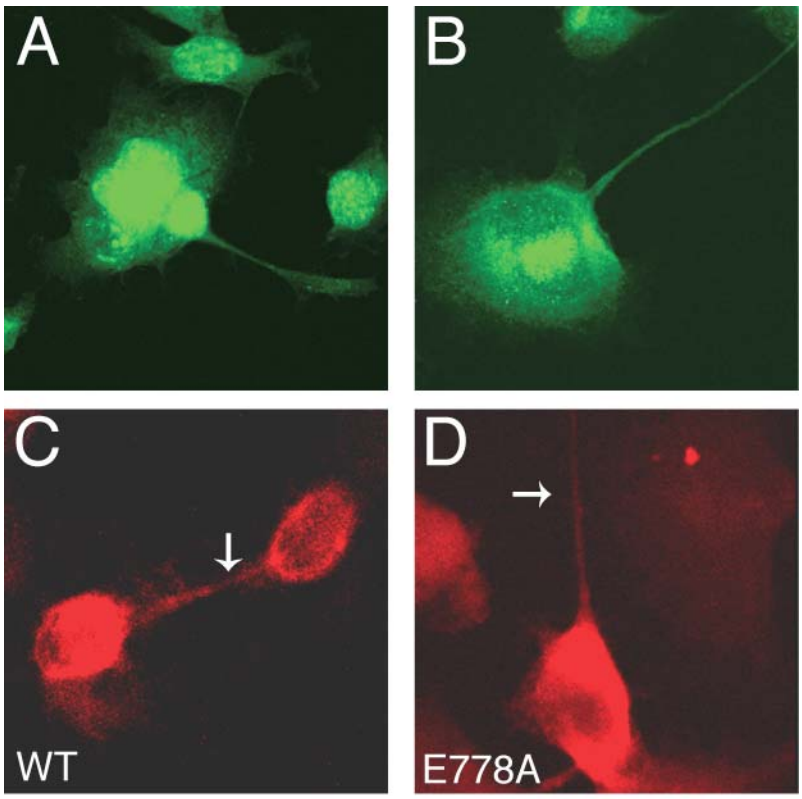
#



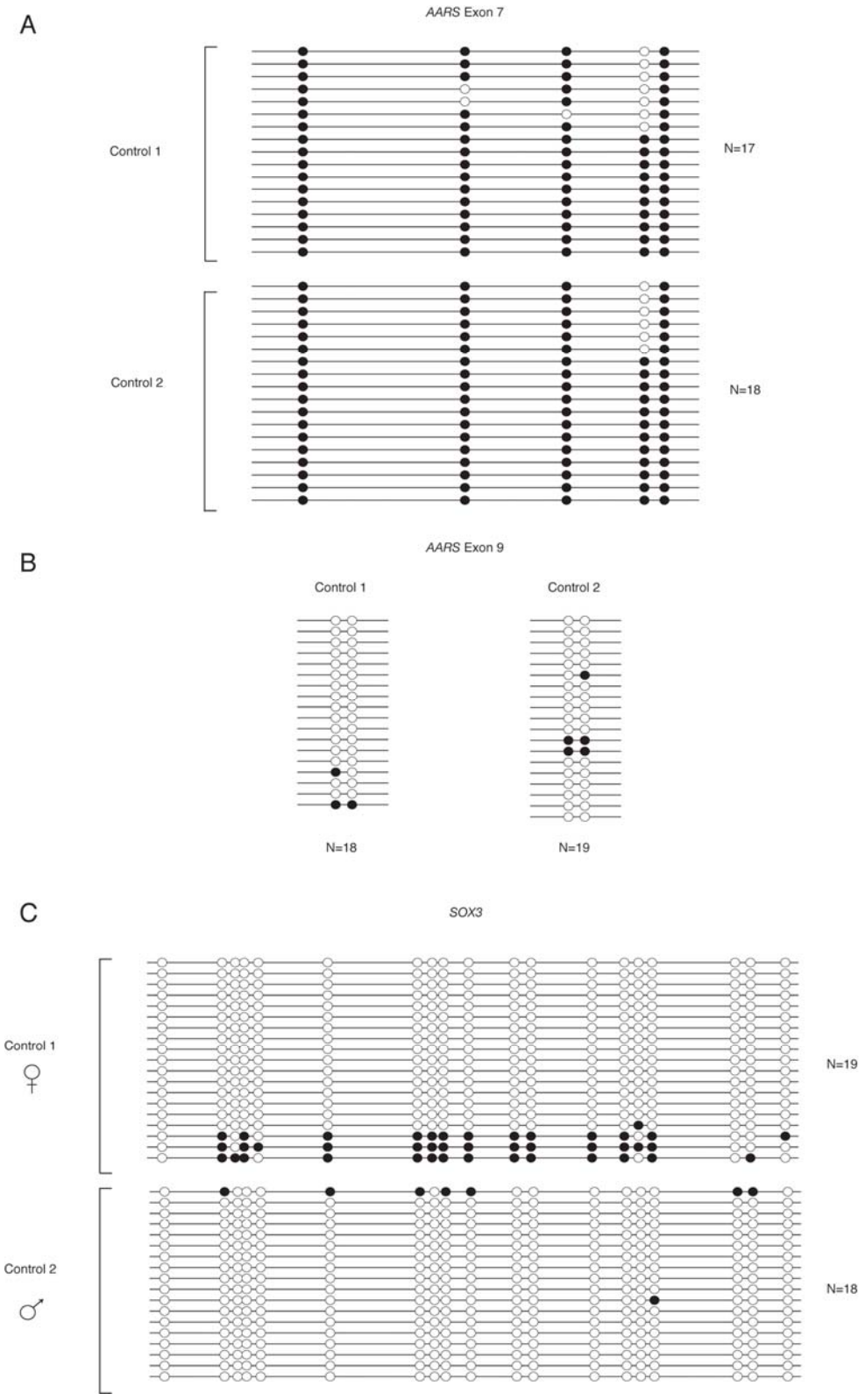
Supp. Figure S1. Heterozygous variants detected in the *AARS* gene. Chromatograms from control and affected ('Patient') individuals are shown for R329H (left) and E778A (right). The nucleotides and resulting amino-acid sequences are shown, with 'R' indicating heterozygosity for a 'G' and 'A' nucleotide, and 'M' indicating heterozygosity for an 'A' and 'C' nucleotide.



Supp. Figure S2. Effect of *AARS* variants on editing activity. Deacylation of the incorrectly charged Ser-tRNA^{Ala} by the wild-type (red), E778A (black), and the previously-described A734E (yellow; see discussion) AARS enzymes is plotted over time. The uncatalyzed deacylation (the no-enzyme reaction, indicated in orange) was run in parallel as a control for background hydrolysis. Values represent the average of two independent experiments, and error bars indicate the standard deviation.



Supp. Figure S3. Evaluation of axonal AARS localization in differentiated MN-1 cells. **A, B**: Differentiated MN-1 cells were stained with an anti-AARS antibody and visualized via confocal microscopy. Endogenous AARS protein was localized diffusely throughout the cell body, nucleus, and neurite projections. **C**: Wild-type AARS tagged with DsRed on the C-termus was transiently expressed in MN-1 cells. After differentiation, localization was analyzed via confocal microscopy. Wild-type AARS was localized diffusely throughout the cell body and neurite projections (arrow). **D**: Similar analyses as described in (**C**) for E778A AARS. Similar to wild-type AARS, E778A AARS was localized diffusely throughout the cell body and neurite projections (arrow).



Supp. Figure S4. Bisulfite sequencing analysis of *AARS* exon 7, *AARS* exon 9, and *SOX3*. **A**: Evaluation of the methylation status of 5 CpGs in *AARS* exon 7. A representation of bisulfite

sequencing products of *AARS* exon 7 is shown for two control individuals (Control 1 and Control 2). Seventeen and eighteen clones were analyzed for Control 1 and Control 2, respectively. Filled circles indicate methylated CpGs. **B**: Similar analyses as described in (**A**) for two CpG dinucleotides within *AARS* Exon 9. Eighteen and nineteen clones were evaluated for Control 1 and Control 2, respectively. **C**: Evaluation of the methylation status of 19 CpGs in a *SOX3* CpG island. The female control (19 clones evaluated) is denoted ♀, while the male control (18 clones evaluated) is denoted ♂.

#