

Description of Additional Supplementary Files

Supplementary Data 1: Genes enriched in sibling cellular and neurite samples. Genes enriched in sibling cellular compartment compared to sibling neurite compartment (fold change > 1.5, $p < 0.05$). Genes enriched in sibling neurite compartments compared to sibling cellular compartment (fold change > 1.25, $p < 0.05$).

Supplementary Data 2: Gene downregulation in neurites (and neurite-specific). 597 annotated genes expressed more in sibling neurites (FC > 1.5) than in null neurites. Genes were filtered to remove those expressed < 20 TpM in sibling neurites. 185 genes annotated genes downregulated more in null neurites than in null cellular samples ($\text{Log}_2\text{FC Neurites} - \text{Log}_2\text{FC Cellular} = < -0.2$).

Supplementary Data 3: Gene upregulation in neurites (and neurite-specific). 221 annotated genes expressed more in null neurites (FC > 1.5) than in sibling neurites. Genes were filtered to remove those expressed < 20 TpM in sibling neurites. 62 genes annotated genes upregulated more in null neurites than in null cellular samples ($\text{Log}_2\text{FC Neurites} - \text{Log}_2\text{FC Cellular} = > 0.2$).

Supplementary Data 4: Initial splicing analysis. All splicing changes (alternative 5'SS (Alt5), alternative 3'SS (Alt3), cassette exon (CE), microexon (MIC), intron retention (IR)) detected using vast-tools. Changes between sibling and null samples required $\text{MV}[\text{dPsi}]_{\text{at}_0.95} = \geq 0.03$ in the respective compartment comparison, and $\text{MV}[\text{dPsi}]_{\text{at}_0.95} = < 0.03$ for the other compartment comparison. No threshold for extent of change (percentage of total transcripts showing the splicing change in question), or gene expression level were applied.

Supplementary Data 5: vast-tools and IRFinder intron retention. 195 introns more retained and 35 introns less retained in null neurites than in sibling neurites (>10% change in either direction of transcripts being intron-retaining and $\text{MV}[\text{dPsi}]_{\text{at}_0.95}$ value ≥ 0.01). In IRFinder analyses, 446 IR events showed increases (> 0.1 increase in IR Ratio) $p < 0.05$, and 86 events showed decreases (< -0.1 increase in IR Ratio) $p < 0.05$ in retention in null neurites when compared to sibling counterparts.

Supplementary Data 6: Genes whose transcripts are preferentially translated in neurites. Ribosomal footprint (Riboseq) data from rat hippocampus indicates that orthologues of 154 zebrafish genes, whose transcripts showing neurite-specific increases in IR, are preferentially translated in neurites.

Supplementary Data 7: Stable versus negative sloping gene lists. Of the genes identified by vast-tools to exhibit increased intron retention in null neurites, 46 show stable downstream exon expression and 135 intron-retaining genes show negative downstream exon expression. Full candidate lists shown before filtering out those with values whose $\text{FDR} > 0.05$. Of the IRFinder identified genes exhibiting increased intron retention in null neurites, 157 show stable downstream exon expression and 252 intron-retaining genes show negative downstream exon expression. Full candidate lists shown before filtering out those with values whose $\text{FDR} > 0.05$.

Supplementary Data 8: ALS-associated human and mouse introns. Chromosomal coordinates of human (hg19) and mouse (mm10) introns perturbed in ALS patient samples and models of ALS.

Supplementary Data 9: Enriched Gene Ontology Biological Processes

Supplementary Data 10: Primers