## FIX ALS GENES

**Project ALS Commitment:** $1.5M

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**Background:** Since Project ALS research advisors Bob Brown and Bob Horvitz identified a mutation in the SOD1 gene as a hereditary cause of ALS in 1995, a strong strategy for slowing or stopping ALS has been to block, or "silence," the errant gene. Now, in 2015, over 30 genes have been identified as contributing to ALS, and the means of delivering gene silencing therapies—including small molecules, siRNAs, and viruses—have been honed to maximize effectiveness.

Some genetic triggers of ALS, like mutations in the TARDBP gene (causing dysfunction in the TDP-43 protein), cannot be silenced without causing massive cell death. Therefore, the Project ALS team is employing new gene "editing" technologies, like the CRISPR/Cas9 technique, to replace mutated gene segments without silencing the entire gene.

**Summary of Progress:** Gene silencing technology has been proven to work in both stem cell and animal models of ALS, and intensive pre-clinical studies are now underway to make sure that these methods are safe for human trial. First patient trials will focus on silencing SOD1 and C9orf72, genes implicated in both familial and sporadic ALS. Meanwhile, in vitro studies to optimize CRISPR/Cas9 in ALS are underway.

**Relevant publications:**
Overview of genetic mutations in ALS
Pre-clinical gene silencing efficacy

Contact us for additional relevant publications or research updates.