Amyotrophic lateral sclerosis (ALS) is a type of neurodegenerative disease characterized by motor neuron death1. Approximately 5% of Familial ALS cases have mutations located in the fused in sarcoma (FUS) gene resulting in reduced muscle mass and impaired motor movement1,2. *FUS* plays a critical role in providing regulation for transcription, translation, and facilitating DNA repair mechanisms3,4,5. Mutations tend to predominate in the non-conventional nuclear localization signal region (NLS), near the C-terminal domain2. Specifically, alterations in this segment have shown to result in severe juvenile onset occurring as young as 11 years old compared to other regions2,6. Recent studies have demonstrated that FUS alterations in the NLS region result in the formation of aggregates and altered DNA repair mechanisms5. These studies *fail to address the complete mechanism for the FUS-related DNA repair pathways and their downstream effect on neurodegeneration*5,7*.*

The **objective** of this study is to determine the impact of multiple missense mutations across various domains and discover which regions are involved with DNA repair mechanisms. I **hypothesize** that alterations in the NLS segment, specifically P525, will disrupt DNA repair mechanisms and result in earlier neuron death compared to other regions. *D. rerio* will be used to test this hypothesis due to conserved homology, transparency during development, opportunity for ploidy manipulation, and anatomical similarity of motor neurons in the spinal cord7. The **long-term goal** of this research is to determine the effect on neurodegeneration due to these alterations, while providing a comprehensive mechanism for the FUS-related DNA repair pathways.

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