The blood-brain-barrier (BBB) plays a critical role by being highly selective and controls the passage of substances in and out of the CNS. Small molecules and lipid soluble proteins cross the BBB easily, larger ones need receptor-mediated transcytosis. BBB dysfunction is associated with many neurodegenerative diseases.

Amyotrophic lateral sclerosis (ALS) cases are classified as ”sporadic” ALS (sALS) or “familial” ALS (fALS). With the fALS form, the disease is inherited. It has been reported that mutations of genes have been associated with fALS. And for this model, we will focus on the mutated FUS/TLS gene on chromosome 16. The FUS/TLS protein binds to RNA, single-stranded DNA and double-stranded DNA. It also interacts with gene-specific transcription factors and appears in double-strand break sites for repair of DNA damages. Mutations in the FUS NLS (Nuclear localization sequence) impairs the poly (ADP-ribose) polymerase (PARP)-dependent DNA damage response. This impairment leads to FUS aggregate formation which appear be a common pathologic hallmark of ALS.

AIM: Accumulation of defects in the endothelial cells of the BBB is correlated to neurodegenerative diseases.

<https://pubmed.ncbi.nlm.nih.gov/19251627/>

https://en.wikipedia.org/wiki/RNA-binding\_protein\_FUS

Amyotrophic lateral sclerosis (ALS) is a fatal degenerative motor neuron disorder. Ten percent of cases are inherited; most involve unidentified genes. We report here 13 mutations in the fused in sarcoma/translated in liposarcoma (FUS/TLS) gene on chromosome 16 that were specific for familial ALS. The FUS/TLS protein binds to RNA, functions in diverse processes, and is normally located predominantly in the nucleus. In contrast, the mutant forms of FUS/TLS accumulated in the cytoplasm of neurons, a pathology that is similar to that of the gene TAR DNA-binding protein 43 (TDP43), whose mutations also cause ALS. Neuronal cytoplasmic protein aggregation and defective RNA metabolism thus appear to be common pathogenic mechanisms involved in ALS and possibly in other neurodegenerative disorders.