Transposable Elements in Frontotemporal Lobar Degeneration

https://neurodegenerationresearch.eu/survey/transposable-elements-in-frontotemporal-lobar-degeneration-2/

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USA

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Transposable Elements in Frontotemporal Lobar Degeneration

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Frontotemporal Lobar Degenerations, DNA Transposable Elements, protein TDP-43, Retrotransposon, Amyotrophic Lateral Sclerosis

Research Abstract

? DESCRIPTION (provided by applicant): The TDP-43 protein plays a role in a broad suite of neurodegenerative disorders including Frontotemporal lobar degeneration (FTLD), amyotrophic lateral sclerosis, and potentially Alzheimer’s disease. TDP-43 is a multifunctional protein with many known cellular roles. So while the importance of TDP-43 in neurodegeneration is established, the mechanisms of TDP-43 toxicity are unclear. We have discovered a new role for

TDP-43 in regulating retrotransposons. Retrotransposons are virus-like sequences that are encoded in our genomes and are capable of replicating and inserting at new chromosomal positions. The toxic potential of transposons in the germline is established. So our discovery provides a plausible hypothesis for toxic effects of TDP-43 in neurons. Our preliminary studies provide evidence that TDP-43 normally helps to silence transposons and that this function is disrupted both in FTLD patients and a Drosophila disease model. Our proposed experiments will use next generation RNA-sequencing with brain samples from FTLD patients to profile expression of retrotransposons. We also will examine the small RNAS a chromatin mark that normally help to silence retrotransposons. We will test three specific hypotheses: 1- that retrotransposon expression is increased in FTLD and ALS brain tissue. 2- that small RNA silencing of retrotransposons is perturbed in FTLD and ALS brain 2- that H3K9me histone silencing mark is perturbed in FTLD and ALS brain tissue

Further information available at:

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