Angiogenin as a therapeutic for the treatment of ALS

https://neurodegenerationresearch.eu/survey/angiogenin-as-a-therapeutic-for-the-treatment-of-als/

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Angiogenin as a therapeutic for the treatment of ALS

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Research Abstract
Amyotrophic lateral sclerosis (ALS) is a fatal neurological condition. Mutations in the Angiogenin (ANG) gene have been originally detected in 15 individuals of Celtic and other ethnic origin, of whom four had familial ALS and 11 apparently ‘sporadic’ ALS. Several independent clinical/genetic studies have confirmed that mutations in ANG are associated with ALS and, recently, Parkinson’s disease. Previous research from our group has shown that Angiogenin is expressed and enriched in motoneurons and functions to protect motoneurons from stress-induced cell death in vitro. We also have new exciting findings showing angiogenin protein delivery to increase lifespan, delay onset of disease progression, and improve motor performance in the SOD1 G93A mouse model of ALS when tested in accordance with

internationally accepted community guidelines. Therefore, we now seek to further develop angiogenin as a new therapeutic for the treatment of ALS. Prior to future testing in clinical trials, it is important that the efficacy of Angiogenin and its mechanisms of action is clearly documented and established. In line with preclinical testing guidelines, we will investigate the effect of angiogenin protein delivery in two further mouse models, FUS(1-359) mice which shows a progressive ALS disease phenotype, and TDP-43 A315T mice. In a second aim, we will address the key question whether angiogenin is taken up and acts in endothelial cells, astrocytes, and motoneurons in vivo, and whether an increase in angiogenesis relates to the protective activity of angiogenin. We have recently also demonstrated that angiogenin is a stress-inducible RNAse that triggers tRNA cleavage in both motoneurons and astrocytes. The final aim of our project is therefore to explore whether tRNA cleavage into tiRNAs is detectable during treatment, and whether tiRNA delivery replicates the effect of angiogenin on motoneuron survival, hence delivering a mechanism of action, companion biomarkers, and potentially new IP.

Further information available at:

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