Understanding the role of altered ubiquitin homeostasis in motor neuron diseases.

https://www.neurodegenerationresearch.eu/survey/understanding-the-role-of-altered-ubiquitin-homeostasis-in-motor-neuron-diseases/

Name of Fellow

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Institution
Funder

Wellcome Trust

Contact information of fellow
Country

United Kingdom

Title of project/programme

Understanding the role of altered ubiquitin homeostasis in motor neuron diseases.

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The project/programme is most relevant to:

Motor neurone diseases

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Amyotroph | Motor Neuron | Spinal muscular atrophy

Research Abstract
SMA and ALS are progressive and fatal neurodegenerative diseases for which there is currently

no treatment. Recent work has shown that UBA1-dependent pathways are an important feature of SMA pathology. Loss of UBA1 activity in different SMA models was found to cause aberrant accumulation of downstream UBA1 target proteins, including beta-catenin. Strikingly, pharmacological inhibition of beta-catenin ameliorated the neuromuscular phenotype observed in different models of SMA. Pilot experiments s uggest a marked decrease of UBA1 and subsequent accumulation of beta-catenin in spinal cord of ALS patients compared to control, thereby supporting a general role for UBA1-dependent pathways in regulating neuromuscular pathology in MND. This project aims to further determine the contribution of UBA1-dependent ubiquitin pathways to the pathogenesis of a range of MNDs. Using mouse models of SMA and ALS, human ALS patient tissue samples, as well as a variety of cellular and biochemical techniques I will extend our understanding of the contribution of UBA1-dependent pathway changes to MND. I will use this knowledge to provide new insights into shared molecular mechanisms spanning multiple MNDs, and examine the possibility that these pathways represent a common therapeutic target for ALS and SMA.

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