Mechanisms Mediating NMJ Dennervation

https://www.neurodegenerationresearch.eu/survey/mechanisms-mediating-nmj-dennervation/

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USA

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Mechanisms Mediating NMJ Dennervation

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Research Abstract

? DESCRIPTION (provided by applicant): Amyotrophic Lateral Sclerosis (ALS; Lou Gehrig's Disease) was first described by Dr. Charcot 140 years ago in 1869; however, its causes remain largely unknown and effective, long-term treatment strategies are not available. My laboratory has a long-term interest in mechanisms mediating motoneuron (MN) cell death during development and in diseases such as ALS. The proposed project builds on years of research whose results have led us to hypothesize that muscle may regulate MN survival not only in development, but also in pathological conditions and aging. In many neurodegenerative diseases initial damage appears to occur at synapses, the neuromuscular junctions (NMJs) in

ALS. It is not known whether NMJ denervation is initiated autonomously at that site or by pathology in the cell body, in non-neuronal cells or even in non-MNs. But all NMJs do not appear to be affected initially, only those on fast fatigable muscle fibers. The experiments will specifically investigate if muscle composed predominantly slow type fibers express a distinct complement of RNA and proteins that may promote NMJ innervation whereas the distinct complement expressed by fast fibers may make MNs susceptible to NMJ denervation in pathology and aging. Much ALS research has focused on pathology in the spinal cord; however, effective treatment strategies for ALS will involve targets in both spinal cord and at the NMJ. The experiments in this proposal will target an under-investigated area in ALS. We will begin to determine if muscle is a key mediator axon/synapse loss in ALS and possibly provide foundation for therapeutic development.

Further information available at:

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