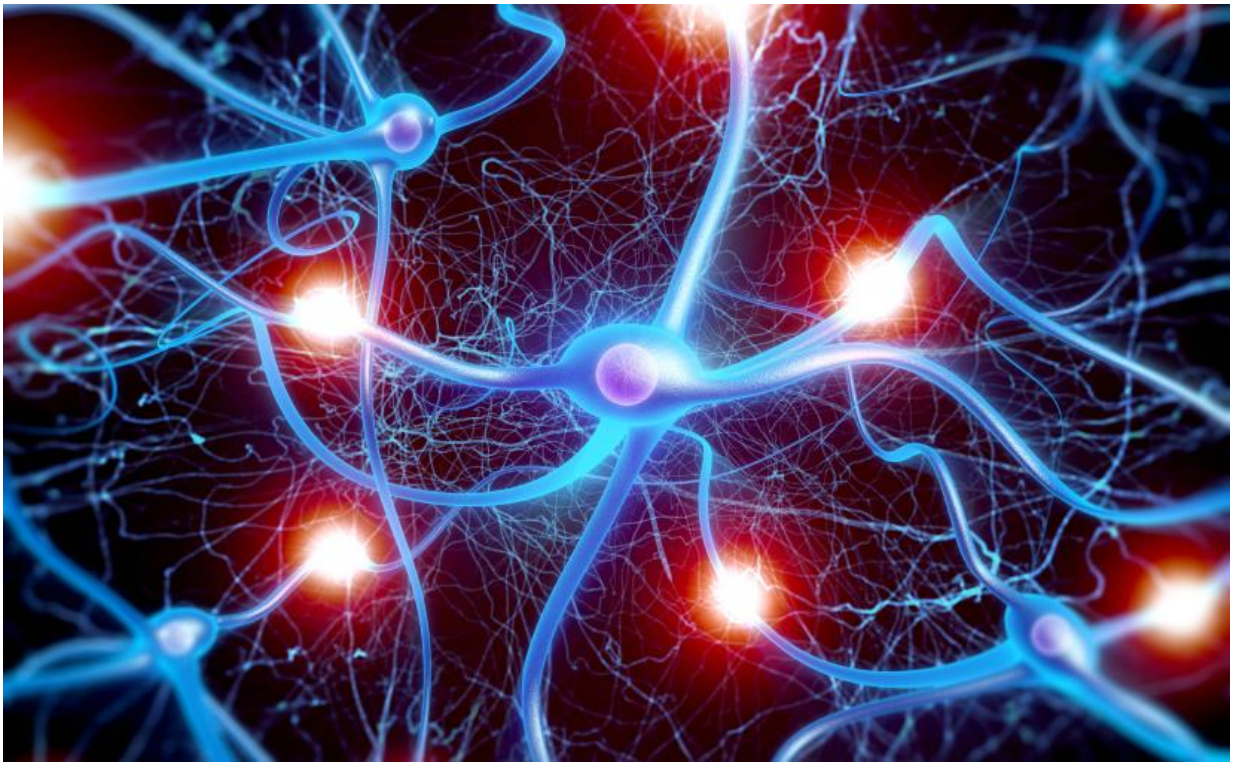

# A New Study Supported by The ALS Association May Provide a Novel Therapeutic Strategy for ALS

Research funded by The ALS Association found that defects in the mechanism that transports proteins and RNA between the nucleus and cytoplasm of cells within the human body may lead to ALS and that regulation of those systems could present a novel therapeutic strategy for ALS.

Details of the study are provided in a new paper entitled, "Modulation of actin polymerization affects nucleocytoplasmic transport in multiple forms of amyotrophic lateral sclerosis," which was released August 23, 2019, in the journal *Nature Communications*.

Within each of the cells in our body, there is the nucleus, which contains our DNA, surrounded by the cytoplasm, which is a jelly-like substance where all of our necessary biochemical reactions happen. Proteins, RNA, and solutes flow between the nucleus and cytoplasm through nuclear pores, which are essentially tiny passageways.

It has been hypothesized that defects in this transport mechanism may cause ALS. This study supports the idea that common genetic mutations can affect the normal function of proteins that regulate transport. Defects in the cytoskeleton are often observed in ALS patients. The study also shows that through altering the cytoskeleton, a network of filaments in every cell providing strength and support, we can normalize nuclear pore function and correct the defects in the transport, thus providing a unique therapeutic strategy for ALS.

“Here, we have connected two processes that are often flawed in ALS patients, nucleocytoplasmic transport and the cytoskeleton. Further, improving one process helped to correct the other,” said John Landers, Ph.D., University of Massachusetts Medical School one of the researchers on this study.

Claudia Fallini, Ph.D., co-leader on the research study stated, “This investigation establishes a novel link between the cytoskeleton, nucleocytoplasmic transport, and RNA regulation, three processes that have been independently connected to ALS. Our data suggest a new model where different pathways affected in ALS are not independent from each other but rather interconnected, generating a vicious cycle that leads to neuronal degeneration.” John Landers, Ph.D., and the other lead researcher added, “…improving one process helped to correct the other. As such, our hope is that a therapeutic strategy does not need to address all defects in patients, but rather only a subset since they may all be connected.”

John Landers, Ph.D. and Claudia Fallini, Ph.D. jointly led the study and received a multi-year grant from The ALS Association. The first author is Anthony Giampetruzzi, Ph.D. All three researchers are affiliated with the University of Massachusetts Medical School. Fallini and Giampetruzzi are past recipients of The ALS Association’s Milton Safenowitz Fellowship. Landers recently received a grant from The ALS Association to create a central genomic data repository.