AMERICAN ACADEMY OF NEUROLOGY®

AAN 65th ANNUAL MEETING ABSTRACT

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Abstract Title: Transplantation of iPSCs-Derived Neural Stem Cells as Therapeutic Approach for Amyotrophic Lateral Sclerosis

Press Release Title: Stem Cells May Hold Promise for Lou Gehrig's Disease (ALS)

Objective: The aim of the study was to investigate the therapeutic potential of iPSC- derived neural stem cells (NSCs) transplantation in an animal model of ALS.

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Background: Amyotrophic lateral sclerosis (ALS) is a progressive, fatal, neurodegenerative disease characterized by the loss of motor neurons. The possibility of reprogramming adult somatic cells into induced pluripotent stem cells (iPSCs) allows obtaining a promising cell source for modeling and cell therapy.

Design/Methods: We generated iPS cell lines derived from human skin fibroblasts with a non-viral non integrating method based on the expression of reprogramming factors with episomal vectors. We differentiated iPSCs using a protocol to promote neuronal stem cells fate. We isolated by FACS a primitive NSC fraction based on their high ALDH activity and low side scatter (ADLHhiSSClo). The phenotype of these cells was analyzed by morphological, gene expression and protein analysis. Finally, iPSC-purified NSCs were transplanted intrathecally or by systemic intravenous injection into ALS mice (SOD1G93A mice).

Results: ALDH(hi)SSC(lo) NSCs from iPSCs are self-renewing and multipotent and can differentiate in vitro into the three neuroectodermal lineage in vitro. Both intrathecally and systemically grafted NSCs migrated into the parenchyma and engrafted the host spinal cord, expressing neuronal precursors- and neuronal mature-specific markers. Cell transplantation significantly prolonged disease duration and lifespan in SOD1G93A mice, promoted the survival of motor neurons and improved neuromuscular function.

Conclusions: The major finding of the present study is that minimally invasive injection of ALDHhiSSClo cells in a mouse ALS model results in consistent engraftment of cells and is associated with an amelioration of the disease phenotype. These data suggest that iPSC derived NSCs represents a promising avenue for effective cell-based treatment for ALS and other neurodegenerative diseases.

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