

Derivation of Astrocytes from Human Embryonic Stem Cell (hESC) for Spinal Cord Injury Therapy

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Every year about 300,000 patients in the U.S. suffer traumatic injury of the brain or spinal cord requiring hospitalization, of which 250,000 survive. Due to the limited regenerative capability of adult central nervous system (CNS), these patients are facing the debilitating consequence of their injuries. Taking advantage of the neuroregeneration promoting properties of glial cells, we have developed a cell therapy for SCI using a specific type of astrocyte. Previously we have shown that transplantation of BMP-induced astrocytes (GDAs^{BMP}) derived from either rat or human embryonic glial-restricted precursor (GRPs) cells promotes extensive neuronal survival, axonal regeneration, and functional recovery in a rat spinal cord lesion model. With the recent advances in embryonic stem cell (hESC) technology and the ability to generate autologous pluripotent stem cells (iPSCs), we hypothesize that hES and iPS cells can be used as a source for generating astrocyte populations with therapeutic potential. Using step-wise differentiation through an intermediate neural progenitor stage, we have derived distinct types of human astrocytes from hESCs. Our data indicate that these hESC-derived astrocytes recapitulate characteristics of rodent precursor-derived astrocytes with respect to cell morphology and expression marker expression. We have also developed a high-throughput in vitro neuronal survival and axonal outgrowth assay by using the Cytellect Celigo adherent cell cytometer. Our results show that astrocytes derived from hESC by BMP induction selectively support the survival and axonal growth of embryonic cortical and dorsal root ganglion neurons. Furthermore, we demonstrate that distinct types of astrocytes can also be derived in a similar manner from inducible pluripotent stem cells (iPSC). These results set the stage for testing the therapeutic potential of hESC-derived astrocytes for spinal cord injury regeneration.