Developing Human Embryonic Stem Cell for Use in Cell and Tissue Therapies

S. Stice;
Univ of Georgia, Athens, GA.

Statement of purpose: Embryonic stem (ES) cells are undifferentiated cells that have piqued scientific curiosity primarily due to their inherent pluripotent nature. The isolation of human ES cells has generated enormous interest due to their ability to differentiate into derivatives of all three embryonic germ layers and form virtually any cell type in the body. Two major areas of study in current ES cell research include analyses and maintenance of pluripotency involving the continued culture of the cells in an undifferentiated state, and development of uniform and directed differentiation strategies for the production of different cell types of specific interest. Although proof of principle of human ES cells developing into many differentiated phenotypes has been demonstrated, successful in vitro differentiation will require a well-characterized starting pluripotent ES population. Transcriptional analyses of the pluripotent state of human ES cells will help uncover or further define signaling pathways and molecular mechanisms involved in the maintenance of the undifferentiated state and initial loss of pluripotency. A detailed understanding of these molecular mechanisms will thus be essential for developing human ES cells as in vitro model systems for studying embryonic development and for harnessing the differentiation potential that makes them highly attractive for cell-based therapies. Research focusing on neurological disorders would benefit from a reliable and well-characterized source of primary cultures of human motor neurons. Recently, functional human motor neurons were isolated from telomerase-immortalized human spinal cord cells. These immortalized cell lines and primary motor neurons derived from embryonic stem cells will positively impact research on motor neurons in the future. Embryonic stem cells have the potential to differentiate to a number of cell types but differentiation of these cells to motor neurons cells has not previously been demonstrated.

Results/Discussion: Here, we report the differentiation of human embryonic stem cells to generate cells of a motor neuron phenotype. First, a renewable source of neuroepithelial cells was generated from human embryonic stem cells, and introduced extracellular signals induced motor neuron differentiation and related gene expression. OLIG2 and HLXB9 gene expression was increased by the addition of basic fibroblast growth factor, retinoic acid and sonic hedgehog, and motor neuron phenotype (Islet1, ChAT) was observed. This study demonstrates that neuroepithelial cells derived from human embryonic stem cells are renewable progenitors capable of generating motor neurons at levels which may be therapeutically useful. Sonic hedgehog, basic fibroblast growth factor and retinoic acid differentially influence human motor neuron differentiation by mechanisms that remain to be defined.

Conclusion: Development of a reliable source of motor neurons from human embryonic stem cells will provide a research tool that will compliment existing models and enhance research motor neuron disease and other neurological disorders.