Comparison of Human and Rat Neural Stem/Progenitor Cell proliferation and differentiation: Implications for the Successful Translation of Rodent Stem Cell Therapies to Humans

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Introduction

While several promising neural stem/progenitor cell (NSPC) therapies for spinal cord injury have been developed in animal models, therapeutic translation to humans has often failed. While the direct comparison of human and rodent NSPCs to assess intrinsic cell differences may improve the translation, this comparison using identical culture conditions has not been reported previously due to the difficulty in obtaining viable human spinal cord tissue to allow the culture of NSPCs.

Methods

Regional ethics board approval was obtained. To compare the intrinsic proliferative and differentiation potential of human and rat spinal cord NSPC, we obtained viable human spinal cord tissue from organ donors (n=10) and Sprague Dawley rats (n=6) and isolated NSPCs from this tissue. Using identical cell culture conditions, human and rat NSPCs were assessed for proliferation in media containing epidermal growth factor and fibroblast growth factor -2. Proliferation was assessed with BrdU, Sox2+ and DAPI labeled cell counts. Differentiation potential was assessed with 1% fetal bovine serum administration. Response to retinoic acid (RA), BMP4, or PDGF-

Results

Rat NSPC proliferation rate was twice (2.3±0.8) that of humans. Rat NSPCs differentiated more into astrocytes (71.8±5.6%) compared to neurons (15.2±4.2%) and oligodendrocytes (2.82±1.3%). Human NSPCs differentiated more into neurons (68.5±16.9%) with little (<2%) gliogenesis. RA stimulated both human and rat NSPC differentiation into neurons, while PDFG only increased rat NSPC oligodendrocytic differentiation, and BMP4 only increased human NSPC astrocytic differentiation.

Conclusions

Due to the intrinsic differences between human and rodent NSPCs, translation of rodent NSPC therapy to humans may require longer duration of therapy because of the relative decrease in human NSPC proliferation rate, and exogenous growth factor administration may require modification given the differences in the intrinsic differentiation potentials and response to growth factors.

Learning Objectives

By the conclusion of this session, participants should be able to:

1)Identify that human and rodent neural stem/progenitor cells have different proliferation potentials.

2) Identify that human and rodent neural stem/progenitor cells have different differentiation potentials.

3) Identify that human and rodent neural stem/progenitor cells have respond to growth factors differently.

References