Therapeutic Effects of Combined Hepatocyte Growth Factor and Human Induced Pluripotent Stem Cell-derived Neural Stem/progenitor Cells Transplantation in Subacute Spinal Cord Injury

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Introduction

The cell transplantation therapy is highly dependent on the degree of damage and its effect is only modest.

HGF activation is involved in cell proliferation, differentiation, pre-angiogenic, anti-apoptotic, and anti-inflammatory.

Material & Methods

Severe contusion SCI and HGF administration rat model

• Severe contusive SCI was induced in RNU nude rats, and recombinant human HGF protein was administered continuously into the subarachnoid space with an osmotic mini-pump immediately after SCI for 2 weeks.

• Histological and RNA-Seq gene expression analyses were conducted 2 and 7 days after SCI.

• To assess the effectiveness of combined therapy, subsequent to the HGF administration, hiPSC-NS/PCs were transplanted into the injured spinal cord at 9 days post-injury.

• Motor functions were assessed by the BBB score, Diggigait analysis, Kinematics.

• Histological analyses were performed at 12 weeks after SCI.

Result

Angiogenesis

Anti-inflammation

Neurogenesis

Transplanted cell engraftment

Spinal cord area

• HGF pretreatment induced better survival of transplanted cells.

• Enhancement of synapse formation by increasing the regenerated nerve fibers.

Combination therapy resulted in synergistic improvement of locomotor functional recovery and potentiation of neurotransmission.

Conclusion

HGF treatment not only preserved host neurons through angiogenesis, neurogenesis, and anti-inflammatory effects, but also enhanced survival of transplanted hiPSC-NS/PCs. Consequently, the augmented formation of synaptic connections between the graft and host neurons facilitated the restoration of motor function.

Therefore, the combined therapy of HGF and hiPSC-NS/PCs transplantation represents a novel and highly promising therapeutic strategy for acute to subacute severe SCI.