Abstract #582.docx

Human induced pluripotent stem cells generated from intervertebral disc cells improve neurologic functions in spinal cord injury

Introduction:

The induced pluripotent stem cells (iPSC) have been considered as the new cell source for the autografting in regenerative medicine. Recently, it has been found that iPSC derived from human fibroblast could differentiate into neurons and improve neurologic functions in experimental spinal cord injury (SCI) model. During the human SCI treatment, we remove large amount of disc cells as a waste product during anterior cervical decompression and fusion. Therefore, disc cells should be utilized as a potential substrate for generating iPS cells. To provide the new therapeutic paradigm in SCI management, we used the human intervertebral disc cells for establishing neural progenitor cells (iPSC-NPC) and differentiate iPSC-NPC to neurons in vitro. Moreover, we transplant iPSC-NPCs into mouse SCI models and investigate the therapeutic effect of iPSC-NPC on neurologic recovery.

Materials and Methods

Human iPSC-NPC were generated from human intervertebral disc cells which were isolated from lumbar discectomy L4/5 specimen. We differentiated human iPSC-NPC into neurons in EGF/FGF2 free media. Mouse SCI was induced at the 10^{th} thoracic level (T10) with clip application model. Neuronal and glial differentiations were identified with immunocyto/histochemical staining using Tuj1, GFAP and electrophysiological study. Behavioral analyses were performed to identify the neurologic improvement after SCI.

Results:

The iPSC-NPC was strongly positive with Nestin in growth media containing EGF/FGF2. The most of iPSC-NPC were differentiated into the Tuj1 positive neuron in media without EGF/FGF2. In addition, these cells showed the neuron specific electrical signaling (Figure 2). To investigate the therapeutic effect of iPSC-NPC on SCI model, cells were transplanted into the injured mouse spinal cord at 9 days after SCI injury. We identified that transplanted cells were survived, which was confirmed by human nuclei immunostaing, in mouse spinal cord at 5 week after transplantation. Most of transplanted cells were either Nestin-positive neural precursor cells or Tuj1-positive neurons. Few of transplanted cells were differentiated into GFAP-positive astrocytes. Behavioral analyses demonstrated neurologic improvement from two weeks after the initial injury until 6 weeks after SCI.

Discussion and Conclusion:

We developed the iPSC-NPC from human intervertebral disc cells. These iPSC-NPCs could generate neurons and improve neurologic outcomes in mouse SCI model. Therefore, we suggest that autologous NPC generated from intervertebral disc cells could be one possible stem cell source for SCI.