

# Stem Cells Used for Therapy Following Spinal Cord Injury

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March 10, 2008

Spinal cord injuries (SCI) are devastating to any one that they are inflicted upon. The majority of patients are left with severe motor and other neurological disabilities. SCIs affect 10,000 North Americans per year and about 200,000 patients are left with associated disability. Of these disabled patients 70% are under 40 years of age. In 1995 an estimated \$7.7 billion was spent on treatment and it can only be assumed that the cost has increased since then.

Injuries are the result of tension or compression resulting in damage to nerves, blood vessels, or the spinal cord itself. Mild injury may cause a cord concussion and brief neurological defects. However severe injury will result in axonal and neuronal injury, with permanent paralysis as a result. In the severe cases of injury primary trauma leads to a series of cascades that result in a secondary injury. The force of impact determines the magnitude of both primary and secondary injuries however secondary injuries tend to be more difficult to reverse. Prevention of secondary injury has become one of the main focuses of treatment. Through the use of decompressive surgery and the administration of Methylprednisolone (anti-inflammatory drug), there have been advances in the treatment of the secondary injury. Both of these treatments deal with inflammation. Inflammation is caused by reactive astrocytes which are a response to SCI. The reactive astrocytes also cause changes in gene expression, hypertrophy, and in certain cases cell division. Also scar tissue can impede axon regeneration and is considered detrimental to functional recovery.

Through the use of stem cells there is a hope to promote regeneration and repair of injury because they can differentiate into any potential cell phenotype. Two specific cell types would be neuronal precursors to replace destroyed neurons and oligodendrocytes to promote remyelination. Stem cells can also promote axonal growth or secrete growth factors which will allow surviving neurons to repair damage and connections. Evidence now shows that stem cells present within CNS can be stimulated to proliferate and differentiate and stem cells from surrounding areas may be induced to move into the injured region of the CNS. Also other stem cells like bone marrow progenitor cells have given rise to the creation of neural cells including neurons. This is extremely significant because it was previously believed that only pluripotent neural stem cells could create neural tissue.

There are three major stem cell sources Human Embryonic Stem Cells, Human Embryonic Germ Cells, and Human Adult Stem Cells. Hematopoietic Stem Cells which are isolated from blood and bone marrow are another source. The following cell types have been used to replace damage neurons: Neuro-epithelial stem cells - Differentiate into neural and glial cells upon transplant into CNS; Lymphohematopoietic stem cells (LHSC) - Easily obtained via chemotherapy and growth factors and have only been proven to differentiate into muscle cells; Mesenchymal stem cells (MSC) - Derived from bone marrow and can migrate through the brain when transplanted and differentiate into neural and glial cells.

There are several cases of successful stem cell therapy in mice and rats. These therapies have resulted in improved functional recovery of hind limbs, reduced cystic cavity, increased area of white matter, and regeneration of axons following an SCI. It has also been noted that due to the invasive nature and possible danger, of direct transplantation of the stem cells to the afflicted area, that there is a need for effective intravenous (IV) administration of these stem cells. The IV injection of the stem cells requires a large number of cells so that enough reach the injury and make a difference in the therapy. Cytokines have been studied for use in increasing the number of stem cells in an area. Two such cytokines are G-CSF and GM-CSF. The use of G-CSF with stem cell factor in studies has shown an increase in bone marrow stem cells by a factor of 250, and also increases the LHSC present. Treatment of this combination can facilitate movement of stem cells and increase the probability that they will differentiate into neural cells. G-CSF also has protective advantages. When released with LHSC into the blood it will repopulate injured area with neural progenitor cells, resulting in re-established neural circuitry, extends cell life by delaying apoptotic cell death, and helps with reduction of the inflammatory response to traumatic injury. The reduction of inflammatory response is due to the suppression of microglial cell activation which release inflammatory cytokines. These hematopoietic cytokines control activation, proliferation, differentiation, and survival of neural stem cells.

The use of stem cells from a variety of sources has been proven to improve motor function in animals after a spinal cord injury. Therapeutic treatment with G-CSF following injury has been proven to increase the number of stem cells present at the site of the injury. The use of stem cell therapy in conjunction with G-CSF therapy should greatly improve neurological and motor function following an injury to the spinal cord. More pre-clinical study is required to prove these effects and hopefully improve the life of patients with SCI.

## References

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