HuCNS-SC® Therapeutic Development Program

(Human Neural Stem Cells)

About Spinal Cord Injury

Nearly 1.3 million people in the U.S. alone are estimated to be living with chronic spinal cord injury.

Chronic spinal cord injury is characterized as a point in time after injury in which inflammation has stabilized and behavioral recovery has reached a plateau. In spinal cord injury patients, the chronic phase typically does not set in until several weeks or months following the injury. To date, treatment approaches have generally targeted the acute and sub-acute time points post injury, which are considered to be hours or days following injury. Realization of a treatment that could be administered at later time points beyond the acute injury phase to restore some degree of function could have a transformative impact on the field as there are no effective treatment options today for chronic spinal cord injury patients.

The loss of sensation and motor function resulting from spinal cord injury is often associated with neuron loss and "demyelination," in which a once-healthy myelin sheath is damaged or destroyed. Myelin is a substance that surrounds and insulates axons (communications fibers of nerve cells). Without this protective myelin coating, axons are unable to properly transmit nerve impulses from the brain to areas below the level of injury.

Hope for the Future

StemCells human neural stem cells have been shown in preclinical studies to treat the neuron loss and myelin deterioration resulting from spinal cord trauma, and to subsequently restore motor function. These results suggest that the use of human neural stem cells may be a viable approach for the treatment of spinal cord injury. StemCells hopes to address a broad population of spinal cord injury patients by extending the post-injury window of opportunity for therapeutic intervention to months or even longer, and by targeting a wide range of injury levels and degrees of impairment.

Milestones

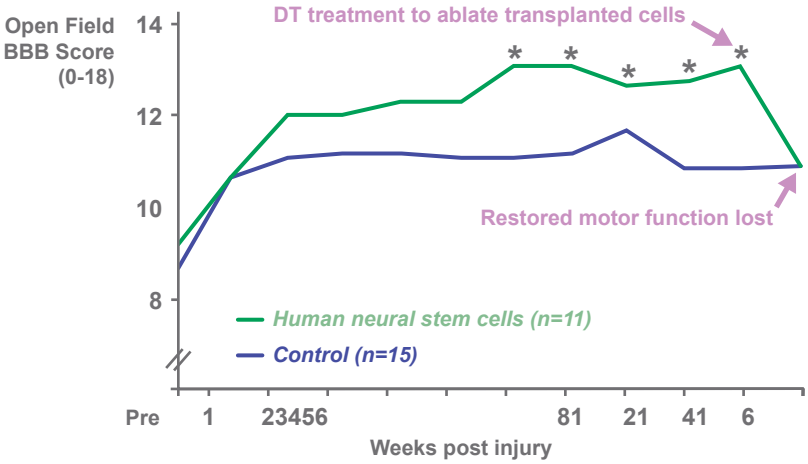
StemCells, Inc. is conducting a Phase I/II clinical trial in spinal cord injury.

- **2002:** Entered into collaboration with researchers at the University of California, Irvine (UCI) to evaluate StemCells human neural stem cells in spinal cord injury
- **September 2005:** *In vivo* proof of principle published in *PNAS* showing that StemCells human neural stem cells restore motor function when transplanted in mice with sub-acute spinal cord injury
- **August 2010:** Data published in *PLoS* showing that StemCells human neural stem cells restore motor function when transplanted in mice with chronic spinal cord injury
- **December 2010:** Secured Swissmedic authorization to initiate a Phase I/II clinical trial in chronic spinal cord injury
- **March 2011:** Initiated Phase I/II trial at the Balgrist University Hospital, Univ. of Zurich

Preclinical Proof of Concept

The results of numerous preclinical studies, conducted in collaboration with researchers at UCI, demonstrate the significant therapeutic potential of StemCells human neural stem cells for the treatment of spinal cord injury. Data published in several peer-reviewed journals show that the cells engraft, migrate along the spinal cord to the point of injury, and then differentiate into neurons and specialized cells called oligodendrocytes, which create the insulation (myelin) necessary for proper transmission of nerve impulses from the brain to below the level of injury. When transplanted in spinal cord-injured mice at both sub-acute and chronic injury time points, the cells have been shown to form protective myelin sheaths around damaged nerve axons and enable a significant and persistent recovery of walking ability.

StemCells human neural stem cells promote long-term functional motor recovery.



Repeated measures ANOVA p<0.01 *** Individual time points p<0.05**

StemCells human neural stem cells were transplanted into a group of spinal-cord injured mice and their motor function over time was compared against a control (non-transplanted) group of similarly injured mice as measured by the BBB score (a standard measure of function). The motor function of the transplanted mice was shown to be higher to a statistically significant degree. When the transplanted human cells were subsequently ablated by the researchers using Diphtheria toxin (DT), the greater function of the transplanted group was lost, demonstrating that the presence of the human cells was necessary for the functional motor recovery.

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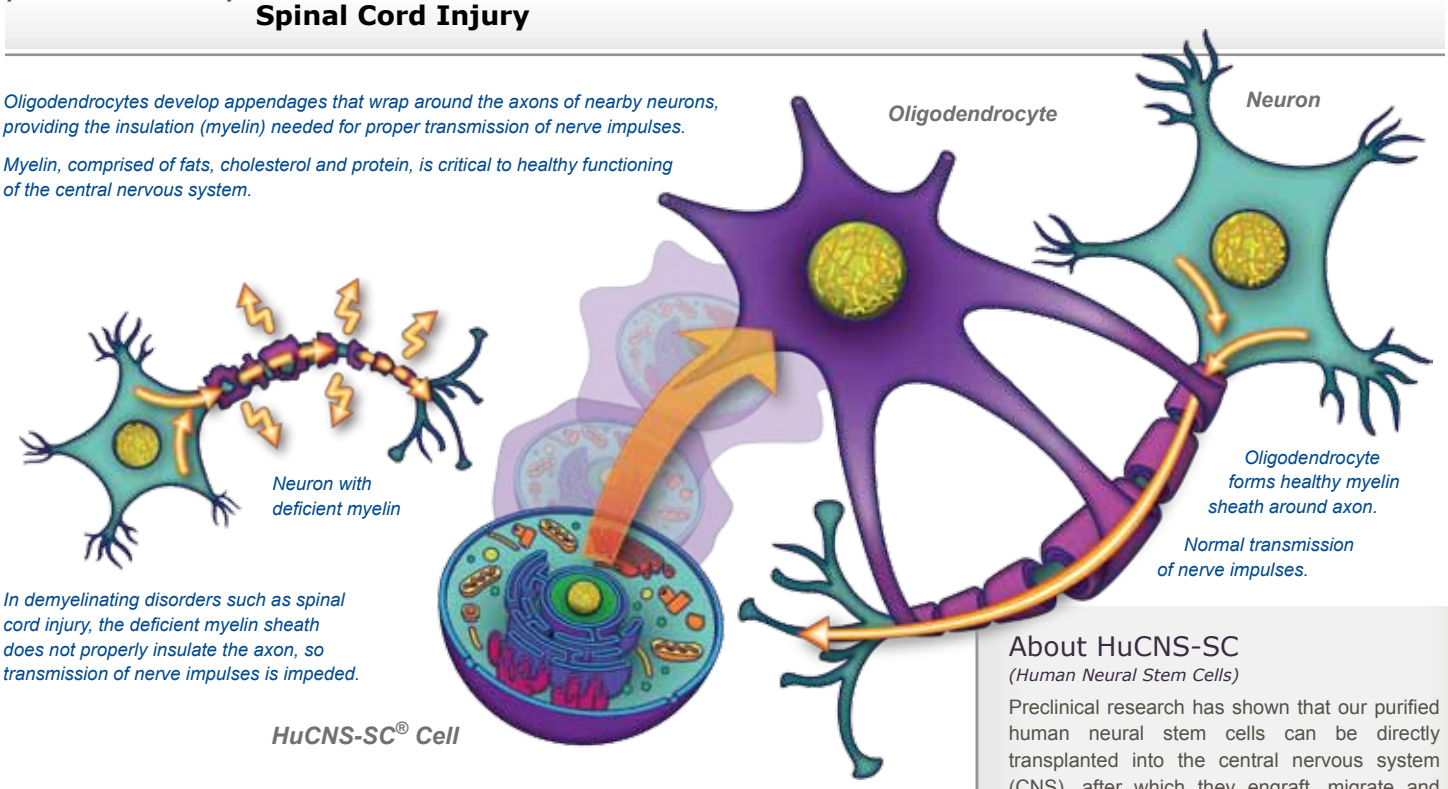
Spinal Cord Injury

Oligodendrocytes develop appendages that wrap around the axons of nearby neurons, providing the insulation (myelin) needed for proper transmission of nerve impulses.

Myelin, comprised of fats, cholesterol and protein, is critical to healthy functioning of the central nervous system.



In demyelinating disorders such as spinal cord injury, the deficient myelin sheath does not properly insulate the axon, so transmission of nerve impulses is impeded.

The StemCells Approach: Myelin Production to Protect Nerve Cells

When StemCells human neural stem cells are transplanted in animals, they migrate to the sites where myelin is deficient. They differentiate into oligodendrocytes, which form healthy myelin sheaths to protect axons, helping nerve cells communicate with each other.

Phase I/II Trial in Spinal Cord Injury

In December 2010, StemCells, Inc. received authorization from Swissmedic, the Swiss regulatory agency for therapeutic products, to initiate a Phase I/II clinical trial of its HuCNS-SC product candidate (purified human neural stem cells) in chronic spinal cord injury. This trial was subsequently initiated in March 2011, and is being conducted in Switzerland at the Balgrist Univesity Hospital, University of Zurich.

The trial is designed to assess both safety and preliminary efficacy in patients with varying degrees of paralysis who are 3-12 months post injury, and will progressively enroll patients based upon the severity of injury. The trial will enroll 12 patients in Europe with thoracic (chest-level) spinal cord injury, and will include both complete and incomplete injuries as classified by the American Spinal Injury Association (ASIA) Impairment Scale. The first cohort will include patients classified as ASIA A. These patients have what is considered to be a “complete” injury, or no movement or feeling below the level of the injury. The second cohort will progress to patients classified as ASIA B, or patients with some degree of feeling below the injury. The third cohort will consist of patients classified as ASIA C, or patients with some degree of movement below the injury. In addition to assessing safety, the trial will evaluate preliminary efficacy using defined clinical endpoints, such as changes in sensation, motor and bowel/bladder function.

All patients will receive HuCNS-SC cells through direct transplantation into the spinal cord, and will be temporarily immunosuppressed. The patients will be evaluated regularly over a 12-month period post transplant in order to monitor and evaluate the safety and tolerability of the HuCNS-SC cells, the surgery and the immunosuppression, and to measure any recovery of neurological function below the injury site. As StemCells intends to follow the effects of this therapy long-term, a separate 4-year observational study will be initiated at the conclusion of the trial.

STEMCELLS Groundbreaking **science.** Breakthrough **medicine.**™

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Preclinical research has shown that our purified human neural stem cells can be directly transplanted into the central nervous system (CNS), after which they engraft, migrate and differentiate into neurons, astrocytes and oligodendrocytes, surviving long-term with no sign of tumor formation or adverse effects. This suggests the possibility of a durable clinical benefit following a single transplantation. In 2009, data from our first clinical trial demonstrated the safety and tolerability of our HuCNS-SC product candidate and the transplantation process. Additional data reported in 2011 provides evidence that HuCNS-SC cells persist long after immunosuppression is discontinued. We are currently developing our HuCNS-SC product candidate for the treatment of several indications including:

- Spinal cord injury (Ph. I/II trial underway)
- PMD (Ph. I trial underway)
- Retinal disorders (Ph. I trial targeted for 2012)
- Alzheimer’s disease and stroke (preclinical)

Processed in compliance with cGMP standards, our HuCNS-SC cells can be expanded, cryopreserved and then stored in banks for future use as “stem cells in a bottle.”

About StemCells, Inc.

Driven by nearly 20 years of pioneering research and innovation, StemCells, Inc. is applying its scientific and industry leadership in stem cell biology to discover, develop and commercialize novel therapeutics and enabling tools and technologies for use in stem cell-based research and drug discovery.

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