Number 24, Winter 2013

Reeve-Irvine Research Center Publication

# Spinal Connections

On March 16th 2013 we hosted our 13th annual "Meet the Scientists" forum, where community members and the public can come hear about the progress RIRC members are making in spinal cord injury (SCI) research. The goal of this forum is to help educate and inform the community on new discoveries relevant to SCI. It is also an opportunity for people living with SCI and their family members to tour our labs and talk directly with our researchers and clinicians.

This year we were pleased to welcome back Dr. Suzy Kim, MD as she has rejoined the RIRC and UC Irvine's Physical Medicine and Rehabilitation department. We also had two new RIRC members, Drs. Catherine Cahill and David Luo join our research presentations as well as this year's special guest Dr. Volkar Sonntag. Dr. Sonntag is a Neurological surgeon and Vice Chair of Neurological Surgery at the Barrow Neurological Institute in Phoenix, Arizona. For the past 30 years Dr. Sonntag has performed thousands of surgeries on patients and specializes in spinal disorders and degenerative spine diseases. He has made significant contributions to the understanding of spinal disorders and we were honored to have him join us this year.

This past year in addition to our usual breakout sessions we expanded our event by integrating company or industry involvement in an area called the "products area". Companies that attended displayed informational booths on treatments for spasticity (Allergen and Medtronic), catheters (Coloplast and Cure Medical), existing and upcoming neck and back braces (Aspen Medical products) and therapeutic technology for rehabilitation (Flint Rehabilitation). Although not represented in a booth, The Joy Factory also had product information regarding their new iPAD tablet mounts for wheelchairs users. This was the first time we have opened our doors to industry or company involvement and we therefore kept this area restricted to these 7 companies. The feedback for this part of our event was well received and we are planning on extending this area to incorporate more companies in the upcoming 2014 year.

We were pleased to see you all this past year and hope that you will join us again in 2014. The forum will be held on March 16th 2014 in our building on UC Irvine's campus. We would love to see you all there and look forward to answering your questions!

If you would like to check out last year's presentations and questions session, please see the link on our website (http://www.reeve.uci.edu/videos-meet-the-scientists-2013.html).

For more information please contact Tania Jope at (949) 824-5925 or tania.jope@uci.edu in January. You can also follow us on facebook at facebook.com/ReeveIrvineResearchCenter.

More pictures on pg. 11

Meet the Scientists 2013


Dr. Oswald Steward

# SCI Therapies...Are we there yet?

In this and the previous issue of "Spinal Connections", Dr. Maya Hatch's "Anatomy 101" feature takes a close look at the ongoing clinical trials involving stem cells for spinal cord injury. It seems appropriate to do this now as we start the 10th year of existence of the California Institute of Regenerative Medicine, which was established through passage of Proposition 71 in 2004. The nine year time period seems short to scientists, but of course is an eternity for people living with spinal cord injury. For scientists, it's remarkable that three different clinical trials for spinal cord injury have been launched, sponsored by Geron, Stem Cells Inc., and Neuralstem. But these early stage trials have mainly focused on safety and it will still take a while to move through the clinical trial process. It's important to emphasize that things don't always go perfectly. There will be bumps in the road, and perhaps dead-ends, but trials ARE underway, which could not be said 10 years ago.

At the end of the day, are any of the approaches currently in trial likely to be a miracle cure? The answer, based on the animal research backing the trials is, probably not. The degree of improvement seen in animals is meaningful, but occurs in a setting of partial injury where there is already some recovery. And the recovery that is seen in the animal studies is not complete. Most importantly, it isn't yet clear whether any of these approaches will prove beneficial for people in the chronic injury phase. This means that basic research on stem cell (and other) applications for spinal cord injury is still critical. I believe that the trials being tested now will eventually be superceded by other approaches that yield more extensive recovery, and do so in the chronic injury phase. I also believe that stem cell therapies will be combined with other approaches to enable long-distance regeneration of connections, which remains the holy grail for full recovery of function. This is the reason that my personal research focuses on axon regeneration, and most recently the use of stem cells to create a better bridge for growing axons at the injury site.

***I believe that the trials being tested now will eventually be superceded by other approaches that yield more extensive recovery, and do so in the chronic injury phase.***

It's an exciting time for scientists because the pace of progress continues to escalate. But we continue to need YOUR help. As we move some treatments forward, it's important to go back to the drawing board to develop the next generation of therapies that will be more effective and bring us even closer to achieving full recovery. The first stage of trial and error, when the story is too immature to be competitive for federal funding, depends critically on private donations. All of us at the RIRC thank you for your previous support and look forward to working together to develop the cures that will restore full function for those who are living with SCI.

## In this issue...



RIRC
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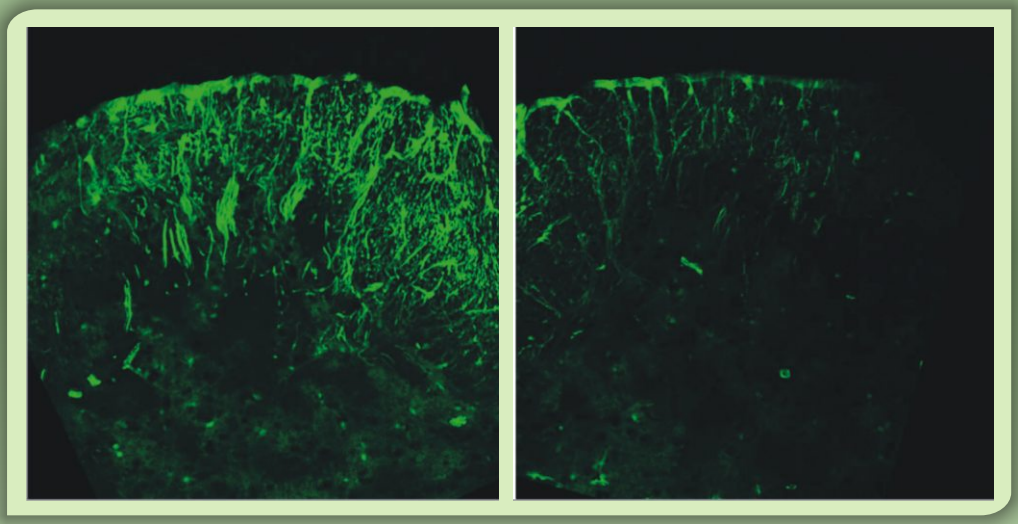
# Luo Laboratory Update

The Luo laboratory studies cellular mechanisms of neuropathic pain. Neuropathic pain sensations occur following injuries to the peripheral or central nervous systems, including spinal cord injuries. Currently, neuropathic pain is treated with the same medications used for other types of pain including opiate drugs. Unfortunately, these medications are usually not effective because neuropathic pain is due to completely different mechanisms than other pain. For this reason, defining the mechanisms of neuropathic pain will hopefully identify novel targets for more specific medications for management of neuropathic pain. To tackle this, the Luo laboratory has been using a multidisciplinary approach to discovery of new targets and pathways involved in neuropathic pain processing including state of the art neurohistological techniques, genomic screening, target validation, electrophysiology and behavioral pharmacology.

The latest discovery from the Luo laboratory in collaboration with the Reeve-Irvine Research Center includes identification of a potentially new target – an extracellular matrix protein called thrombospondin-4, for neuropathic pain interventions. The discovery came from studies using rodent models of neuropathic pain. Using gene chip microarray analysis on tissue samples from animals displaying neuropathic pain, the Luo laboratory discovered an increased level of messenger RNA for thrombospondin-4 gene. Increased messenger RNA usually means an increased amount of protein production of that particular gene. Data from in vivo biochemical validation studies indicated that thrombospon-4 protein production is indeed increased in non-neuronal cells in the spinal cord after nerve injuries which correlates with the development of neuropathic pain states. Electrophysiological studies indicated that increased thrombospondin-4 in the spinal cord caused hyper-sensitization (increased sensation) of spinal cord neurons responsible for sensory information processing. Importantly, this could be the driving force for neuropathic pain because mild and sub-threshold sensory input now could activate neurons that give rise to pain pathways, leading to exaggerated pain perception. To confirm the contribution of thrombospondin-4 to neuropathic pain development, the Luo laboratory team showed that blocking injury-induced thrombospondin-4 messenger RNA prevented spinal cord injury-induced thrombospondin-4 overproduction and eliminated neuropathic pain states. These findings support that injury-induced thrombospondin-4 overproduction may play an important role in the development of spinal cord injury-induced neuropathic pain states. Blocking this pathway may represent a new strategy for the development of more specific and safer pain medications for neuropathic pain management.



Fluorescent images of spinal cord sections showing an increased production of thrombospondin-4 labeled by green fluorescence on the injured side of the dorsal spinal cord (left) compared with that in the non-injured side (right).

# REHABILITATION CORNER: Pain

Xing Zhao, MD, Sujin Lee, MD
Maya Hatch, PhD, Eric Chang, MD

*As mentioned in our previous newsletter (number 22), we have recently collaborated with various physicians working in UCI's Physical Medicine and Rehabilitation department for this section of our newsletter. This section will highlight important rehabilitation research, techniques, and/or information relevant to SCI rehabilitation.*

Physiatrists (doctors who specialize in physical medicine and rehabilitation) treat many of the secondary complications associated with SCI including pain, spasticity and bladder dysfunction. In this article we focus on one of the most common secondary complications: pain. Up to 80% of people with SCI suffer from pain, which impacts quality of life as well as cognitive, physical, and emotional functionality. The goal of this article is to provide an understanding of the unique types of pain that are common following SCI, including "central pain" and "neuropathic pain" and how these pain syndromes are managed.

## Spinal cord injury and pain:

Of all the post injury complications in people with SCI, pain is one of the most difficult conditions to treat. Pain is generally defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Although this definition seems easy enough to understand the fundamental problem is that pain following SCI is often NOT related to actual or potential tissue damage. Instead, it is due to abnormal/excessive activation of central pain pathways. Also, pain following SCI is complex because several types of pain may exist simultaneously making it difficult to diagnose and treat effectively. Because the mechanisms of the pain are different, pain following SCI is often refractory to treatments currently available.

## Why does pain happen?

SCI triggers a series of events that lead to anatomical and physiological changes within the spinal cord and even the brain. Although we don't fully understand the mechanisms, some of the changes lead to different types of pain including allodynia, hyperalgesia, and spontaneous pain.

## Classification System:

The definition and classification of pain syndromes following SCI has not been well established. In fact, there are 29 different SCI pain classification schemes, making it virtually impossible to determine the prevalence of various types of pain. The different terminology also creates miscommunications between clinicians, researchers and health officials. To address this, in 2012 a group of 15 pain experts developed a clearly defined, unified pain classification system called the International Spinal Cord Injury Pain Classification (ISCIP). The new ISCIP organizes SCI pain into a three tier hierarchy format that is easy for experienced and non-experienced clinicians and researchers to understand. The first tier includes the general type of pain (nocicieptive, neuropathic, other or unknown). The second tier includes the subtypes of pain in tier I, and the third tier uses the source of pain as an identifier. Here, we focus on the general definition and classification of SCI pain. More detailed information on specific types of pain will be discussed in upcoming newsletters.

## Classification of SCI Pain:

Nociceptive pain is something that everyone experiences. It is NOT abnormal.

Nociceptive pain is defined as pain generated from the activation of nociceptors (peripheral nerve endings) located in peripheral tissues that are capable of reacting to a noxious stimuli. Noxious stimuli are events that potentially damage tissue and they can be mechanical (like pinching), chemical (acids or irritants) or thermal (extreme temperatures).

Nociceptive pain can be sub-divided into cutaneous, musculoskeletal and visceral. Cutaneous pain is what you feel when you cut yourself. Musculoskeletal pain refers to the pain that arises from muscle, tendons, ligaments, joints or bones. This type of pain can be described as 'dull' or 'aching'. Visceral pain comes from internal organs. Examples of visceral pain include pain from constipation, urinary tract infection, kidney stones, cholecystitis and myocardial infarction. This type of pain can be described as 'cramping', 'dull', or

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## The Next Generation joins the Plymouth Rock n Run Turkey Trot

Many of you probably know that Tania Jope, RIRC Director of Community Development, was due to deliver twins in early October. Well, it happened a bit early, about 2 months early to be exact, and so the Jope family has been busy dealing with two preemies. We're happy to report that the twins (Ryan and Sophia) were home with mom and dad by October and we were all delighted that the entire family including the twins did the 5K in the Plymouth Rock n Run Turkey Trot on Thanksgiving day. The twins seemed to enjoy the ride, sleeping peacefully among the crowd of over 2000 runners. Tania is on maternity leave until after the first of the year, and we look forward to her return to the RIRC then.

We would also like to thank everyone that participated as well as the many volunteers that made this event happen. A special thanks to Research for Cure who organized the event!


ResearchforCure.org


Please consider including
The Reeve-Irvine Research Center
in your estate plans.

Your planned gift can help
create tomorrow's cures.

For more information please contact:
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**The Annual**

**CALIFORNIA SPINAL CORD INJURY "MEET THE SCIENTISTS" FORUM**

**Saturday, March 15th, 2014**

William J. Gillespie Neuroscience Research Facility
University of California, Irvine

**Save the Date!!!**

# Anatomy 101: An informative NSC "stem off" part II

By Maya Hatch, Ph.D.

For part I of our "stem off" (see newsletter 22, page 8-9), we described ongoing stem cell clinical trials via a comparison chart. Here in part II, we provide more detailed information on the cells and the pre-clinical work in animals that lead up to the trial approvals. Here, we include only the information available from published scientific journals, Clinicaltrial.gov or corporation websites. It may help to re-familiarize yourself with the part I prior to reading this second piece.

*Please note: Both of these trials are using "neural stem cells (NSC)" and not human embryonic stem cells (HuESCs), as was the case with the Geron trial. More information on what neural stem cells are can be found in a previous Anatomy 101 entitled "NSCs: What are they and what can they do?" in Spinal Connections newsletter, number 22.*

## Stem Cells Inc.

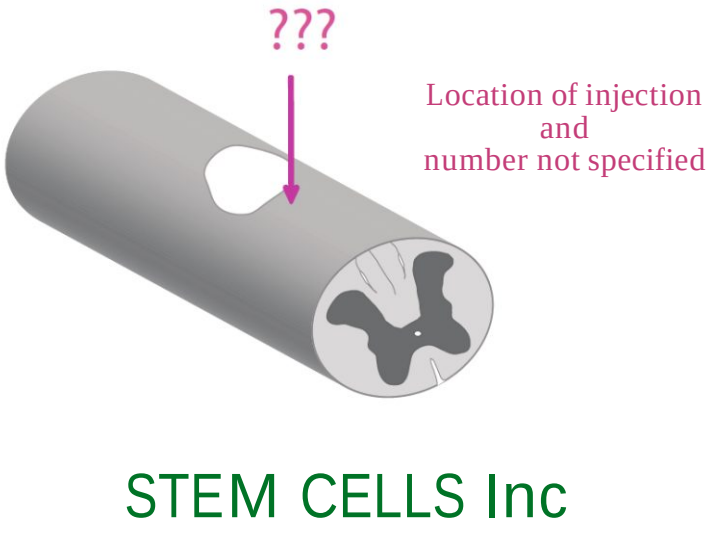
### The Cells

Stem Cells Inc. states that their NSCs (called HuCNS-SCs) are a "highly purified population of human neural stem cells" that can be "expanded for a number of generations" while retaining their potential to differentiate into neurons, astrocytes and oligodendrocytes. The cells were originally isolated from 16-20 week old fetal brain tissue[1]. These isolated cells were propagated as neurospheres (cluster of free floating NSCs) and fed with media devoid of animal-derived supplements with human basic fibroblast growth factor (bFGF), epidermal growth factor (EGF) and lymphocyte inhibitor factor (LIF) added to keep the cells from differentiating. At various passages master and working cell batches were frozen and stored in liquid nitrogen. All of these procedures were carried out under good manufacturing practice (GMP) conditions. These cells were first tested for safety in clinical trials involving two severe developmental disorders--Neuronal Ceroid Lipfuscinosis (NCL; ClinicalTrials.gov #:NCT00337636) and then Pelzaeus-Merzbacher Diease (PMD; ClinicalTrial.gov #: NCT01005004).

For use within the SCI clinical trial (ClinicalTrial.gov #:NCT01321333), the information provided publically (on Stem Cells Inc's website, or on ClinicalTrials.gov) did not state the exact procedure that would be used for injection. Presumably, upon delivery and prior to surgery, the cells will be dissociated into single cells. Per federal regulations all cells used will also be tested and free of antibiotics, preservatives, endotoxins and pathogens.

### The preclinical animal work

Much of the published preclinical work for this SCI trial was directed by two faculty members at the University of California, Irvine; Drs. Brian Cummings and Aileen Anderson. The initial aim of their preclinical work was to determine if the HuCNS-SCs were able to survive and differentiate when transplanted in a thoracic traumatic spinal cord injured environment[1]. Results indicated that HuCNS-SCs were able to survive and migrate, when transplanted 9 days after a contusion injury. Significant locomotor recovery was also seen in HuCNS-SC transplanted animals and the survival of HuCNS-SCs was required for[2] and directly related[3] to locomotor recovery.




Further preclinical work also showed that HuCNS-SCs could be safely transplanted at sub-acute (30 days post injury)[4] and, most recently, chronic (60 days post injury)[5] time points without incidences of increased allodynia or hyperalgesia. For the rodent studies, HuCNS-SCs were transplanted at 4 sites (2 rostral and bilateral, and 2 caudal and bilateral to the injury site). Each injection was 250nl at a concentration of 75 cells/nl for a total of 75,000 cells. Transplanted cells differentiated mainly into oligodendrocytes, with some neurons and few astrocytes regardless of the transplantation time post injury. No tumors were detected in any studies.

Continued on pg 8, column 1

Neural Stem, Inc.

The Cells

Neuralstem states that their cells (NSI-566 or HSSC) are "regionally specific cells that are already suited [for] the task prescribed to them once transplanted into the CNS" and that they "do not become any cell other than that to which they are fated". This means that NSI-566 cells are derived from the spinal cord and will only become cells of the spinal cord; astrocytes, oligodendrocytes or neurons. The cells were derived from the cervical and upper thoracic spinal cord of a single human fetus at approximately 8 weeks gestation. The cells were propagated as a single line, with no genetic manipulations or modifications, and as a single adherent monolayer of cells in tissue culture dishes fed with media devoid of feeders and animal-derived supplements. Cells were grown for 60 passages and supplemented with bFGF to keep the cells from differentiating. At various passages, cells were harvested, frozen and stored in liquid nitrogen. All of these procedures were carried out under good manufacturing practice (GMP) conditions. These cells are being tested for safety in Neuralstem's ALS trial (clinicaltrial.gov #: NCT01348451).

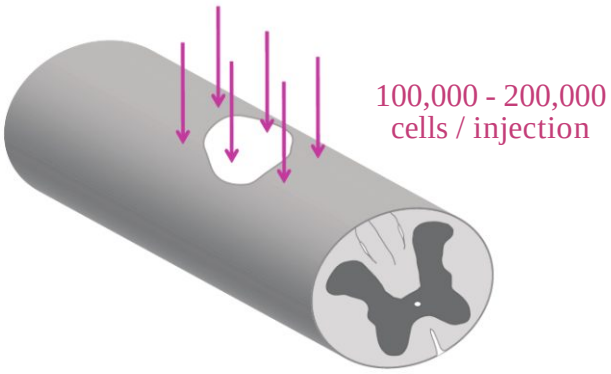
For use within the SCI clinical trial, cells will be thawed one day prior to surgery, washed and prepared at a density of 10,000 cells per microliter in "hibernation media". Cells will then be shipped overnight to the surgery site and tested for viability for transplantation. Any cells to be used for transplantation in the trial will also be tested and free of antibiotics, preservatives, endotoxins and pathogens.

The preclinical animal work

The published preclinical work for this SCI trial (ClinicalTrial.gov #:NCT01772810) was by scientists at the University of California, San Diego. One study involved an ischemia-induced SCI in a rat model; the other involved complete transection injuries, also in rat.

The aim of the preclinical work from the ischemia-induced SCI model was first to examine the effects, if any, the HSSC had on motor recovery. Results indicated that cells were able to survive and differentiate mostly into neurons in rats with ischemic injuries. There was recovery of motor function in transplanted animals, and the degree of recovery seemed dependent on the number of cells injected. In addition, these studies also determined the optimal time frame and dosing of the HSSC1. Results indicated that a total of 200,000-600,000 cells over 10 bilateral injections (10,000-30,000 cells per injection for a total of 20 sites) into the spinal cord 21 days after injury was optimal (no tumors were detected however this was not an extensive tumorigenicity study).

Because there are obvious differences in spinal cord dimensions and environments in rats vs. people, a follow-up study by this group investigated the optimal HSSC dosing regimen in a species with spinal dimensions closer to humans (minipig)[2]. Using a 5 bilateral injection procedure in the same ischemia-induced injury model, data in the minipig demonstrated that injections of >50,000 cells/injection, or volumes >6ul lead to tissue disruption whereas lower doses did not. Thus, the injection regimen used in the rats (max of 30,000 cells/injection in max of 2ul volumes) may be the maximum that can safely be delivered into the spinal cord unless there is a lesion cavity.




NEURALSTEM Inc

The aim of the preclinical work with the severe SCI rat model was to determine if transplanted HSSCs were able to overcome the inhibitory nature of the injured cord to enable CNS axonal regeneration in the most severe form of SCI, a complete spinal cord transection model[3]. In this study, cells were treated with a cocktail of growth factors in a fibrin matrix and then transplanted into the lesion cavity 1 week post injury. The cells survived, differentiated,

Continued on pg 8, column 2

continued from p. 6

The details of the clinical trial

Stem Cell Inc's SCI trial is a Phase I/II safety trial for subacute (3-12 months after injury) spinal cord injury. The primary goal is to determine the safety and toxicity of the HuCNS-SCs by measuring the incidence and severity of adverse events in transplanted individuals for 1 year after transplantation. Since this is a Phase I/II study Stem Cells Inc. is also requiring enrollment of patients into their long-term follow-up study for an additional 4 years. The primary outcome measure of the long-term study (ClinicalTrials.gov #: NCT01725880) is the American Spinal Injury Association (ASIA) impairment scale (a neurological examination); there will also be continuing safety monitoring.

Since this is a safety trial, certain precautions will be taken. This trial is only enrolling 12 thoracic level SCIs (T2-T11) and excluding penetrating SCIs, individuals who are under 18, those that have other spinal diseases, previous transplantations, gene transfers or current malignancies. Anyone with a history of traumatic brain injury will be excluded as well. The first cohort of patients will include ASIA A (complete) injuries and the second cohort will include ASIA B (sensory incomplete) injuries, with some degree of sensation below the injury. Finally, the third cohort will consist of ASIA C (motor incomplete) injuries representing individuals with some degree of movement below the injury. The number of cells to be transplanted is not specified in the information on ClinicalTrials.gov or on Stem Cell Inc's website; These sites only state that enrolled patients will receive a single dose of HuCNS-SCs into the spinal cord.

All patients in this trial will receive routine standard of care for surgery and will be put on a immunosuppressive regimen for 6 months. In addition to the assessment of safety, the trial will also evaluate changes in sensation, motor and bowel/bladder function, which may be important for

Continued on page p.9 column 1

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and integrated with the host tissue. There was extensive outgrowth of axons from the graft and some regeneration of host axons into the graft. Importantly, cell survival was minimal if cells were transplanted without growth factor treatment.

The two bodies of work above are the bulk of the published work behind the planned Neuralstem cell trial yet, the preclinical (please see Neuralstem's website) and clinical work (ClinicalTrial.gov #: NCT01348451) they have already done in Amyotrophic Lateral Sclerosis (ALS) likely contributed pertinent information for this trial as well. Interestingly, most HSSCs differentiated into neurons in vivo. This is in contrast to the cells from Stem Cells Inc. which preferentially form oligodendrocytes.

The details of the clinical trial

Neuralstem's SCI trial will be a Phase I safety trial using their proprietary HSSCs (NSI-566) for chronic spinal cord injury (between 1 and 2 years after time of injury). As a Phase I trial their primary outcome is to determine the safety and toxicity of the HSSCs by measuring the incidence and severity of adverse events in transplanted individuals over a 60 month period. Precautions include enrolling people with thoracic level injuries (T2-T12 only) only, who have ASIA A (complete) levels of impairment. This trial is also excluding SCIs due to gun shot or stabbing wounds, individuals who are under 18, have other spinal disease, or those with complete spinal cord transection. Another important step employed in this trial is the dose escalation of HSSC cells. The trial will consist of 2 groups. Group A1 will consist of 4 patients receiving 3 bilateral injections (total of 6 injections) consisting of 100,000 cells/injection. After Group A1 is considered safe, Group A2 will consist of 4 patients receiving the same 6 injection sites as Group A1 but using 200,000 cells/injection. This will help determine the maximal dose of cells that can be safely transplanted.

Continued on page p.9 column 2

## StemCells, Inc.

## Neuralstem, Inc.

Stem Cells, Inc. continued from p. 8

future clinical phases. This trial is currently being conducted in Switzerland at the Balgrist University Hospital. It also has recently been approved for extension into the US and Canada.

[1] B. Cummings et.al.,(2005) in PNAS, Vol. 102 (39), pp. 14069-74.

[2] B. Cummings et.al., (2006) in Neurological Research, Vol. 28 (5), pp. 474-81.

[3] M. Hooshmand et. al., (2009) in PLoS One, Vol. 4 (6), pp. e5871.

[4] D. Salizar et. al., (2009) in PLoS One, Vol. 5 (8), pp. e122272.

[5] K. Piltti. al., (2013) in Stem Cells Translational Medicine, Vol. 2 (12), pp. 961-74.

Neural Stem, Inc. continued from p. 8

All patients in this trial will receive routine standard of care for surgery and will be put on a immunosuppressive regimen consisting of Basiliximab for 3 months. In addition to the assessment of safety, the secondary outcome of this clinical trial will be to evaluate the graft survival by MRI, as well as the ability of the HSSC cells to improve bowl and bladder function, pain and various motor and sensory scores. This information will be important for future clinical phases (phase II,III). This trial will begin in 2014 and will be conducted at the Shepard Center in Atlanta, GA.

[1] D. Cizkova et.al.,(2007) in Neuroscience, Vol. 147 (2), pp. 546-560.

[2] D. Usvald et.al., (2010) in Cell Transplantation, Vol. 19 (9), pp. 1103-1122.

[3] P. Lu et. al., (2012) in Cell, Vol. 150 (6), pp. 1264-1273.

As you will notice in both the Stem Cells Inc. and Neuralstem trials the approved Phase I clinical trials often do not exactly mirror the preclinical animal work. For example, the amount of cells transplanted in the Neuralstem clinical trial is larger than in the rodent studies. This is partially due to the differences encountered when crossing into larger species. The human spinal cord, and its anatomical structures like the gray matter, are much larger than in the rat. It would seem reasonable to assume that the human cord can take larger amounts of transplanted cells. However, preclinical data by Neuralstem's colleagues showed seemingly small increases in cell doses in the minipig (a much larger species) causing significant tissue disruption. Indeed, other studies have shown that although the larger species are anatomically larger, the distribution of specific cell types (like neurons and glial cells) may not be similar. This suggests that there may be a fine line between injecting the amount of cells that the spinal cord is capable of housing vs. the number of cells needed to be functionally incorporated.

Other differences between the preclinical animal work and the clinical trials exist and include the types of injuries studied, the number of injections performed and specific groups to exclude. More detailed information about why these differences exist will not be discussed in this issue.

We bring these differences up to emphasize the fact that preclinical animal studies, more often than not, will not be EXACTLY what will be translated into humans. We can't expect them to. Instead, preclinical animal studies simply provide us with information that will help design a plausible protocol, and/or it can inform us as to the overall capabilities of a new therapy.

## REHABILITATION CORNER

Continued from p. 4

'tender'. Pain that does not fall into cutaneous, musculoskeletal or visceral pain, like autonomic dysreflexia or headaches, can be referred to as other nociceptive pain.

Neuropathic pain is usually caused by a lesion or disease of the somatosensory system. SCI causes three types of neuropathic pain; at-level, below-level, and other neuropathic pain. At-level neuropathic pain is a result of a lesion to the spinal cord or nerve roots. It is perceived in a segmental pattern, unilaterally or bilaterally, in locations within the dermatome of the injury itself and up to 3 dermatomes below the injury. Below-level neuropathic pain is similar to at-level pain but it is perceived in locations more than 3 dermatomes below the level of injury. Both at-level and below-level neuropathic pain may involve either increases or decreases in the ability to feel touch or pressure within the area of neuropathic pain. Pain is described as 'hot-burning,' 'tingling,' 'pricking', 'pins and needles', 'sharp', 'shooting', 'squeezing', 'painful cold' and 'electric shock-like'. Although most SCI patients experience one type of neuropathic pain, it is possible to experience two separate and distinguishable pains, one at-level and another below-level. When this occurs, it is classified and documented as two separate pains.

Other neuropathic pain refers to pain that can be at the level of an injury or below but not pathologically related to the SCI. Some examples are pain associated with diabetic neuropathy, and pain due to “pinched nerves” in the back.

Treatment for pain:

As mentioned nociceptive pain is not abnormal and over the counter anti-inflammatory agents like ibuprofen are sufficient for pain reduction. Neuropathic pain is not as easy to treat and it can start as early as 1 month after an SCI. Before pharmacological agents are prescribed, physiatrists will first check for correct seating position, proper transferring techniques and correct application of assistive devices. If the pain persists, pharmacological agents may be prescribed. Some of the options for neuropathic pain are opioids, anti-epileptics, anti-spastics and others (more details on treatments will be in upcoming articles). Regardless of the pain type, it is important to see a physician as soon as the pain starts so that early diagnosis and treatment can be given. If not treated early, acute neuropathic pain can lead "wind-up" or plasticity changes in the CNS that lead to chronic neuropathic pain.

Footnote: The information provided here is a distilled version of a recent review article soon to be published in Critical Reviews in Physical and Rehabilitation Medicine.

## Reeve-Irvine Research Center

For questions regarding our educational and scientific programs or general information on the Reeve-Irvine Research Center, please contact:

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949-824-3993

### Interested in fundraising or making a donation?

Please contact:

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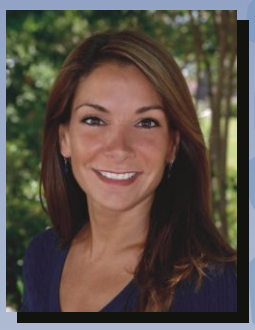
949-824-5925



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## Meet the Scientists, continued from cover.


Picture 1: Attendees at research presentation session.
Picture 2: Special guest Dr. Volkar Sonntag speaks during the research presentations.
Picture 3: Attendees interacting with companies at the "products area".


**RIRC is pleased to continue its sponsorship of tours for school children in Orange County. Here, Dr. Kelli Sharp introduces issues of spinal cord injury research to a group that is part of the home-schooled network.**

Dr. Sharp also organized the RIRC component of the summer program for high school students whose goal it is to become doctors (Summer Research program: School of Medicine at UCI). The students were exposed to both basic science and translational research with an emphasis on bench to bedside methodology. A goal of the RIRC is to continue to promote the scientific minds of our youth and community. If you, or a group, are interested in learning more about spinal cord injury research, contact Dr. Kelli Sharp by email at sci@uci.edu or phone (949) 824-5145.

# Ways to Give....

Since there are a variety of ways one can support the Reeve-Irvine Research Center at the University of California, Irvine, it's important you choose the options that are most appropriate for you. Planned giving enables a donor to arrange charitable contributions in ways that maximize his or her personal objectives while minimizing the after-tax cost. Listed below are just a few ways to send your gift to support the critical spinal cord injury research happening today and in years to come.

Should you have questions or if you would like to receive more information on giving, please contact

Tania Jope
(949) 824-5925 or tania.jope@uci.edu.

Those wishing to make a donation directly may send checks payable to the UCI Foundation/Reeve-Irvine to the address below:

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University of California, Irvine
2107 GNRF
Irvine, CA 92620-4292

Or donate on line by visiting our website at
www.reeve.uci.edu

## *Check out our website!*


We would like to say a special thanks to
Shad Davis a personal friend of Roman Reed
for donating his time to update our website!

*Thank you Shad!*

**www.reeve.uci.edu**

## New at the RIRC!

# Monthly Lab Tours

For more information
on touring the laboratories
and hearing more about our research programs
please contact

Kelli Sharp, DPT
sci@uci.edu or call (949) 824-5145

RIRC
Reeve-Irvine Research Center

## Study to understand trunk stability and control.

- Subjects with spinal cord injury will receive truck stability testing.
- The session will be held in Irvine on the UC Irvine campus.
- Participants will receive $10.00 for completing each session.

**3 session minimum. 10 session maximum.**

- If your SCI occurred at least 1 year ago you may be eligible.

*All personal information will be kept confidential.*

If interested, contact Kelli Sharp, DPT
sci@uci.edu or call (949) 824-5145