New Hope for Reversing the Effects of Spinal Cord Injury, a Successful Study by NJ Researcher.

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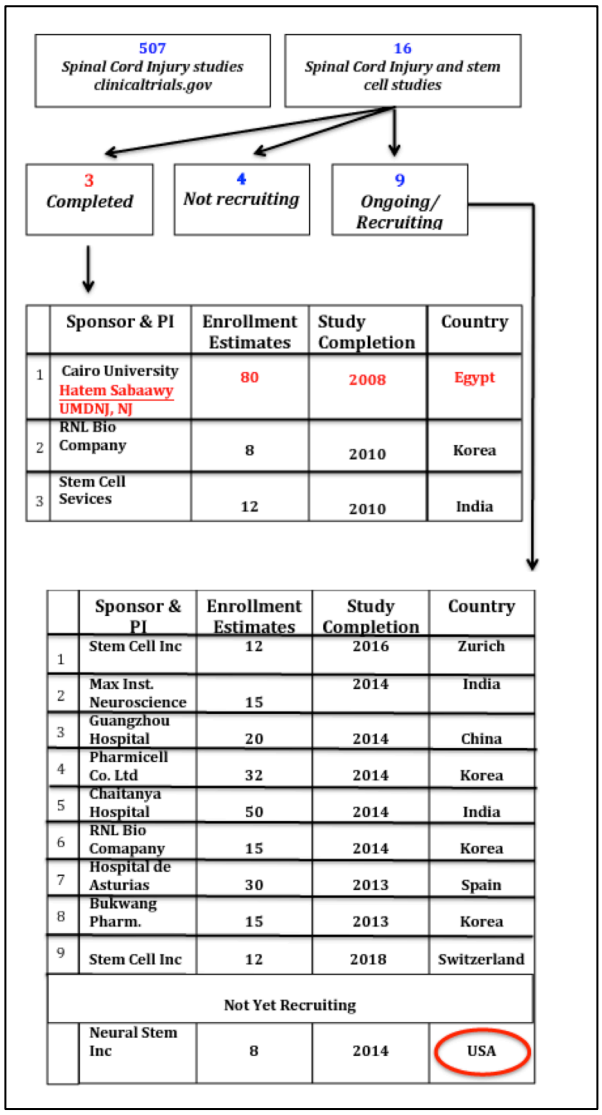
Spinal Cord Injury (SCI) is a devastating ailment that results in drastic life style Changes. At one time considered irreversible, impressive research endeavors using stem cell treatments have ushered in an era of new hope. We now stand at a historic threshold, observing these studies as they translate into therapies for patients with SCI. A testimonial to the trend is the huge surge in clinical trials attempting to define treatment using stem cells for SCI, as depicted in the table on the right (Clinicaltrial.gov)

Unfortunately, none of these studies have been conducted in US. This is not due to the lack of research expertise or knowledge, but rather due to public misconceptions that drive a non-supportive stance of regulatory agencies. To date, only one study (not yet recruiting patients), has been approved to conduct clinical trials in US. So despite having a plethora of basic research to support initiation of these studies, leaders in stem cell research at US institutions cannot translate their research into applied cures. Consequently, they have to explore options available in other countries despite prohibitive costs

In an attempt to address the challenges faced by US based stem cell researchers, I spoke with Dr. Hatem Sabaawy, MD, PhD, lead investigator of the largest, oldest and most successful phase I & II clinical trial listed on clinicaltrial.gov for stem cell treatment for SCI.

Dr. Hatem Sabaawy, M.D., Ph.D.
Assistant professor of medicine at UMDNJ-Robert Wood Johnson Medical School and the Cancer Institute of New Jersey,
Founder of Celvive Inc.



	Sponsor & PI	Enrollment Estimates	Study Completion	Country
1	Cairo University Hatem Sabaawy UMDNJ, NJ	80	2008	Egypt
2	RNL Bio Company	8	2010	Korea
3	Stem Cell Sevices	12	2010	India

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1	Stem Cell Inc	12	2016	Zurich
2	Max Inst. Neuroscience	15	2014	India
3	Guangzhou Hospital	20	2014	China
4	Pharmicell Co. Ltd	32	2014	Korea
5	Chaitanya Hospital	50	2014	India
6	RNL Bio Comapany	15	2014	Korea
7	Hospital de Asturias	30	2013	Spain
8	Bukwang Pharm.	15	2013	Korea
9	Stem Cell Inc	12	2018	Switzerland
	Not Yet Recruiting			
	Neural Stem Inc	8	2014	USA

Q: Congratulation for the completion of a successful study. Can you summarize the highlights of the study recently published in *Cell Transplantation*?

Our phase I/II clinical trial study was conducted on 70 patients with chronic SCI, previously not responding to physiotherapy treatment for at least 6 months. While the control group received only physical therapy treatment, the test group of patients was given physical therapy along with stem cells (derived from their own bone marrow, ABMCs) via intrathecal injections near the injury site. Using the American Spinal Injury Association Impairment Scale (AIS), patients received neurological and physical evaluations monthly for 18 months to determine if sensory and motor functions were improved. While

none of the control patients showed any significant improvement more than 1-2 points, patients in the test group responded to tactile and sensory stimuli as early as 4 weeks into the study. At 12 weeks, they experienced improvements in sensation and muscle strength, which was associated with enhanced potency and improved bladder and bowel control that eventually allowed patients to live catheter-free. Patients who showed improvement based on the AIS were also able to sit up and turn in their beds. At the end of 18 months, 23 of the 50 test patients showed a significant improvement of at least 10 points on the AIS motor score with significant sensory and functional improvements, and several patients were able to walk with assistance. Most importantly, there were no side effects in patients treated with stem cells during the course of our investigation.

Q: Do you think treatment of spinal cord injuries is currently possible?

Although not a complete cure, adult patient-derived bone marrow cells (ABMCs) can currently be offered as a treatment option for patients with SCI. Our study along with numerous other reports show the beneficial effects of bone marrow derived stem cells. It is clear that the regenerative and secretory properties of bone-marrow derived stem cells can improve symptoms of paralysis in some patients when coupled with the current standard of care that physical therapy provides. However, more studies are needed with a larger number of patients to test different cell dose levels and intervals at which stem cell therapy should be delivered.

Q: You have utilized adult patient-derived bone marrow in your studies. What is your opinion on utilizing embryonic stem cells and induced pluripotent stem cells (iPSCs) for treatments?

Rigorous research endeavors over the past few decades have identified protocols for efficient use of autologous bone marrow derived stem cells for treatments. Extensive experience with autologous bone marrow transplantation is available in most hospitals. Numerous studies have shown the beneficial effect of using BM cells for injury repair and I personally favor the use of these cells for treatment regimens since they are much better studied. However, at the same time, I also strongly support research utilizing embryonic stem cells as well as induced cells. Being relatively new technologies, iPSCs and iNs need to be better characterized before they can be ready for human testing. I think we are at least 5-10 years away from having a product ready for large-scale human trials in this category. ABMCs are currently available treatment option with no side effects while safety issues using embryonic stem cells and iPSCs are still in exploratory phase.

Q: Many establishments promise miraculous cures for spinal cord injuries. What is your opinion about public education for patients approaching institutions for possible cures?

Unfortunately, unwary patients are exploited in establishments that offer cell therapies with no clear cut clinical data to support the outcome and without really understanding the mechanisms involved. This results in:

a) Hype of high, unrealistic expectations in patients.
b) Bad publicity for the good research and regulated trials being conducted by responsible experts in the field.
c) Stem cell tourism that resulted in many disappointed patients.

I strongly advocate public education enabling a systematic patient approach to clinical trial and treatment options. It is of utmost importance to help patients understand in advance by proper review of publications and data supporting the treatment. It is also important to educate them by reviewing internationally acceptable regulations for the conduct of the clinical trial in which they plan to participate. Additionally, there should be international regulations implemented on the participation of patients in clinical trials and therapies in countries other than their home country, and all therapies should only be offered under protocols approved by local regulatory authorities and following international standards.

Q: Has it been easy to follow up with the regulatory agencies in US regarding the promising results of the study?

Since the publication of our study, I have been contacted by numerous patients and their physicians to explore the possibility of being included in the trial. A safe treatment protocol for improving the quality of life for individuals with SCI has already been established by the study. Yet, we are not in a position to offer the treatment to patients here in the US until a long-term safety follow up study for patients treated in phase I is

completed and the treatment is investigated in a larger number of patients in phase II dose escalation studies in multicenter trials. I would say that the initial response from the FDA has been very encouraging. However, it is extremely important for FDA and other global regulatory agencies to look beyond political ramifications and expedite monitored, regulated clinical trials in USA.

Q: Does an academic environment support this kind of innovative research?

Being part of a thriving research environment offers numerous advantages for staying ahead in cutting edge research. However, large-scale commercialization of new treatments is extremely difficult due to monetary limitations. Having established the foundation in academia, I expedited the process by founding Celvive Inc. Under this framework, I hope to accelerate the availability of treatments for patients within USA. I also hope to work with FDA to get approval for multi-center clinical trials in collaboration with other investigators in the field.

Q: Do you think there is a requirement to harmonize clinical trials and treatments for spinal cord injuries using stem cells internationally?

Despite the tremendous increase in research study numbers in this field all over the world, there is no co-ordination between different study protocols. For example, many investigators use BMSCs for treatment, but there is no standardized protocol for their collection, storage, expansion or injection. This often creates discrepancies in results. There is therefore an urgent requirement to synchronize studies being conducted worldwide. This effort to standardize cell therapies for spinal cord injury was pioneered by Dr. Michael Fehlings, a Toronto-based neurosurgeon, and world expert on spinal cord injury repair and cell therapy. Joining hands with fellow investigators and clinicians from around the globe, we have started a Stem Cell Global Blueprint conference (GBC) to exchange knowledge and define criteria for cell therapies, and to have a unified approach towards the next phase of clinical trials. Besides establishing designs for next set of trials, we also want to ensure better education of the public in context to stem cell therapy.

Spinal cord research and New Jersey Commission on Spinal Cord Research (NJCSCR).

- New jersey is one of the very few states to have a specifically designated commission to support spinal cord injury research projects.
- The New Jersey Commission on Spinal Cord Research (NJCSCR) was established in 1999.
- The NJCSCR is one of only nine publically funded organizations nationally that together with National Institute of Health, the Centers for Disease Control and few other entities, provide the essential support for the research needed to find solutions for this devastating injury.
- Since 2001, NJCSCR has awarded over $33.6 million to individual scientists in the state.
- NJCSCR also supports a central registry of spinal cord injured people in NJ.
- The work of NJCSCR is supported entirely by a statutory one-dollar surcharge on all traffic and motor vehicle fines. Revenue collected by State Treasurer is deposited into NJCSCR Fund. No part of the operating budget is funded by general tax revenue.

Q: What are your plans for the future?

There is still a lot of follow up work required to define mechanisms of the beneficial effects. We need a better profiling of phenotypic markers involved in the regenerative process. One immediate requirement is the development of a universal system to isolate ABMCs in a closed environment that can subsequently be processed under identical conditions for studies all over the world. This will ensure utilization of identical cells in studies worldwide instead of stem cells that have been exposed to extremely variable conditions.

Conclusion for NJ residents.

This is an exciting phase in the field of SCI treatment. NJ is fortunate to have accomplished researchers as well as the financial support of organizations like NJCSCR. A concerted effort is now required to progress to the next phase of offering treatments for SCI that are safe, effective and harmonized all over the world. If the US expects to stay at par with the rest of the world in this field, there is an immediate requirement for correct public education along with appropriate policy modification that are in sync with the rapid changes happening in the rest of the world.