International Society for Stem Cell Application

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- Greetings from Chairman
- Recent Trend of Stem Cell Treatment, Dr. Daeyong Kim, Founding President / CEO of N-BIOTEK Inc.
- Hello, Chapter Directors!
- Upcoming Events of ISSCA in 2018
- ISSCA Sponsors

Contents

Greetings!

It is the time of the low fertility, aging, and anti-aging/well-being now days.
In the past, it has been the age of disease treatment with conventional medicine, but now with increased lifespan we are pursuing the quality of life with regenerative medicine.
It is the age to judge the quality of life.
According to increasing the lifespan, also there are many troubles with incurable disease and cancers. Although the endless efforts of mankind have brought many improvements in the treatment of diseases, the solution is still limited by the treatment method.
“Stem Cell Therapy”, called Regenerative Medicine, is the most interesting part in the medical fields in the 21st century because stem cell therapy can be the best solution not only for the incurable disease but for anti-aging. Moreover, it is expected as the supreme bio drugs to develop bio industry with many areas like clinical trials and cosmetics. Through all that, I am expecting that ISSCA can be the excellent role model in of stem cell application parts to contribute the development of regenerative medicine through co-researches and international exchanges in the world.
Congratulations on issuing the first ISSCA magazine!

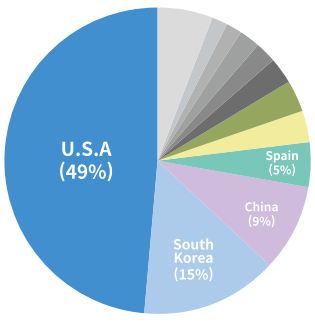
CHAIRMAN Sung Duck Choi M.D

Recent Trend of Stem Cell Treatment

1. Recent Trend of Stem Cell Clinical Trial

Based on the different mechanism from conventional medicine, stem cell-based medicine presents possibility of treatment in areas that could not be solved by conventional medical treatment. Competition to develop stem cell-based medicine is fierce in the international community because of an expectation that it can offer patients with intractable diseases whose life is at risk or whose quality of life is significantly lowered with a new possibility for treatment and thereby creating high added value. A total of seven stem cell-based medicine including four approved in Korea has been approved for sales internationally followed by a conditional approval system introduced in Japan in 2016 which approved two items to be sold in the market as a 'new renewable medical product.' Therefore, understanding international R&D and policy trends is not only important for developing strategies for developers, but also provides a basis for establishing support and regulatory direction at a national level.

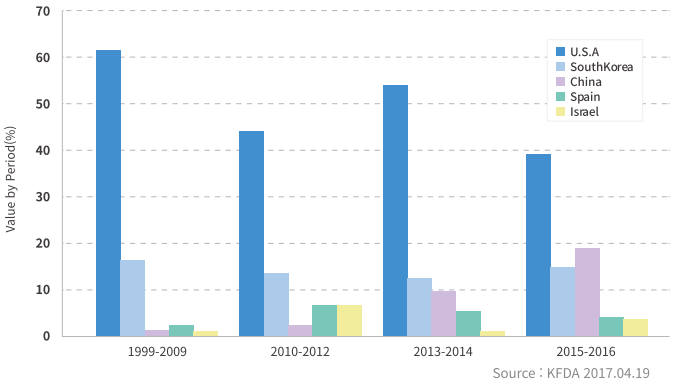
Since the first company-initiated clinical trials began in 1999, as of December 31, 2016, a total of 314 commercial trials, including 47 clinical trials newly registered in 2016, are either completed, in progress, or scheduled to be performed. While clinical trials for commercial purposes reached its peak in 2011, there has been a slight slowdown from 2012 to 2013. However, in 2014 and 2015, 45 and 51 trials were registered respectively followed by 47 new trials in 2016. That is, commercial clinical trials are on the steady rise. Of the total 314 clinical trials performed between 1999 and 2016, Korea registered 46 cases recording the second largest number of clinical trials in the world after the United States that enrolled 155 clinical trials. (Figure 1) In 2016, the United States enrolled 23 new clinical trials while China enrolled eight and Korea enrolled five. Taiwan, followed by the United States, Korea, and China, made a meteoric rise registering three new clinical trials and Spain and Israel have also added two clinical trials, maintaining the status of the world's fourth and fifth largest country in terms of the number of commercial clinical trials. The period of clinical development from 1999 to 2016 was divided into four periods, and the change in the share of the top four clinical trial development countries in each period was analyzed (Figure 2). The United States accounted for 60% of the entire clinical trials in the early stage of clinical research; the proportion of newly registered clinical trials in the last two years has fallen to 40%. Korea has steadily been increasing its clinical research since 2007, leading to a 15% or so proportion throughout the entire period. China has started commercial clinical trials since 2009 and as a results, its ratio of newly registered clinical trials in the past two years has exceeded Korea by about 20%. Clinical trials of Spain and Israel experienced a sharp increase between 2010 and 2012 and have steadily added the number of clinical trials every year, recording 5% of clinical trials approximately. While the United States was in absolute advantage at the beginning of commercial clinical development, its share of clinical trials has decreased by half compared to the initial stage due to a steady increase in Korea, China, and other countries.



Country	Number of cases
U.S.A	155
South Korea	46
China	29
Spain	15
Israel	11
Germany	10
India	9
U.K	7
Belgium	7
Taiwan	6
Canada	
etc.	19

Source : KFDA 2017.04.19

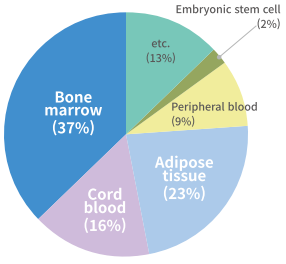
(Figure 1) Clinical Research Status by Country



Source : KFDA 2017.04.19

(Figure 2) Change in the Share of Clinical Trials by Period

Stem cell-derived tissues were divided into marrow, fatty tissue, and cord blood to analyze the status of clinical trials (Figure 3).During the entire analysis, marrow-derived stem cells accounted for the highest percentage of 37%, followed by fatty tissue and cord blood by 23% and 16% respectively. When it comes to stem cell-derived tissues, 13% of them were not classified according to the conventional classification methods and there have been a significant number of cases that directly harvested stem cells from a tissue including placenta, spinal cord, and cephalin derived from an aborted fetus. While marrow has been used as a major source of cellular material in the early clinical trial development stages along with peripheral blood, its proportion has decreased since 2010 when clinical trials began in earnest. The number of stem cells derived from marrow has increased to 55% between 2010 and 2012 during the middle of the period, but has decreased to 20% to 30% for the last four years since 2013. Fatty tissue and cord blood have been steadily increasing since the mid-term of clinical trial development stages; especially, the use of fatty tissues and cord blood during the last two years has increased to 35% and 19%, respectively. Clinical trials using embryonic stem cells showed four cases between 2010 and 2012 and two cases in 2015, showing a somewhat stagnant status of clinical trials using embryonic stem cell. The results of this analysis suggest that fatty tissue and cord blood have widely been used as a source for obtaining stem cells, considering the ease of obtaining source materials and efficiency of isolating stem cells.



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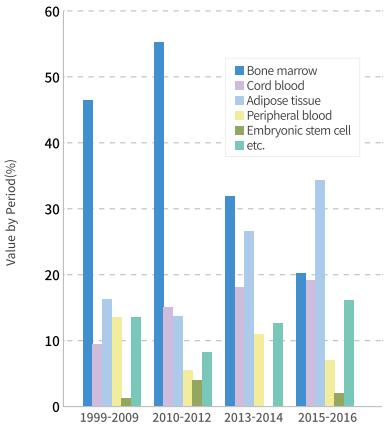
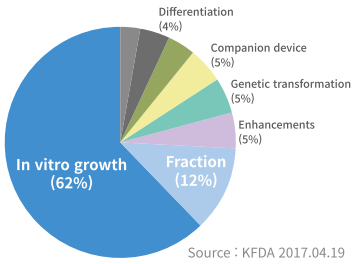


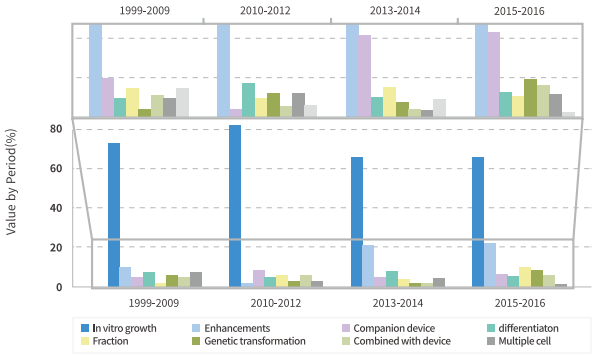
(Figure 3) Clinical Development Status by the Cell-Originated Tissues

We analyzed the status of clinical trials depending on the type of in vitro operation (Figure 4 and 5). After analyzing them throughout the whole period, in vitro proliferation and isolation were the most common in 71% of all clinical trials, followed by fractionation of 14%. When analyzed periodically (Figure 5), the clinical trials of cells undergoing in vitro proliferation and separation were slightly decreased in the last four years. This decline in the rate of in vitro proliferation and segregation may be attributed to the rapid increase in the number of clinical studies using fractionated cells to 20% over the same period. This may be related to the outburst in the clinical use of SVF obtained from fractionation in the last four years. There has not been a significant trend observed in regards to the proportion of clinical trials involved in manipulation, differentiation induction, and genetic modification for functional enhancement whereas clinical trials on stem cells that are administered as complexes with support and on companion devices to obtain fraction regarded as stem cells or for special culture are continue to grow.



Source : KFDA 2017.04.19

(Figure 4) Status of Clinical Research and Development by the Type of In Vitro Operation



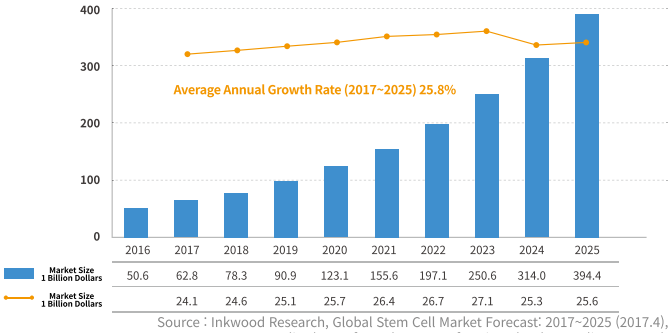
(Figure 5) Status of Clinical Research and Development by Periodical and the Type of In Vitro Operation

2. R&D Trends on Clinical Indications

The indications on which the most number of clinical trials have been conducted are neurological and musculoskeletal diseases, which have dethroned heart disease in the number one position until 2015 in terms of clinical trials to third. Analysis of 47 clinical trials in 2016 showed that commercial clinical trial development for the nervous system, respiratory, musculoskeletal, and immune system diseases increased significantly whereas clinical trials on heart disease and gastrointestinal diseases, which dominated in the early clinical trial development stages, have added one and two clinical trial (s), respectively. Although heart disease was hit by nervous system diseases and musculoskeletal diseases in the total number of clinical cases, it was the most advanced indications since they had the highest clinical rate in the final stages; the number of clinical trials performed on neurological diseases was high, the number of clinical trials in the final stages was low as an earnest onset of clinical trials has started relatively late compared to heart diseases. As a result of analyzing the status of indications development by country, the U.S. showed high clinical share in heart diseases, neurological diseases and musculoskeletal diseases. Korea showed significant clinical and relative superiority in nervous system, musculoskeletal system and skin diseases compared to other countries. China has the lowest diversity of diseases among countries and showed a relative strength in the nervous system, musculoskeletal system and respiratory diseases. In addition, as the developer of Holoclar, the first EMA-approved product, Spain recorded a high percentage of musculoskeletal disorders, including eye diseases; Israel has a relative advantage in malignant diseases.

3. Global Market Prospect of Stem Cells

According to the 'Global Stem Cell Prospect 2015-2025' published in the latest issue of Bioindustry, the stem cell market in Korea is estimated to be $ 1.1 billion in 2016 and is expected to grow to an annual average of 26.67% by 2025 to reach $ 9.5 billion.



	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
Market Size 1 Billion Dollars	50.6	62.8	78.3	90.9	123.1	155.6	197.1	250.6	314.0	394.4
Market Size 1 Billion Dollars		24.1	24.6	25.1	25.7	26.4	26.7	27.1	25.3	25.6

Source : Inkwood Research, Global Stem Cell Market Forecast: 2017~2025 (2017.4), Edited Date from the Center for Biotechnology Policy Research

The Status and Outlook of the Global Stem Cell Market (2016-2025)

North America, which accounts for about one-third of the stem cell market in 2016, is expected to continue to grow, mainly due to an increase in cancer patients. The U.S. stem cell market is the largest in terms of market share with $ 13.8 billion in 2016 and will grow to an annual average of 26.45% over the forecast period of 2017-2025 and will expand to $ 112.4 billion by 2015. As the number of patients with chronic diseases such as cancer continues to increase in the United States, studies on stem cell research and therapeutic drug development are active and related. That is, investments are on the rise.

In Europe, companies involved in the stem cell market are actively making investment, and the increase in cancer and cardiovascular diseases is a major factor in market growth, similar to North America. The U.K. stem cell market is worth $ 2.7 billion in 2016, accounting for the largest portion of the European market, and is expected to grow at an annual average of 24.31% by 2025 to $ 19 billion. The U.K. is renowned for its government-run, world-class National Health System (NHS) and a variety of private medical centers that provide up-to-date health management services. With rise in investment in stem cell research in step with increased chronic diseases, stem cell-related markets in the U.K. are expected to grow. The stem cell market in France has grown to $ 2.6 billion in 2016 and is projected to grow to an annual average of 24.61% by 2025, to $ 18.9 billion. Korea is expected to grow at an annual average of 26% until 2025 in the stem cell market. The growth of the Asian stem cell market is expected to be the fastest in the world due to the economic development and income improvement in developing countries in Asia and the increase in investment in medical tourism and medical treatment due to low cost of treatment. In particular, clinical cases of stem cells will likely increase sharply if stem cell regulation is relaxed as Korea has been experiencing a steady increase in the number of those who who experienced stem cell treatments applying cultured adipose derived stem cells since 2017.

Deayong Kim, Ph.D.

Founding President of ISSCA

Hello, Chapter Directors!

Benefits of STEM Cells and PRP in Hair Restorations

In last few years, PRP hair restoration is on the rise and people have different opinion and response about the outcome of this therapy. However in recent times with the addon of STEM Cells along with PRP therapy, more positive response is being noticed.

In my hair transplant and hair restoration practice, I have noticed that use of good quality PRP and adipose tissue derived mesenchymal STEM Cells produce excellent results in majority of my patients. Initially patients notice decrease hair loss along with healthier hairs and finally in 6 to 9 months new hair growth is noticeable. There have been many published research articles showing the benefits of STEM Cells in the treatment of alopecia.

I have been using both PRP and adipose tissue derived STEM Cells for few years along with mesotherapy. In my practice, I have developed Triple Therapy® protocol which is a 14 weeks course which is initiated with adipose tissue derived mesenchymal STEM Cells followed by PRP and mesotherapy. This protocol is extremely beneficial for patients who have poor donor area and despite hair transplant they are still hoping to get some fullness and want to slow down their ongoing hair loss.

Beside the use of mesenchymal STEM Cells, there has been some articles about the new research which is being conducted at University of Southern California STEM Cell Laboratory by a postdoctoral researcher Mingxing Lei and his team who are treating patients with alopecia with the use of organoids, which are clusters of STEM Cells grown in vitro that can self organized into an organ like structure. This study shows six step process of hair growth where progenitor cells were used in the first step which soon aggregated in step two, then these aggregated progenitor cells turned into polarized cysts in step three which then transformed into so called coalesced cysts in step four followed by formation of planar skin in step five which were formed into follicles in step six. These follicles were implanted into a mouse which produced hair. See more detailed about this on the article by Ana Sandoiu published on August 14th, 2017.

Junaid Syed, M.D., F.A.C.P.
Medical Director of Orlando Hair Clinic
ISSCA (International Society of STEM Cell Application) Chapter Director of USA

Junaid Syed, M.D., F.A.C.P.
Medical Director of Orlando Hair Clinic
ISSCA (International Society of STEM Cell Application) Chapter Director of USA

Junaid Syed, M.D.

Orlando Hair Clinic
New U Med Spa
Hormone Replacement Therapy Orlando
Instant Medical Care

7300 Sandlake Commons Blvd
Suite 227
Orlando, Florida 32819

OHC: 888-430-6115
NUMS: 888-689-3070
HRTO: 888-430-6293
IMC: 888-846-2551

FAX: 407-809-5243
Cell: 407-734-2950
E-Mail: drjunaidsyed@gmail.com

www.OrlandoHairClinic.com
www.NewUMedSpaOrlando.com
www.HRTOrlando.com
www.InstantMedicalCare.com

Junaid Syed, M.D.

Chapter Director in U.S.A

Thank you for allowing me to introduce myself, theinstitution and to be a part of such a great organization, International Society for Stem Cell Application (ISSCA). I finished my education in the USA and currently hold board certification in Neurology and Psychiatry, Pain Management, Interventional Pain, Sleep Medicine, Clinical Neurophysiology, and Internal Medicine. I finished my education and training in 2005. I am currently a fellow of the American College of Physicians (F.A.C.P.), a fellow of the Interventional Pain Physicians (F.I.P.P.); granted by the World Institute of Pain, a Fellow of the American Academy of Neurology (F.A.A.N.) and a Certified Principal Investigator (C.P.I).

In 2007, I established The NeuroMedical Institute in Panama City, Florida. The Institute was built with the mission to provide state-of-the-art evidence-based-medicine, multidisciplinary diagnostic and therapeutic services for neurologic, sleep and pain disorders with compassion and respect under one roof. The Institute houses five centers within it; The NeuroPain Center, The NeuroImaging Center, The NeuroSleep Center, The NeuroRehab Center, and The ElectroDiagnostic Center. In addition, we established three sister companies in 2012; iNaturally, The American Research Center and DME USA. All five centers and the sister companies work in harmony to provide patients with a holistic approach to pain, sleep and neurological disorders withwellness and aesthetics under one roof.

iNaturallyis becoming the focus of our practice. It is a wellness center that focuses on the well-being of a person to include nutrition,weight loss, vitamins, supplements, and aesthetics. DME USA is a fully equipped center providing our patients, nationally and internationally, with DMEand medical supplies. The American Research Center participates in major clinical trials with major pharmaceutical companies. Theycollect data from our patients in the regenerative medicine department and also house sleep laboratories for sleep-related clinical research.
What sets our centers apart from others is the innovative technologies and unique tools and techniques we use to diagnose and treat our patients. Patients can receive conventional therapies or participate inresearch-based therapies. Our research center was one of the national centers participating in a major pharmaceutically-funded clinical trial of stem cell therapy for stroke patients with motor deficits. Adult bone-marrow-derived stem cells that have been transiently transfected with a plasmid construct encoding the intracellular domain of human Notch-1 were injected into the brain-strokedarea. The trail had positive results and many patients benefited.Since our centers treat patients with neurologic, sleep and pain disorders, we have a huge patient data base with those disorders, which can be treated with cell therapy.

In 2014, we established a multi-specialty center in Palestine, diagnostically and therapeutically, with the main focus on regenerative medicine. It has become a huge success in a very short time. We have brought to the country new technologies and therapies that never existed in this part of the world before. In 2017, we established three centers in Israel with huge success. Currently we are considering expanding in Jordan, Turkey and the Gulf region.

I hope that through the ISSCA,we as an organization with its leadership and members,can put our minds and hearts together to bring the field of cell therapy into main stream medicine by contributing with clinical research andsupportive evidence.We want to extend these innovative therapies to as many patients worldwide as possible. I hope to open the dialoguebetween members and leaders of the society to learn from each other's experiencesand share our wealth of knowledge. The experience of many scientists and physicians together is far better than each individually.

Mustafa Hammad, M.D

Chapter Director in U.S.A

EFFECTS OF MESENQUIMAL STEM CELLS ON RHEUMATOID ARTHRITIS

Rheumatoid arthritis (RA) is the most frequent cause of autoimmune arthritis. It has an incidence of 0.3 to 1.2% of the world population. Annually, between 5 and 50 per 100,000 new adults are reported. It affects more women than men and its appearance coincides with the most economically productive stage, this being a very important situation to take into account because RA results in a chronic degenerative disabling disease in many cases.

In order to help diagnosis and not confuse RA with other diseases that can cause arthritis or inflammation of the joints, a list has been proposed and accepted with a series of criteria in which a series of parameters related to the symptoms, the laboratory data and the radiological images.

The classification criteria for RA are considered seven parameters, although to confirm the diagnosis of RA it is enough for a patient to collect four of them:

1. Morning stiffness lasting more than an hour for more than six weeks.
2. Arthritis in at least three joint areas, with evident swelling and joint effusion, for more than six weeks.
3. Arthritis in the joints of the hands (wrist, bases of the fingers and / or base of the second phalanx) for more than six weeks.
4. Symmetric joint inflammatory inflammation for more than six weeks.
5. Presence of rheumatoid nodules (subcutaneous).
6. Presence of radiological changes typical of RA (such as erosions or osteoporosis in the wrists).
7. Positive rheumatoid factor.

The immune response in AR

Rheumatoid arthritis is an autoimmune disease that arises when the patient's defenses attack the body itself. In the case of rheumatoid arthritis, many types of cells and chemicals of the immune system are involved, which participate in the inflammatory process that occurs in the joint lining or synovial membrane.

The inflammatory process or cascade begins when an antigen - a substance capable of triggering an immune response - comes in contact with the T lymphocyte, one of the main cells of the immune system. The antigen and the T lymphocyte come into contact thanks to a cell called the antigen presenting cell.

The antigen presenting cell communicates with the T lymphocyte through two signals. The first of these allows the cell of the immune system to recognize the antigen, while the second, called the costimulation signal, causes the complete activation of the T lymphocyte.

Upon activation, the T lymphocytes multiply and release chemicals that in turn activate other cells of the immune system. Finally, this process stimulates the release of substances that attack the joints, causing inflammation and destroying them.

In CD4 T lymphocytes (LT) two types of collaborative responses (Th) have been identified: Th1 (cellular or delayed immunity) and Th2 (humoral immunity). The Th1 participate in the elimination of intracellular pathogens and the Th2 in the elimination of extracellular microorganisms.

T-lymphocytes are activated by the presentation of self-antigens and costimulatory signals by antigen-presenting cells (APCs) through the HLA class II; Th1 are the secreting lymphocytes of interferon gamma (IFN-g) and interleukin 2 (IL-2), and Th2 are the lymphocytes that release cytokines IL-4, IL-10 and IL-13, mentioning that in the activation of T cells, in addition to the Th1 differentiation promoted by IL-12 and Th2 by IL-4 [, there is a subgroup of CD4 + T lymphocytes called Th17 promoted by the transforming growth factor b (TGF-b) and IL-6, which secrete IL-17 and that coordinate the immune response in a different way than Th1 or Th2, in turn, Th also stimulate B lymphocytes (LB) to produce autoantibodies. The Th17 are associated with chronic inflammatory and autoimmune processes promoted primarily by the proinflammatory effect of IL-17 and are the IL-23 that induce its proliferation. IL-17 has been implicated in the development of various autoimmune diseases, among which RA stands out, since it has been found that IL-17 expression is elevated in affected areas. In AR, IL-17, in addition to enhancing the activity of IL-1 and TNF-alpha (tumor necrosis factor alpha), stimulates the differentiation of osteoclasts and promotes the destruction of cartilage and bone. TNF-alpha also participates in the activation of neutrophils, LT, stimulates the production of cytokines and co-stimulates the production of antibodies by LB. Another proinflammatory cytokine is interleukin 6 (IL-6). IL-6 was identified as a factor produced by LT and, like IL-1, contributes to the development of osteoporosis and joint destruction in RA through the proliferation of synovial fibroblasts and differentiation of osteoclasts Previously it was believed that LB played a collateral role in the pathogenesis of RA. However, it is important to point out that its participation involves various mechanisms including the production of autoantibodies, the activation of LT and the secretion of soluble proinflammatory factors and effectors such as IL-6, IL-10, TNF-a, etc. Mesenchymal stem cells, obtaining and properties Mesenchymal stem cells are multipotent cells, with fibroblastoid morphology, originated in embryonic mesoderm and which has the potentiality to differentiate into osteocytes, chondrocytes, adipocytes and fibroblasts. Because of their easy obtaining, trophic and immunomodulatory capacity, MSCs they are a very appreciated resource in regenerative medicine. Obtaining Form: There are several protocols for obtaining and processing mesenchymal stem cells. In our particular case we use fresh techniques with minimal manipulation, for which the patient is subjected to a mini liposuction of 60 cc of pure fat which is processed by enzymatic digestion with collagenase at 37° and then centrifuged for separation by decantation. The so-called SVF stromal vascular fraction will be reintegrated into the patient. Trophic capacity: As previously stated, MSCs have the ability to differentiate into cell lines of the same mesodermal layer, however recent studies have shown their ability to generate cells from the ectoderm. and endoderm (transdifferentiation) in vitro. Some researchers think that it is due to the stress to which the cells are subjected or to the presence of certain factors in the culture medium. On the other hand, these cells release a set of bioactive substances through exosomes into the medium, these substances have the purpose of stimulating angiogenesis , inhibit apoptosis, inhibit fibrosis, immunodular, and favor the migration of different cells to the site of injury. Immunomodulatory properties many times mesenchymal cells require activation by IFN gamma for the release of immunomodulatory substances.

Some of these substances are :

IDO	- Catalyzes the degradation of tryptophan
	- Inhibits the proliferation of T cells
Prostaglandin E2	- Inhibits the mitogenesis of T cells and the synthesis of IL-2
	- Stimulates the production of IL-10 in macrophages
	- Blocks the differentiation of immature dendritic cells (DC) to mature
IL-6	- Inhibits the differentiation of monocytes to CD, decreasing their ability to stimulate T Cells
	- Delays the apoptosis of lymphocytes and neutrophils HLA-G5
	- Suppresses the proliferation of T cells - Decreases the cytotoxicity of NK and LT
	- Promotes the production of T-reg

CONCLUSION

Undoubtedly mesenchymal cells play a fundamental role in the treatment of rheumatoid arthritis, due to their immunomodulatory capacity can help to reduce the direct attack by the immune system to different tissues and their ability to differentiate into different tissues and by create a suitable medium for the regeneration of tissues, at the local level an improvement of the joint tissue and less permanent damage is observed. Therefore, we recommend the intravenous infusion of mesenchymal cells associated with infiltrations of large joints. The question we ask ourselves is how long is this immunomodulation, in my personal experience, no more than 4 months when we use the stromal vascular fraction -SVF-. These patients are the so-called "multidose patients", due to the need to permanently perform SVF infusion, in our experience patients never abandon the traditional immunomodulatory treatment such as metrotexate, biological medication - etanercept, adalimumab, abatacept etc- No place to doubts, in countries where the regulations allow the cultivation, cell expansion and cellular reintegration to the patient, the treatment is less complex for the patient since he would undergo a single extraction of adipose tissue and presumably the immunomodulation time should be higher secondary to a greater cellular population obtained through cell culture and expansion. However, in countries where reimbursement is not allowed after culture and cell expansion, treatments with mesenchymal cells derived from adipose tissue is an excellent alternative to treatment, allowing to enter remission of disease, recovering damaged tissue and avoiding permanent deformations, always remembering to maintain to the immunomodulated patient through traditional measurement for rheumatoid arthritis and using new infusions and infiltrations of mesenchymal cells when the patient is again in an outbreak

Pastrana Lopez Silvina MD

Medical Director

Stem Cell Center Buenos Aires Argentina

Regentherapy s.a

Silvina Pastrana, M.D.

Chapter Director in Argentina

Mesenchymal Stem Cells Heal a Large Foot Ulcer Resulting From a 30,000 Volt Electrocution

Abstract:

Juan,a 45 year-old electrician,suffered a 30,000 volt shock when his left arm contacted a high tension power line. The current travelled down the back of his left leg and exited via a 12cmx10cm wound on the dorsal aspect of his left foot leaving the underlying structures exposed. He subsequently fell from the platform and spent 2 months inthe hospital.

Three months after his injury, Juan's foot ulcer had not closed and he opted to undergo an autologous StromalVascular Fraction stem cell procedure.. Four weeks after the first procedure, the ulcer showed significant (70%) closure with clear new growth visible circumferentially around the ulcer. An activated PRP Procedure was then performed to further stimulate the cell division. Two weeks later, Juan was walking in shoes and underwent a final stem cell procedure.

Over a period of 5 weeks, the ulcer closed and the patient attained a new lease on life, recovering the ability to look after himself, and perform his daily activities. It is expected that he will return to work shortly

Introduction:

History of Present Illness: 45 y/o electrician sustaining a 35,000 volt shock and subsequent fall from a platform on 9/3/17, requiring 2 months of hospitalization. The exit wound left a 10cmx7cm ulcer on the dorsal aspect of his left foot with underlying structures exposed. On December 12, 2017, the patient was evaluated for stem cell therapy. At the first evaluation the wound exhibited only minimal closure leaving the patient in danger of gangrenous necrosis.

Physical Exam: On exam there is a 12cmx10cm ulcer on the dorsal aspect of his left foot and significant scarring on the posterior of his left thigh. He is unable toplace any weight on the affected foot and walks with a crutch. He expresses significant concern about his future.

Treatment Plan: Stromal Vascular Fraction (SVF) autologous stem cell transplantation with activated Platelet Rich Plasma (PRP) to be injected into the wound and intravenously followed by 21day re-evaluation.

On December 13, 2017, the SVF procedure was performed. The patient was sedated with midazolam, morphine, and propofol and 100cc of adipose tissue was extracted from his right flank. The mesenchymal stem cells were separated with collagenase and programmed with immunologically privileged nucleotides for bone, muscle, skin, and tendon. The stem cells were then mixed with activated PRP drawn from the patient prior to sedation and injected directly into the borders and center of the ulcer. An IV Infusion was also given. The wound was cleansed with chlorhexidine, covered with a hydrogel containing collagen and hyaluronic acid, and wrapped with a bandage

On January 14, 2018 the patient had his first follow up appointment and significant closure of the ulcer was observed. The size of the wound was reduced by 70% leaving a 4cm x 3cm ulcer with no underlying structures exposed.

On Feb 4, 2018, the patient had his second follow up appointment and the wound was observed to be 2cm x 1cm. The patient was ambulatory and able to wear shoes. A final Bone Marrow Aspirate Concentrate (BMAC) stem cell procedure was performed. A 50cc of bone marrow was extracted from his right ilium, activated with the same nucleotides as the first procedure, and injected into the wound as well as intravenously.

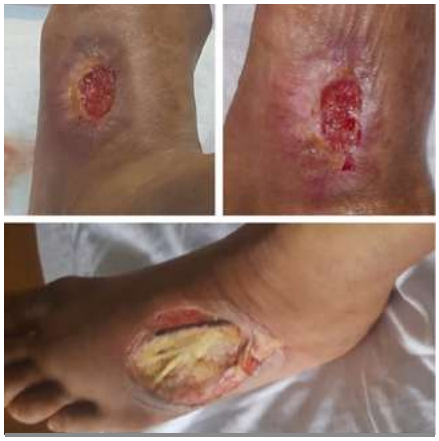
Discussion:

Autologous stem cell transplantation gave this patientthe chance at a full recovery; a chance he would not have had without the stem cell transplantation. The level of healing achieved with stem cell treatement prevented the possibility of gangrenous necrosis and the potential loss of his limb. The patient is now ambulatory and able to return to his daily activities.

Conclusion:

Mesenchymal stem cell procedures, both SVF and BMAC, offer the significant potential for healing when no other options exist. We have demonstrated their efficacy in wound closure in this patient.

-The patient's wound upon discharge from hospital



-Bottom: Patient's wound on Dec 12 upon first evaluation for stem cell procedure
-Top Left: Patient's wound 1 month post SVF Procedure
-Top Right: Patient's wound immediately following PRP

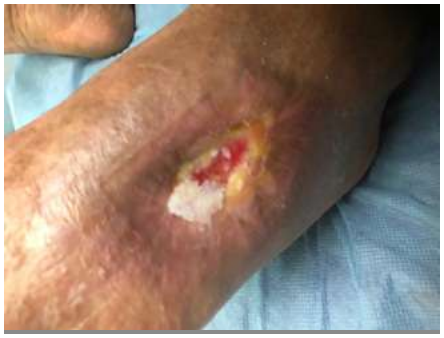
Leslie Mesén Martínez, M.D.

Dr. Mesen is the founder and Chief Medical Officer of the Stem Cells Transplant Institute in San Jose, Costa Rica. Established in 2013, he is a co-founder and the Chief Medical Officer of the Anti-Aging and Wellness Clinic. Under his direction, the Anti-Aging and Wellness Clinic has grown to four clinics in three countries; two clinics in Costa Rica, one clinic in Tijuana, Mexico and one clinic in Panama City, Panama. He previously served as Chief Medical Officer at Costagenics Age Management Program from 2007-2010 and Chief Medical Officer at Anti-Aging Institute of the Americas from 2010-2013.

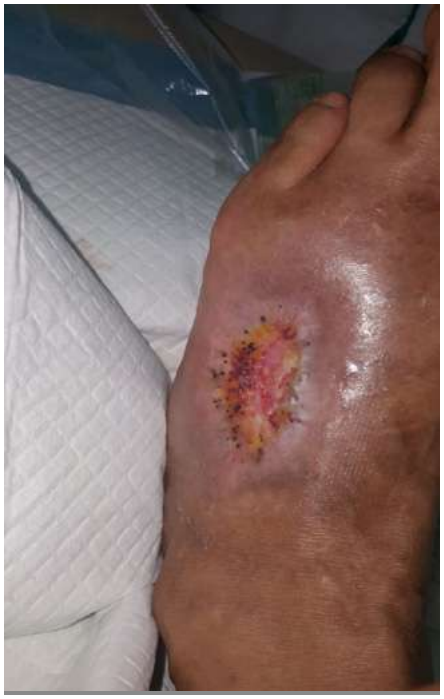
Since 2009, Dr. Mesen has been an active member of the American Academy of Anti-Aging and Regenerative Medicine (AAARM) and the American College of Physicians Central America. In 2015 he became a member of the International Organization for Training and Medical Research (IOCIM). This organization is committed to ensuring quality healthcare to the countries in Latin America. In 2015the organization awarded Dr. Mesen the "Prize to the Medical by Achievement for a Better Life" award for recognition of his excellent academic career and continuing education and commitment to improving human life. Dr. Mesen also received the Award for Excellence in Healthcare from the IOCIM for his leadership, outstanding performance and quality of service.

Dr. Mesen has a passion for helping patients and has built both, the Stem Cells Transplant Institute and the Anti-Aging and Wellness Clinic, on a foundation of research and scientific innovation and individualized patient care. His focus is to improve the quality of life of each patient he treats while gaining a better understanding of cellular senescence and regeneration.

Dr. Mesen earned his degree in Medicine and Surgery from the University of Ibero-America and completed his fellowship in Emergency Medicine at the University of Miami. In 2005, Dr. Mesen received additional training in Pediatric Medicine and Internal Medicine from CajaCostarricense de Seguro in Costa Rica.In 2017 he completed his fellowship in stem cell therapy with A4M is board certified by the American Academy of Anti-Aging and Regenerative Medicine. He is in the process of completing his Ph.D. in Medicine and Surgery at the University of Salamanca in Spain.



-The patient's wound on Feb 4, 2018 just before his final BMAC Procedure



-The wound on the date of publication: February 10, 2018

Leslie Mesen, M.D.

Chapter Director in Costa Rica

Upcoming Events

Istanbul in Turkey, April 28th, 2018

Coordinator:

Mr. Salih Yildirim, CEO of BioTrend

University of Buenos Aires School of Medicine in Argentina , August 25th, 2018

Coordinator:

Dr. Silvina Pastrana, Chapter Director in Argentina

Jeju in Korea, November 24th, 2018

Coordinator:

Dr. Daeyong Kim, Founding President of ISSCA/
CEO of N-BIOTEK Inc.

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Stem Cell Center es una plataforma entre Médicos y Científicos . Hemos compuesto una red mundial con profesionales de primera línea quienes comparten vía online sus experiencias y estudios en Terapias Celulares. Los miembros con licencia en el Grupo, han sido entrenados, equipados y reciben asesoramiento de Global Stem Cells Group para la investigación y tratamiento de pacientes.
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Insights from Industry

Salih YILDIRIM

CEO, BioTrend

"Regenerative medicine is an exciting, expanding field of medicine. The human body has the inherent power to heal itself but in some instances it just needs a little help."

"As BioTrend, we provide applications of tissue engineering, stem cell therapy, medical devices and other biological therapies to repair and regenerate damaged or diseased tissues and organs.

BioTrend entered the regenerative medicine field a decade ago, starting with PRP and Bone Marrow Concentration applications. In 2010, the first Multi-Center Hearth Failure trial in which bone marrow derived stem cells had been injected during angioplasty was designed and sponsored by BioTrend in Turkey. The results were very promising. Currently, we can isolate blood, bone marrow, skin and adipose tissue with point of care systems.

BioTrend will continue to research and provide regenerative medicine technologies in order to best serve the needs of partners, customers and patients. On this journey, I am very pleased to meet Mr. Daeyong Kim who has been great partner. Our business partnership is now in its fourth year and I would like to extend our warmest appreciation to him and his team for joining hands in business. I believe ISSCA is the new authority for Global Stem Cell Network with the publications, research, education and certified training programs."

Company

BioTrend was established in 2004 in Cleveland, OHIO USA. Since 2006, BioTrend has been serving the Turkish health sector. As a part of the textile and construction company group, BioTrend benefits from the group`s 35 years of international business experience to move forward stronger and more professionally.

BioTrend focuses on genetic, biochemistry, molecular biology, biomaterials and stem cell technologies; the company has introduced a significant number of innovative technologies to the Turkish healthcare industry. The technologies and products which are safe, high technology and proved their quality in the world are marketed and distributed by BioTrend in Turkey, Azerbaijan, Kazakhstan, Georgia, North Cyprus. Iraq, Saudi Arabia, Oman and UAE.

About Salih YILDIRIM: Salih Yıldırım currently serves as the CEO of BioTrend BioTechnologies, a leading biotechnology supplier of regenerative medicine products. He is responsible for growing the business's global activites that included recent aquisition of ReGen Virtual Clinic, an innovative global medical provider.

During his position at BioTrend, between 2013 to 2016, Mr. Yıldırım served Cleveland Clinic, one of the best healthcare organizations in the world, as International Business Developer. He earned his MBA Healthcare Management degree from Cleveland State Universtiy, USA.

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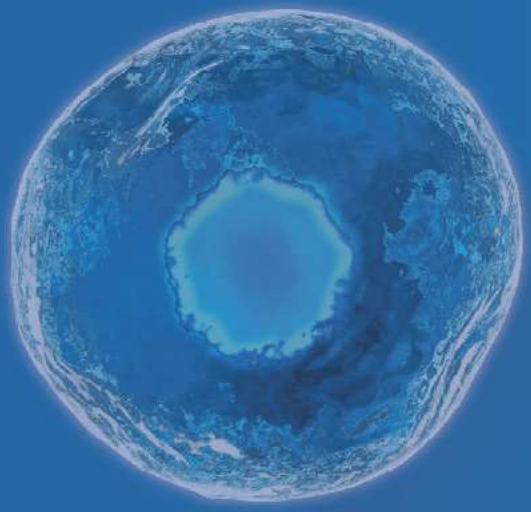
Tel +82-70-4006-4385
Fax +82-32-328-2372
E-mail joinissca@gmail.com
Address 402-803 Technopark, 655 Pyeongcheon-ro, Bucheon-si, Gyeonggi-do, Korea (14502)



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