

REGENERATIVE MEDICINE AND STEM CELL

Life is Beautiful

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OUR GOAL

The Liv Hospital Regenerative Medicine and Stem Cell Production Center is the first in-hospital center of its kind complying with international GMP (Good Manufacturing Practice) standards in Turkey. High quality, safe biological products are produced for targeted treatments.

Based on our passionate belief in an inter-disciplinary approach involving close collaboration between all relevant medical fields of specialization, our aim is to offer our international patients personalized, tailor-made stem-cell and stem-tissue genetic engineering products and future genetic treatment options in line with the extraordinary advances achieved in recent years by scientists and physicians around the world and the applicable scientific and ethical rules and regulations.

OUR MISSION

To offer our patients and their loved ones life-changing, high-quality healthcare services through the application of cells and stem cells in the field of “Cellular Therapy” as well as through the development of new treatment technologies in line with recognized treatment protocols.

OUR VISION

With its perfectionist approach, our Regenerative Medicine and Stem Cell Research and Production Center aims to improve the quality of life and to extend it to patients who suffer from various diseases and injuries by transforming high technology stem cell and tissue engineering treatments into clinical products.

WHAT CONDITIONS CAN BE TREATED?

The Regenerative Medicine and Stem Cell Production Center can offer treatments for the following medical conditions:

- Peripheral arterial diseases (such as Buerger's Disease)
- Chronic critical limb and foot ulcers
- Incurable chronic injuries
- Cartilage degeneration
- Soft tissue and wound treatments
- Plastic surgery
- Breast reconstruction
- Tendon damage
- Burns, injuries and injury scar repair

Cosmetic applications:

- Skin rejuvenation and firming
- Filing applications
- Facial bone and soft tissue trauma
- Maxillofacial surgery
- Facial deformities
- Immunotherapy treatments (such as graft versus host disease GVHD treatment)

Our center has been licensed by the Turkish Ministry of Health as a production center with a view to offering our patients healthcare services in the above fields; the following cellular products isolated and produced at our center are as follows:

- Adipose tissue-derived stem cells,
- Umbilical cord stem cells,
- Synovium-derived stem cells,
- Fibroblasts,
- Cartilage cells,
- Adipose tissue-derived stem cell-enriched vascular fraction,
- Bone marrow-derived stem cell-enriched vascular fraction.





THE ERA OF REGENERATIVE MEDICINE
AND STEM CELLS HAS DAWNED

The most significant advances in medical science have occurred in cellular and molecular biology, and genetics. In particular, our understanding of cells and stem cells has expanded at an incredible pace as result of parallel developments in stem cell studies and their scientific results. We have learned about normal hair growth, post-incision skin renewal, and how millions of blood cells are generated within the space of a few minutes in the bone marrow by the action of stem cells located in the tissue and organs. We then established that could not only generate cells in

the tissue and organs in which they are located; laboratory extraction showed they could do so in other tissues and organs. Consequently, scientists had the idea of using stem cells with the capacity to transform into different cells to treat previously untreatable conditions that shared one characteristic – namely that organ failure and dysfunction were caused by the cells in the diseased organ. This is why so much of the research carried out in the past 10 to 15 years has been in the field of Regenerative Medicine.

PUTTING PATIENTS' HEALTH AND
WELLBEING FIRST

Liv Hospital established the Regenerative Medicine and Stem Cell Production Center as a pioneer in the field of stem cells. At our Center all scientific and ethical rules are strictly applied to prioritize patients' health and wellbeing.

THE ERA OF STEM CELL
AND REGENERATIVE
MEDICINE

Although advances in the diagnosis and treatment of diseases continue at a dizzying pace, some diseases have remained incurable even by the latest surgical methods. Modern medicine is based on a desire to achieve greater health, to cure diseases and achieve a state of healing that will restore patients to as close as possible to their original condition. Treat-

ments that had long been regarded as the best possible solutions in which everyone said "This is as good as it gets" have been rapidly surpassed over the past 20 years; conditions that could only be partially treated can now be dealt with comprehensively. Tissue renewal and regeneration using the patient's own cells or stem cells in cases that had until very recently been seen as beyond the reach of even stem cell science, is now within the realms of possibility through cell or stem-cell based treatment; these treatment protocols are rapidly gaining ground.

LET YOUR BODY REGENERATE ITSELF

The Liv Hospital Regenerative Medicine and Stem Cell Production Center offers solutions to medical and cosmetic issues by using regenerative cells obtained from the patient's own tissue.

Working in conjunction with all clinical branches, our Center treats unhealthy or non-functioning cells and tissue using recognized cellular treatment methods in line with the applicable legal and scientific procedures.



WHAT IS REGENERATIVE MEDICINE?

Regenerative medicine is a procedure of creating live and functional tissues in order to repair or change some tissues or organs which lose their function due to age, disease, damage or at birth. Success in regenerative medicine can be achieved in two ways:

- 1) By inducing some organs or tissues that were previously untreatable in a way that they heal and treat themselves through stimulation of regenerative cells located in these tissues and organs by surgical or chemical signaling communications mechanisms.
 - 2) In cases that the body cannot repair itself, cells / stem cells from the patient or obtained from a suitable donor are reproduced in laboratory conditions for re-transplantation or the transplantation of 3-D tissue / organ grafts produced from these cells and the use of tissue engineering technologies.
- This new discipline of medical and life sciences encapsulates all the studies and work carried out in clinical sciences including applications in immunology, cell biology, chemistry, tissue and biomaterial engineering, molecular biology, developmental molecular biology, and genetic and regenerative medicine.

HOW COMMON IS STEM CELL TREATMENT?

Stem cell treatments have become more common in recent years around the world, especially in the treatment of health issues that cannot be treated using conventional methods. However, they can only be applied using products from centers and universities that are licensed and certified in line with internationally applied criteria.

IS THERE AN AGE LIMIT FOR STEM CELL TREATMENT?

Stem cell treatments are generally evaluated based on the age, disease and clinical condition of a patient. All factors need to be considered. For instance, the age limit for the cell treatment to repair joint damage with cells obtained from the patient's own cartilage tissue is 55. Mesenchymal Stem Cells widely used in the clinic can cause immunologic side effects in the recipient when transplanted from another individual. Therefore, treatment is conducted using stem cells obtained from suitable third party donors in age-related cases where personalized stem cell treatment cannot be carried out; this is common in GVHD treatment, for example.

HOW LONG DOES IT TAKE TO PRODUCE A STEM CELL?

This depends on the tissue source of the stem cells and the method of processing. Reproducing the required number of stem cells for transplantation by separating and cultivating them from tissue biopsy samples usually takes a period of 4-6 weeks.

HOW LONG CAN THE MANUFACTURED STEM CELLS STAY ALIVE?

The shelf life of cells from the time they leave the production laboratory is 24-72 hours, but transplantation is preferably carried out in the shortest possible time (24 hours at most). While their lifespan depends on production conditions, their optimum level of life is up to 72 hours when transplantation is carried out within a transfer kit with the temperature in the laboratory at +4 °C.

According to clinical evaluation of the patient's condition, the cells can be stored by freezing them at -196 °C; cell treatment can then be repeated as required, by a specific and meticulous method of thawing.



WHAT ARE STEM CELLS?

Stem cells are undifferentiated cells that have the potential to be able to divide into specialized cells. They are found in multi-cellular organisms. Cells that we now call 'stem cells' have important characteristics that distinguish them from normal (somatic) body cells within our bodies' organisms. The most important distinguishing features are their high capacity to reproduce and their ability to differentiate between the various other types of cells in our bodies. Because of their long-term self-renewal capacity in live or laboratory conditions without losing this ability to differentiate, their response to appropriate signals (in live cases generally damage signals, in the laboratory various chemical stimuli), and their ability to distinguish between different tissue / organ cells, they have gained the status of important biologic material primarily in modern cell-based treatments, experimental developmental biology, drug toxicity studies and in understanding the pathogenesis of diseases.

Stem cells' high multiplication potential is attributable to their high telomerase enzyme activity; if this function resumes without differentiation, they maintain it by means of ongoing transcription factor expressions related to the activation of signal pathways originating in their micro-environments (niche; bed) that are responsible for self-renewal.

WHO CAN BENEFIT FROM STEM CELL TREATMENT?

Patients who have diseases that are amenable to stem cell treatment can benefit from treatments, depending on their age and physical condition.

HOW ARE STEM CELLS PRODUCED IN A LABORATORY?

This process can only be carried out in a laboratory licensed and certified by the Ministry of Health in accordance with Good Manufacturing Practice (GMP) criteria. Stem cells are produced in a laboratory by using a biopsy sample (such as bone marrow or adipose tissue) taken from the patient's own tissue (autologous) related to the patient's disease. First of all, related cells are isolated from this biopsy sample and are reproduced by constant nourishing and controlled under proper conditions. Transfer in a form that is ready for transplantation is performed only after the appropriate number of cells has been reached and the quality control stage, involving flow cytometry, telomerase activation, gene expression, endotoxin and mycoplasma testing, has been completed.

FROM WHERE CAN A STEM CELL BE OBTAINED?

Stem cells can theoretically be obtained from any body tissue or organ, but the most widely used cells for treatment purposes are derived from the bone marrow, umbilical cord, synovial fluid or membrane, and heart and adipose tissue.



REGENERATIVE MEDICINE AND STEM CELL APPLICATIONS

ORTHOPEDICS AND TRAUMATOLOGY

STEM CELL TREATMENTS IN ORTHOPEDICS

- Cartilage Problems
- Tendon injuries and tendinitis / tendinosis problems
- Applications for joint degeneration
- Sport injuries, especially soft tissue problems

CARTILAGE AND DEGENERATIVE JOINT DISEASES

There have been very significant advances in stem cell applications in orthopedics, especially cartilage problems. At this point with the help of regenerative cells that are produced from the patient's own tissues through a biopsy, it is possible to observe cartilage formation even in areas where there is almost no cartilage. Therefore, functional and structural renewal is possible for the cartilage areas.

Tissue loss is an extremely important issue for our skeleton as well as the cartilages that enable our joints to move freely. The Liv Hospital Regenerative Medicine and Stem Cell Production Center is able to offer various treatment opportunities in order to replace these tissues. Especially for cases of cartilage loss, procedures for producing cartilage from a cartilage tissue, as well as stem cell applications, can be carried out in GMP laboratories by using the most advanced technology, and can be implanted in patients.



EYE DISEASES

HOW COMMON IS STEM CELL TREATMENT?

In our daily lives, our cells and tissues are being renewed even though we do not realize it. This renewal occurs with the help of stem cells. Stem cells are also needed for eye tissue as for other body tissues, in order to renew tissue and to replace cells which are lost. This ongoing renewal can be affected by diseases which cause a deficiency in stem cells. As a result, vision and the general health of the eye can be severely affected. The causes of stem cell

damage include genetic diseases in the cornea of the eye which cause a deficiency in stem cells, improper contact lens usage, radiotherapy, immunosuppressive treatments, certain immunological-related eye diseases, chemical burns, eye infections and eye allergies. Stem cell applications are a key factor for the treatment of these diseases.

EFFECTIVE IN TREATING EYE SURFACE DISEASES

Stem cells that are produced in the laboratory and then transplanted enable patients to regain sight by restoring the cornea surface. Nowadays, reproduction and transplantation of limbal cells are used for the treatment of eye surface diseases, while studies continue for the treatment of congenital or age-related retina diseases through the usage of limbal cells. Some positive results are being reported following various procedures that have been carried out using amniotic membrane or using Cell Sheet technology with stem cells derived from the limbal region (limbal cell cells) or the oral mucosa.

Work is ongoing with respect to using surface disease treatment by means of generating limbal cells for transplantation and the treatment of congenital and age-related conditions such as macular degeneration.

Positive results are being reported in animal testing. Official authorization has been granted in the United States and Japan for obtaining retina pigment epithelia cells to treat macular degeneration using iPS (induced pluripotent stem cells).



COSMETIC AND PLASTIC SURGERY

Stem cell applications for plastic reconstructive and cosmetic surgery can be divided into two main categories. The first one is for cosmetic applications. Stem cell applications have an important potential especially for the skin resurfacing. Fat injections enriched with stem cells are efficient anti-ageing treatment methods for the face and hands. Using their own tissue prevents some side effects or allergic reactions. It is not possible to achieve permanent results by using filling or other materials. However by using the patient's own tissue, there is a potential to obtain more lasting and effective results compared to other methods.

RENEWING AGEING AREAS

Renovators obtained from the patient's own body enable skin renewal in ageing areas. This treatment is done in 3 steps. In the first step, fatty cells are taken from a patient through a biopsy or liposuction. Regenerative cells obtained from these tissues are then refined and concentrated. Regenerative cells are injected separately or combined with other natural mixtures according to the patient's needs.

HOPE FOR UNHEALED WOUNDS

The second application area for plastic reconstructive and cosmetic surgery is unhealed wounds, disturbed blood flow or skin tissue, and subcutaneous tissue disorders or changes related to radiotherapy, and other diseases in which medication has a limited effect. Stem cell applications are a hope for those difficult clinical problems and hold the prospect of lasting remedies.

Regenerative cells obtained from the patient's own body can also be used for cosmetic applications. Renovators obtained from the patient's own body enable skin renewal of ageing areas. The treatment procedure is performed in 3 steps:

- Fatty cells are taken from the patient's own body through a biopsy or liposuction
- Regenerative cells obtained from these tissues are refined and concentrated.
- Regenerative cells are injected separately or combined with other natural mixtures according to the patient's needs.

FACE AND BODY FILLING (ANTI-AGING)

In fillings carried out with artificial products such as implants, up to 70% of the filling may be reabsorbed by the body. However, this problem can be minimized by using regenerative cells obtained from the patient's own body for a natural, permanent and more youthful appearance. In this case, a single injection carried out by using regenerative cells will be sufficient, rather than multiple operations.

TREATMENTS OF WOUNDS AND SKIN SCARS

Regenerative cells obtained from the patient's own body are used for the treatment of face and body wounds and scars. The probability of allergic reaction is low. The deformed area can regain its previous natural form after the treatment.

BREAST RECONSTRUCTION

Breast cancer is the most frequently occurring cancer in women. As part of the process that often concludes with surgical removal of the breast, cancer tissue under the breast and lymph nodes, regenerative cells are now often used in breast reconstructive surgery.

BURN TREATMENTS

Severe burns and third-degree burns are some of the most difficult cases that cosmetic surgery faces. The Liv Hospital Regenerative Medicine and Stem Cell Production Center uses regenerative cell applications in order to allow patients to regain a healthy appearance in place of chronic burn tissue.



DERMATOLOGY

SKIN RESURFACING AND REJUVENATION

Stem cells are used for the treatment of age-related wrinkles, spots and other problems such as faded skin. The aim of the treatment is to repair the tissue that has been damaged due to age and to enable a more youthful appearance. For that reason, a 3 mm biopsy sample is taken from behind the ear or from other parts that are not exposed to sun, and younger fibroblasts belonging to the patient are produced in a special culture environment. Injections are carried out with 15 to 30 days intervals over 3 or 4 sessions in total. Injections are performed by conventional mesotherapy techniques. No side effects have been reported.

ACNE SCARS

Acne scars can be a major issue for many people. Few studies have been reported for the treatment of acne scars based on autologous fibroblast injections. Fibroblasts obtained through similar techniques are applied as dermal injections. Laser or Dermaroller procedures can also be integrated into the treatment.



ENDOCRINOLOGY AND METABOLISM DISORDERS

DIABETIC FOOT WOUNDS

Foot wounds are observed in 25 percent of diabetic patients; currently, 8% of these cases result in amputation of the toes or the entire foot. Regenerative cells are used for treatment of the surgical area wound, facilitating a cure for diabetic foot wounds.

CARDIOVASCULAR SURGERY

Limb Ischemia Problems

Regenerative cells obtained from the patient's own body enable a solution to vascular occlusion problems as well as other diseases. For this disease some medical treatments such as drugs, ozone or high pressure are administered. Amputation (removal of parts in which vascular occlusion has occurred) or sympathectomy (removal of the sympathetic nerve) can be performed as a last remedy for surgical operation. However, regenerative cell applications which effectively cure wounds and restore circulation can be counted as an effective and new procedure.




NEW HOPES

UROLOGY

Tissue or organ loss related to chronic diseases is one of the most challenging problems facing medicine today. In the past 10 to 15 years, successful results in animal experiments have led to an increase in the popularity of stem cell use in the treatments of chronic diseases in humans. These animal experiments in urology increase the hopes for applications on the human body. The most important feature which makes stem cell treatment attractive is the stem cells' ability to develop and to turn into the desired cells in the target tissue in which they are implanted, as well as their ability to trigger certain substances which can regenerate malfunctioning cells in the target tissue, which ultimately makes tissue and organ repair possible.

THE FIRST FIELD OF APPLICATION IS URINARY INCONTINENCE

In the field of urology, successful results have been observed with stem cell applications in animal experiments with respect to kidney diseases, bladder disorders, urinary incontinence, infertility, erectile dysfunction, and Peyronie's disease. The first application area has been urinary incontinence, which has produced successful results. Male infertility, erectile dysfunction and Peyronie's disease are expected to be the conditions in which stem cell treatments make the most rapid advances in terms of medical treatment. As Liv Hospital's Urology Team, having obtained precursory results from animal testing in particular on erectile dysfunction, which we have shared through international peer publications, we are now completing our preparations for human trials. After obtaining the required official authorization, we shall soon start our clinical work (Phase 1 / 2) in parallel with studies in other developed countries.



Cardiovascular diseases, which are some of the most frequently occurring conditions today, and the resulting heart attacks, can severely affect the patient's life quality. Stem cell implantation is now used in the treatment of post-heart attack cardiac deficiency. In case of vascular occlusion in coronary veins, the heart cells supplied by these veins start to die within 20 to 30 minutes. If the blockage is not removed, most of the cells die in 6 hours. Scientific evidence indicates that this period can be reversed by using stem cells obtained from bone marrow.

CARDIOLOGY

BONE MARROW AS HEART RESTORER

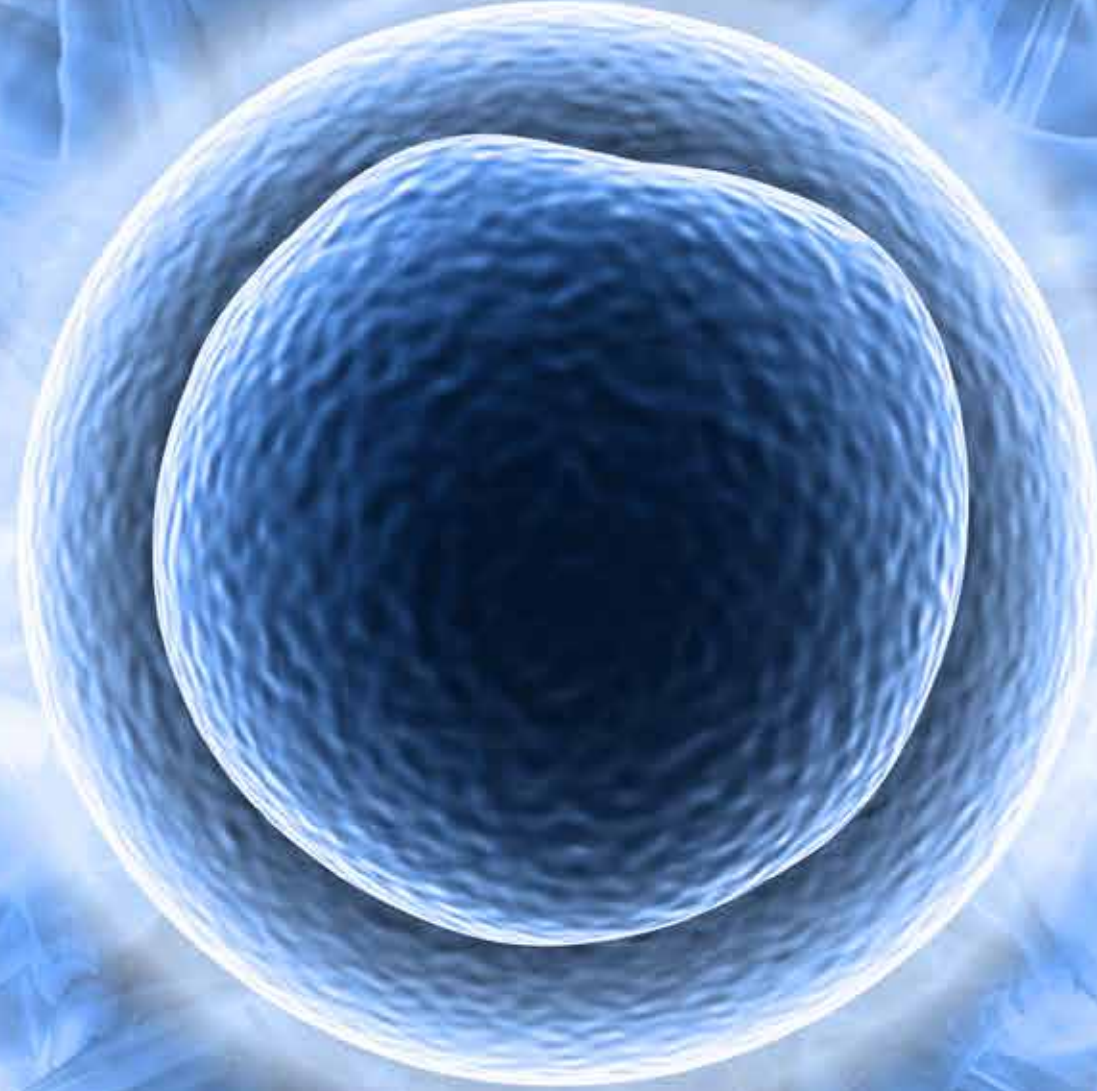
Heart muscle cells cannot be regenerated when they die due to a heart attack. It has been noticed since the early 2000s that stem cells exhibit properties to repair sickly tissues. This development marked a new era in stem cell treatment. Stem cell treatment in heart disease has been the main focus of these efforts. The heart muscles are irreparably damaged after an infarct. Stem cell treatment is used to repair this damage in the heart muscle and also in severe cardiac failure. Stem cells taken from the patient's bone marrow are injected into the coronary veins of the patient suffering from an infarct. This method can result in the generation of new veins. In studies so far, it has been observed that the damaged areas in the heart can heal completely in 6 months and the heart beat strength increases. Alternatively, studies in the United States have shown that heart stem cells derived from small biopsy samples obtained from the patient's own heart can have a therapeutic effect.


WHAT DOES IMPLANTATION INVOLVE?

Stem cell implantation is performed in a similar way to angiography, by introducing a tube into the inguinal vein and guiding it to the heart tissue, without the need for surgery. This procedure is performed either on the artery or vein, depending on the patient's condition and disease.

YOUR OWN CELLS ARE INJECTED

The stem cell to be implanted into the heart tissue is not taken from a relative or someone else, but from the patient himself or herself. The stem cell is obtained from the sample taken from the patient's own bone marrow. For this reason, there is no possibility of cell rejection.





With its perfectionist effort, Our Center of Regenerative Medicine and Production of Stem Cells, aims to improve the quality of life, and to extend it to patients who suffer from various illnesses and injuries, by transforming stem cells to high tech and treatments engineered tissue engineering, in products.

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