

ADIPOSE TISSUE-DERIVED MESENCHYMAL STEM CELLS: COSMETIC AND PLASTIC APPLICATIONS

- Today, adipose tissue-derived mesenchymal stem cells (AT-MSC) are widely used in the treatment of persistent chronic wounds (such as diabetic wounds) and burn injuries, congenital anomalies (eg. Lipodystrophy, cleft lip or palate) , peripheral vascular disease (such as Buerger's Disease and ischemic foot), tissue damage that can occur after surgery to remove a tumor (such as post-mastectomy breast filling), facial fillers, hand and face rejuvenation (wrinkle reduction), as well as correcting soft tissue defects.
- Various scientific studies have shown their capacity to form strong new blood vessels and how the numerous protective factors they secrete can regain the regenerative capacity of tissue throughout the period of life.
- As well as their applications in orthopedics, plastic surgery and dermatology, AT-MSCs are easily obtained sources whose tissue characteristics make it possible to obtain the in large numbers. Nowadays, they constitute a viable alternative source to bone marrow-derived MSCs. For this reason, they are now used as an alternative source, especially in the clinical processes associated with immune suppression (like GVHD).
- In addition, phase 1/2 research studies are ongoing into the effectiveness of AT-MSCs in all clinical trials and research studies involving bone marrow-derived MSCs such as cardio vascular diseases, organ failure, and neuro-degenerative diseases.

SINOVIAL TISSUE-DERIVED MSCs

- The synovium is a stem cell-rich vascular connective tissue surrounding the inner surfaces of the bone capsule outside the cartilaginous bone areas.
- Nowadays, synovial tissue-derived stem cells that are used especially in the treatment of joint damage are obtained from biopsies taken from patients in arthroscopic surgery.

SINOVIAL TISSUE-DERIVED MSC APPLICATIONS

- Joint cartilage damage is generally very difficult to treat. In spite of successful outcomes from biologic treatments with autologous chondrocyte transplantation, damage to the area from where the chondrocytes are obtained and its restricted cell source mean that this is not a suitable form of treatment in certain cartilage applications.
- Since their discovery in 2001, synovial tissue-derived mesenchymal stem cells have shown promising results in the treatment of skeletal muscle regeneration, especially in cartilage, bone, tendon and muscle damage cases.
- Today, successful results are obtained in cartilage therapies using mesenchymal stem cells. Scientific studies indicate that in spite of the existence of various sources for stem cells, the most promising candidate for repairing cartilage damage are synovial tissue-derived stem cells with their high chondrogenic potential and low hypertrophic differentiation.

MSC

MSC
Cellular therapy

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MSC

STEM CELLS

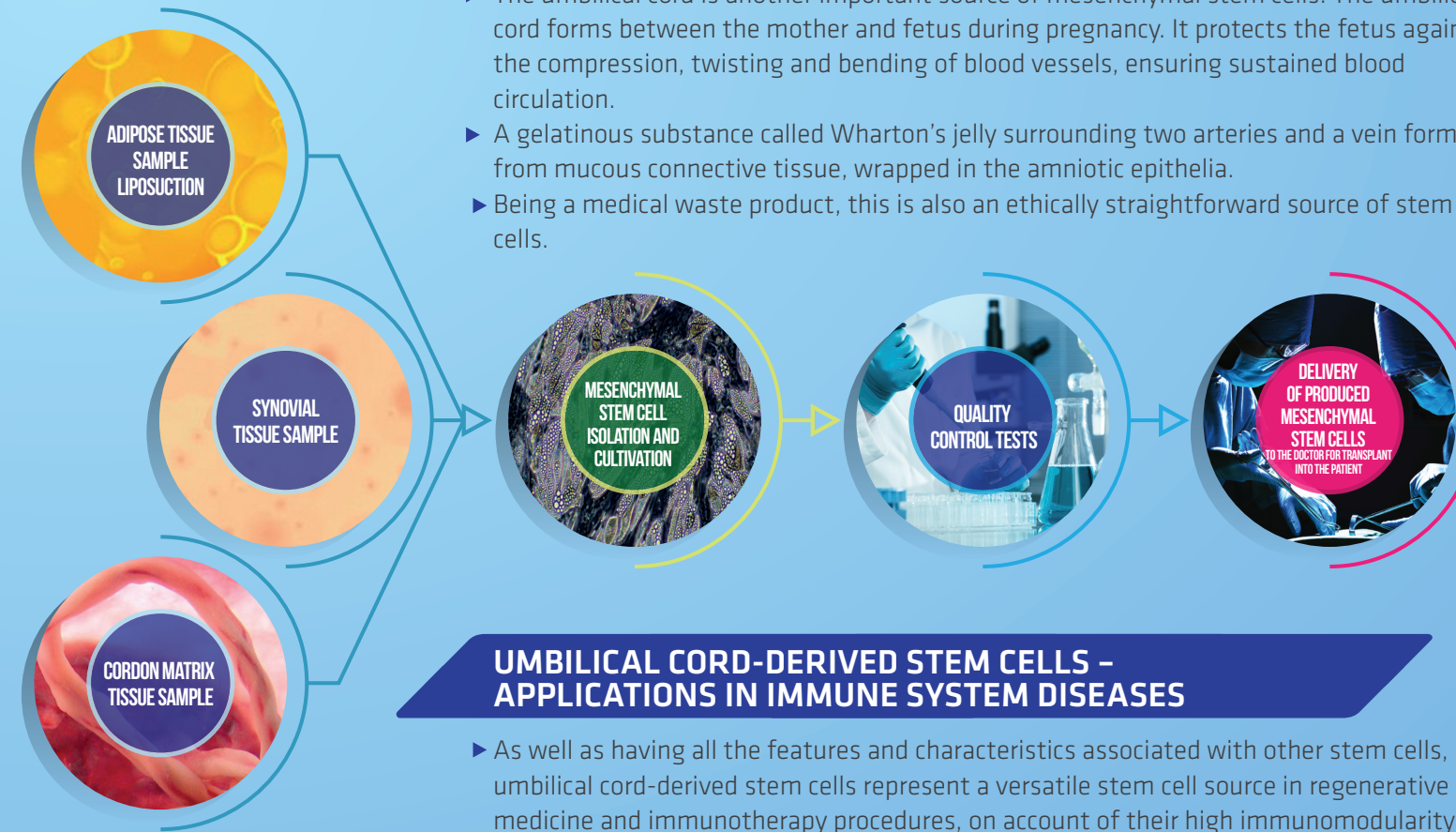
- Stem cells are undifferentiated cells that renew themselves and possess infinite divisibility capacity through asymmetric mitotic division.
- As well as their ability to remain undifferentiated, they can actively differentiate when necessary and turn into different cell types.
- Stem cells derived from various tissues and organs, play a role in the function of damaged or lost tissue and organ regeneration.
- Furthermore, because of stem cells' immune regulatory properties, they have been clinically widely used in several *in vitro* and *in vivo* procedures as important biological agents of cellular therapies.
- Today, stem cells are also used in cardiovascular system disorders, auto-immune and inflammatory diseases as well as treating orthopedic, skin and soft tissue damage.

FAT (ADIPOSE) TISSUE

- Located in the layer of skin called the hypodermis, adipose tissue performs a crucial role in filling the body cavities, insulating against heat loss and cushioning certain anatomic parts of the body.
- Divided into two types (white and brown), adipose tissue contains fibroblasts, endothelial cells, macrophages, smooth muscle cells and stem cells.

ADIPOSE TISSUE-DERIVED MESENCHYMAL STEM CELLS

- Adipose tissue is found in nearly every part of the body and is rich in stem cells. The patient's stem cells are obtained from the waste adipose tissue called lipoaspirate following the lipoaspiration procedure. It is therefore a repeatable, low-risk procedure.
- Isolation of stem cells from the adipose tissue obtained from the patient is carried out under laboratory conditions. The isolated cells are proliferated. When they have reached a sufficient number for transplantation, they are subject to quality control tests before being conveyed to the specialist doctor who is going to perform the procedure.



UMBILICAL CORD-DERIVED STEM CELLS

As well as being a rich source of stem cells obtainable from the donor without the need for surgical intervention, they can be obtained from different layers of the umbilical cord (Wharton's jelly, veins, arteries, cord layers and the lower amniotic and perivascular regions). The protection of the placental barrier lowers the risk of contamination and there none of the disadvantages specific to the wear and tear of life.

UMBILICAL CORD

- The umbilical cord is another important source of mesenchymal stem cells. The umbilical cord forms between the mother and fetus during pregnancy. It protects the fetus against the compression, twisting and bending of blood vessels, ensuring sustained blood circulation.
- A gelatinous substance called Wharton's jelly surrounding two arteries and a vein forms from mucous connective tissue, wrapped in the amniotic epithelia.
- Being a medical waste product, this is also an ethically straightforward source of stem cells.

UMBILICAL CORD-DERIVED STEM CELLS - APPLICATIONS IN IMMUNE SYSTEM DISEASES

- As well as having all the features and characteristics associated with other stem cells, umbilical cord-derived stem cells represent a versatile stem cell source in regenerative medicine and immunotherapy procedures, on account of their high immunomodularity impact.
- They are suitable for autologous and allogeneic use. Before allogeneic applications, genetic and chromosomal tests are required to determine the health of the patient.

GRAFT VERSUS HOST DISEASE (GVHD)

- Transplantations of allogeneic hematopoietic stem cells (HSCs, responsible for the production of blood cells) are widely used in the treatment of blood-borne malignancies and genetically-based blood diseases, in Turkey and around the world.
- Although these transplantations have saved lives of many patients struggling with malign diseases, they can also give rise to potentially terminal Graft Versus Host Disease (GVHD) in which the donors T-lymphocytes reproduce, damaging their target organs in recipient's bone marrow, skin, liver and gastrointestinal system.
- Nowadays, high dosage immuno-suppressive medications (corticosteroids) are used to treat GVHD. However, resistance to these medications can develop in the acute stage, with severe consequences including even the expiry of the patient.

GVHD STEM CELL THERAPY

- Due to their strong immuno-suppressive characteristics, MSC transplantation is used in the prophylaxis and treatment of acute GVHD that can develop after allogeneic stem cell transplantations.
- It has been shown to be especially effective in treating skin and bowel symptoms in steroid-resistant Stage III – IV
- GVHD cases, yielding successful results in 6 out of 8 cases. More than 250 GVHD cases have been treated using MSCs in Turkey; the reported success rate is very high.
- The American Society for Blood and Marrow Transplantation reports no long-term post-procedure risks associated with the officially approved use of allogeneic MSCs in mesenchymal stem cell treatment, from 2010 to the present day.

APPLICATION

- Stem cells are prepared and injected under strict GMP conditions in line with the number of cells specified by the specialist for the patient (the product is produced as a suspension in a vial or by membrane-seeding). It is transplanted into the patient in recurring sessions at set intervals, as required.
- Suspension and membranous product may be used in combination, as demanded.
- The Liv MedCell Stem Cell manufacturing period is 4 to 6 weeks.
- Anesthesia may be required during the procedure.
- The product needs to be transplanted into the patient 24 – 48 hours after production.
- Autologous or allogeneic stem cell applications are carried into those parts of the body specified by the specialist doctor. Stem cells can either be administered to the damaged region, or into the circulatory system.

SIDE EFFECTS AND INTERFERENCE WITH MEDICATION

- As well as not interfering with any medication in any way, there are no known side effects.
- Testing on usage during pregnancy and breast feeding has not been carried out.