

## Offer of the Tissues and Stem Cells Bank and the Fat Tissue and **ADSC Transplant Clinic:**

- · adipose tissue collection and isolation of ADSC stem cells
- · banking of the collected adipose tissue and ADSC stem cells
- · conducting research in medical treatment based on cellular technology
- · preparation of ADSC stem cells for treatment in:







AESTHETIC MEDICINE (ADSC mesotherapy, scars, regeneration)



PLASTIC SURGERY(breast augmentation, tissue defects, ADSC uplift surgery)



ANTI-AGING THERAPIES (ADSC infusions, tissue and organ regeneration)



DIABETOLOGY (treatment of type II diabetes)



OPHTHALMOLOGY (optic nerve atrophy - ONA)



VASCULAR SURGERY AND CARDIOLOGY (ischemia, post-infarction regeneration)



MAXILLOFACIAL SURGERY (bone reconstruction, osteoarthrosis, implantology, dentistry, tissue regeneration)



LARYNGOLOGY (bone reconstruction, chronic sinus inflammation)





NEUROSURGERY AND NEUROLOGY (discopathies, post-stroke conditions, ischemia)





## Capabilities of the Tissues and Stem Cells Bank

The Tissues and Stem Cells Bank is authorized to collect, test, process, store and distribute adipose tissue and mesenchymal stem cells derived from adipose tissue. The Bank's activity gives patients professional and safe care of the collected adipose tissue and ADSC stem cells. The Tissues and Stem Cell Bank, thanks to its Quality Assurance System guarantees the quality of stem cells products. All donations have bacteriological tests, and are evaluated in terms of the number of contained stem cells and their viability.

In the Tissues and Stem Cells Bank new possibilities of stem cell treatment for doctors and patients are available. After the usual liposuction procedure, patients have the option of freezing their adipose tissue or stem cells for future treatments. ADSC stem cells are frozen under validated conditions in liquid nitrogen vapor, so that preparations (after thawing) are available to patients for many years from the date of collection. The Tissues and Stem Cells Bank is the perfect place to conduct scientific research with the use of regenerative medicine.



## One liposuction, ADSC stem cells for life

Thanks to the collection of excess adipose tissue and ADSC stem cells isolation, the cellular product can be divided into portions. The amount of the portions is determined individually with the patient's physician. This is a revolutionary change in the planning of stem cells therapy, in which the patient has only one liposuction to collect adipose tissue. Stem cells isolated from one procedure can be given to the patient repeatedly, in outpatient settings. This is a great convenience, especially in plastic surgery, aesthetic medicine, orthopedics, diabetology or neurosurgery, where it is not enough to administrate ADSC stem cells in only one injection/infusion to achieve a satisfactory clinical response.



# Stem cells therapy in treatment of many diseases

The ADSC stem cells isolated and stored in the Tissues and Stem Cells Bank are used in the treatment of many diseases and degenerations, e.g. in neurosurgery (discopathy), orthopedics (entezopathies, shoulder, knee, wrist), diabetology (type II diabetes) or oral surgery. ADSC stem cells can be used to improve beauty, in plastic surgery (facial, breast lipofilling), aesthetic medicine (mesotherapy, facial, breast and body treatments).



## Cooperation with Bank Tissues and Cells

We offer access to modern therapies based on stem cells to hospitals, scientific institutions and patients. We enable short-and long-term storage of ADSC stem cells for the needs of ongoing therapies We encourage hospitals and clinics from all over Poland and Europe to cooperate with our Tissues and Stem Cells Bank. After signing the contract, you can direct your patients to our facility. An experienced team of specialists from our Hospital makes a medical qualification and then isolates ADSC stem cells from the patient's fat tissue. After isolation of ADSC stem cells, we obtain ready-made cellular products for clinical use. Then, depending on the therapeutic decision, the stem cells product can be sent to your medical facility fresh (on the same day/next day) or at the right time (after many weeks, months) in a frozen form (in dry ice).

We are convinced that we will offer you a satisfactory and longterm cooperation model that ensures your facilities and patients treated with constant access to modern cellular therapies.



## Discopathy

#### WHAT IS DISCOPATHY?

Discopathy is a disease which affects intervertebral discs, which are disks found between two of the vertebrae in the vertebral column. The most common type of the disease is degenerative discopathy which is a process that mainly takes place due to osteoarthritis. It can be described as the stiffening, and also gradual settlement of the discs, which commonly affects those found at the base of the lumbar, between the L5 and S1 vertebrae. Discopathy is the most common vertebral column disease.

#### TREATMENT OF DISCOPATHY WITH ADSC STEM CELLS

An innovative and effective method of treating discopathy is injection of mesenchymal ADSC stem cells isolated from the patient's own body fat. ADSC stem cells have the innovative ability to transform into different types of specialized cells, building, among others, cartilage, muscles, bones, tendons and ligaments. They also stop scarring processes, promote angiogenesis and stop the process of cell death due to hypoxia. These cells strengthen the natural capacity of tissues to regenerate them.

The treatment of ADDC stem cell discopathy involves the removal of adipose tissue by thin-needle abdominal liposuction, purification, preparation and administration directly to the damaged site to initiate tissue regeneration and repair. The procedure can be performed under local or general anesthesia.

#### WHAT CAUSES DISCOPATHY?

Discopathy occurs due to the deterioration or wear and tear of one or several intervertebral discs over time, linked to osteoarthritis. The latter disease is a chronic ailment that can be identified through persistent joint aches and pains which are caused when the cartilage and the joint itself become abnormally worn down.

Discopathy can occur at any age, despite the fact that old age is one of the contributing factors. The disease usually occurs because of repetitive microtrauma or physical stress, but it can also be caused by congenital anomalies. Intervertebral disc wear can appear anywhere along the spine, but it quite often occurs in the lower back, the lumbar.





### Stroke

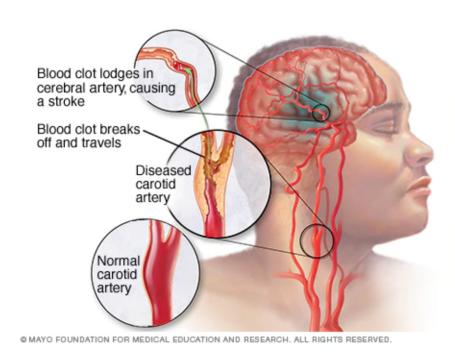
#### WHAT IS STROKE?

Stroke is a disease that affects the arteries leading to and within the brain. It is the No. 5 cause of death and a leading cause of disability in the United States.

A stroke occurs when a blood vessel that carries oxygen and nutrients to the brain is either blocked by a clot or bursts (or ruptures). When that happens, part of the brain cannot get the blood (and oxygen) it needs, so it and brain cells die.

#### TREATMENT OF STROKE WITH ADSC STEM CELLS

The adipose-derived stem cell (ADSC) treatment effectively improves the neurological deficits during stroke by reducing neuronal injury, limiting proinflammatory immune responses, and promoting neuronal repair, which makes ADSC-based therapy an attractive approach for treating stroke.



#### STROKE TREATMENT METODHS

Worldwide, stroke is one of the main causes of death and disability in adult patients and has become a serious public health problem. Current therapeutic approaches focus on removing the blockage of the blood vessel by thrombolysis and surgery. However, these treatments usually have small time window and have no limiting effect on neural repair after the injury and, therefore, can help 10% of the patients. There is a need for new therapies that can both limit ischemic brain lesion and promote neural repair.

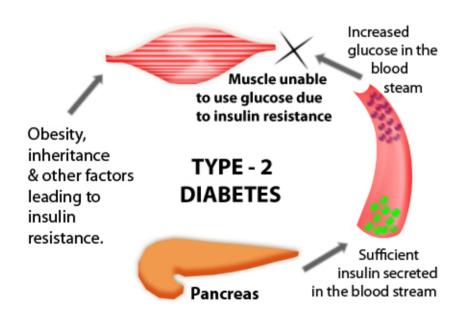


# The use of adipose derived stem cells to treat microvascular complications of type 2 diabetes

#### WHAT IS DIABETES TYPE II?

Diabetes is a chronic (lifelong) disease marked by high levels of sugar in the blood. Glucose enters the bloodstream when food is consumed. Glucose is the source of fuel for the body. The pancreas produces insulin, which moves the glucose from the bloodstream into muscle, fat, and liver cells, where it can be used as fuel. People with diabetes have high blood sugar, because the pancreas does not make enough insulin or their muscle, fat and liver cells do not respond to insulin normally, or both.

In Diabetes Type II, the pancreas does not make enough insulin to keep blood glucose levels normal, often because the body does not respond well to insulin.



The project anticipates the use of mesenchymal stem cells (MSCs) from patients' own adipose tissue (ADSC - Adipose Derived Stem Cells) for the treatment of diabetes mellitus type II (T2DM) and its complications. The aim of the project is to develop innovative therapy and evaluate its effectiveness in the treatment of T2DM and organ complications: angiopathy and diabetic retinopathy, cardiomyopathy, nephropathy, diabetic polyneuropathy. Previous treatment proceedings in diabetes was based on symptomatic treatment and consisted of the use of oral drugs or exogenous insulins (controlled injection form to compensate the level of sugar in the blood). In recent years, MSCs obtained from various tissues are the subject of research and are also used in the treatment of diabetes. This is due to the ability of MSCs to unlimited renewal, immunomodulatory properties, ability to migrate to damage sites, and differentiation into specific cells and tissue. MSCs from adipose tissue can be used in diabetes treatment, taking into account the fact that these stem cells have the ability to: differentiation into pancreatic beta cells that produce insulin; regeneration of existing Langerhans cells of the pancreas by secretion of cytokines and growth factors (VEGF, IGF-1, PDGF-BB, angiopoietin-1, etc.); protection of endogenous islet cells through immunoregulatory and antioxidant activity and inhibition of T cell proliferation; improvement of organ and tissue insulin sensitivity through secretion and activation of various factors; reduction of proinflammatory cytokines and chemokines; stimulation of M1 macrophages transfer into anti-inflammatory M2. MSCs activity in diabetes helps to stabilize blood glucose levels and is effective in the treatment of chronic complications of organ diabetes listed above. Most research uses stem cells derived from bone marrow, umbilical cord blood, or mature cells of various tissues that have been restored to stem cells.

## Amyotrophic lateral sclerosis (ALS)

#### WHAT IS ALS?

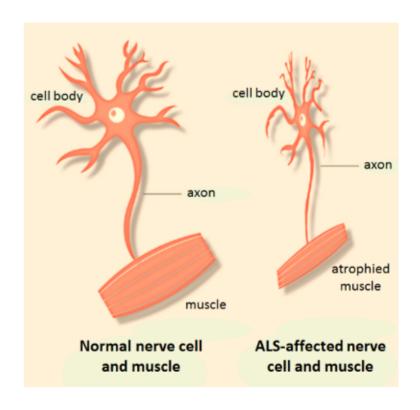
Amyotrophic lateral sclerosis (ALS) is a rare fatal neurodegenerative disease which is characterized by the loss of upper and lower motor neurons resulting in muscle weakness, progressive paralysis and mortality 3 to 5 years after the clinical onset due to respiratory failure. It is estimated that about 30,000 people in United States are struggling with ALS with a higher incidence rate in men. ALS can be divided into two forms, including sporadic ALS (sALS) with 90% prevalence and the familial ALS (fALS) affecting only 10% of patients with a possible link to some genetic mutations.

#### TREATMENT OF ALS WITH ADSC STEM CELLS

Adipose-derived stem cells (ADSCs) are regarded as potential source of regenerative medicine, since their multipotency, abundance and minimal ethical consideration. In addition to direct replacement of damaged cells using stem cells, recent studies have reported that stem cells secrete various beneficial factors and modulate a hostile environment during illness. In many reports, this is called a bystander or paracrine effect. ADSCs express and secrete multiple factors for the paracrine effects and have a high proliferation rate with a ower senescence than other tissue-derived stem cells. Thus, ADSCs are reliable source for paracrine function based stem cell therapy.

#### ALS TREATMENT METODHS

The presence of blood brain barrier (BBB) is the main problem in the treatment of central nervous system (CNS)- related diseases such as ALS. The newly designated methods especially drug delivery vectors may help to solve this problem. There are two types of drug delivery tools,including synthetic and natural vectors. In general, synthetic vectors are products of chemical reactions from lipophilic compounds. Liposomes are the main type of synthetic tools utilized by researchers, however, regarding their possible side effects such as immunogenicity, accumulation in tissues and unknown consequences of this method, applying natural vectors instead is being considered.



## Multiple sclerosis (SM)

#### WHAT IS SM?

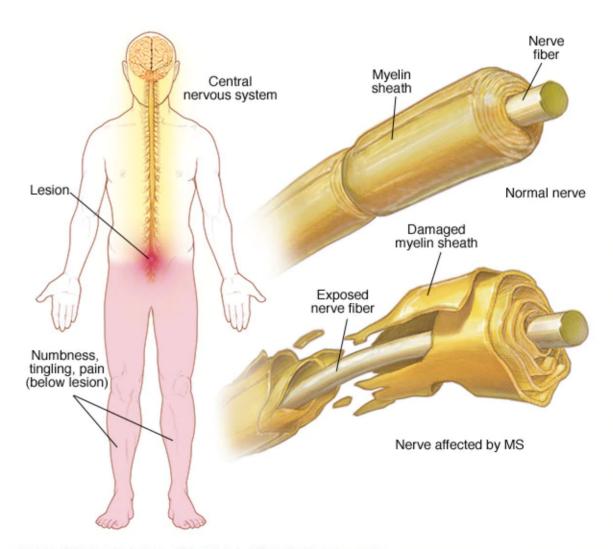
SM is a demyelinating disease in which the insulating covers of nerve cells in the brain and spinal cord are damaged. This damage disrupts the ability of the nervous system's to communicate, resulting in a range of signs and symptoms, including physical, mental, and sometimes psychiatric problems. Specific symptoms can include double vision, blindness in one eye, muscle weakness, trouble with sensation, or coordination. MS takes several forms, with new symptoms either occurring in isolated attacks (relapsing forms) or building up over time (progressive forms). Between attacks, symptoms may disappear completely; however, permanent neurological problems often remain, especially with the disease progression.

#### TREATMENT OF SM WITH MESENCHYMAL STEM CELLS

The therapeutic effects of MSC in MS have been demonstrated in several animal studies. In one of the first studies of immune modulation, Zappia et al. demonstrated administration of MSC subsequent to immunization with encephalomyelitis-inducing bovine myelin prevented onset of the mouse MS-like disease EAE. The investigators attributed the therapeutic effects to stimulation of Treg cells, deviation of cytokine profile, and apoptosis of activated T cells. It is interesting to note that the MSC were injected intravenously. Several other studies have shown inhibition of EAE using various MSC injection protocols. To our knowledge there is only one publication describing clinical exploration of MSC in MS. An Iranian group reported using intrathecal injections of autologous culture expanded MSC in treatment unresponsive MS patients demonstrated improvement in one patient (EDSS score from 5 to 2.5), no change in 4 patients, and progressive disease in 5 patients based on EDSS score. The study revealed, that six patients had improvement in their sensory, pyramidal, and cerebellar functions. One showed no difference in clinical assessment and three deteriorated.

#### SM TREATMENT METODHS

There is no known cure for multiple sclerosis. Treatments attempt to improve function after an attack and prevent new attacks. Medications used to treat MS, while modestly effective, can have side effects and be poorly tolerated. Physical therapy can help with people's ability to function. Many people pursue alternative treatments, despite a lack of evidence of benefit. The long-term outcome is difficult to predict, with good outcomes more often seen in women, those who develop the disease early in life, those with a relapsing course, and those who initially experienced few attacks. Life expectancy is on average 5 to 10 years lower than that of an unaffected population.



### Alezheimer's disease

#### WHAT IS ALZHEIMER'S DISEASE?

Alzheimer's disease (AD) is the most common type of dementia with cognitive deficits, resulting from progressive neuronal death in the hippocampus and the cerebral cortex. It is well known that the accumulation of amyloid beta (AB) is responsible for the progression of AD, which includes widespread neuronal dysfunction and ultimately, cell death. Pathologically, the brain of AD patients is characterized by an accumulation of senile plaques, atrophy of neurites, and neurofibrillar tangles. The plagues contain large amounts of AB peptide derived from cleavage of the amyloid precursor protein (APP). In familial AD, mutations in APP have been shown to increase the production of AB42 leading to disease, and this association has led to the hypothesis that  $A\beta$  is the key to the pathogenesis of AD.  $A\beta$ accumulates in the mitochondrial membrane and impairs mitochondrial functions. This results in the induction of pro-apoptotic factors such as caspases, whose activation induces apoptosis. p53, known as a tumor suppressor, has a critical role in determining cell fate. There is abundant evidence that p53-dependent cell death is increased by oxidative damage of cells during AD. p53 induces apoptosis by regulating apoptotic proteins such as Bcl-2-associated X (Bax) and caspase-3.

### THE CAUSE OF ALZHEIMER'S DISEASE AND IT'S TREATMENT METODHS

The cause of Alzheimer's disease is poorly understood. About 70% of the risk is believed to be inherited from a person's parents with many genes usually involved. Other risk factors include a history of head injuries, depression, and hypertension. The disease process is associated with plaques and neurofibrillary tangles in the brain. A probable diagnosis is based on the history of the illness and cognitive testing with medical imaging and blood tests to rule out other possible causes. Initial symptoms are often mistaken for normal ageing. Examination of brain tissue is needed for a definite diagnosis. Mental and physical exercise, and avoiding obesity may decrease the risk of AD; however, evidence to support these recommendations is weak. There are no medications or supplements that have been shown to decrease risk.

No available treatment can stop or reverse the progression of the disease, though some may temporarily improve symptoms. Behavioral problems or psychosis due to dementia are often treated with antipsychotics, but this is not usually recommended, as there is little benefit with an increased risk of early death.

#### TREATMENT OF ALZHEIMER'S DISEASE WITH MESENCHYMAL STEM CELLS

Current reports suggest that ADSCs may be a promising new cell source for regenerative cure, which can be regenerative treatment of Alzheimer's disease. Ma et al. showed that intracerebral administration of ADSCs has the potential efficacy to restore spatial learning/memory ability in APP/PSI double transgenic mice. The improvements were believed to arise due to a dramatic reduction in amyloid-b aggregation, which is one of the fundamental pathologies of the disease, and also included learning and memory recovery. It was evident that administration of ADSCs could alter microglial activation, as well as mitigate dementia symptoms and alleviate the cognitive downturn. IV administration of ADSCs also palliated dementia symptoms and had therapeutic effects in another Alzheimer's disease mouse model. Pérez-González et al. investigated the issue of neurogenesis in the adult hippocampus. They proposed the possibility that leptin, an adipose-derived hormone, could promote neurogenesis, as well as its mechanism of action. The results indicated that the proliferation of neuronal precursors was increased in APP/PSI double transgenic mice following leptin, as well as neuroprotective consequences. In summary, transplantation of ADSCs might have potential beneficial effects in preventing the pathological development of Alzheimer's disease.