DESCRIPTION FOR THE GENERAL PUBLIC

Systemic lupus erythematosus, systemic sclerosis and ankylosing spondylitis are incurable rheumatic diseases leading to disability and/or precocious death. Pathogenesis of these diseases is not fully understood and available medical treatment is not effective. Therefore, there is a need of developing new therapies improving patients' quality of life.

Systemic lupus erythematosus and systemic sclerosis have autoimmune background and are characterized by chronic inflammation and accumulating damage of numerous tissues and internal organs. In ankylosing spondylitis it is easier to control inflammation but the major clinical problem is how to stop pathological bone remodelling and prevent disablement.

The potential therapy of autoimmune disease is mesenchymal stem cells (MSCs) administration. These cells, in contrary to embryonic stem cells evoking many ethical concerns, are localized in tissues of adults organisms. MSCs are present in bone marrow, adipose tissue, periosteum or umbilical cord blood. These cells possess regenerative and immunosuppressive properties: they are able to regenerate injured tissues (e.g. cartilage, bone, adipose tissue) and to suppress activity of other immune cells. Because of these two attributes, MSCs can be beneficial in autoimmune disease treatment.

Presently, intensive research is conducted on MSCs derived from adipose tissue – ASCs. MSCs derived from adipose tissue are of special interest with regard to their therapeutic application. The reasons for this are their non-invasive, easy isolation (by liposuction) and very abundant number (500-times more than in bone marrow). Our knowledge about ASCs function and potential clinical application is expanding quickly. ASCs are administered in heart infarction or craniofacial reconstruction, but their use is not very common yet.

It is known that autologous bone marrow-derived MSCs (BMSCs) failed to bring benefit to rheumatic patients and there are reports showing functional abnormalities of these cells and their probable contribution to pathological processes. Thus, it is likely that depending on local milieu, MSCs may exert beneficial or detrimental effects. Although allogeneic BMSCs and umbilical cord-derived MSCs have been shown to give clinical improvement in these patients, it would be more rational and convenient to use autologous MSCs with preserved immunomodulatory and/or regenerative properties. We hypothesize that MSCs derived from subcutaneous adipose tissue, not exposed to strongly inflammatory milieu, are intending candidates to achieve this goal.

In the proposed project we will verify if autologous subcutaneous ASCs possess properties suitable for their therapeutic use in patients suffering from systemic lupus erythematosus, systemic sclerosis and ankylosing spondylitis, as well as whether contribution of ASCs to particular disease is beneficial or detrimental. The work plan of proposed project includes assessment of ASCs regenerative and immunomodulatory potential. Especially, we are interested in explanation what is the impact of disease-specific ASCs on immune cells (T and B cells) and whether ASCs contribute to pathogenic processes. Several laboratory techniques will be used: *in vitro* cell cultures, ASCs differentiation towards cells building bone, cartilage and adipose tissue, analysis of surface and intracellular proteins (by flow cytometry), quantitative detection of secreted factors (by immunoenzymatic tests), quantitative evaluation of genes expression, histochemical stainings.

All described in this project diseases are incurable and disabling. The prevalence of ankylosing spondylitis is relatively high (0.25%-1% of population), which represents an important social and economic problem. Systemic lupus erythematosus and systemic sclerosis are rare so the number of people affected is rather low, however the severity of these diseases and poor prognosis for patients constitute a huge medical problem. The significance of the project is therefore obvious since it would contribute to the development of new therapeutic strategy.