Rheumatoid arthritis (RA) is an incurable, autoimmune diseases affecting about 1% of Polish population. What is very important, the RA onset occurs is relatively young age of about 30-40 years. The disease affects mainly women in their most active period of life. RA is associated with chronic inflammatory process in joints leading to their destruction caused by joint cartilage and bone degeneration. In the course of RA, cardiovascular morbidities occur and are the cause of precocious death. It has to be underlined that RA leads to severe medical, social and economic problems. People suffering from this disease become unable to work and need help in normal, everyday avtivities. The real problem in Poland is that the availability of modern, biologic therapies which for many patients represents the only way to avoid disability, is highly insufficient comparing to other UE countries. Taking into consideration all these facts, there is a great need of innovative therapies which would enable to cure RA or to limit its symptoms.
One of the potential autoimmune disease therapy is mesenchymal stem cells (MSCs) administration. These cells, in contrary to embryonic stem cells evoking many ethical concerns, are localized in tissues of adult organisms. MSCs are present in bone marrow, adipose tissue, periosteum, skeletal muscles or cord blood. These cells are of special interest because of their regenerative and immunosuppressive properties: they are able to regenerate injured tissues (e.g. cartilage, bone, muscles, adipose tissue) and to suppress activity of other immune cells. Because of these two qualities MSCs can be beneficial in autoimmune disease treatment, e.g. RA.
Presently, intensive research is being conducted on MSCs derived from adipose tissue – ASCs. The reason for this is high availability and abundancy of these cells as they are about 500 times more frequent in adipose tissue than in bone marrow.
Our knowledge about ASCs function and potential clinical application is expanding quickly. ASCs are being administered in heart infarction or craniofacial reconstruction, but so far their use is not very common. ASCs possess properties of affecting T lymphocyte subsets which leads to attenuation of immune response. It is reported that ASCs suppress proinflammatory Th17 lymphocytes subset and promote activity of anti-inflammatory T regulatory cells (Tregs).
Because of the autoimmune nature of RA and its destructive and debilitating impact on joints, the basic science project has been proposed to verify whether rheumatoid ASCs function is altered and whether rheumatoid ASCs are still exerting their immunosuppressive abilities. To this aim, ASCs localized in the place of inflammation will be analyzed. We will use ASCs derived from intra-articularly localized infrapatellar fat pad.
The main objective of the proposed project is the evaluation of ASCs isolated from infrapatellar fat pad of RA patients on rheumatoid T cells and their differentiation towards Th17 and Tregs. The hypothesis of the study assumes that ASCs localized in the rheumatoid joint, contrary to ASCs from healthy donors, may promote proinflammatory Th17 subset development and do not induce immunosuppressive Treg cells.
In proposed experiments we will assess the effect of direct contact between ASCs and T lymphocytes, the effect of soluble factors secreted by ASCs and the effect of microvesicles released by ACSs. Microvesicles are spherical membrane structures released by many cell types. It is known from the literature, that MSCs exert part of their effects by microvesicles secretion. The experiments will evaluate T cells activation, proliferation, percentage of Th17 and Tregs and secretion of various proinflammatory and anti-inflammatory factors. Several laboratory techniques will be used: in vitro cell cultures, flow cytometry, immunoenzymatic tests. Interaction between T lymphocytes and ASCs or microvesicles will be also assessed using confocal microscopy enabling accurate pictures of in vitro cultured cells. Moreover, we will verify if under ASCs treatment, T lymphocytes become able to inhibit activity of other T cells and acquire immunosuppressive function.
Results of proposed basic science research will provide important information on MSCs function in inflammatory microenvironment. Analysis of ASCs localized in the infrapatellar fat pad will enable evaluation of cells originated from the site of chronic inflammation. Results of the proposed project will be very valuable in an aspect of mesenchymal stem cell therapy of RA.