DESCRIPTION FOR THE GENERAL PUBLIC

Osteoarthritis, as a result of joint cartilage damage, is the most frequent musculoskeletal system disease and the third cause of disability in the world's population as far as the frequency of occurrence is concerned. However, treatment methods for osteoarthritis used so far do not ensure the permanent improvement of the state of patients. That is why new methods of the treatment of joint cartilage damage are being searched for, the ones that use the possibilities created by tissue engineering that enables the growth, differentiation and metabolic activity of cartilage tissue cells (chondrocytes). The most recent direction of research in the area of joint cartilage reconstruction leans towards using differentiated ones in the direction of chondrocytes, various populations of stem cells such as mesenchymal stem cells (MSCs) and induced pluripotent stem cells (iPSCs). The MSCs of bone marrow or fat tissue are an easily accessible source of cells. However, with the age of the donor the differentiation capacity of these cells decreases and this prevents an increase of culture scale and thereby their potential therapeutic effect is diminished. The iPSCs are an alternative. Their features are similar to embryonic stem cells, and they are created from the mature cells of adults via the forced expression of those genes responsible for the state of pluripotency. The differentiation of stem cells in the direction of chondrocytes requires the supplementation of culture medium by suitable growth factors as well as cytokines. Currently, there are several methods of the differentiation of iPSCs to chondrocyte-like cells. However, even strictly controlled lab conditions may not mirror the environment inside human joints. A pro-inflammatory environment may affect negatively the implantation of the obtained cells by increasing their mortality. According to recent research, factors that are secreted by iPSCs into the culture medium possess cytoprotective qualities. The method of differentiation of iPSCs developed by us allows obtaining the amount of material that is sufficient to fill large articular cartilage defects. The chondrocyte precursors obtained by this method may thus be a perfect material for implantation in the places of damaged articular cartilage. Despite the existence of several methods of the differentiation of stem cells in the direction of chondrocytes, neither of them is sufficiently efficient nor takes into consideration the impact of synovial fluid that is in their natural environment.

The aim of the project is the development of an efficient method of chondrocyte precursor cell culture as a result of the differentiation of iPSCs in the presence of synovial fluid collected from patients with advanced degenerative changes in the knee joint. We are planning to make a detailed analysis of synovial fluid collected from, a selected group of patients with a degenerative disease of the knee joints and to examine the influence of synovial fluid upon the differentiation, viability and aging of chondrocytes in the primary culture, as well as their precursors obtained as a result of the differentiation of iPSCs. This will enable determining the influence of a microenvironment of the inflamed knee joint on the function of chondrocytes dedicated for implantation in the place of damaged cartilage. In the final stage we are planning to examine the influence of conditioned medium, gathered from iPSCs which is culture free from nutritional cells and serum, as a factor that delays the aging of cells as well as neutralizing the negative impact of a pro-inflammatory environment upon chondrocytes.

We expect that our project will allow the determination of the usefulness of iPCSs in the reconstruction of damaged joint cartilage as well as assessing if their therapeutic effect depending on the degree of osteoarthritis and the micro-environment of the knee joint is taken over by the disease process. The obtained results would constitute a considerable progress in the damage of articular cartilage treatment using a tissue engineering method.