

## Objective of the project

The aim of the project is to determine whether tauroursodeoxycholic acid (TUDCA), which is a substance commonly known as chemical/pharmacological chaperone, could be beneficial in resolving endoplasmic reticulum stress (ER stress) in chondrocyte cells. Second goal is to evaluate the modulatory effect of TUDCA on chondrocytes supplemented with glucosamine sulfate (GS). We suspect that alleviation of ER stress may help in the restoration of the proper functioning of articular cartilage in osteoarthritic joints. We assume that ER stress can underlie the main causes of chondrocyte dysfunction, such as reduced biosynthesis of extracellular matrix (ECM) components, enhanced cell death, and decreased cell proliferation rate. In this respect, we decided to check if TUDCA can alleviate ER stress, resulting in general improvement of those parameters. This assumption is justified, since the avascular cartilage tissue, deprived of glucose and oxygen supplies, is naturally predisposed to develop ER stress.

Additionally, osteoarthritic joints tend to develop severe inflammation, which is also known inductor of ER stress. Therefore, if we manage to prove the *in vitro* efficacy of this pharmacological chaperone, in the future it will be possible to use it as a non-invasive method of osteoarthritis treatment or perhaps, improve the efficiency of widely available nutritional supplements containing glucosamine sulfates and chondroitin sulfates (CS), in cartilage rebuilding.

## Basic research to be carried out

The basic concept of our study is to obtain the report concerning the efficacy of pharmacological chaperone – TUDCA in the alleviation of the ER stress state in chondrocyte cells. We decided to conduct our studies on both, the commercially available chondrocyte cell line, as well as the chondrocytes isolated from patients subjects to total knee arthroplasty surgery. Our project assume experimental scientific work, that will enable us to obtain new knowledge about the influence of the endoplasmic reticulum stress on chondrocytes' functioning and the potential use of chemical chaperones in treatment of osteoarthritis. Our studies will make an impact into contemporary knowledge concerning changes developed under the influence of ER stress, and its connections with chondrocyte apoptosis and turnover. Moreover, our studies will bring an insight into possible role of tauroursodeoxycholic acid in cartilage restoration in osteoarthritic joints. Obtained results will let us broaden the horizons about new potential anti-arthritis therapies.

## Reasons for choosing the research topic

Osteoarthritis is characterized by the progressive degradation and loss of articular cartilage. It is also considered to be the most common arthritic disease which incidence increases with age. As population demographics changes in a way to include more elderly individuals, this disease will have a serious impact on life quality of modern societies. Currently, we still did not develop any specific treatment to prevent or retard cartilage degradation in osteoarthritis. The premises that led us to investigate this problem is constant disability of today's medicine to treat or prevent osteoarthritis, and the controversial role of commonly taken dietary supplements containing glucosamine and chondroitin sulfates (its good efficiency in *in vitro* studies, and lack of the efficiency in clinical trials) in improving cartilage condition (Fig.1).

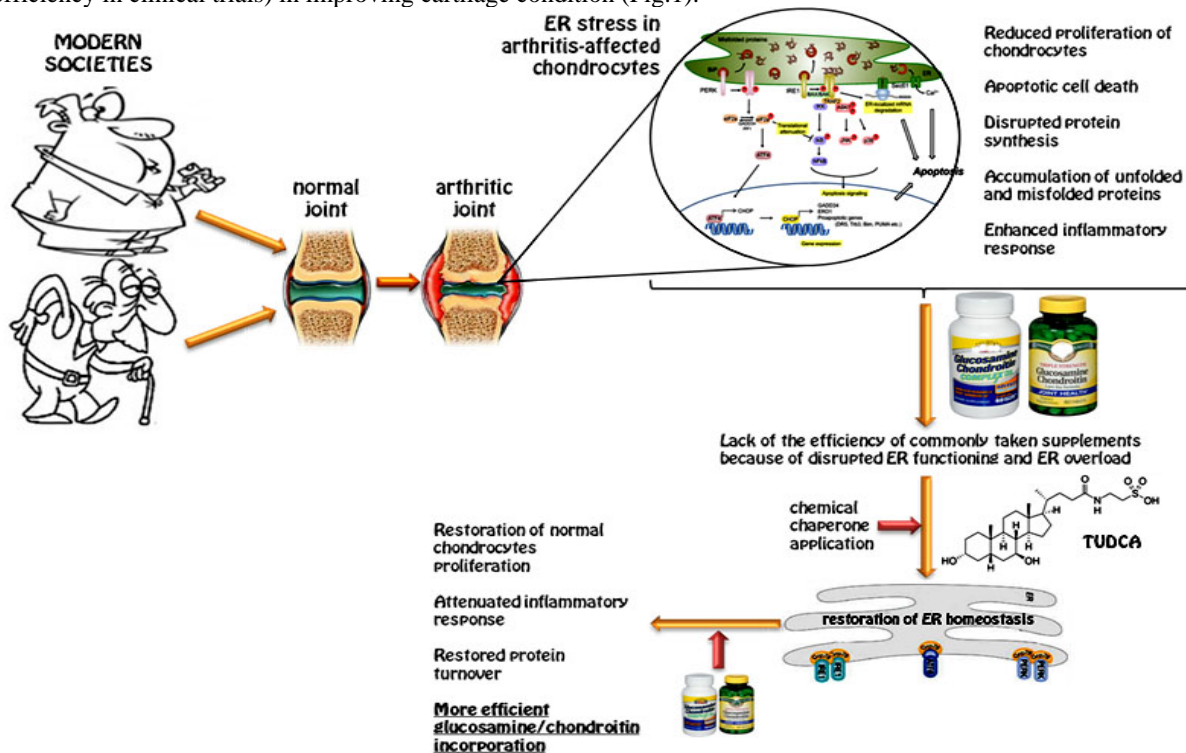


Fig. 1. Schematic presentation of the reasons for choosing the research topic.