Objective of the project: Osteoarthritis (OA) is the most common chronic condition of the joints. OA mostly affects cartilage, but it also affects the subchondral bone, the synovium and periarticular tissues. Patients with OA experience crunching feeling or sound of bone rubbing on bone when the joint moves. The stiffness and pain tend to be worse in the morning with improvement during the day as the person carries on his or her daily activities. OA may affect any joint, but predominantly it attacks joints of knees, hips, spine or hand. OA usually develops over a long period of time. Risk factors include previous joint injury, joint malformation and genetic burdening. Threat is greater in those who are overweight and have a job that puts stress on the joints.

For a long time, the diseasewas believed to be caused by mechanical stress on the joint and wasusually explained as wear-and-tear arthritis, meaning that it is related to aging.Currently, the scientific communitytends to change this paradigm. More and more results indicate that OA may be a result of misdirected inflammation.Inflammation is a process by which the body's immune cells and substances they produce protect us from infection. However, in some diseases, the body's defense system - the immune system - triggers an inflammatory response when there are no foreign invaders to fight against and then causes damage to its own tissues. When inflammation occurs, some defending chemicals are released into the blood or affected tissues. Reactions to the substances released during inflammation increase the blood flow to the area of injury or infection and may result in redness, warmth and swelling. Moreover, the increased number of immune cells and inflammatory substances within joints of OA patients can be observed. The most important defending substances are cytokines, metalloproteinasses, neuropetides and prostanoids, small signaling proteins and lipids that aid cell-to-cell communication duringimmune response.These inflammation processes may irritate nerves within the knee causing more pain. Nowadays, there are emerging evidences that imbalance in levels of above described immunomodulating agents may play a critical role in the diseaseinitiation,its development and in the disease-related pain occurrence. All that above, implicates that osteoarthritic joint tissues host a heightened number of migratory inflammatory cells and of some of the substances these cells secrete, this make us wonder if inflammation is an important player in OA.

Description of the basic research to be carried out: To test our hypothesis whether damage to the joint sets in motion a chain of molecular events we will use commercially available primary Human Fibroblast-Like Synoviocytes (HFLS) derived from joints of healthy donors and those suffering from Osteoarthritis (HFLS-OA)and compare them to corresponding cell-derived cultures from patients, who underwent knee replacement surgery. We want to gain more understanding of the effect and the consequences of local inflammation, so by stimulation of these cell lines, will take a closer look on how they respond, what inflammatory mediators they produce and to what extent they contribute to the disease progression and pain development.

Reasons for choosing the research topic: The development of drugs and other treatments for specific symptoms or conditions relies heavily on our understanding of underlying mechanisms. Because OA is extremely serious public and individual health struggle we decided to address this problem in our research. Pain in patients suffering from OA affects their work and normal daily activities. As pain may prevent physical activity, muscle loss may occur. Knee or hip pain may lead to a sedentary lifestyle that promotes weight gain and possible obesity with further higher risk of development of diabetes, heart disease and high blood pressure. Globally, approximately 250 million people have osteoarthritis of the knee (3.6% of the population as of 2010) causing moderate to severe disability of many people worldwide. According to the Centers for Disease Control and Prevention OA affects more than 25 million men and women over the age of 25 in the USA accounting for 25% of visits to primary care physicians and half of prescriptions. It is estimated that almost half of the adult population of the USA will have symptomatic knee OA by the age of 85, with the highest risk among those that are obese. There are over 8 million people in the United Kingdom living with OA and a 2003 survey of almost 2000 people with OA found that 81% are in constant pain or are limited in their scope to perform everyday tasks. Since OA is a major cause of joint pain and disability and the most common reason for total hip and knee replacement it also has huge economic implications due to an increasing number of joint replacements, increasing hospital charges and ageing population. In 2004 the USA national bill for hospital charges for hip/knee replacements was US$26 billion. If the current trend persists, it was estimated that 600,000 hip replacements and 1.4 million knee replacements will be performed in the US in 2015. With an aggregate cost of $14.8 billion ($15,400 per stay), it was the second-most expensive condition seen in USA hospital stays in 2011. By payer, it was the second-most costly condition billed to Medicare and private insurance. Summarizing, societal burden due to OA is outstanding and the need of further research on OA is urgent.