Flavonoids present a large family of compounds synthesized by plants that have a common chemical structure. There are many scientific evidences that dietary flavonoids promote health and prevent disease in humans. Many of the biological effects of flavonoids appear to be related to their ability to modulate cell-signaling pathways but also to their antioxidant activity. Some of flavonoids, like genistein and kaempferol were found previously to modulate efficiency of synthesis of glycosaminoglycans (GAGs), compounds which are accumulated in cells of patients suffering from mucopolysaccharidoses (MPSs). The mucopolysaccharidoses are a group of rare, inherited, heterogeneous and progressive lysosomal storage disorders that are clinically characterized by abnormalities in multiple organ systems and reduced life expectancy. MPS disorders, due to deficiency or malfunction of specific lysosomal enzymes, leads to an abnormal accumulation of certain complex carbohydrates (glycosaminoglycans naed formlelly mucopolysaccharides) especially in the arteries, skeleton, eyes, joints, ears, skin, and/or teeth. This accumulation causes permanent, progressive cellular damage that affects appearance, physical abilities, organ and system functioning, and, in most cases, mental development. Depending on the type of mucopolysaccharidosis, affected individuals may have normal intellect or may be profoundly retarded, may experience developmental delay, or have severe behavioral problems. Physical symptoms generally include coarse or rough facial features, thick lips, an enlarged mouth and tongue, short stature with a disproportionately short trunk (dwarfism), abnormal bone size or shape (and other skeletal irregularities), thickened skin, enlarged organs such as the liver or spleen, hernias, and excessive body hair growth.

Mucopolysaccharidosis type I (MPS I) is characterized by diminished degradation of the glycosaminoglycans heparan sulfate (HS) and dermatan sulfate (DS). Patients present with a variety of symptoms, including severe skeletal disease. Current therapeutic strategies have only limited effects on bone disease. The isoflavone genistein has been studied as a potential therapy for the mucopolysaccharidoses because of its putative ability to inhibit GAG synthesis and subsequent accumulation. Therefore, genistein and other tested flavonoids have been proposed as potential drugs for the use in substrate reduction therapy (SRT) for MPS disorders and other lysosomal storage diseases (LSDs). Cell, animal, and clinical studies, however showed variable outcomes. The aim of this work is to determine effects of selected flavonoids, used alone or in combinations, on expression of genes of mouse fibroblast mucopolisaccharidosis type I (MPS I) model *in vitro.* Testing the effects of flavonoids on human fibroblast (HDFa) transcriptome, we found that genistein, kaempferol and combination of these two compounds induced dose- and time-dependent remarkable alterations in transcript profiles of GAG metabolism genes. They included genes coding for enzymes involved in GAG biosynthesis, as well as those required for GAG degradation. Interestingly, effects of the mixture of genistein and kaempferol were stronger than those revealed by any of these compound used alone. Interestingly, monitoring particular mRNA levels in HDFa, we found that tested flavonoids significantly stimulate expression of TFEB, a gene coding for the transcription factor which was demonstrated previously to act as a master positive regulator of lysosomal biogenesis. Further analysis to elucidate gene expression modulation in mouse *in vitro* model is necessary to answear the question about differences between influence of flavonoids on MPS patients and mouse MPS model.

DNA microarray analysis, which is one of the fastest-growing new technologies in the field of genetic research, which allows to measure the expression levels of a large number of genes simultaneously, would stand for the basic analysis of this project. Cultures of wild-type and MPS I mouse fibroblasts will be treated with flavonoids (genistein, kaempferoland mixtures of them), and transcriptomic signatures will be determined by DNA microarray analyses, followed by quantitative real-time PCR (qRT-PCR) designed for selected gene panel.

Understanding the control of gene expression under tested flavonoids' is critical for answear the question of their impact on modulation of glycosaminoglycan metabolism in case of mucopolisaccharidosis. Analysis included in this project would fulfill the lack of information about mechanism of flavonoids' action in different MPS models.