Title:

Rescue from bone loss, diminished mineral density and strength in mice after treatment with steroid and non-steroid anti-inflammatory drugs by injection of exosomes enriched with agomir miRNAs.

Treatment with anti-inflammatory drugs like diclofenac or glucocorticoids results in many negative side effects on the mineralization of bones, strength, mechanical resistance, and healing of fracture and postoperative healing of bone defects. Postoperative convalescence and recovery requires anti-inflammatory treatment because pain and inflammation are usual post-operative complications. The project aims to develop new strategy of protective treatment to increase bone strength. This strategy bases on short RNA molecules, which can reach bone cells and induce bone mineralization and strength.

In this study laboratory mice will be treated with non-steroid (diclofenac) or steroid (methylprednisolone) anti-inflammatory drugs within four weeks. After this time, the animals will be sacrificed and their femurs will be analyzed using methods dedicated to test bone strength. Bone fragments will be prepared to dynamic mechanical analysis (DMA) and visualization methods computed microtomography (μ-CT) and atomic force microscopy (AFM). Bone fragments will be studied also using biochemical methods. Short synthetic RNA molecules will be injected to laboratory mice, which were administered with diclofenac or methylprednisolone for 4 weeks. Other cohort of these mice treated with anti-inflammatory drugs will not be injected, but kept in conditions enabling physical activity, which will be monitored. After four weeks all animals will be sacrificed and strength of their femurs will be measured by DMA. This study will reveal changes in mineralization in the group of animals receiving short RNA and the group with access to physical activity. The impact of short RNA and physical activity on bone regeneration will be compared.

The design of protective therapies to treat patients suffering drug-induced or natural bone loss, is a key argument to develop this studies on targeting short RNA to bones. The main disadvantage of nucleic acids is their transport to affected tissues. This project will improve the method of nucleic acid delivery to bones, and could be applied in future also in other tissues.