C1. DESCRIPTION FOR GENERAL PUBLIC.

In accordance to World Health Organisation (WHO), osteoporosis is skeletal disorder characterized by low bone mass, deterioration of bone microarchitecture and in consequence its increased susceptibility to fractures. Osteoporosis in elderly results from alternation in bone metabolism during aging, activity of cells making up bone tissue and hormones regulating bone formation. It was estimated, that risk of osteoporotic fracture in life came to about 40%. That kind of bone trauma has become a real plaque- in Europe it occurs 3 million times per year- one per 30 seconds. Moreover, huge epidemiologic studies indicated that, risk of proximal femur fractures is higher than the risk of mammary gland, uterus or ovary cancer occurrence.

Bone is very metabolic active tissue- during life the processes of renewal, resorption and repair take place simultaneously. In physiological conditions, both bone formation and lysis works together in synergistic way in order to maintain tissue homeostasis. Osteoblasts are cells responsible for bone remodelling, they synthetize bone matrix, while osteoclasts breaks down bone tissue by disassembling its composites. Bone remodelling take place during whole life of the organisms and it is conditioned by genetic factors. In case of osteoporosis, imbalance between osteoblast and osteoclasts acidity is observed, which leads to fractures and difficulties in its healing. The main therapeutic approach in bone fractures is application of plaster cast or if necessary endoprosthetics, replacement of natural bone for artificial, metallic implant.

Patients suffering from osteoporotic bone fractures may benefit from the achievement in the field of tissue and biomaterial engineering which aim to synthetize innovative materials to improve fracture healing. For that reason, in presented project we would like to fabricate novel scaffold aid in bone regeneration in elderly as an alternative for metallic implants. Designed by our team material will consist of hydroxyapatite (nHAP) crystals- inorganic component of bone responsible for its mechanical properties and micro RNA (miRNA) molecules. miRNA particles are build up by approximately 20 nucleotides and are known for tremendous biological activity as they regulate gene expression profile in many cell types. Between nHAP and miRNA magnetic linker in the form of iron oxide nanoparticles (Fe_2O_3/Fe_3O_4) will be incorporated. That system provides ability of controlled in time release of therapeutic miRNA depending on the bone healing rate. In order to release miRNA application of static magnetic field (0,5 T) in the area of biomaterial implantation is necessary to break bonds between material' compounds. nHAP will enrich bone matrix while miRNA affect metabolism of cells responsible for bone remodelling regulation. Presented material will be synthetize using two distinct types of miRNA. miR-21 will be released as first to stimulate mesenchymal stem cells which give rise to osteoblasts while miR-124 diminish activity of causing bone lysis osteoclasts.

Effectiveness of fabricated materials will be tested *in vitro* with bone marrow mesenchymal stem cells (BMSC) and osteoclasts cells line 4B12. In this stage biocompatibility, osteogenic properties and effectiveness in miRNA into host cells will be assessed. The most potent material will be next tested *in vivo* using animal model of osteoporosis- SAM/P6 mice. Critical size calvarial bone defects in animals will be filled with biomaterial. At different time points, animals will be exposed to static magnetic field in order to release therapeutic miR-21 and miR-124. Molecular biology techniques, immunohistochemistry and micro-tomography analysis will be performed to evaluate material' therapeutic potential construed as new bone formation effectiveness.

We assume that, fabricated by our group scaffold, because of targeted regulation of distinct cell populations will enhance bone regeneration in experimental animals. Obtained results will deliver valuable data about the synthesis of innovative biomaterials with controlled drug release system. Moreover, it will elucidate the mechanisms of bone regeneration in osteoporotic patients.