Contagious diseases are not unusual and have been around mankind for centuries. However, it is remarkable that the other diseases affecting humanity are neglected in the pandemic time (COVID-19). Moreover, after infection the people often struggle with ailments resulting from extensive damage to tissues and organs. Therefore, the diagnostic and regenerative aspects in medicine are so important in pandemic and post-pandemic era. Tissue engineering wants to face these neglects through looking for new solutions related to the regeneration of organs and tissues. The fundamental elements used in tissue engineering are biomaterials, stem (progenitor) cells and bioactive molecules. These elements create the so-called **triad of tissue engineering**, promoting (together or separately) the process of tissue regeneration and remodelling. The creation of biomaterials which simultaneously act as carriers for stem cells and bioactive substances is vital for the rebuilding of functional tissue and determines the therapeutic effectiveness. This approach is especially important in the context of treating extensive tissue damage, such as critical bone or nerve defects resulting from trauma or resection of bone affected by cancer, as well as craniocerebral injuries and spinal cord injuries.

In the project, it has been planned to obtain and characterize a multi-element system based on the use of nanosized phosphate-silicate compounds with apatite structure (**nSi-HAp**) doped with lithium ions (**Li^+**) and co-doped with rare earth ions (**RE^{3+}**) for stem cell stimulation. The developed system will influence the proliferation and phenotypic plasticity (ability to differentiate) of stem cells, favouring the regeneration processes. The main goal of the project is to study the effect of nHAp material structurally modified with Li^+ and RE^{3+} (e.g. Eu^{3+}, Sm^{3+}, Tb^{3+}, Yb^{3+}) ions and chemically modified with chemotherapeutic agents (e.g. metronidazole, tynidazole) enclosed in the obtained biodegradable polymers (e.g. polylactide (PLA), poly(l-lactide) (PLLA) or poly(D,L-lactide) (PDLA) or poly(D,L-lactide-co-glycolide) (PDLLGA)), the proliferative and metabolic potential, and the tissue-directed differentiation of progenitor cells. Our pilot studies have shown that nSi-HAp modified with Li^+ and RE^{3+} ions can have a positive effect on the activity of established animal cell lines, including macrophages, as well as multipotent adipose and glial progenitor cells. The resulting multi-disciplinary team will determine how human progenitor cells isolated from the bone marrow act in the presence of engineered nanoparticles. The research will be related to the understanding of the mechanism of operation of the obtained systems, and the main molecular pathways related to the regeneration processes of bone, cartilage, adipose and nervous tissue will be analysed.

The result of the project will be the production and detailed characterization of multifunctional biomaterials, based on nanosized phosphate-silicate compounds with apatite structure, structurally modified with ions and modified with chemotherapeutic agents closed in the obtained biodegradable polymers as biocomposites of potential importance in tissue engineering. The research will include the synthesis of nanocrystalline phosphate-silicate compounds with apatite structure modified with Li^+ and RE^{3+} ions and chemically with the drug, determining their structural and morphological properties, and a study of interfacial connection mechanisms with biodegradable polymer and evaluation of its functionality related to stimulation of tissues and organs after implantation into the body (so-called bioactivity). In addition, tests are aimed to determine whether Li^+ and RE^{3+} ions can be released from the designed samples. The strategy related to the modification of nanomaterial surfaces with biodegradable polymers allows for increasing the compatibility of such systems and enables more stable attachment of active substances to their surfaces. The drug should then be released in a more controlled and sustained manner, which is important for effective therapy, including the elimination of side effects and, finally, overcoming multidrug resistance (MDR). Furthermore, the research is aimed at the detailed characterisation of osteogenic, chondrogenic, adipogenic and neurogenic properties of biomaterials both in an in vitro model (progenitor cells) and using an *in vivo* model (ectopic tissue formation study).

The research conducted under the project will fulfil current strategies realized in tissue engineering related to the development of innovative biomaterials for precision/personalised medicine supporting the regeneration of critical tissue and organ defects at the site of damage (regeneration in situ). The planned work in the project will contribute to the development of modern and advanced research methods crucial for advances in personalized medicine and theranostics.