

Chemotherapy with application of compounds of natural origin, for example paclitaxel, is of great importance in the treatment of neoplastic diseases due to the unique therapeutic activity and the ability of these compounds to act on many molecular targets. On the other hand, serious bacterial infections accompanying the chemotherapy or resulting from surgery or implantation are also a serious therapeutic problem, and the necessity of their prevention is a challenge. The treatment of cancer and the serious problem of the growing resistance of cancer cells and bacteria in the case of severe inflammations still require the development of new therapeutic strategies. In both cases, it is reasonable to use natural compounds with a broad activity profile. Unfortunately, their poor solubility, and thus low bioavailability, limits their effectiveness in any therapies. Nanocarriers that improve the bioavailability as well as can influence the overall biological activity of such systems are a response to the above-described problems. The combination of natural compounds (phenolic compounds, other biomolecules of plant origin, biopolymers) and metal nanoparticles (Au NPs, Au/Ag NPs) as both active ingredients and/or carriers can turn out to be much more advantageous than the use of monotherapy. Such an approach may also lead to the discovery of previously unknown additive and/or synergistic therapeutic effects.

The main goal of the project is to answer the question of how to consciously synthesize new hybrid/composite biomaterials by controlling their spatial and modular structure to achieve the desired activity. Biomaterials will be designed based on Au NPs, phenolic compounds of plant origin, and biopolymers (chitosan) as the main building blocks of nanomaterials with various spatial and composite structures: *i*) colloids, *ii*) fibers and *iii*) films (coatings). The obtained materials will be precisely characterized in terms of size and morphology (SEM, TEM, DLS, NTA), electronic surface states (XPS), crystal structure (XRD), and the presence of an organic coating (IR-ATR, TGA). The reactivity will be tested *in vitro* in condition mimicking the biological environment. The stability of the organic coating will be assessed, interactions with macromolecules important from the therapeutic point of view (including blood plasma proteins, DNA) as well as the kinetics and mechanism of Au NPs release from the developed fibers and coatings will be investigated. A novel non-optical method of tracking the formation of the protein corona in complex biological media will also be used. NPs will be labeled with fluorophores or ¹⁹F, and their diffusion coefficient will be measured by Fluorescence Correlation Spectroscopy (FCS) or ¹⁹F Nuclear Magnetic Resonance Diffusion Spectroscopy (NMR, COSY). In addition, a significant novelty in this project is the application of the latest *in vitro* research approaches based on 2D and 3D cell models: co-cultures of eukaryotic and prokaryotic cells and spheroids/organoids, respectively. In turn, the use of high-resolution microscopic visualization techniques and advanced research at the level of nanomaterial-cell interactions make this project groundbreaking. Detailed research on both the physicochemical and biological characteristics of the obtained nanomaterials will allow the selection of the most interesting materials for more detailed research and will allow to indicate the advantage of one form of material with a specific spatial and modular structure over another.

Concluding, the project focuses on gathering scientific evidence that the controlled and targeted use of well-characterized formulations containing metal nanoparticles is both safe and therapeutic. **A novel approach is to study the interaction of the spatial and modular system for three different types of nanomaterials containing Au NPs (colloids, fibers, coatings) on the biological response in the most advanced *in vitro* model systems mimicking the environment of an infected wound (cultures of human macrophages infected with selected bacterial strains) and microenvironment of a solid tumor (spheroids, organoids).** This approach is characterized by the advantages of near-physiological experimental conditions over the simple monoculture approach of eukaryotic and prokaryotic cells significantly deviating from natural conditions.