Reg. No: 2018/31/B/NZ6/02476; Principal Investigator: prof. dr hab. Robert Bucki

Increasing drug resistance of microorganisms resulting from the uncontrolled and often inappropriate use of antibacterial drugs has caused bacterial and fungal infections to become one of the main burdens and threats to public health. A decrease in the therapeutic efficiency of modern antibiotics due to this increased drug resistant-associated morbidity and mortality has motivated the search for novel, effective compounds with antimicrobial activity. The employment of nanotechnology-based approaches and natural antimicrobial peptides (AMPs) is an especially attractive option. Literature reports clearly indicate that LL-37 peptide, one of the best-known representatives of this group, is characterized by multi-directional biological action, including a broad spectrum of antimicrobial activity, regenerative properties and the ability to modulate the host's immune response. It is believed that such pleiotropic action of the peptide is conditioned by its interaction with a number of membrane receptors and intracellular factors, the activation of which results in diverse biological effects. It is postulated that ceragenins due to chemical and structural similarity, could show corresponding properties and equally multifaceted action. To date, it has been demonstrated that ceragenins are characterized by a broad spectrum of antimicrobial activity, also against bacterial and fungal strains resistant to modern antibiotics and chemotherapeutics. However, the exact mechanism of action of these compounds at the molecular level has not been fully understood, nor has the exact potential of these compounds in terms of their use as regenerative and immunomodulatory agents been examined.

Considering the reports indicating the possibility of using metal nanoparticles, including gold nanoparticles, as drug carriers and factors to enhance the activity of other biologically active compounds, we plan to perform the synthesis and physicochemical analysis of nanosystems in which different ceragenins (CSA-13, CSA-44 and CSA-131) will be immobilized on the surface of gold nanoparticles. We also plan to create a system employing cyclodextrins - cylindrical polysaccharides, which are widely used in the pharmaceutical and cosmetic industries to reduce the toxicity and adverse effects of drugs, improve their solubility and bioavailability, and thus, increase biological activity.

It is assumed that conducting experiments in both cell culture and animal model, as well as extensive computer simulations, will result in the creation of new nanoantibiotics with significant activity against drug-resistant pathogens and will enable comprehensive assessment of the therapeutic potential of ceragenins and nanosystems as modern immunomodulatory and regenerative agents.