DESCRIPTION FOR THE GENERAL PUBLIC

Antimicrobial peptides (AMPs) represent a group of widely distributed compounds with wide spectrum of antibiotic activity (against bacteria, fungi, viruses and parasites) produced by most of the living organisms. Besides antimicrobial mode of action, they are also involved in the intracellular processes of wound healing and angiogenesis, modulation of the immune response and toxin neutralization.

Due to the uprising incidents of the drug-resistance among pathogenic strains of bacteria and fungi, many of the research groups from both academy and pharmaceutical industry have focused their effort on the development of novel anti-infective drugs exploring the antibiotic potential of AMPs.

The aim of our project is to utilize the antibiotic properties of the selected AMPs in two types of conjugates that could be effective in eradication of intracellular infections and biofilm. Both intracellular invasion and development of biofilm represent mechanisms responsible for development of antibiotic tolerance of pathogenic microbes, that in consequence leads to failure of standard antibiotic therapies.

Trying to answer this problem , we propose synthesis of two types of conjugates:

a) **AMP-Vitamin**, where AMP is covalently bound to molecule of specified **vitamin (B3,B6, H or E)** . From our point of view, conjugation with vitamin will enable AMP non-invasive permeation of eukaryotic cell membrane and further neutralization if intracellulary entrapped bacteria. To test the effectiveness of this type of bicomponent compound, we will use the model of macrophage (human and mice) infection with pathogenic strain *Staphylococcus aureus* within collaboration with research group of professor Jan Potempa (Jagiellonian University), who established this method to study mechanisms of intracellular persistence of this bacteria.
b) **AMP-nanoparticle**, where AMP will be covalently linked to functionalized **quantum dots of ZnO** (10-30 nm diameter) (the particle will have surface exposed free amine group). This particular model of compound will be utilized by us for eradication of biofilm developed by pathogenic bacteria (*Pseudomans aeruginosa*, *S. aureus*) and fungi (*Candida albicans*).

The biological properties of the obtained compounds (both initial AMPs and their conjugates) will be thoroughly established in several *in vitro* tests aimed at evaluation of their antimicrobial activity, potential cytotoxicity towards human cells and, finally, ability to eradicate biofilm and intracellular *S. aureus* engulfed within macrophages.

In case of promising results of microbiological tests combined with confirmed low toxicity towards mammalian cells, the proposed conjugates could be potentially utilized for treatment of chronic wounds and reoccurring skin infections (AMP-Vitamin) or production of novel polymeric materials with antimicrobial and antibiofilm properties.