Description for the general public

The rapid development and spread of a variety of microorganisms resistant to conventional antibiotics has become a serious epidemiological and clinical global concern in last years. In addition, the problem is getting more substantial by appearance of new and re-emerging infectious diseases. Antimicrobial peptides (AMPs) are promising therapeutic compounds because (i) they act against a broad spectrum of microorganisms (bacteria, viruses, fungi), (ii) they do not induce resistance mechanisms in microbes, (iii) they can efficiently neutralize toxins released by pathogens and (iv) modulate the host immune response. Among various AMP families are defensins, dermaseptins, cathelicidins and temporins. In our proposal we designed the group of 12 peptide conjugates consisting of two components: one characterized with antimicrobial properties (e.g. analogues of temporin-1 CEb) and second with high affinity to phospholipids membranes (such as: dalargin or carnosine) facilitating conjugates internalization by eukaryotic cells. The conjugates were designed based on results of our preliminary study carried out on the derivative of temporin. Our data showed that tested peptides possess a strong antimicrobial potency against intracellular pathogens. Moreover, we revealed their ability to neutralize proinflammatory activity of selected pathogen associated molecular patterns (PAMPs). Therefore, the main goal of the project is to evaluate the role of proposed conjugates in the elimination of intracellular pathogens expressing those PAMPs. We will analyze the action of our conjugates against obligatory intracellular pathogens (e.g. *Legionella pneumophila*, herpes simplex virus, coxsackievirus), as well as facultatively intracellular bacteria (*Staphylococcus aureus* and *Porphyromonas gingivalis*). The objective of this proposal is to select novel peptide conjugates with the potent antimicrobial activity against intracellular pathogens, which are safe for the mammalian host. Additionally, in our project we will investigate immunomodulatory activity of designed compounds. The biological properties of conjugates will be examined using various biological tests, which allow to determine their potential cytotoxicity to mammalian cells and ability to penetrate into eukaryotic cells. Taking into account that cationic peptides are being considered as a new generation of antibiotics, obtained data in distant perspective can serve as an excellent entry platform for development of novel peptide-based drugs against intracellular pathogens.