Description for the general public

The growing resistance to commonly used antibiotics has become a great threat nowadays. There exists an established list of so called alarm pathogens, which are responsible for majority of mortality and morbidity events in the world as far as infectious diseases are concerned. Among several species, the list includes methicillin resistant *Staphylococcus aureus* (MRSA). Under this name we mean strains resistant to routinely administered β-lactam antibiotics including methicillin, oxacillin and others, however such phenotype is very often accompanied by multiresistance to other antibiotics. In recent years, growing number of *S. aureus* strains resistant to vancomycin and other glycopeptides has been reported. The rate of resistance acquirement exceeds that of novel drugs introduction, pointing out at the fact that new antimicrobial compound discovery is a very challenging task.

Currently the emphasis is put on the development of new techniques allowing to overcome a multidrug resistance in microorganisms, which either can be applied alone or can be used in combination with classical applications. One of such alternatives is an antimicrobial photodynamic inactivation (PDI) – a method historically used in cancer treatment, but lately gaining much popularity in antimicrobial research. PDI is based on combined action of photosensitizing compound (photosensitizer), light of a proper wavelength and oxygen. When applied together, they lead to generation of reactive oxygen species and trigger local stress environment in which surrounding cells are being damaged and killed. This approach has a potential especially in treatment of skin lesions and wound infections and can serve as a potent complementation of antibiotic therapy.

Despite the availability of many research models in the field, the mechanisms that take place in bacterial cell upon action of light-activated compound still remain elusive. As a result, a conventional PDI method is often unequally efficient towards strains of high biochemical diversity. Currently, new strategies to improve classical photoinactivation method are under investigation, aiming to obtain a higher specificity and efficacy towards microorganisms. This project concerns a combination of light-activated porphyrin and a small molecule adjuvant farnesol, which can specifically potentiate porphyrin's antibacterial action against *S. aureus*. Compounds used in the study – light-absorbing porphyrin of complex name 5.10.15.20-tetrakis(1-methyl-4-pyridinio)porphyrin, abbreviated as TMPyP and farnesol, a natural compound of plant origin – reveal a synergistic action, thus the activity of combined compounds is greater than summarised activities of compounds used separately. This phenomenon has not been examined so far and its molecular background remains unknown. The main goal of the project is to characterize the mechanism of TMPyP and farnesol's combined antimicrobial action. This will be achieved by identification of bacterial genes specifically induced in response to applied mixture of compounds and light. Complementation of the project will shed light on processes taking place in *S. aureus* cells. This is the first step to elucidate the mechanism of antibacterial action of analysed compounds.