Molecular mechanism of the biological activity of the antifungal antibiotic amphotericin B

Owing to a dramatic rise in mycotic infections their effective treatment is a topical and highly important issue. Amphotericin B belongs to a group of life saving antibiotics, used as a gold standard to treat deep-seated mycoses. Unfortunately, high effectiveness of this antibiotic is associated with the severe toxic side effects to patients. A research activity of numerous laboratories worldwide is focused on the problem of elaboration of a pharmacological formula of amphotericin B effective in combating mycotic infection and characterized by a minimized toxicity to human cells. Within the present research project we plan to address this problem with application of microscopic techniques based on fluorescence lifetime imaging and on resonance Raman scattering. These techniques allow to image localization of molecules of amphotericin B in human cells and cells of fungi. Moreover, these techniques allow to study specific organization and interaction to other biomolecules, such as sterols and lipids, responsible for the biological activity of the antibiotic and the toxic side effects. One of the aims of our project is to separate the pharmacologically desired biological activity of amphotericin B from the toxicity of this drug to patients via engineering nanoscale structures specifically involved in different modes of action of the drug with respect to cell membranes. We hope that our studies will substantially broaden our knowledge on the detailed molecular mechanisms underlying biological activity of amphotericin B. We also hope that expected results will bring us closer to achieving the goal of developing a safe to patients pharmacological formula of the antibiotic.