OPUS 10 - National Science Centre (Poland)

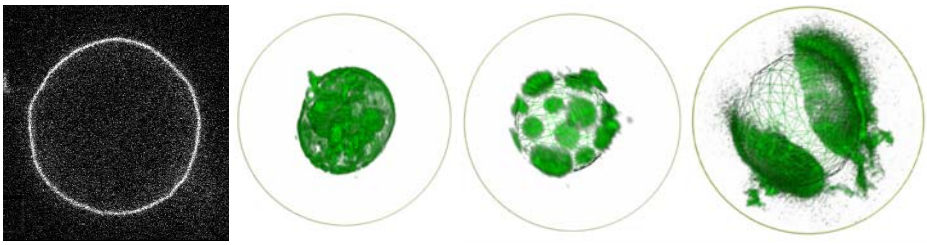
INNOvative antiSEPTic agents for a therapy with a broad spectrum of action "INNOSEPT"

The scientific goal of the project is to develop a molecule, that will cause mechanical stress in bacterial membranes, for medical applications in the treatment of infections caused by antibiotic-resistant strains.

The bacteria are becoming more and more resistant to antibiotics. The widespread use of antibiotics in medicine and breeding led to rapid evolution of bacteria resistant to several antibiotics. One of the most promising ideas is to provide a molecule that will be able to change the mechanical properties of bacteria membrane that will lead to its destabilization or at least will alter those mechanical properties, that it will be possible to distinguish the bacteria from the rest of the environment. It is a very advantageous solution, since the cell has a little possibility of creating a genetic resistance to mechanical attack. However, to create such a form of attack on the cell it is necessary to find a parameter that would be the determinant of the effectiveness of bacteria membrane destabilization.

For this purpose, the newest technologies will be used to peek deep into the bacterial membrane and to understand the mechanisms allowing it to be selectively destroyed. The 3-years project involves the use of powerful computing centers, consisting of tens of thousands of computers to find parameters describing this particular phenomenon. Then a staff of scientists specialized in pharmaceutical analyses, and guided by the parameters set by computers, will conduct the cutting-edge research experiments aiming to select the most effective molecule. Finally, to verify the actions taken, they will use the newly developed hybrid research methodology consisting on microscopic observation of bacterial membranes in 3D and in a real time, combined with an automated numeric processing. This method is able to illustrate the mechanism of membrane destruction far below the resolution of standard optical microscopes (*flicker noise fluorescence method, see figure below*). Finally, for the most effective molecule it will be developed a special liposome carrier known from cosmetics industry, in order to facilitate the penetration into infected wounds and to provide a long-lasting effect. The effectiveness of such a developed molecules will be tested using bacterial cultures.

Our experience in the field of computer-aided research on the level of atoms and molecules, as well as many years of experience in developing liposome formulations of drugs for targeted therapies dedicated especially for the treatment of cancer, led us to take an action in global challenge of an increasing antibiotic resistance in bacteria, which presents a real health risk for the whole society. Using the research methods of the XXI century we have the ambition to develop a molecule that can help millions of people around the world. Of course we are aware that before the product enters pharmacies and hospitals, must undergo a long and difficult verification path. A great ideas start with small steps in basic research.



The grease bubble resembling a bacterium. On the left a microscope image, on the right subsequent phases of membrane disruption observed in a real time. Computer-aided flicker noise fluorescence method.