MODULATION OF STABILITY OF VIRIONS – A FIGHT FOR AND AGAINST VIRUSES

As viruses might be our allies (in vaccines, as sensor elements, "messengers" in genetic therapies) or enemies (sabotaging biotechnological processes) it is important to support or deactivate them. The modulation of stability of virions is the main goal of the proposed project.

Viruses are parasites, which hosts are cells. Without cells viruses cannot perform their live cycle. Often virus cause the dead of the host upon release of number of copies of virions. Cascade of progeny virions attack neighboring cells or transfer to another host organism. There are viruses, which attack animals and humans, causing various diseases (like HIV, HPV, Hepatitis A and B, influenza, rotavirus, Zika, rubies to name only a few), plants (Tabaco mosaic virus) or even bacteria. Proposed project within Sonata Bis focuses on viruses attacking bacteria – named bacteriophages, or phages for short.

There are two main reasons for such a choice. First of all phages cause serious problems when they infect the bacteria based biotechnological factories. Within hours a single bacteriophage can be multiplied in millions of copies utilizing biochemical machinery of the host. In each bacterial cell up to few hundreds copies are formed and released. This usually results in death of bacteria. This has profound repercussions as bacteria based processes are one of the most important in biotechnology and dominate a number of branches of industry which exploit natural metabolic capabilities of bacteria to produce active substances All factors, which may cause closures of bacteria-based factories, cause millions of dollars in losses. We would like to explore the possibility of deactivation of virions by external electromagnetic field (in the first approach by the electric field) and its combination with other external factors. We will examine the mechanism of interaction between the field and phages. In contrast to all previous approaches the method will not be invasive. Our preliminary results confirm the existence of the effect, but its nature is unknown. Revealing the mechanism could allow for optimization of the virus deactivation method. The knowledge gained upon realization of the project might be also utilized against pathogenic viruses attacking humans, helping to fight against numerous diseases. We expect that the knowledge gained by realization of this task will help to understand the risks of living close to high voltage lines, which are now under discussion.

Second reason for deciding to focus on bacteriophages is a fact that among them are species (like bacteriophage MS2), which are great models for studying viruses attacking eukaryotic (also human) cells. As such they are great to study the methods for preserving vaccines. We would like to make an impact by developing the method for improving thermal stability of viruses. Maintaining the potency of virions requires keeping vaccines refrigerated during all its lifetime from production to administration. This is especially challenging in remote regions of developing countries – places, where vaccination programs are of most urgent importance. It appears that up to 80% of costs of vaccination programs is generated by the need of storing and transporting of the vaccines in low temperatures (so called "cold chain problem"). It is estimated that this increase a cost of vaccine programs by $200–300 million per year. Another issue is fight against antibiotic resistant bacteria. The advent of post-antibiotic era has started. Phages might be drug of last resort in number of cases, as they disrupt bacterial cells. But there is a need to support/modify them to deceive immune system. The improvement in stability of virions will be obtained by linking the capsid (part of the virion, where genetic information is stored) proteins by adjustable linker by bioconjugation reaction.

Influencing the structure of microorganism by deliberate chemical modification is new way to obtain modified organisms. But instead of GMO (genetically modified organisms) we will open a completely new field of CMO (chemically modified organisms).