D1 DESCRIPTION FOR THE GENERAL PUBLIC (IN ENGLISH)

Due to the development of antibiotic-resistant bacterial strains, there is an increasing need to evaluate and develop alternative methods for antibacterial treatment. Scientist all over the world are looking for an alternative bacterial infection treatments methods, which will be biocompatibility and devoid of generate a new kind of resistant bacterial strains. In addition, the efficiency of vaccines inducing adaptive immune responses could be impaired by the rapid immune evasion of pathogens through their frequent mutations. Recently, it has also been demonstrated that a new allotrope of carbon, graphene oxide, has antibacterial activity, and also been reported to be more effective than some currently used therapeutic antibiotics – kanamycin. Moreover, graphene oxide should devoid of generate a new kind of resistant bacterial strains. The surface of graphene is covered by electron cloud, which predisposes this material to make permanent bonds with many various compounds at this same time, also with biomolecules.

Immunotherapy is the treatment of disease by inducing, enhancing, or suppressing an immune response. Activation immunotherapy is designed to elicit or amplify an immune response. Immunomodulatory regimens often have fewer side effects than existing drugs, including less potential for creating resistance in microbial disease. The natural non-peptide antigens are usually fixed in their structure with less antigenic modulation and are much smaller, so the recognition of these antigens is more quickly and effectively with as fast as 2-3 minutes after exposure, indicating that it is no need for antigen uptake and processing. (*E*)-4-hydroxy-3-methyl-but-2-enyl diphosphate (HMBPP) have been identified as specific bacterial phosphoantigen, an immediate upstream metabolite of isopentenyl diphosphate (IPP). HMBPP is approximately 1000-fold more potent than isopentenyl pyrophosphate for the in vitro activation of T cells, what make it an ideal bacterial phosphoantigen to use in nanoimmunostimulatory biocomplexes.

The possibility to chemically modify graphene oxide allows creation of new biocomplexes that can be adapted to the specific immune intervention. The presence of bacterial phosphoantigens on graphene oxide can facilitate cellular uptake by antigen presenting cells through recognition and activation of surface receptors and trigger the immune system to fast response.

The main aim of the research project is to assess the effectiveness of nanoimmunostimulatory biocomplexes of bacterial phosphoantigen, IL-2 and L-glutamine with graphene oxide deck on the activation of leukocytes in research conducted *in vitro*. Nanoimmunostimulatory biocomplexes will base on graphene oxide platform, which is two-dimensional carbon structure. To the deck will be incorporate non-peptide, specific, bacterial phosphoantigen – HMBPP, enriched by IL-2, together this compounds will stimulate immune system. The complex will be powered by additional source of energy for immune cells, L-glutamine. In the future, this nanoimmunostimulatory biocomplexes could be an alternative to antibiotics therapy for intracellular bacterial pathogens infection.

Research will be conducted on 4 different human cell lines, human leukemic T-cell (Jurkat), primary human peripheral blood T cells, primary human peripheral blood monocytes and peripheral human mononuclear cells. The study will be done in 3 experiments as distinct tasks. Experiment 1 is about synthesis and physicochemical properties characterization of nanoimmunostimulatory biocomplexes. Results of experiment 2 allow to assess the biocompatibility of nanoimmunostimulatory biocomplexes (cell morphology, ultrastructure, proliferation level and viability assays). Project include also experiment 3, where inflammatory mediators secretion analysis on protein and mRNA level will be perform.

Presented research project results will assess the validity of potential use graphene oxide-based nanoimmunostimulatory biocomplexes as bacterial phosphoantigen carriers. Showing the positive results of biocomplexes on immune cell lines activation and intensive proliferation will be a basis to further studies on the application of those biocomplexes in intracellular bacterial pathogens infection treatment, as an alternative for antibiotics. Experiments in proposed project will verify how nanoimmunostimulatory biocomplexes modulate and stimulate immune system by activation, maturation and proliferation chosen immune cell lines (T CD4+ cells, CD14+ monocytes and human peripheral mononuclear cells). The results of this project will be the first reports on the graphene oxide-based nanoimmunostiulator in intracellular bacterial pathogens infection treatment.