Educational project summary

The project is aimed at understanding the mechanisms of formation of sugar coatings on the surface of the pathogen responsible for periodontitis in humans, *Porphyromonas gingivalis*, and use that information to produce new vaccines. Testing of vaccines will be conducted on mice.

Porphyromonas gingivalis is a human pathogen responsible for periodontitis. At present, there are no specific vaccines or therapeutics for protection against infection.

The pathogen has a sugar coating on the surface which is fixed and connected to the second shell which is variable. Variable sugar coating allows the pathogen to escape recognition and destruction by the immune system of the host. On the basis of genetic information, elements making up the core shell are known but the mechanism of formation of coatings is not fully understood. Based on data from other bacteria, part of the synthetic pathway responsible for generating sugar coating of *P. gingivalis* can be reconstructed and compared with the mechanisms of formation of sugar coatings in bacteria and higher organisms. In the proposed design, we want to use this information to isolate a part of the *P. gingivalis* genome to redirect and reconstruct the variable sugar envelope in a commercial *E. coli* strain used for the production of proteins. The envelope will be connected to a protein secreted by the pathogen and known to elicit a strong immune response in the host. Because the sugar part is low-immunogenic in the host, the construct will be combined with the carrier nanoparticle to enhance the host immune response. The final product will be tested in a mouse model of *P. gingivalis* infection in order to determine the effectiveness of the vaccine.

The work plan will be divided into four steps: a) genetic engineering in order to construct a vector producing sugar coating and a modified version of the protein secreted by a pathogen containing the sequence necessary for recognizing a site to join and start the synthesis of shell, b) production of nanoparticles and coupling of the construct with the nanoparticle carrier, c) testing the product stability and toxicity in a cell culture, and d) testing the protection against infection in a mouse model of pathogen infection.

The importance of the project

The project deals with issues in the field of basic sciences for the pathogen of major clinical significance. Studies will include the integration of genetic knowledge and its reflection in the sugar coatings produced by the pathogen. Analysis of the products will increase the knowledge in the area of sugar coatings and mechanisms for their creation. Work on the mechanisms will allow for better understanding of the mechanisms of handling the immune system by the pathogen.

Construction of new media for nanoparticle fusion proteins will may lead to new products with potentially lower toxic effects of new vaccines than those designed by using traditional media and will open a new field of research on such media. Evaluation of the effectiveness of new nanoparticle adjuvants will be carried out in a mouse model of infection.

The success of the project will allow for the development of similar solutions for other pathogens of clinical relevance. Solutions should provide new generations of vaccines in a short time based on correlation of existing data and DNA sequences of known paths of synthesis of sugar shells. This approach will significantly reduce the time to develop vaccines and commercialize them.