Popularizing abstract of the project entitled: The role of milk matrix lipids in programming the immunoreactivity of proteins derived from lactic acid bacteria

The reason for undertaking the specific research topic is the fact that food allergies (FA) remain a global problem despite many years of scientific efforts. It has been estimated that the immune system of about half of newborns is not able to develop tolerance to food proteins. The global FA diagnostics & therapeutics market size was valued at USD 2.69 billion in 2018 and is expected to grow by 7.4% over the next 10 years. An elimination diet remains the only effective way to prevent this condition, but that strategy causes discomfort for the patient and his family. An effective exclusion of allergens from the patient's diet often turns out to be impossible, given that more than 1,000 substances with allergenic potential have been identified so far. Moreover the use of new raw materials and modernization of technological processes favor the emergence of new allergens. The main food-origin allergens that the infant's body is in contact with are cow's milk proteins since they are likely the first cross-species animal protein source encountered. However, in the prenatal period, much earlier in the life cycle, bacterial cells and their components present in the placenta can affect the fetal immune system. It is estimated that each live bacterial cell is capable of producing on average 15 femtograms of proteins so in one cup of e.g. yogurt there is almost 30 mg of bacterial proteins (BP). This amount of proteins for the oversensitive organism might be threatening. The composition and functions of produced BP may depend on the genus of bacteria, its condition and interaction with environmental factors such as media used for their cultivation, additives, and stress (e.g. non-optimal temperature or oxygen concentration). The human immune system in most cases should tolerate BP but preliminary studies of applicants showed that some lactic acid bacteria have in their structure a regions of proteins which can be recognized by the antibody classes E and G1 (associated with FA) and not, as previously thought, only with antibodies A, M and G4 (associated with specific tolerance of commensal microbiota). In addition, it was observed that the profile of produced BP could be influenced by the composition of the culture medium, and lipids appeared to be an important factor. Some compositions appear to be preferable and promote lower production of immunoreactive proteins in bacterial cells. The studies of other groups show that in fact in people with AP there is a much more frequent dysfunction of the MyD88-ROR-γt axis, which is involved in the development of tolerance. This results in the development of hypersensitive reactions even to the proteins of the physiological intestinal microbiota. It means that the reaction to the proteins of the bacteria consumed in the diet can be analogous.

The aim of the project is to program, through the use of specific lipid fractions, selected strains of bacteria of the *Lactobacillus* genus for the production of proteins with the potential to induce mechanisms related to tolerance and inhibit the expression of proteins that induce AP mechanisms.

Functional analysis of proteins produced in bacteria and their impact on the mechanisms occurring in intestinal and immune cells will allow to broaden knowledge about their putative role in the course of the allergic process. We hypothesize that the targeted selection of a raw material with an optimal lipid composition can improve the nutraceutical properties of products containing tested bacteria.
In this project, proteins from bacteria of the *Lactobacillus* genus will be investigated because these bacteria are the most often used in fermented food processing technologies and in probiotic preparations. In general, their use supports natural immunity and alleviates the course of FA, but there are also some ambiguous reports of the deterioration of the health of patients with FA as a result of probiotic supplementation (Martin-Muñoz, 2012). Therefore, in the planned project, it is planned to verify the previously observed potential BP to bind to human IgE and IgG1 antibodies, using sera from patients diagnosed with AP, which may constitute a scientific basis for further steps of the planned research explaining the role of BP in the development of AP and / or tolerance. The properties of these proteins and their roles in individual mechanisms will be then assessed using cell lines of the intestinal mucosa at various stages of maturity (undifferentiated - a model imitating the conditions prevailing in the small intestine of infants, and on the model of differentiated cells - i.e. the model of mature intestine). The immunoreactive effect of BP will also be tested with lymphocyte cells involved in the regulation and control of immunity. Studies involving a mouse model were also planned to check the influence of the tested BP on a living organism.

The results that will be obtained during the course of the project may provide evidence for a new aspect of interactions between the lactic acid bacteria and the human immune system. The targeted selection of a raw dairy material with an optimal lipid composition can improve the nutraceutical properties and safety of products containing these bacteria. The new primary knowledge is a base to implement an "immunoreactivity of bacteria" analysis as a new discriminant of food safety.