Extracellular vesicles as mediators of intercellular communication in an organism exposed to PET microplastics - multi-omic studies in domestic pig model

Plastics have been on the market for over 100 years, and due to their practical properties, the trend to use them in agriculture, industry and even in our daily lives has spread worldwide. In recent decades, global production of plastics has increased dramatically, from 1.7 million tons in the 1950s to 368 million tons in 2019. Considering current consumption and the rate of growth of the world's population, plastic production is expected to quadruple by 2050. Due to improper management and disposal practices, large amounts of plastic waste enter the environment through various pathways, causing serious pollution problems. Among plastic waste, microplastics (MPs) particles smaller than 5 mm, are of particular concern, mainly because of their long residence time in the environment, their small size, and their ability to penetrate cells and cause harmful effects. Microplastics have been found in drinking water – both bottled and tap – beer, table salt, honey, sugar, milk and canned foods, lipsticks, toothpaste, dietary supplements, juice clarifiers and food packaging materials, and in the air. Oral administration of MPs has been shown to lead to accumulation in the liver, kidney, intestine, and brain, which has been shown to lead to oxidative stress, energy imbalances, neurotoxicity, and behavioral disorders.

In the last decade, the role of extracellular vesicles (EVs) as a key player in physiological balance and homeostasis, as well as in disease processes, has been particularly emphasized. EVs are small membrane particles secreted by almost all cell types, and contain proteins, lipids, RNAs, and miRNAs. EVs have been reported to play important roles in numerous pathological conditions, including cardiovascular disease, promotion of cancer progression and metastasis, as well as autoimmune and neurodegenerative diseases. In addition, EVs also serve as mechanisms to eliminate toxic/unnecessary substances from the cell, suggesting their role in maintaining intercellular homeostasis.

The aim of our research is to determine the effects of polyethylene terephthalate (PET) microplastics (one of the most commonly used plastics) on the content of EVs isolated from selected body fluids (blood, bile, and urine) and the transcriptomic, proteomic, and metabolomic profile of tissues (liver and kidney) that are the main source of EVs in bile and urine. The experiment will be performed on sexually immature gilts. The animals will be divided into three groups: 1) control group receiving orally empty gelatin capsules; 2) experimental group receiving orally a low dose of microplastics; 3) experimental group receiving orally a high dose of microplastics. During our preliminary studies, we found that miRNAs in EVs isolated from the serum of piglets receiving oral PET microplastics can affect genes that regulate the tumorigenesis in the pancreas. Therefore, in this project, we decided to determine the *in vitro* effect of these EVs (more of their content) on the transcriptomic profile of pancreatic cells from piglets not treated with PET microplastics. The presence or accumulation of microplastics in the EVs will also be determined. The results obtained will provide new and valuable data on the potential effects of microplastics on various biological functions. The use of sequencing methods: RNA-Seq/Small RNA-Seq for the transcriptome analysis and liquid chromatography/tandem mass spectrometry (LC-MS/MS) for the proteome and metabolome analysis, will provide significant data on the expression of genes, proteins and metabolites associated with the organism’s response to microplastics.