

Plastics in our everyday environment have become a global problem, an integral part of life, and the extent of exposure and potential toxic effects of these contaminants on numerous human organ systems are becoming evident. Microplastics (MP) are tiny pieces of plastic with a particle size up to 5 mm, while nanoplastics (NP) are usually considered to have a particle size of 1  $\mu\text{m}$  and smaller, invisible to the eye. Plastic waste that ends up in the environment includes primary micro- and nanoplastics (MNP), originating from industries such as cosmetics, textiles, automotive, and chemicals, as well as secondary microplastics, which result from the fragmentation of larger plastic debris. Their widespread presence has been detected in water, soil, the atmosphere, and living organisms. The most commonly used plastic is polyethylene terephthalate (PET), a polymer widely used due to its low cost, light weight and ease of transport. Long-term exposure to MNPs can result in inflammation, oxidative stress, tissue damage and metabolic disorders.

Literature reports indicate that MNPs are currently a common source of exposure to harmful substances that can significantly disrupt the hormonal balance and impair intercellular communication. One of the main routes of cellular communication in multicellular organisms are extracellular vesicles (EVs) - small particles of endosomal origin, which are released into the extracellular environment by almost all types of cells and mediate intercellular communication via auto- and paracrine pathways. These structures, equipped with various signaling molecules such as proteins, lipids and various forms of RNA, including microRNA, significantly modify the functioning of recipient cells. In this way, EVs affect various biological processes, including those occurring in the reproductive system, such as growth, proliferation and differentiation of ovarian follicle cells, gametogenesis, oocyte maturation, fertilization, implantation or embryo development. Studies suggest that micro- and nanoplastics can interact with extracellular vesicles, changing their composition and function. Our previous research results indicate that extracellular vesicles isolated from piglet serum can transport PET plastic particles and that PET can change the content of transferred information molecules (miRNA) in the vesicles. In the case of oviduct epithelium, this may have a potentially important role in regulating fertility-related processes, because the altered communication between cells may affect ovarian function, egg transport, and the reproductive microenvironment.

The proposed research will use a novel *in vitro* 3D culture system of porcine oviduct cells. Long-term culture of oviduct epithelial cells will be conducted in microgravity conditions, which will be exposed to different doses of PET micro- and nanoplastics. The aim of the proposed project will be, among others, to analyze the effect of PET MNPs on the content of EVs secreted by *in vitro* cultured spheroids, as well as to determine the effect of EVs content on the biology of porcine oocytes and embryos. The proposed research belongs to the category of basic research. Understanding the role of extracellular vesicles in cell-to-cell communication in the context of micro- and nanoplastic pollution, including PET, will provide new insights into the mechanisms by which MNP pollution impacts human health, including reproductive health.