The ubiquity and accumulation of plastics in the environment pose a serious threat to the living organisms, including human. Production of plastics in the world is being constantly increased; in 2019, it reached 368 million tons.

Plastic may be degraded to microplastic particles with diameters of <5000 nm, and then to nanoplastics with diameters of <100 nm. One of the most commonly used plastics is polystyrene (PS). This substance has found many applications mainly in the production of styrofoam used for insulation of buildings as well as in food packagings (plates, trays, cups) and laboratory equipment. Recently, concerns have been raised about the impact of polystyrene nanoparticles (PS-NPs) on living organisms. PS-NPs enter the body via the respiratory and digestive systems and through the skin. Cox et al. (2019) showed that the annual human consumption of microplastics ranges from 39,000 to 52,000 particles. Recently, plastic microparticles with a size of 5 to 10 μm were determined in women's placenta (Ragusa et al. 2021).

Toxicity of nanoparticles depends on their size, shape, the presence of functional groups, solubility and chemical composition.

The studies that have been conducted by the applicant so far (Kik et al. 2021) have shown that PS-NPs are cytotoxic and exhibit oxidative potential in human peripheral blood mononuclear cells (PBMCs). The largest changes were caused by the smallest nanoparticles of 30-70 nm diameter; therefore the effect of these nanoparticles on human PBMCs will be more thoroughly assessed in this project.

The aim of this project is to verify the hypothesis that PS-NPs in the concentrations, which may be present in human organisms, can induce epigenetic and genetic disruption in human blood cells and, thus they are not safe for humans.

DNA damage and epigenetic changes (including, among others, complete methylation, methylation of the promoter regions of suppressor genes and protocogens, as well as the expression of these genes at the mRNA level) can disrupt numerous cellular processes, which in turn may lead to the development of various diseases, including cancer. Epigenetics is a relatively new branch of science, showing that not only direct DNA damage can result in measurable changes in cell (in human health), but quantitative changes in the levels of many (above-mentioned) proteins are also very important. Increased expression of proto-oncogenes (genes potentially associated with cancer formation) or decreased suppressor genes (genes protecting against cancer development) may also result in pathological processes in normal cells and tissues, and may, consequently, lead to pathological changes in the entire organism.

In this project, we will investigate the effect of PS–NPs on the above-mentioned epigenetic modifications in human blood cells for the first time. Genotoxic action of PS-NPs will be assessed by the analysis of DNA single and double strand-breaks formation, oxidative damage to DNA purines and pyrimidines, as well as evaluation of DNA damage repair.

Human PBMCs (mainly lymphocytes) will be used in this study. These cells are a very suitable research model as they are easy to isolate andabundant in biological material (in blood), and particularly because they play an essential role in the human body. It is well-known that PBMCs protect the human organism against various pathogens and cancer cells, participating in so-called immune response. After entering the bloodstream PS-NPs can disrupt the immune system, leading to the development of various diseases, including cancer. Styrene (the building block of polystyrene) has been shown to be immunotoxic.

The absence of conclusive evidence of nanoparticle toxicity is one of the major challenges in human health risk assessment concerning the effect of these substances. Obtaining the results on genotoxicity and epigenetic action of PS-NPs on blood cells would largely allow us to come closer into the human health risk assessment of plastic nanoparticles, which are widespread in the environment and consequently in living organisms.