Micro and nanoplastics (MNP) are tiny small fragments of degraded plastics. Contamination of the environment by MNP is a very serious problem and its impact on living organisms is still intensively studied. While the harmful effects of MNPs on fish and aquatic invertebrates are fairly well documented, its effect on mammals requires further research. Many studies have shown that MNPs can cross the gut lining and enter the body. In in vivo model on rats it has also been demonstrated that 20 nm nanoparticles of polystyrene were capable to pass the blood-brain barrier. Though MNP has been identified as a risk factor during environmental and occupational exposure of humans, little is known about its effects on the human body at the cellular level.

A wide application of nanomaterials in industry causes their increasing accumulation in the abiotic environment and in tissues of higher organisms. Despite the several years of scientists' efforts to make the nanomaterials safe, we are still unable to precisely determine its impact on environment and living organisms. In addition, environmental exposure of humans and biota to a single nanomaterial or nanoparticle is rather unlikely due to the ubiquitous presence of other types of nanoparticles. Therefore, in this project we will compare the impact of single nanoplastic, single metallic nanoparticle (silver nanoparticles, AgNPs) with the impact of their mixture on model in vitro and in vivo systems. AgNPs are among the most abundant NPs in the environment.

It has been found that accumulation of certain types of nanoparticles in higher organisms is associated with different effects, such as respiratory diseases, allergies, cardiovascular diseases and cancer. At the cellular level, in vitro studies it was shown that nanoparticles induce oxidative stress, which can affect intra- and extra-cellular cellular signaling pathways, including activation of epithelial-mesenchymal transition, one of the earliest stage of carcinogenesis.

Breast cancer is among the most common malignant neoplasm of women in the Polish population. According to the Polish National Cancer Registry in 2012 the number of breast cancers exceeded 16500 yearly (with increasing prognosis during next years). Especially dangerous is the fact that cancer morbidity rate among premenopausal women increased during the last three decades 1.7 times. In patients diagnosed with hormone-dependent cancer, blocking the estrogen receptors by administering their selective modulators, such as tamoxifen or raloxifene to the patient is a key therapeutic issue. However, the preliminary results indicate that silver nanoparticles can stimulate estrogen receptor-activated pathways through a pathway independent of hormone ligand binding and initiate cellular EMT transition.

This project aims to determine the role of AgNPs, MNP and their mixture in the estrogen-independent activation of the ERα, to investigate how nanoparticles will modulate receptor activation especially at low doses of the hormone and in the presence of tamoxifen, and to assess how nanoparticles will affect the expression of ERs in different tissues of animals exposed to nanoparticles.

We will use polystyrene nanoparticles and AgNPs stabilized with citric acid 29 nm diameter. Both types are widely used in scientific investigations model nanoparticles. Since one of the goals of this project is developing of new models for investigation of ERα-dependent signaling pathways, we decided to use model nanoparticles to enable comparison with existing literature. On the other hand, to mimic environmental exposure we decided to use MNP released from commercially available plastic tea bags.

The research model will be cell lines with a differentiated expression of the ERα , which may be a model of breast cancer cells. In addition, the *in vivo* model will examine how silver nanoparticles and their mixture with the nanolastic and the nanoplastic itself will affect the level of estrogen receptors in rat tissues.