BIONANOPARTICLES WITH A MOLECULAR TARGETING DEVICE AS A WEAPON FOR BREAST CANCER

Breast cancer is the second most common cause of death among Polish females. More than 25% of diagnosed cases are HER2-positive breast cancer (HER2+), which is one of the most aggressive forms due to overexpression of the HER2 receptor present on the surface of the tumor cell. In HER2+ breast cancer, the progression of the disease is very rapid and aggressive, with metastases to the lymph nodes and to the central nervous system. The most promising therapy for the treatment of HER2+ breast cancer is targeted therapy, in which treatment is individually tailored to the patient because of a precisely defined molecular target. In the treatment of HER2+ breast cancer, a promising form of treatment is the use of monoclonal antibodies such as Trastuzumab or Pertuzumab conjugated to well-known cytostatic drugs such as Doxorubicin or Tamoxifen. The molecular target of antibody-drug conjugates is to reach the tumor cell, block its activity and deliver the cytostatic drug. Unfortunately, this form of therapy has limitations. These include issues related to the administration of the drug in the body, i.e., short half-life or severe side effects such as cardiac problems, drug resistance, as well as enormous treatment costs amounting to approximately 4 000 Euro every 3 weeks. Thus, there is a continuing need to search for more effective and cheaper drugs in the treatment of HER2 + breast cancer.

The main goal of this project is to use peptide fibrils as nanoparticles as a new class of the drug delivery system for HER2+ breast cancer. Peptide fibrils are nanoparticles with high resistance to physicochemical and mechanical factors. Due to their amino acid structure, they are characterized by high biocompatibility as well as high possibility of chemical modification. In addition, fibrils have a large surface-area-to-volume ratio, which permits for higher drug loading and attachment of targeting molecules. In our project fibril will contain two covalently linked molecules: targeting and blocking HER2 activity - antibody Transtuzumab or affibody ZHER2:289 (Aff) and known breast cancer drug – doxorubicin (DOX). This entire construct (fibril + Ab / Aff + DOX) may be called a nanodrug. The development of universal system transporting the drug in organism, released it from carrier under influence of various factors such as pH change or presence of specific enzymes, would find wide application in treatment of various types of cancer diseases. Construct with fibril + Aff + DOX will be possible to synthesize in a chemical laboratory. Thanks to this, the drug we developed will be much cheaper in production and thus widely available.

We expect that due to the implementation of our project we obtain at least one nano-drug with proven anticancer activity, to be used in targeted therapy in patients with HER2+ breast cancer. The results of our project also contribute to the development of a new class of biological nanoparticles as weapon with molecular targeting device for other diseases.