

In the 21<sup>st</sup> century we have at our disposal unique technologies that make our everyday life easier and significantly improve its comfort. In medicine, modern technologies also have made a huge revolution. An important area in which significant progress has been made are materials for medical use. Modern biomedical materials are biodegradable, nanomaterials, intelligent materials or materials used in personalized and targeted therapies. Their quality, properties and capabilities allow tissue regeneration and effective treatment. Currently conducted basic, preclinical and clinical research on biomaterials is focused mainly on oncology, orthopedics and dermatology. However, gynecology is an example which is worth to increase the research dynamic on new therapies or materials, because of social and economic reasons of this endometriosis. Currently in Poland only 2% of clinical trials conducted annually concern gynecology. At the same time, women suffer from many diseases of which etiology is not well understood yet, and their treatment is only aimed at relieving symptoms, as there is no effective medicine. An example of such disease is endometriosis. Endometriosis is a disease in which cells of the endometrium, the tissue lining the uterus, form inflammatory lesions outside the uterine cavity e.g. on the ovaries, bowels or even skin. This chronic and hormone-dependent disease is characterized by symptoms such as severe pain during menstruation, pain during intercourse and infertility. About 10% (190 million) of the world's female population being in reproductive age suffers from endometriosis. In the most severe cases, endometrial lesions should be removed surgically. Unfortunately, this procedure does not guarantee success, because this disease recurs easily. It has been estimated that the frequency of endometriosis recurrences is 21.5% at 2 years after the procedure and 40–50% within 5 years.

The aim of the project is to develop and analyze the properties of a hybrid material for local drug delivery that could be used in the treatment or supporting therapy of endometriosis. A novel dual drug delivery system (DDS) based on nanofibers and hydrogel will be designed. The nanofibers will be loaded with progesterone, which reduces viability of endometriotic cells. *Anti*-CTLA4 antibodies placed in hydrogel should suppress the local inflammation associated with the disease. A new route of administration of the known bioactive substances may be more effective. So far, the research conducted on drug development confirmed that the change of the administration route may change the effectiveness of the drug. In order to achieve the project's aims, the work will be divided into five phases: material development and optimization (phase I), properties characterization (phase II and III) and *in vitro* (phase IV) and *in vivo* testing (phase V). In the first phase, polymers from the group of polyesters and biopolymers will be tested as a carriers for therapeutic bioactive substances. The selected polymers, which are widely admitted to the medical use, will be processed e.g. by the electrospinning. This method allows to form nanofibers, which are planned to be a progesterone carrier. The nanofibers will be placed in the hydrogel which will also contain the *anti*-CTLA4 antibody. Thanks to the use of superparamagnetic iron oxide nanoparticles (SPIONs), the possibility of controlled drug release through an external magnetic field stimulation will be investigated. The aim of the project is to conduct an extensive studies of drug release kinetics, mucoadhesion (interaction with the mucosa), degradation profile and efficiency in *in vitro* and *in vivo* experiments. A comprehensive analysis of the structure and properties of the DDS will be carried out. *In vitro* tests will verify the cells viability and production of interleukin IL-10 and TGF- $\beta$ , which stimulates the secretion of cytokines accompanying inflammation.

It is expected, that as a result of the project a novel hybrid biomaterial revealing an appropriate mucoadhesion and drug release profile of bioactive substances will be developed. The substances released from the DDS will effectively inhibit the proliferation and activity of endometriotic cells and regulatory T lymphocytes. *In vivo* tests will be carried out on a small animal model in order to initially verify the safety and effectiveness of the developed material.