The urinary tract infection (UTI) is one of the most common infection among people. It is estimated that over 10% of women all over the world, suffers from UTI at least once a year. The cost of UTI antimicrobial therapy, in the United States alone is approximately 8 billion dollars per year - covering the cost of 15% of all antibiotics prescribed in primary health care. *Escherichia coli* is responsible for more than 80% of urinary tract infections. It has been proven that the number of pathogens resistant to conventional therapy with antibiotics is constantly growing. It is also important that fluoroquinolones, one of the groups of medications commonly used in UTI, is characterized by considerable toxicity - one of the most serious side-effects observed in therapy with these compounds is cellulitis, resulting in permanent damage to cartilage and tendons.

The aim of the conducted research is to learn the protective mechanism of the LL-37 peptide and its analogs (ceragenins), in relation to the mucous membrane of the urinary tract which influences its resistance to bacterial infections. A more precise understanding of the mechanisms engaged in the natural immunological response to UTI, can enable us to design new methods of treating these infections.

The mucous membrane of the urinary system constitutes the first line of defence against the invasion of pathogens. This is possible due to the constant presence of cells of the immune system, cytokines and antimicrobial peptides (AMPs) including human cathelicidin LL-37. The level of LL-37 in cells and tissues varies and often increases during a urinary tract infection caused by E. coli bacteria. The biological activity of the LL-37 peptide is antimicrobial, anticancer and immunomodulatory. The process of stimulating the immune system (immunomodulation) of the LL-37 peptide aiming to regulate the immune reaction of the organism to infection, encompasses the ability to promote chemotaxis (movement of cells to infected areas) among the immune system cells, after the activation of a specific membrane receptor fMLP (N-formyl MetLeu-Pro). The wide immunomodulatory spectrum also includes the inactivation of the pro-inflammatory effect of products released from pathogen cells as well as the increasing of the immunity of the mucous membranes (the induction of changes in elasticity of the epithelium cells) under the influence of the LL-37 peptide. What is more, it has been proven that the LL-37 peptide can also activate epithelium cells through interaction with the receptor for EGF (epidermal growth factor), which plays an important role in the healing of damages (regeneration) to the mucous membrane. The usage of cationic analogs of antimicrobial peptides – the ceragenins (CSAs) - in this project can create new possibilities for preventing UTI infections. Ceragenins have a positive surface charge, which has an electrostatic effect on the negatively charged surface of microorganisms, resulting in their death.

The project aims to assess the influence of the LL-37 peptide on the activation of membrane receptors, in the process of changes in the cytoskeleton of epithelium cells of the urinary tract using an atomic force microscope (AFM). The ability of the LL-37 peptide to inhibit the internalization of bacterial cells (E. coli) into the cultivated urinary tract epithelium cells will also be assessed. Additionally, the influence of the LL-37 peptide on the permeability of the membrane of the urinary tract epithelium cells will be investigated. The evaluation of the immunomodulatory and antibacterial effect of the LL-37 peptide in infections of the urinary system is also planned.

The motivation for the planned studies is the fact, to date, the effect of the LL-37 peptide and its analogs (ceragenins) on the resistance of the urinary tract mucous membrane to uropathogen infection was not defined. No attempt was made to assess the therapeutic potential of the LL-37 and its synthetic analogs neither in in vitro nor in vivo conditions in such infections. It is assumed that the results of the planned research will enable development of new methods of UTI treatment.