Endometriosis is a debilitating gynecological disease defined as the presence of endometrial cells in an abnormal or ectopic location outside the uterine cavity. Most commonly affected sites are the pelvic peritoneum, ovaries, uterosacral ligaments, and the rectovaginal septum. The aberrant tissue responds to hormonal stimulation, undergoing cyclical growth, and shedding similar to appropriately located endometrial tissue in uterus. Common symptoms of endometriosis are: painful periods and ovulation, severe pelvic cramping, heavy bleeding, pain during sex, urination and bowel pain, bleeding and pain between periods. Endometriosis occurs in approximately 10-15% of reproductive aged women and is present in 20–50% in women with infertility, and 71–87% in women with chronic pelvic pain. Women wait an average of 8-10 years for a diagnosis. The main method of diagnosing endometriosis is laparoscopy (called the gold standard), which involves excision of endometriotic lesions. Hormone therapy and analgesics are used for treatment of symptomatic endometriosis. However endometriosis often recurs. Therefore, it is important to have a comprehensive and individualized approach to the patient and to find a non-invasive diagnostic marker of the disease. Numerous theories have been proposed to explain the pathogenesis of endometriosis. Sampson's theory of retrograde menstruation is considered to be the most accepted. This theory assumes that endometriosis occurs due to the retrograde flow of endometrial cells through the fallopian tubes during menstruation. However, it has been shown that this process takes place in 90% of women, while endometriosis is diagnosed in only 10% of them. Means, that there must be a mechanism that blocks the immune system from removing endometrial cells, interferes with its function, leading to implantation of the ectopic endometrium and the formation of lesions. The aim of this project is to investigate the role of gene polymorphisms and their protein products of the molecules engaged in HLA class I antigen processing - ERAP1, ERAP2, LNPEP, TAP1, TAP2, LMP2, LMP7, LMP10 and tapasin in endometriosis. Perhaps the polymorphism of the proposed genes influencing the expression of proteins, their activity and substrate specificity may be related to the predisposition and severity of endometriosis. HLA class I alleles will be tested at the high resolution level using the NGS method. We also plan to examine selected microRNAs as negative regulators of expression of the proposed molecules as well as the promoter methylation status of selected genes. We will study 500 patients with endometriosis and 600 control women without endometriosis. Moreover, we will study the expression of these proteins and HLA class I in tissues affected by the ectopic endometrium by immunohistochemistry methods, as well as the expression of the relevant miRNAs by Real-Time PCR. The inability to form the correct HLA class I complexes with the appropriate peptides may result in a lack of immune response by CD8+ and NK cells, contributing to the attachment of the ectopic endometrium and development of endometriosis. So far, in PubMed database, there are no studies on genetic polymorphism and expression of proteins from antigen processing machinery in tissues with ectopic endometrium. Since there are studies confirming the shedding of proinflammatory cytokine receptors such as TNFRα by ERAPs, we also want to check how the level of these aminopeptidases will affect the pro and anti-inflammatory status of patients with endometriosis. We will also test the level of ERAP1, ERAP2 and LNPEP as well as pro and anti-inflammatory profile in the plasma of patients and in the peritoneal fluid. The concentration of aminopeptidases will be tested by ELISA method, while the level of pro and anti-inflammatory cytokines by multianalyte profiling on Luminex. In the next step of the study, we will determine the expression of HLA class I on CD8 + and NK cells in the peripheral blood (by flow cytometry) to check if the expression of HLA class I is altered in patients compared to healthy women. We also want to deepen the analysis of the polymorphisms in HLA-G gene in the 3'UTR (by sequencing method), which might influence miRNA binding leading to increased mRNA degradation and decreased HLA-G production. Therefore, we will also test the level of the soluble HLA-G molecule in the plasma of patients and in the peritoneal fluid. Perhaps our research will contribute to understanding the mechanisms related to the development of endometriosis, and thus help in the treatment of these patients. The use of ERAPs inhibitors seems to be a promising treatment method in the case of over-expression of these proteins. In the final stage of the project, we plan to create an algorithm to predict in patients whether they will develop a mild or advanced form of the disease. This algorithm will be created using artificial intelligence and machine learning methods.