Bladder cancer (BCa) provides 5% of all diagnosed cancers in European Union countries. It is the fourth most common type of cancer among men and eleventh among women. Although this disease can affect people at every age, it is mostly diagnosed in patients above 55 years of age. Additionally, bladder cancer is 4 time more prevalent in men than women. Besides sex and age, main BCa risk factors are connected with life style and can be listed as follows: smoking status, alcoholism, suffering from chronic urinary bladder inflammation, medicines intake e.g. bisacodyl. Also environmental factors and specific working environment (exposure for such carcinogens as: benzidine, 4-aminobiphenyl, α- and β-naphthylmine) increase risk of BCa development. However, the etiopathogenesis of bladder cancer is still not fully explained. In above of 90% of cases, bladder cancer developed from the urothelium (it is an example of "transitional epithelium", which covers most of the urinary tract). Bladder cancer is characterized by long time of latency, which makes it more difficult to diagnose at early stage of the disease. Main clinical symptom of bladder cancer is hematuria, which may become a microscopic hematuria (observed only under the microscope) or macroscopic hematuria (visible to the naked eye). Less characteristic symptoms include frequent urination, unexpected need to urinate, bladder spasms, while in advanced stage of the disease, patients suffer from pelvic and flank pain, peripheral oedema and enlarged lymph nodes. Episodes of hematuria are the basis for further diagnosis of bladder cancer. The process of diagnosis is multi-step and encompasses such methods as: physical examination, blood and urine tests, chest roentgenography, ultrasonography of the abdomen and urinary tract, urography, urine cytology. Nevertheless, the definite diagnosis of bladder cancer requires implementation of cystoscopy and histopathological examination of biopsy samples obtained during trans-urethral resection of the bladder tumor (TURbt). Unfortunately, available diagnosis methods are invasive andexpensive. Because of that, less invasive and more specific methods, allowing for the diagnosis of bladder cancer at early stage of the disease, are sought.

For many years, a substantialinterest about the role of modified nucleosides in the pathomechanism of different diseases is notified. This hypothesis refers to one of the metabolic process, which is a RNA turnover. Rapid metabolism of RNA was observed in pathophysiological disorders, for example inflammation, disorders of the immune system or cancer diseases. One of the products of RNA turnover, nucleosides, undergo reutilization and degradation. On the other hand, modified nucleosides, which are also products of post-transcriptionalRNA modification, are not degraded or reutilized instead, are excreted with urine. Because of that, a higher level of nucleosides and modified analogues in urine were observed in different diseases, including breast cancer, hepatocellular cancer, leukemia, nasopharyngeal cancer.

Preliminary studycovered development and validation of an analytical method for the detection of chosen, modified nucleosides in urine with the use of high-performance liquid chromatography hyphenated with mass spectrometry technique. Developed method was applied for the determination of chosen nucleosides and modified nucleosides in urine samples from healthy volunteers and patients suffering from urinary cancer diseases. Results of preliminary studies, showed the statistically significant difference in the levels of selected nucleosides between patients suffering from genitourinary cancers and healthy volunteers. Consequently, the aim of presented study is to verify the hypothesis, that previously observed changed levels of nucleosides and modified nucleosides in urine of patients diagnosed with bladder cancer in comparison to healthy volunteers, is related to the presence of bladder tumor.

Main part of the proposed project will be a prospective study covering quantitative analysis of urine and plasma samples collected during the cystoscopy at different time points before and after the surgery of BCa tumor resection. Quantitative changes in urine and plasma will be monitored only of normal and modified nucleosides, selected in preliminary studyas significantlydifferentiating patients with urogenital cancer, including bladder cancer, with healthy volunteers.

Results of theproposed projectwillenrich the knowledge about the role of modified nucleosides in the pathomechanism of BCa as well as evaluate their diagnostic potential as a marker of different stages of the BCa as well as the condition before and after the tumor resection.