## Reg. No: 2016/23/N/NZ7/02875; Principal Investigator: mgr Julia Jacyna

Bladder cancer (BCa) consists one of the most common cancer in human population worldwide. Based on demographic data and the observed increased incidence of BCa in the past, it is estimated that in 2035 the number of cases of BCa can double as compared to 2012. The diagnosis of BCa is based on complex, costly, and often invasive and hardly available procedures, such as cystoscopy, ultrasound, computed tomography, magnetic resonance imaging, urography or histopathological evaluation of biopsy. Some of mentioned procedures are characterized by low sensitivity and that is the reason why some BCa cases are not diagnosed (it usually concerns tumors in the early stages of the disease). Moreover, tests for the diagnosis of BCa are usually performed only at the moment of presence of the late symptoms of the disease. This is because the early symptoms BCa are very non-specific (e.g. frequent urination, pain and burning sensation during urination, hematuria, the presence of clots in the urine), which are often mistaken for signs of other genitourinary tract diseases, like kidney or bladder inflammation. Symptoms such as anuria, pain in the lower abdomen, pain in the lumbar region, usually occur only in the advanced stages of the disease, which causes reducing chances for implementation of an effective treatment. Therefore, there is a need for specific and non-invasive methods for diagnosis of BCa that may be used for early detection of bladder tumor, e.g. during screening tests.

Known risk factors of BCa include mainly smoking (it is estimated that smoking is responsible for about 50-60% of all cases), age, obesity, lack of physical activity and gender (men suffer from BCa three times more often than women). However, the pathomechanism of BCa development has not been fully explained yet.

Recently, to study the mechanisms of development of many diseases, including civilization diseases, metabolomics approach is often implemented. Metabolomics is one of the branches of systems biology, i.e. science dealing with the study of living organisms and concentrated on detailed knowledge of biological processes occurring in cells. It focuses on the analysis of the metabolome, i.e. the total number of metabolites in organism, which reflects the current physiological or pathophysiological state of an organism. Metabolomics research usually includes two research approaches: metabolic profiling and targeted metabolomic analysis, and the most popular biological materials for the study are urine, blood, plasma, or saliva.

Preliminary studies included metabolic profiling, i.e. the analysis of as many metabolites in the tested urine samples as possible, from samples of both healthy volunteers and patients diagnosed with BCa. Three complementary analytical techniques used for this purpose, allowed the selection of compounds that may play a potential role not only in explanation of the causes of BCa, but also in its future diagnosis. In the project, the targeted approach will be applied to urine samples with the use of two complementary separation techniques (gas and liquid chromatography) coupled with mass spectrometry, for accurate determination of concentrations of metabolites selected in the preliminary studies. In addition, the data on the concentrations of the metabolites in healthy subjects will be correlated with the epidemiological data (smoking status, age, obesity, gender). The proposed approach will answer the question, which metabolites have the greatest significance for the classification of patients regardless of the associated risk factors. Subsequently, the evaluation of samples derived from individuals diagnosed with BCa at different stages of the disease, will provide information whether there is a correlation between the BCa stage and the concentration of selected metabolites. The combination of the results obtained in all the stages of the project will relate to the metabolome changes arising solely from the presence of cancer progression, regardless of the existence of factors predisposing to BCa. The results obtained within the project can be used not only for more detailed explanation of the molecular mechanisms responsible for the development of BCa, but will also provide an insight into clinical progression of the disease.

Therefore, the obtained results can offer a greater understanding of pathomechanism of developing bladder cancer and may also contribute to the verification of hypothesis on potential of metabolomics approach in the diagnosis of this disease. The results will be published in impacted scientific journals and will be presented during conferences.