Sepsis and septic shock are considered to be one of the most serious causes of life threatening. Currently, the bacteria that mostly contributes to the development of sepsis is *Escherichia coli*. In recent years, the importance of this bacteria as a pathogen has increased significantly due to its increased virulence and resistance to antibiotics. In addition, results obtained from both standard blood biochemical tests and microbiological blood/urine culture tests do not always provide sufficient information about the sepsis occurred in the organism. Such a common situation of low sepsis diagnosis rate is very dangerous for the patients due to rapid progression of the disease and consequently very high risk of death.

In the proposed project, we intend to develop and examine a comprehensive study involving the integration of 3 complementary research approaches (biochemistry, genetics and metabolomics) to explore the pathomechanism of urosepsis caused by *E.coli.* The assessment of genetic and metabolic factors influencing the development of urosepsis will be also carried out, including the analysis of additional blood biochemical tests of patients.

The study will be performed on the patients with urosepsis (n = 50) and patients without urosepsis (n = 50) but with UTI - isolates causing symptomatic infection caused by *E. coli*. Patients' selection to urosepsis and control groups (n=100, participants selected from 450 preliminary classified patients with sepsis suspicion) will be based on the results obtained from microbiological blood/urine culture tests and clinical inclusion/exclusion criteria. For selected two groups of patients, additional biochemical blood tests will be carried out in order to search for new indicators responsible for the development of urosepsis. The clinical part of the project will be carried out by the Department of Emergency Medicine Medical University of Gdansk.

The *E.coli* strains isolated from patients enrolled into the study will be subjected to appropriate genetic tests to assess bacterial virulence and potential factors affecting them (including the ability to encode siderophores). The genetic stage will be carried out by a research team from the Department of Molecular Biotechnology and Microbiology at the Gdansk University of Technology.

Next, metabolic studies will cover the analysis of the whole set of bacterial metabolites (the so-called metabolic fingerprints) from *E. coli* strains isolated from patients, as well as metabolites secreted by this bacteria (the so-called metabolic footprinting). Metabolomics studies will lead to the selection and identification of metabolites that, based on statistical studies, will be characteristic for urosepsis triggered by *E. coli*. The obtained data from genetic, metabolomic and biochemical studies will then be subjected to advanced chemometric methods including Bayesian hierarchical modelling and correlation analysis. These methods will be used in terms of searching for linkage between the degree of virulence of the bacteria, its metabolic composition, secreted toxins and patient biochemistry. Metabolomic and chemometric studies will be carried out by a team from the Department of Biopharmaceutics and Pharmacodynamics Medical University of Gdansk.

The expected result of the project will be a selection of a panel of factors that can complement the current knowledge regarding pathomechanism of urosepsis development triggered by *E. coli*. In addition, the obtained results will be validated based on targeted metabolomic studies of urine samples derived from patients enrolled into the project. Such studies will be carried out in order to verify the results obtained from bacterial isolates and will consist in quantitative measurements of concentrations of previously selected metabolites in order to confirm their significance in the development of urosepsis caused by *E.coli* with the association of biochemical and genetic results. Such step is necessary to confirm the role of genetic-biochemical-metabolomic factors in the pathogenesis of urosepsis.