DESCRPTION FOR THE GENERAL PUBLIC

According to the European Centre for Disease Control and Prevention (ECDC) surveillance report for 2012, the Ventilation-Associated Pneumonia (VAP) is the most common type of hospital acquired infection (HAI) in critically ill patients. Nowadays, the infections caused by antimicrobial-resistant species are becoming an increasing menace. Currently used methods for pneumonia diagnosis are time consuming, often non-specific to lung infection and require invasive procedures. Therefore, fast and non-invasive methods for detection of microbial lung infections in combination with host response monitoring are required.

In this project we propose the analysis of Volatile Organic Compounds (VOCs) in exhaled breath for effective, painless and totally non-invasive detection of bacterial lung infections and therapy control. The basis for this innovative approach is a fact that bacteria (alike all living cells) produce numerous volatile metabolites, of which some may be species-specific and thus provide a "biological fingerprint" of pathogen presence. Detection of such bacteria-derived metabolites in exhaled breath is completely non-invasive and can be performed repeatedly without any burden to the patient. This approach is increasingly recognised by researchers and by specialists in critical care medicine as an innovative and promising diagnostic technique for early detection of emerging pulmonary infections. Furthermore, breath analysis has high potential to advance precision diagnosis of pathogens as it reflects individual susceptibility to disease causing agents and also to therapeutic agents. Apart from this, the potential for non-invasive "real-time" analysis of exhaled biomarkers for personalised monitoring of disease state and therapy progress is a clear advancement beyond the current state-of-the-art in clinical practice. Such breath biomarkers, when thoroughly characterized and validated in multicentre study, in combination with the currently observed rapid advancement in nanotechnology can only now enable production of substance-specific sensor-based devices. Ultimately such methodology could lead to more timely and hence more effective antibiotic use, contributing to de-escalation of worldwide problem of antibiotic resistance.

The primary **aim** of this project is the identification and thorough characterization of VOC biomarkers for pathogenic bacteria. To correctly address this research problem, project is divided into three stages:

1) **The *in vitro* experiments** with antibiotic resistant and sensitive bacteria cultures for identification of volatile metabolites differentiating bacteria.
2) **The clinical study** where breath samples will be collected from mechanically ventilated patients admitted to the Clinical Department of Anesthesiology and Intensive Care of the 10th Military Hospital in Bydgoszcz to verify the existence of bacterial metabolites in breath gas of infected patients. Moreover, an on-line breath analysis will carried out at the Clinic for Anesthesiology and Intensive Care of the Gdańsk Medical University in cooperation with the Gdansk University of Technology to investigate the dynamic changes of exhaled markers and reveal its potential for personalized therapy control and host immune response monitoring. A database of bacterial VOC markers will be established and a Biobank of patient-derived pathogens will be created enabling legacy studies in the future.
3) **The Validation** of gathered results in three-center clinical study (Bydgoszcz, Gdańsk, Innsbruck) with independent cohorts of ventilated patients in order to evaluate clinical relevance of breath-markers for VAP diagnosis where the key parameters of a future breath test (e.g. sensitivity and specificity) will be compared to those obtained for currently used clinical methods.

This project will translate *in vitro* findings (biomarker discovery) into hospital settings at intensive care unit and reveal the clinical usefulness of newly developed breath test for non-invasive and immediate diagnosis of ventilation-associated pneumonia. Early detection of infection, potential identification of a causative pathogen, monitoring of a host-immune response and control of a personalized therapy combined in one completely non-invasive test, result of which is available within 2-3 hours since sample collection is clearly beyond the current state-of-the-art in the field of diagnosis of infectious diseases in humans, and testifies about high novelty of the here proposed project.