The aim of the project is to investigate the role of the activation of protein complex of inflammasome in the response to *Acinetobacter baumannii* pneumonia secondary do septic peritonitis. Formation of inflammasome complex is one of major early mechanism of the host cells response to infection. It results in the release of active interleukin-1β and usually leads to the cell death. Our hypothesis claims that exaggerated activation of inflammasome in response to secondary *A. baumannii* infection impairs the protective immune response to this infection. Infections with multi-drug resistant *A. baumannii* strains became an emerging problem in the intensive care units (ICUs) worldwide. *A. baumannii* very rarely causes infections in healthy humans. In the ICUs the most common form of *A. baumannii* infection is pneumonia in septic patients with disturbed immunity who require mechanical ventilation. Infection with *A. baumannii* is a significant mortality risk factor in such patients. Due to the emergence of highly antibiotic resistant strains, immunomodulatory therapies may become one rescuing option. Development and clinical introduction of such therapies require, however profound understanding of the mechanisms of immunopathogenesis of a given infection. This knowledge should be gained in the context of specific clinical situation. For this reason in this proposed research we plan to develop a disease model on the mice with human immune cells. Such mice are known as the humanized mice. In our previous studies we have established a method of humanization of immunodeficient mice by the transplantation of human hematopoietic stem cells. Then, humanized mice were undergoing surgical cecum ligation and puncture (CLP) to induce septic peritonitis. This allowed us to evaluate the impact of sepsis on the human hematopoietic stem cells in bone marrow. In our current project, we intend to establish the humanized mice model using mice with the expression of human stem cell factor (SCF) which enhances development and maintenance of human immunocompetent cells. Humanized mice will then undergo the CLP surgery with following treatment with analgesics and antibiotics. Then, mice will be mechanically ventilated and receive intratracheally suspension of *A. baumannii* to induce pneumonia. By the measurement of early mortality biomarkers the animals will be assign to groups of low and high probability of death. Mice will be sacrificed under general anesthesia and human myeloid cells from their lungs and bone marrow will be analyzed. The expression of inflammasome-related genes will be evaluated by Real-Time PCR technique. Inflammasome formation will also be investigated on the protein level using confocal microscopy on tissue sections. The comparison of the activity of inflammasome genes and proteins between groups of low and high risk of death will help to identify the protective and harmful effects of inflammasome activation. In order to confirm the outcome-related significance of the activity of inflammasome indicated in the abovementioned experiment, we plan to perform experiments with silencing of the expression of specified inflammasome gene. To accomplish this, we will use the siRNA knockdown technology dedicated to the *in vivo* application. The efficacy of gene silencing will be confirmed by the Real-Time PCR technique. The endpoints in this experiments will be the number of alive bacteria in the lungs and the degree of lung injury in mice infected 24 hours earlier.

By the use of a unique clinically-relevant model which is based on humanized mice we hope to indicate new targets for the immunomodulatory therapies in severe *A. baumannii* infections. Establishment of such complex model will also serve in the future as a translational research platform for the pre-clinical studies of immunomodulatory therapeutics.