

Lung cancer is the most common malignancy in Poland and in the world and belongs to cancers with the worst prognosis – the overall 5-year survival is usually below 15%. In the last years the development of different immunotherapy strategies, including therapies based on antibodies blocking immune checkpoints, in other words costimulatory receptors with suppressive functions. The aim of these therapies is to boost an effective anti-tumor response and to overcome the immunosuppression induced by tumor cells. Still problematic is the very heterogeneous and hardly predictable response to this kind of treatments, therefore the requirement for effective implementation of these treatments is the identification of appropriate prognostic biomarkers. Increasingly more studies indicate that the individual extend of suppression of the patient's immune system, especially in the tumor microenvironment, considerably influences therapy effectiveness. Our own previous studies as well as studies from other researchers point out the key role of exosomes, small membrane vesicles released by different cell types, in the modulation of anti-tumor response. Exosomes, as one of the key elements of intercellular communication within the tumor microenvironment and carrier of genetic material and functional suppressive molecules derived from the tumor, are an essential mediator of local and systemic immune suppression. Currently many studies explore exosomes from peripheral blood as easy accessible sources of biomarkers of the patient's immune status, which allow to choose the optimal treatment and to monitor treatment response. However the changes detected in peripheral blood may not reflect the actual changes within the tumor microenvironment, which are significant for treatment. The aim of our project is to elucidate if the exosome profile in systemic circulation reflects the profile of exosomes from the tumor microenvironment and may be a marker of immune dysfunctions within the tumor lesion. An innovative aspect of the project is the implementation of bronchoalveolar lavage (BAL) as a method for the isolation of exosomes from the tumor microenvironment. It is a low-invasive, standardized procedure which can be performed during diagnostic bronchofiberoscopy routinely done for very patient with suspected lung cancer .We plan to perform a comprehensive analysis of the molecular profile of exosomes present in BAL fluid in reference to the immune status within the tumor microenvironment of non-small cell lung cancer patient. We assume that the individual molecular profile of exosomes present in the tumor microenvironment will significantly affect the local immune response as well as the response to potential immunotherapy, which we want to check in a murine model of lung cancer. We hope that the in-depth molecular and functional analysis of BALF exosomes will contribute towards the identification of exosomes as tumor markers and provide a target for novel anti-cancer strategies.