Roles of polarized neutrophils on lung tumour development in an orthotopic lung tumour mouse model

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Body: Lung cancer is a highly deadly disease and results of current treatments are still deceiving. It has recently become evident that inflammation contributes to enhance tumour development by modifying the tumour microenvironment. Neutrophils represent the most abundant type of white blood cells and are an essential part of the innate immune system, suggesting their important functions in tumour biology. The aim of this study was to understand the potential impact of neutrophilic inflammation on lung tumour development in a non invasive orthotopic mouse model. For this, Lewis Lung Carcinoma (LLC) tumour cells were intratracheally injected with or without a pro-inflammatory agent. We report that neutrophilic inflammation induced by a polysaccharide compound is able to enhance lung tumour development while the LPS-induced inflammation only modestly increased tumour volumes. Interestingly, neutrophils isolated from lungs of mice stimulated by this inflammation-inducing polysaccharide displayed more often N2-protumoral phenotype when compared to neutrophils isolated from LPS-challenged lungs. Higher levels of β2-integrin were measured in polysaccharide-challenged lungs and an increased number of interactions of neutrophils expressing β2-integrin with ICAM-1 molecules present on epithelial pulmonary cells might be hypothesised as a mechanism for enhanced tumour development. We propose in this study that N2-neutrophils enhance lung tumour cells anchorage on the airway epithelium by bridging the tumour cells with the epithelium. Importantly, inflammatory agents inducing N2-neutrophils mainly seem mandatory for a pro-tumour effect.