Abstract

Esophageal cancer belongs to the gastrointestinal malignancies with the worst prognosis. Current treatment options, including surgical resection, chemotherapy, radiotherapy, or a combination of these methods, have low efficacy and the five-year survival rate for patients with esophageal cancer is approximately 10 to 15 %. In the last decade, immunotherapy has become the leading treatment modality for metastatic tumors. However, the success of immunotherapeutic approaches does not only depend on the infiltration of the tumor microenvironment with immune cells but also on the phenotype of these infiltrating cells.

The aim of this project was to evaluatethe immunological features of tumor-infiltrating lymphocytes obtained from different tissue compartments (tumor, peritumoral tissue, adjacent healthy tissue, and lymph node) of patients during surgical resection and to compare them with clinical and histopathological data of patients.

We observed that the distribution of NK (natural killer) cells, CD8 and CD4 positive T cells was different in each tissue compartment. While the lymph nodes had the highest percentage of T cells, the opposite was seen in NK cells. The proportion of NK cells was the lowest in the lymph nodes. The expression of death receptors FasR and DR3 (death receptor 3) was the lowest on CD4 T cells infiltrating the lymph nodes. Furthermore, we demonstrated that significantly lower proportions of peritumoral T cells and NK cells were shown in patients that were actively smoking. Furthermore, these cells displayed also a very high expression of death receptors. Our results thus demonstrated that active smoking has a critical impact on the tumor microenvironment and the adjacent tissue infiltrating immune cells and can significantly affect the prognosis of patients with esophageal cancer. In the next study, a significantly higher levels of CD47 molecule were expressed on the CD8 T and NK cells rather than on the tumor cells. These data suggest that esophageal cancer may not be suitable for the treatment with anti-CD47 monoclonal antibodies, as they will preferentially target immune cells.

Keywords: esophageal carcinoma, immunotherapy, tumor-infiltrating lymphocytes (TIL), death receptors.