Abstract

Head and neck cancers (HNSCC) are a heterogeneous group of tumors that are induced by tobacco and alcohol use or persistent human papillomavirus (HPV) infection. The incidence of virally induced HNSCC is increasing worldwide. The viral etiology positively influences patient survival and effectiveness of antitumor treatment, which may be explained by the presence of a specific immune response directed against HPV viral antigens. The main objective of this study is to characterize in detail the microenvironment of cancers of viral and non-viral etiology with a focus on *in situ* detection and quantification of immune cells. For this purpose, advanced methods for studying the tumor microenvironment were introduced and optimized, such as multispectral immunohistochemistry or mass cytometry. The frequency of immune cells, expression levels of selected genes and selected proteins in HNSCC were evaluated in relation to tumor etiology and prognosis with the aim to identify potential therapeutic targets. Our results indicate that the microenvironment of HPV-positive tumors shows higher levels of pro-inflammatory and anti-tumor immune cells and factors, compared to the immunosuppressive microenvironment of HPV-negative tumors. Higher levels of PD-$1^{+}$$CD8^{+}$ (programmed cell death protein 1, cluster of differentiation 8) T lymphocytes, GLUT1 (glucose transporter 1) and Hif-1α (hypoxia-inducible factor 1α) producing cells are associated with better survival, whereas higher level of arginase 1 mRNA predicts poorer survival of HNSCC patients.