ABSTRACT

Head and neck squamous cell carcinoma encompasses a complex and heterogeneous group of malignant diseases. Originally, this tumor type was associated with tobacco and alcohol consumption. However, a significantly expanding subset of tumors associated with oncogenic human papillomavirus infection arising in deep tonsillar crypts was identified within the last decades. Due to the essential role of the immune system in antiviral and anticancer immune response, the prognosis of patients is significantly influenced by the volume, composition and functional capacity of the immune infiltrate. The immunosuppressive landscape of head and neck cancer leads to unfavorable outcome of patients and decreased efficacy of immunotherapy. The response rate to standard treatment is high, however, standard therapy is accompanied by considerable toxicity influencing the quality of life. In 2016, the first immunotherapeutics for the treatment of patients with recurrent squamous cell carcinoma of the head and neck were approved – the anti-PD-1 immune checkpoint inhibitors nivolumab and pembrolizumab. This type of therapy, based on mitigation of immunosuppression, shows strong efficacy and less toxicity in combination with other therapies. Therefore, anti-PD-1 immunotherapy was recently approved in the first-line treatment setting as monotherapy or in combination with chemotherapy for patients with metastatic or unresectable, recurrent head and neck cancer. Despite the therapeutic benefit of immune checkpoint inhibitors, there is still a large proportion of nonresponding patients. Thus, better understanding of the individual immune cell populations playing key role in anticancer immune response could reveal the principles influencing functional orientation of the immune response. Personalized immunotherapeutic protocols created with respect to these principles could enhance the efficacy of current therapeutic strategies. This dissertation thesis broadens the knowledge of the significance of HPV-specific CD8+ T cells, B cells and other immune cell populations infiltrating to the tumor microenvironment of HPV-associated vs. HPV-negative tumors of head and neck. This thesis also highlights the importance of combined immunotherapy based on the elimination of immunosuppression, which arises due to a chronic activation of adaptive immune system and consequent expression of inhibitory molecules.