THE TUMOR IMMUNE MICROENVIRONMENT OF HEAD AND NECK CANCER IN RELATION TO ANATOMICAL SITE CLASSIFICATION

Background: Head and neck squamous cell carcinomas (HNSCCs) arise in the mucosal linings of the upper aerodigestive tract. Risk factors are smoking, excessive alcohol consumption and infection with human papillomavirus (HPV). Tumors are classified according to stage, HPV status, and to anatomical site: oral cavity, hypopharynx, larynx and oropharynx. Immune checkpoint inhibitors belong to the treatment arsenal for HNSCC but are effective in only a minority of patients. Treatment response and prognosis are influenced by the tumor microenvironment (TiME). Generally, HPV-related HNSCCs are associated with increased immune infiltration, but for different HNSCC anatomical sites such data are lacking.

Materials and Methods: Using flow cytometry, we investigated the TiME of 58 fresh HNSCC samples. We further examined the spatial distribution of CD8+ subsets using multiplex immunohistochemistry (mIHC) on 20 samples. Additionally, single cell RNA-sequencing (scRNA-seq) was performed on five samples to obtain a comprehensive understanding of individual cells in the TiME of HNSCC.

Results: Increased T cell frequencies were observed with flow cytometry in oral cavity squamous cell carcinoma (OCSCC) in comparison to HPV-unrelated HNSCC at other anatomical sites. Using mIHC, no significant differences were found in tissue-resident or proliferating CD8+ densities between sites. However, a trend towards increased proliferating CD8+ densities within 30 μm from tumor cells was highest in OCSCC. Moreover, the number of infiltrating CD8+ cells within 30 μm from tumor cells was highest in OCSCC. Using scRNA-seq, we were able to annotate cell types and perform subclustering. This enabled us to distinguish among others CD8+ exhausted T cells.

Conclusions: Our data indicate that, compared to other anatomical sites, oral cavity SCCs are more often populated by T cells. This suggests that particularly OCSCC may more easily respond to immunotherapy strategies aimed at activating T cells.


A CAR-T CELL-BASED APPROACH FOR THE TREATMENT OF MALIGNANT T CELL DISEASES

Background: The T cell receptor (TCR) is uniformly expressed in monoclonal T cell lymphoma (TCL) populations and would thus represent an ideal target antigen for a CAR-based immunotherapy.[1] However, the TCR is present on all T cells including malignant, healthy and CAR-T cells. Strategies to increase tumor specificity of TCR-specific CAR-T cells are therefore required.

Conclusions: In the first case the off-tumor activity would affect about 50% of T cells, which could lead to impaired T cell immunity in the patient. The latter approach is highly specific to the malignant T cell clone but would require creation of individual CD3-specific CARs for every patient which is currently impracticable. The TCR V-segment chains can be grouped into families and targeting TCR malignancies via V-family-specific CARs would spare the majority of healthy T cells. [4–6] Targeting the TCR V-segments would unite high tumor specificity with the limited effort of creating a panel of CAR molecules that could be used for all patients.