

Role of the programmed death-ligand 1 (PD-L1) and antigen presenting natural Killer (AP-NK) cells in immunosuppressive tumor microenvironment (TME) of oral squamous cell carcinomas

I.Varghese¹, S. Durab¹ J. Wu¹, J.N. Holland M. Williams², Y. Lou¹ and N. Vigneswaran¹

¹Department of Diagnostic and Biomedical Sciences, University of Texas School of Dentistry at Houston

²Department of Pathology, University of Texas MD Anderson Cancer Center, Houston.

Objective: Immune checkpoint blockade (ICB) response rate targeting PD-1/PD-L1 in oral squamous cell carcinomas (OSCC) is lower (< 20%) than other solid cancers. Identifying factors contributing to an immunosuppressive TME may inform cancer progression. AP-NK cells co-expressing CD8 α and HLA-DR antigens promote immunosuppression by selectively killing effector T-cells.

Methods: Tissue microarray of OSCC (n=64), oral epithelial dysplasias (OED, n=14), proliferative verrucous leukoplakia which progressed to OSCC (PVL; n=6), and oral lichen planus (OLP; n=5) were used in this study. By immunohistochemistry (IHC), evaluated PD-L1 expression (Clone 22C3) in tumor cells by the Tumor Proportion Score (TPS) and in tumor infiltrating lymphocytes (TIL). IHC for CD3, CD8, and CD8 & HLA-DR double labelling was used for phenotyping the TIL. We used Fisher's exact tests to compare categorical variables and Student's t-test for continuous variables.

Results: PD-L1 expression in TIL (negative: 0-5%; positive > 5%) showed significant correlation with tumor site, nodal status and survival. OSCC were classified into four TME types based on their TPS and the number of CD3-positive TIL. (1) PD-L1 negative (TPS <5%) and scant CD3+TIL in 39% (2) PD-L1 negative (TPS <5%) and high CD3+TIL in 34% (3) PD-L1 positive (TPS >5%) and a high CD3+TIL (ICB responders) in 14% (4) PD-L1 positive (TPS > 5%) and scant CD3+TIL in 13%. CD3+ve T-cells were significantly lower (p=0.0075) in OED and PVL compared to OLP. There was a trend for increased AP-NK cells and % of AP-NK/CD3 cells in OED (56.7 $\pm$ 10.1; 2%) and PVL (64.5 $\pm$ 24.2; 7%) compared to OLP (30.5 $\pm$ 7.4; 0.7%). There was no statistically significant correlation between TPS and age, gender, smoking status, tumor site, histology grade, tumor stage, nodal status, survival and TIL density.

Conclusion: In addition to PD1/PD-L1 pathway, our data supports AP-NK cells playing a role in promoting immunosuppressive TME in OSCC.