Comparing the Tumor Immune Microenvironment of the ROC1 Oral Cavity Across Time

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Objectives: Head and Neck Squamous Cell Carcinoma (HNSCC), the sixth most common cancer worldwide, is associated with high-risk subtypes of Human Papillomavirus, tobacco, and alcohol over-consumption. Current immunotherapy strategies require frequent administration, resulting in off-target toxicity due to systemic delivery. The recurrent/metastatic HNSCC cases treated with immunotherapy have less than 20% response rates, furthering the need to understand the immunosuppressive tumor immune microenvironment (TIME). We are investigating a HNSCC preclinical non-HPV model with p53 mutations, Roberto Rangel Oral Cancer 1 (ROC1), to understand the TIME and responses to immunotherapies. Herein, we investigated the TIME in the ROC1 oral cavity tumor model. We hypothesize that the TIME contributes to the immunosuppressive ROC1 tumor growth kinetics.

Experimental Methods: The ROC1 cell line was provided by Dr. Roberto Rangel (MDACC) and the cell line was maintained in culture according to our collaborator's protocol. C57BL/6 mice were injected with the ROC1 cells in the oral maxillary vestibule. Tumors were collected at different growth time points 9mm^2, 25mm^2, and 49mm^2 for immune cell analysis by flow cytometry.

Results: Across the tumor growth kinetics, ROC1 tumors become immune cell infiltrated with an increase from 5% to 20%. As the tumor growth progresses, CD4 T cells increase up to 5% while CD8 T cells decrease. Of the T-cells present in the TIME, exhaustion markers like PD-1 are expressed in over 70% CD4 T cells and increased in CD8 T cells from 10% to 60%.

Conclusion: Herein, we established and characterized an immunosuppressive orthotopic model of oral cancer. Our results indicate an increasing immunosuppressive TIME in the ROC1 oral cavity model as tumor growth progresses. Further studies will apply intra-tumoral delivery of biomaterial-based immunotherapies in the preclinical model and validate the TIME of heterotopic tumors.

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