HPV-POSITIVE MOUSE MODEL OF ORAL SQUAMOUS CELL CARCINOMA: DEVELOPMENT AND TRANSCRIPTOME ANALYSIS

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Head and neck cancers are a heterogeneous group of tumors that includes oral squamous cell carcinoma (OSCC). One of the risk factors for the development of some anatomical subtypes of OSCC is persistent infection with high-risk human papillomavirus (HPV) strains, such as HPV-16. Clinical data indicate, that some patients with HPV-positive OSCC have a better prognosis and respond better to various treatment modalities, including radiotherapy and immunotherapy. To evaluate the differences between HPV positive and HPV negative OSCC and therapies based on adaptive immune response, immunocompetent mouse models are essential. Nevertheless, HPV-positive mouse model of OSCC are still scarce due to the species specificity of HPV. Therefore, the aim of our study was to establish and characterize a mouse model of HPV-positive OSCC. We established two monoclonal MOC1-HPV cell lines (MOC1-HPV K1 and MOC1-HPV K3) by transduction of murine OSCC cell line MOC1 with LXSN16E6E7 retrovirus, which encodes the HPV-16 E6 and E7 open reading frames. We confirmed a stable expression of HPV-16 E6 and E7 in both monoclonal MOC1-HPV cell lines on mRNA and protein level with quantitative PCR and immunofluorescent staining, respectively. *In vitro* characterization demonstrated differences in cell morphology and cell migration capacity, where MOC1-HPV K3 cells migrated significantly slower in the wound healing assay compared to the parental or MOC1-HPV K1 cell line. *In vivo*, we characterized the tumor microenvironment (TME) of the newly established tumor models by immunofluorescent staining of blood vessels (CD31), hypoxic areas (EF5), and proliferation (EdU). MOC1-HPV K1 tumors were less hypoxic, with a higher proportion of proliferating cells compared to MOC1 and MOC1-HPV K3 tumors. Both in vitro and in vivo results correlate with transcriptome analysis results of the three cell lines, where the 20 most enriched gene ontology “biological process” terms in MOC1-HPV K1 cell line include terms related to angiogenesis and blood vessel formation, as well as cell migration and motility. In conclusion, we established a mouse model of HPV-positive OSCC that can be used to study basic characteristics as well as tumor microenvironment and immune responses to different therapies of HPV-positive OSCC.