Programming immunity: a tetravalent mucosal nanovaccine for enhanced local and systemic antitumor response in head and neck cancer

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Introduction

With the rising incidence of head and neck cancers (HNCs) linked to the human papillomavirus (HPV), the viral oncoproteins E6 and E7 have become key therapeutic targets because they are the primary drivers of malignant cell growth.

Methods

This study details the development of a therapeutic intranasal vaccine against HNC. We produced a tetravalent mucosal vaccine (Qβ-HPVag) by conjugating four elongated HPV16 E6 and E7 synthetic peptides to Virus-Like Particles (Qβ) loaded with a TLR9 agonist.

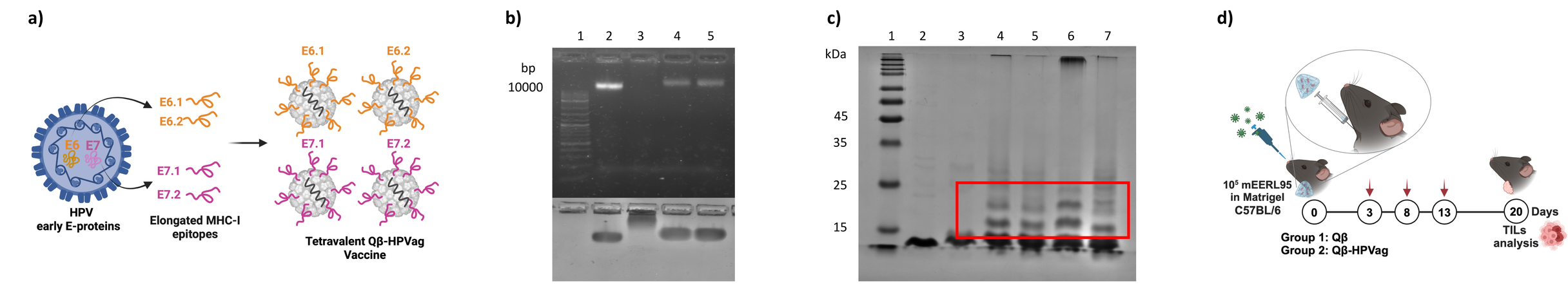

Fig. 1 - a) A schematic representation of the development of the tetravalent VLP-based vaccine (Qβ-HPVag), **b)** 1% agarose gel of Qβ-VLPs after ssRNA digestion and re-packaging with Type B CpG, stained with SybrSafe (top) and Comassie Blue (bottom), **c)** SDS-PAGE stained with Comassie Blue. Coupling efficency is shown with red box, **d)** Visual representation of the experimental setup.

Results

Intranasal Qβ-HPVag Vaccination Enhances Intratumoral CD8⁺ T Cell Infiltration Accompanied by Increased Dendritic Cell Recruitment

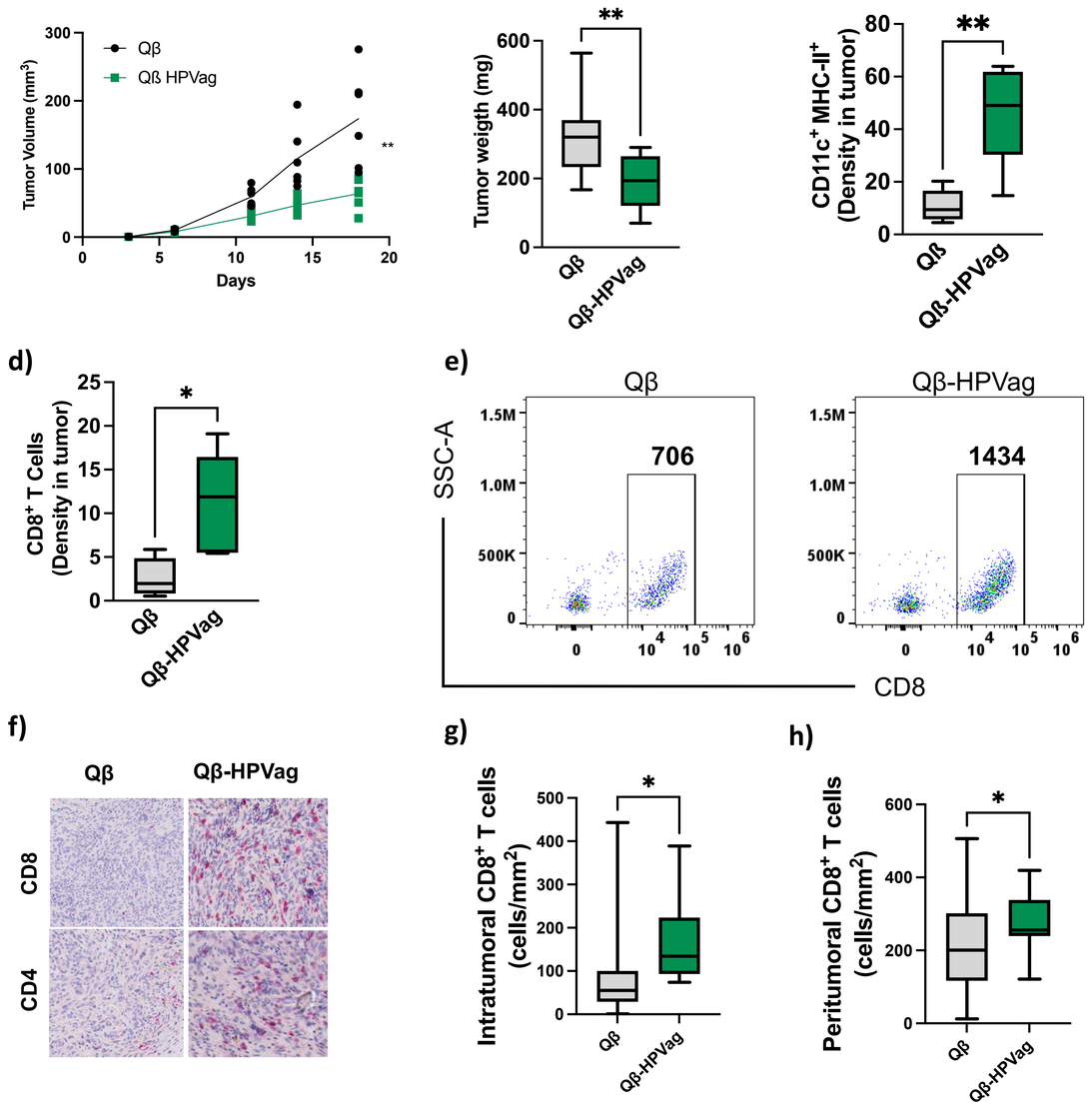

Fig. 2 - a) Tumor volume mm^3, **b)** Tumor weight mg, **c)** Densities of CD11c$^+$ MHC-II$^+$ cells, **d)** Densities of CD8$^+$ T cells, **e)** flow cytometry plots illustrating the total number of CD8+ T cells acquired from each tumor on day 20, **f)** Representative IHC sections stained for CD4+ or CD8+ T cells for the control and vaccinated group, **g)** Intratumoral CD8$^+$ T cells, **h)** Peritumoral CD8$^+$ T cells. Statistical analysis (mean ± SEM) by Student's t test. Significance levels are denoted as follows. ***p<0.001, **p<0.01, *p<0.05.

Qβ-HPVag Drives Tumor-Infiltrating B Cell Responses Including Memory B Cells and Plasmablasts

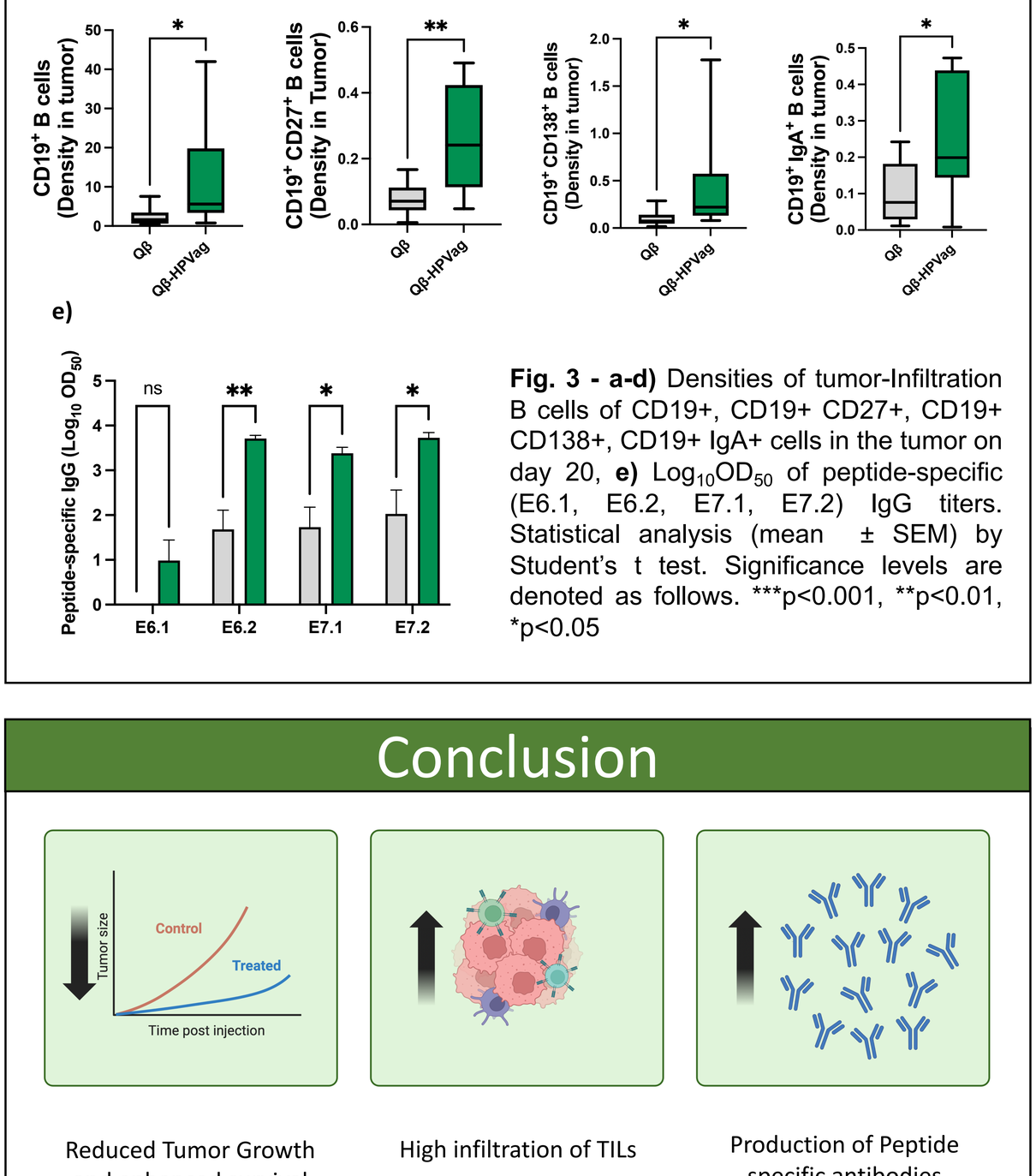

Fig. 3 - a-d) Densities of tumor-Infiltration B cells of CD19+, CD19+ CD27+, CD19+ CD138+, CD19+ IgA+ cells in the tumor on day 20, **e)** $Log_{10}OD_{50}$ of peptide-specific (E6.1, E6.2, E7.1, E7.2) IgG titers. Statistical analysis (mean ± SEM) by Student's t test. Significance levels are denoted as follows. ***p<0.001, **p<0.01, *p<0.05

Conclusion

Contact

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