

Supplementary Online Content

Zhu G, Amin N, Herberg ME, et al. Association of tumor site with the prognosis and immunogenomic landscape of human papillomavirus-related head and neck and cervical cancers. *JAMA Oncol*. Published online November 18, 2021. doi:10.1001/jamaoto.2021.3228

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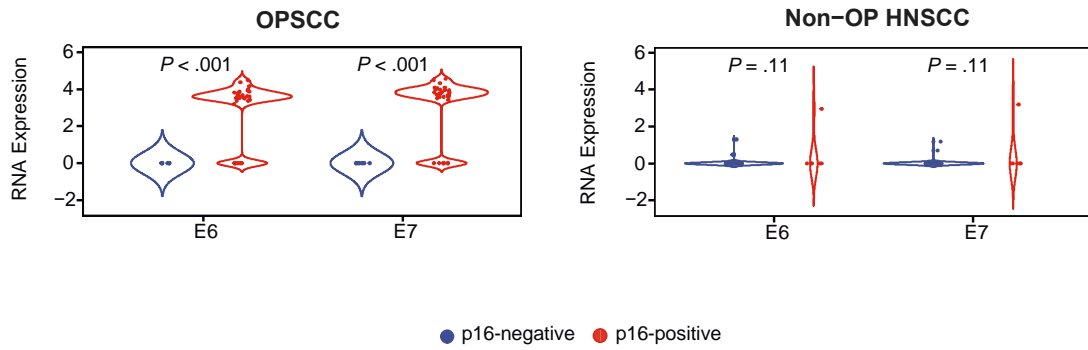
eFigure 8. Comparative Analysis of Immunogenomic Metrics Between HPV-positive and -negative Patients Within Each Tumor Site—TMB and CNV

This supplementary material has been provided by the authors to give readers additional information about their work.

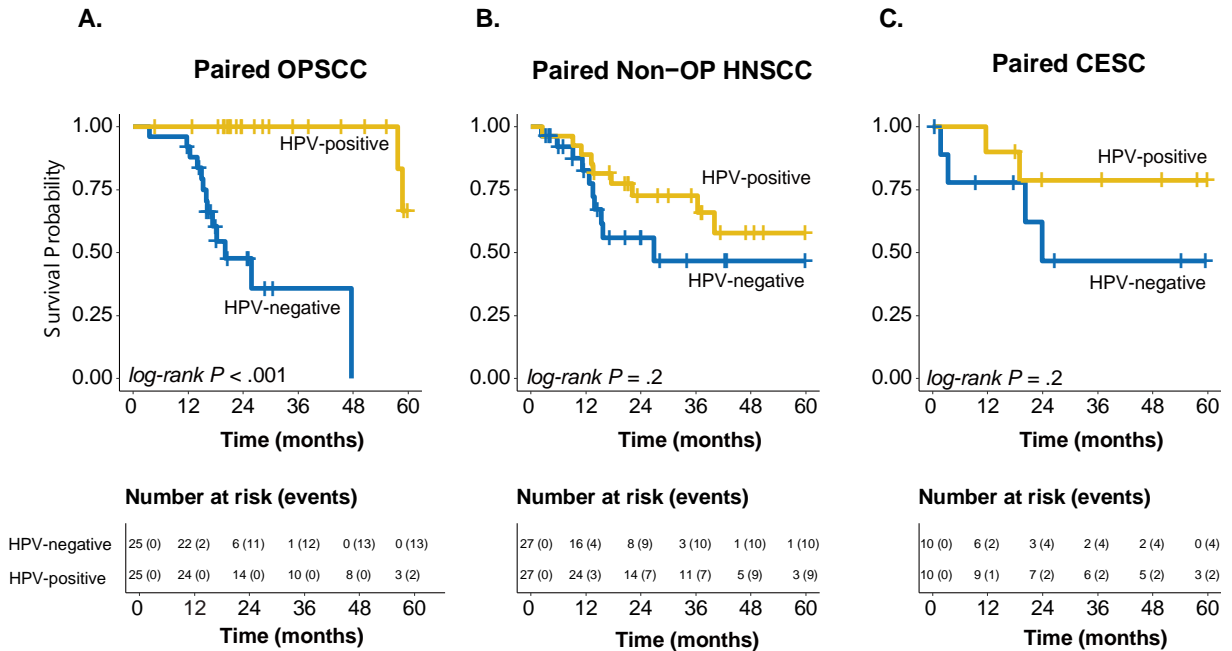
eTable. The Characterization of HNSCC and Cervical Cancer Patients in TCGA by HPV status

	N					
	HPV-negative			HPV-positive		
	OP (N=26)	Non-OP (N=408)	Cervical (N=10)	OP (N=53)	Non-OP (N=27)	Cervical (N=244)
Age						
Mean (SD)	57.4 (10.2)	61.6 (12.2)	60.4 (15.2)	55.3 (8.73)	62.9 (7.92)	48.2 (13.9)
Median [Min, Max]	57 [38, 79]	62 [19, 90]	57 [34, 81]	56 [35, 77]	61 [49, 82]	46 [20, 88]
Gender						
Female	6	123	10	4	1	244
Race						
White	22	340	7	51	26	163
Others	4	68	13	2	1	81
Smoking history						
Current smoker	14	146	3	9	7	53
Lifelong non-smoker	3	88	5	20	6	107
Current reformed	9	163	1	23	14	55
Unknown	0	11	1	1	0	39
T						
T0, T1, T2	11	151	6	37	8	165
T3, T4	15	257	1	16	19	26
Unknown	0	0	3	0	0	53
N						
N0, N1	12	251	4	18	14	154
N2, N3	14	153	0	35	13	0
Unknown	0	4	6	0	0	90
M						
M0	23	398	3	52	25	99
M1	1	3	3	0	1	5
Unknown	2	7	4	1	1	140
Clinical stage						
I, II	6	92	7	8	3	181
III, IV	20	316	3	45	24	56
Unknown	0	0	0	0	0	7
Histologic grade						
G1, G2	20	310	0	a	15	NA
G3, G4	4	89	0	a	12	NA
Unknown	2	9	10	a	0	244
p16 status						
Positive	1	5	NA	31	1	NA
Negative	7	62	NA	1	2	NA

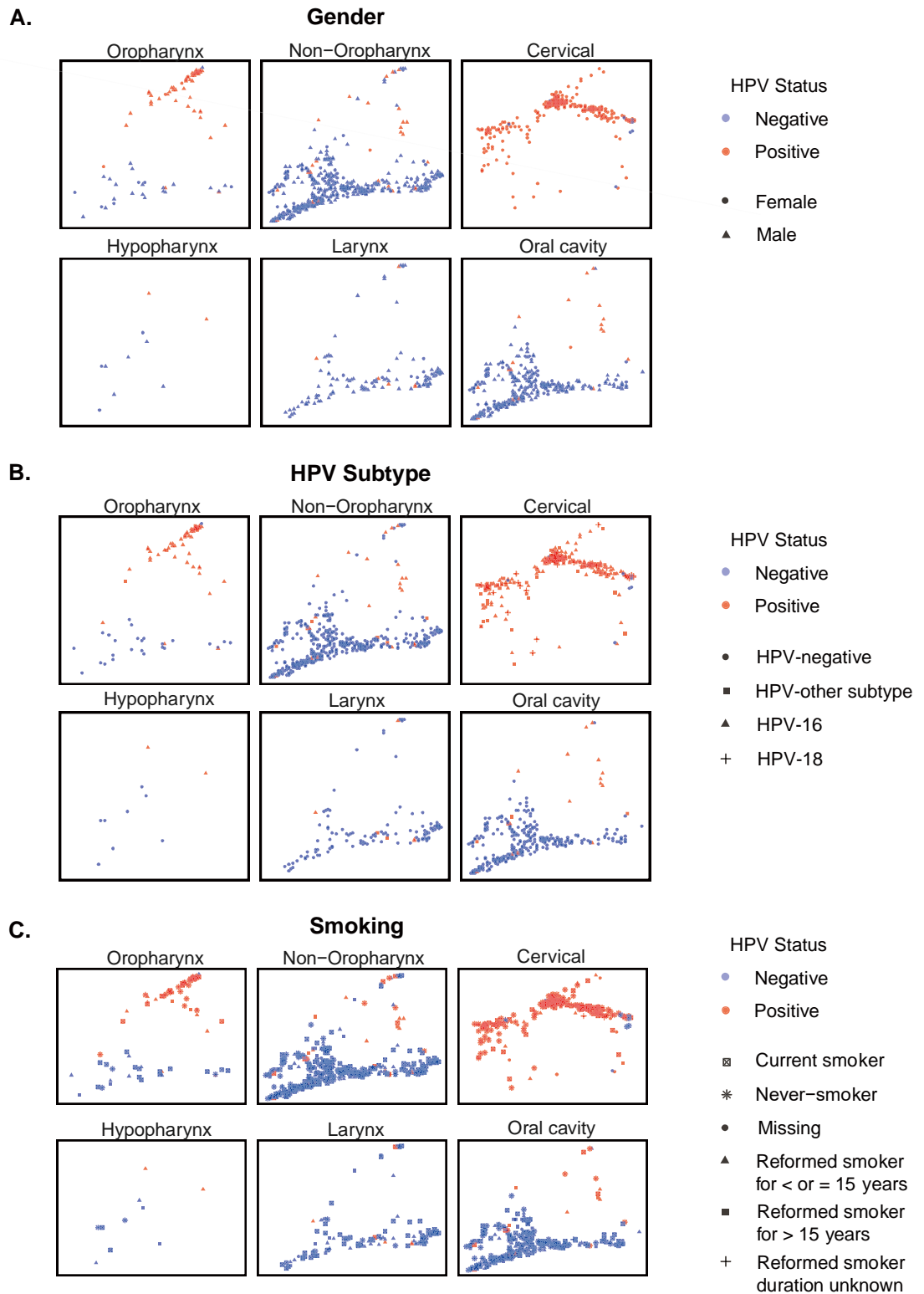
OP: oropharynx; Non-OP: non-oropharynx; SCC: Squamous cell carcinoma; ^a: Tumor grade or differentiation status reporting not recommended for HPV-positive OPSCCs per College of American Pathologists guidelines.



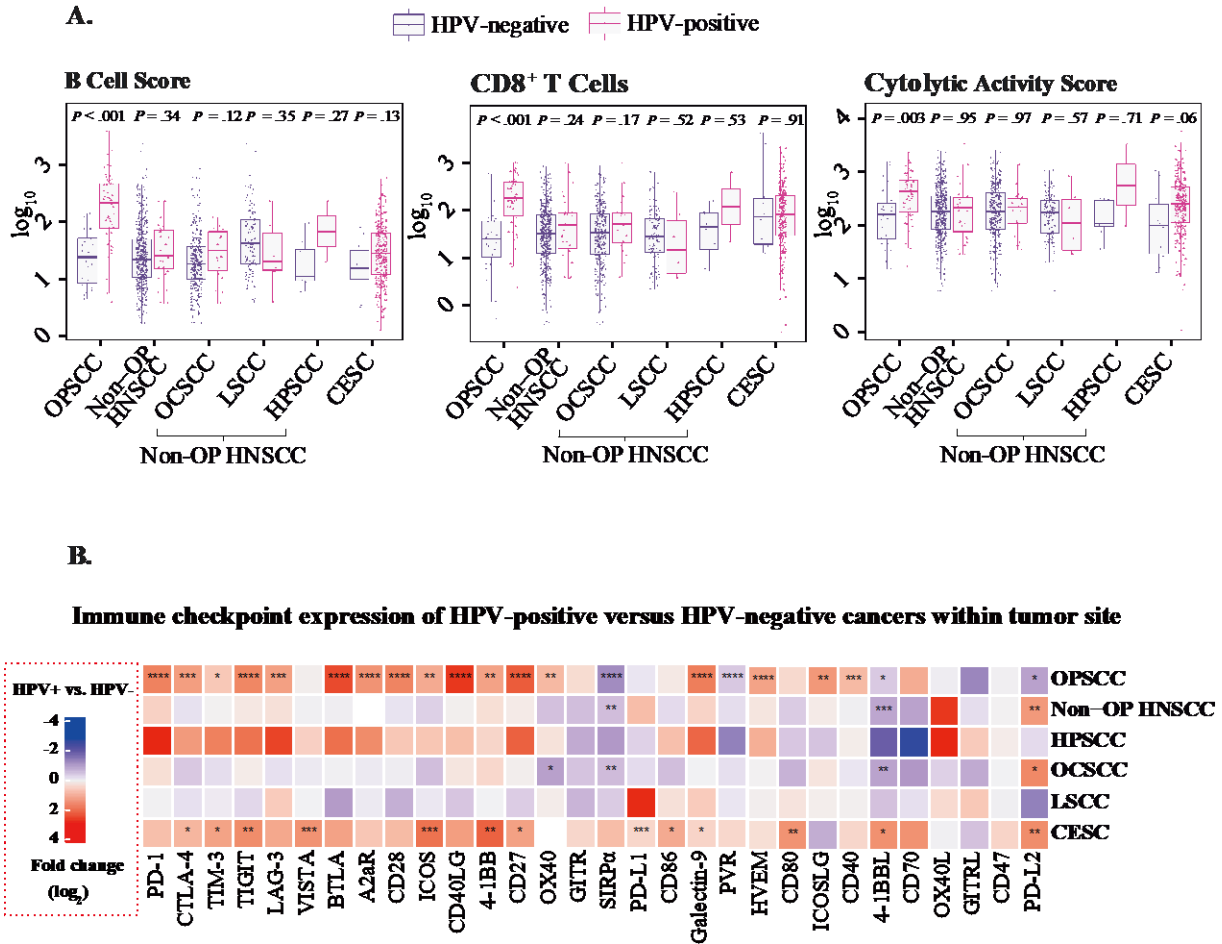
eFigure 2. The expressions of E6 and E7 transcripts in OPSCCs and non-OP HNSCCs by p16 testing. RNA expression measured in $\log_{10}(\text{Read counts} + 1)$; OPSCC: oropharyngeal squamous cell carcinoma; non-OP HNSCC: non- oropharyngeal squamous cell carcinoma in the head and neck.



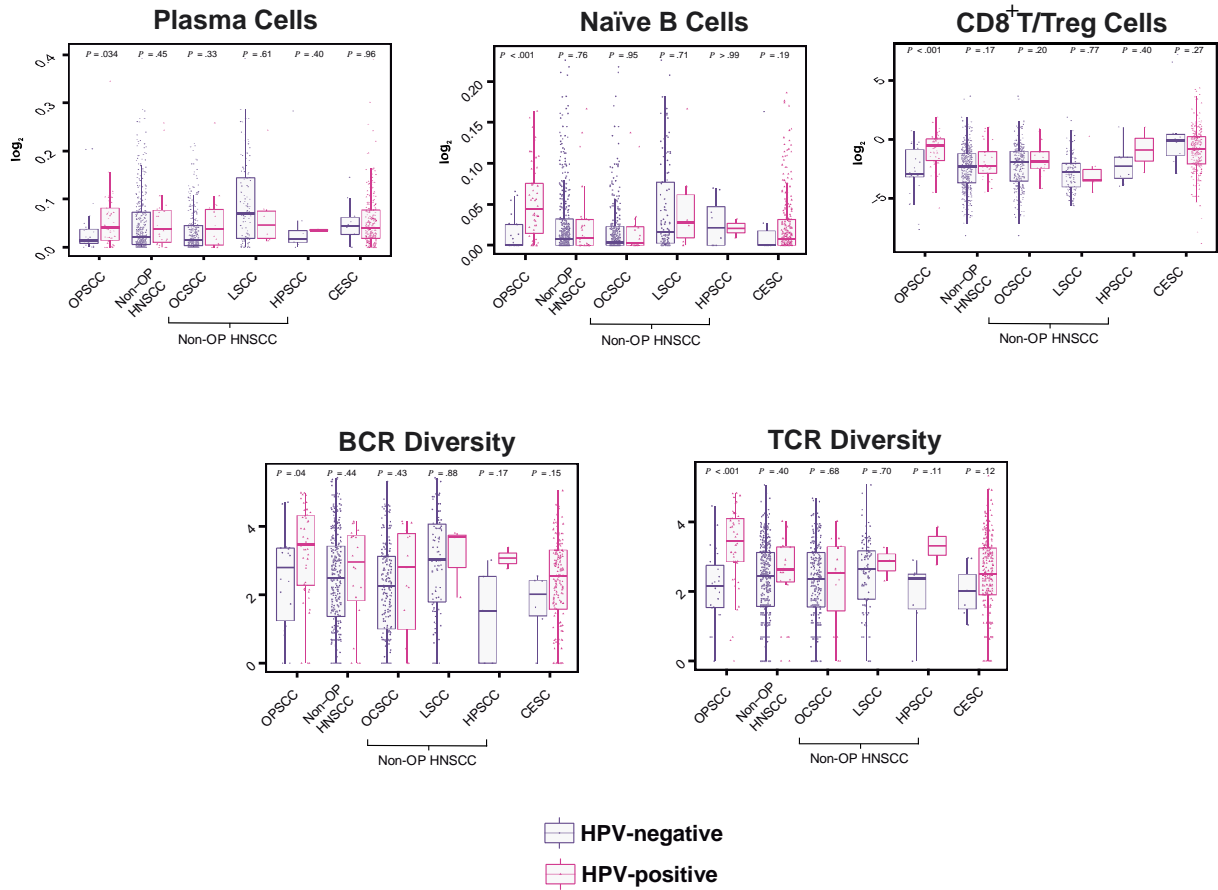
eFigure 3. Overall survival differences between propensity-score matched patients with HPV-positive and -negative cancers. Kaplan-Meier survival analysis displaying differences in overall survival between propensity-score matched patients with HPV-positive and -negative cancers arising from the oropharynx, OPSCC (A), non-oropharyngeal head and neck cancer, non-OP HNSCC (B), and cervix, CESC (C). HPV-positivity, age, smoking history, gender, and TNM were matched by propensity-score in these cases.



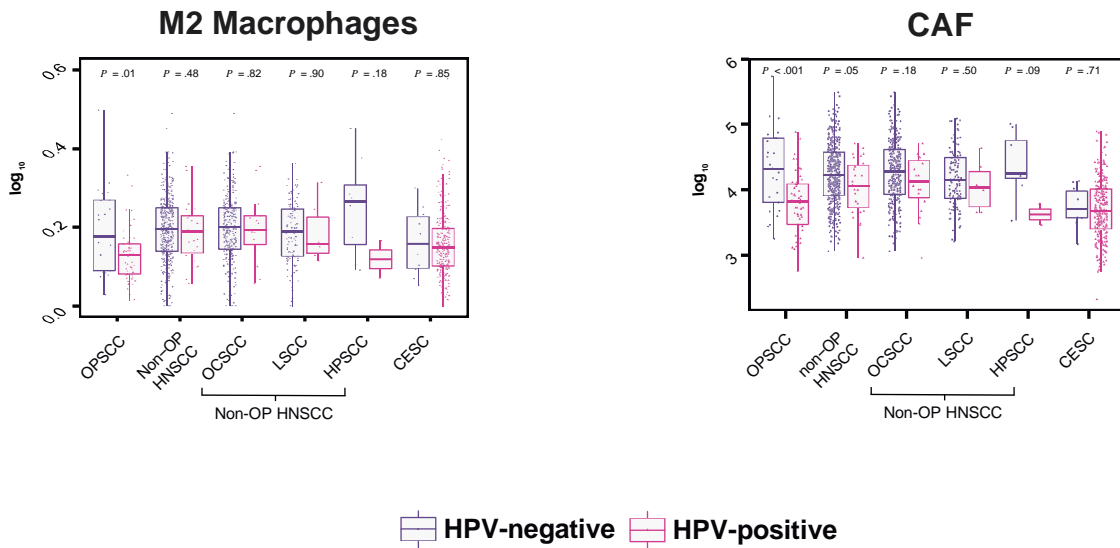
eFigure 4. A two-dimensional reduced visualization based on 2,630 immune-related transcripts in HNSCC and CESC patients. The TumorMap discretized by gender (A), HPV subtype (B), smoking history (C) for each site: oropharynx, non-oropharynx, cervix, hypopharynx, and oral cavity. Red = HPV-positive; blue = HPV-negative.



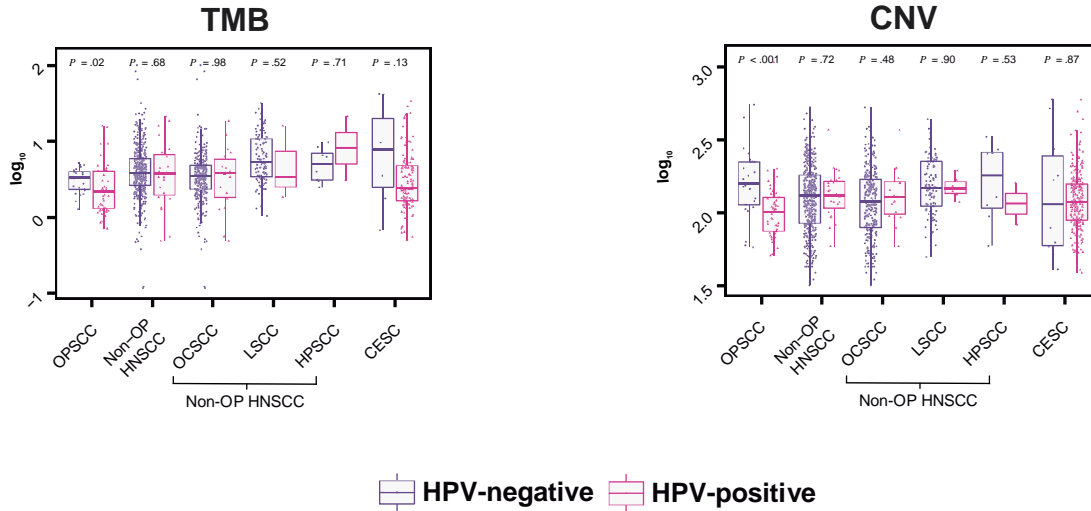
eFigure 5. Comparative analysis of immunogenomic metrics between HPV-positive and -negative patients within each tumor site. HPV-positive and -negative non-OP HNSCC and CESC are similar with regards to B cells, CD8⁺ T cells, and cytolytic activity scores. Significant differences are seen in the above parameters between HPV-positive and HPV-negative OPSCC (A). The landscape of differentially expressed immunomodulatory checkpoint receptors and ligands between HPV-positive and -negative tumors (B); Color gradient reflects fold change of normalized gene expression in HPV-positive over HPV-negative patients; * $P < .05$, ** $< .01$, *** $< .0001$, **** $< .00001$. OPSCC: oropharyngeal squamous cell carcinoma; non-OP HNSCC: non-oropharyngeal squamous cell carcinoma in the head and neck, which includes the oral cavity, larynx, and hypopharynx; OCSCC: oral cavity squamous cell carcinoma; LSCC: laryngeal squamous cell carcinoma; HPSCC: hypopharyngeal squamous cell carcinoma; CESC: cervical squamous cell carcinoma.



eFigure 6. Comparative analysis of immunogenomic metrics between HPV-positive and -negative patients within each tumor site. HPV-positive and -negative non-OP HNSCC and CESC are similar with regard to plasma cells, Naïve B cells, CD8⁺ T/Treg cells, TCR diversity, BCR diversity. Significant differences are seen in the above parameters between HPV-positive and HPV-negative OPSCC. OPSCC: oropharyngeal squamous cell carcinoma; non-OP HNSCC: non-oropharyngeal squamous cell carcinoma in the head and neck, which includes the oral cavity, larynx, and hypopharynx; OSCCC: oral cavity squamous cell carcinoma; LSCC: laryngeal squamous cell carcinoma; HPSCC: hypopharyngeal squamous cell carcinoma; CESC: cervical squamous cell carcinoma.



eFigure 7. Comparative analysis of immunogenomic metrics between HPV-positive and -negative patients within each tumor site. HPV-positive and -negative non-OP HNSCC and CESC are similar with regard to M2 macrophages, and CAF (cancer-associated fibroblasts); Significant differences are seen in the above parameters between HPV-positive and -negative OPSCC. OPSCC: oropharyngeal squamous cell carcinoma; non-OP HNSCC: non-oropharyngeal squamous cell carcinoma in the head and neck, which includes the oral cavity, larynx, and hypopharynx; OCSCC: oral cavity squamous cell carcinoma; LSCC: laryngeal squamous cell carcinoma; HPSCC: hypopharyngeal squamous cell carcinoma; CESC: cervical squamous cell carcinoma.



eFigure 8. Comparative analysis of immunogenomic metrics between HPV-positive and -negative patients within each tumor site. HPV-positive and -negative non-OP HNSCC and CESC are similar with regard to TMB (tumor mutation burden) and CNV burden, however, HPV-positive OPSCC has a significantly lower TMB and CNV burden than HPV-negative OPSCC. OPSCC: oropharyngeal squamous cell carcinoma; non-OP HNSCC: non-oropharyngeal squamous cell carcinoma in the head and neck, which includes the oral cavity, larynx, and hypopharynx; OCSCC: oral cavity squamous cell carcinoma; LSCC: laryngeal squamous cell carcinoma; HPSCC: hypopharyngeal squamous cell carcinoma; CESC: cervical squamous cell carcinoma.