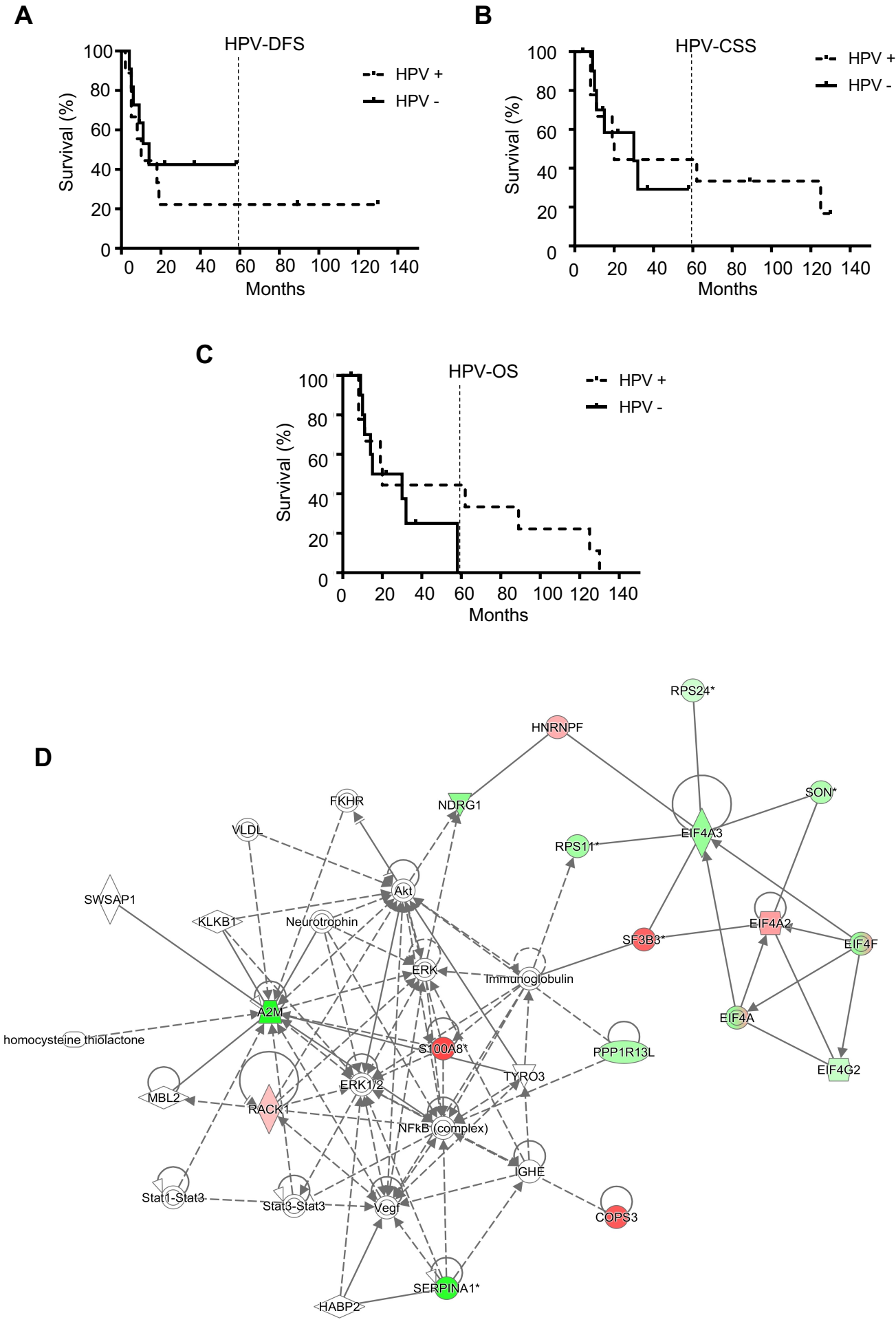
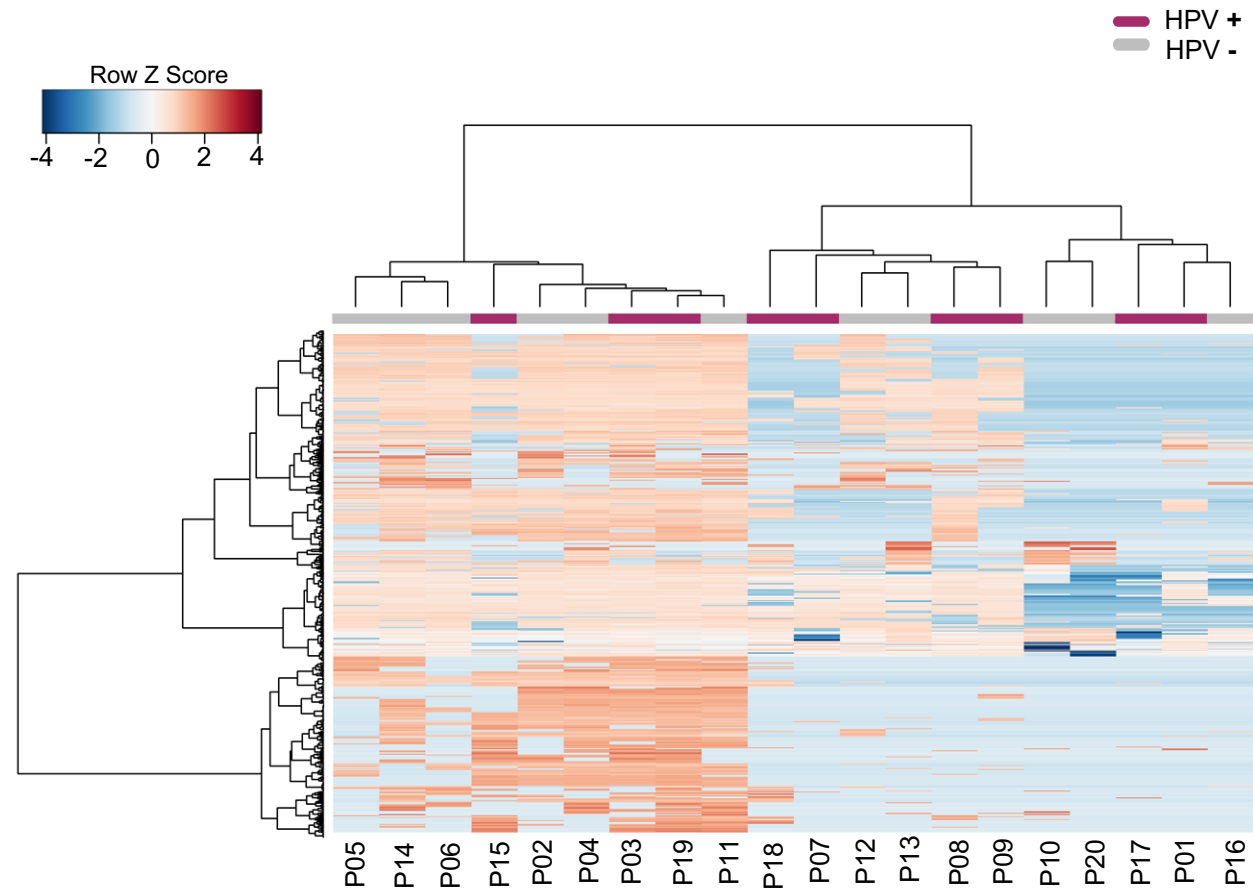


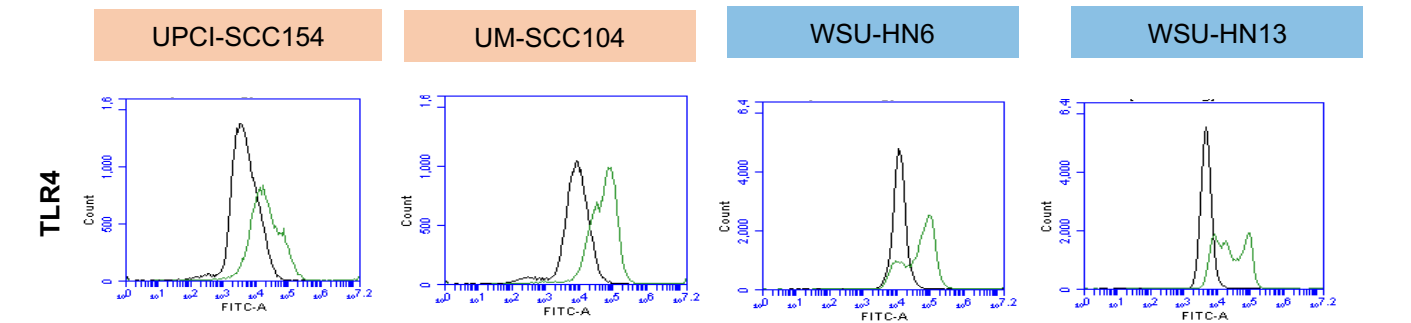
Supplementary Figure 1



Supplementary Figure 2



Supplementary Figure 3



SUPPLEMENTARY TABLES

Supplementary Table 1. Sociodemographic and clinicopathological features of the patients included in the proteomics analysis.

<i>Feature</i>	<i>HPV(+)</i>	<i>HPV(-)</i>	<i>p value</i>
	<i>n (%)</i>		
Age			
Mean	34,7	32,7	
Median	37	35	0.656
Range	20-40	20-39	
Sex			
Male	6 (66,7)	6 (54,5)	0.670
Female	3 (33,3)	5 (45,5)	
Tobacco consumption			
Yes	5 (62,5)	10 (90,9)	0.262
No	3 (37,5)	1 (9,1)	
Alcohol consumption			
Yes	3 (37,5)	10 (90,9)	0.041
No	5 (62,5)	1 (9,1)	
Anatomical site			
Tongue	3 (37,5)	4 (40)	0.84
Floor of the mouth	3 (37,5)	2 (20)	
Other	2 (25)	4 (40)	
T classification			
T1/T2	0 (0)	3 (27,3)	0.218
T3/T4	9 (100)	8 (72,7)	
N classification			
N0	5 (55,6)	3 (27,3)	0.362
N1-N3	4 (44,4)	8 (72,7)	
Histological differentiation			
I	5 (55,6)	6 (54,5)	0.055
II	4 (44,4)	3 (27,3)	
III	0 (0)	2 (18,2)	
Surgical margins			
Negative	6 (85,7)	7 (63,6)	0.596
Positive	1 (14,3)	4 (36,4)	
Treatment			
Surgery	3 (33,3)	4 (36,4)	1
Surgery +RT	5 (55,6)	5 (45,5)	
Surgery +RT + CTX	1 (11,1)	2 (18,2)	
Recurrence			
Yes	7 (77,8)	6 (60)	0.628
No	2 (22,2)	4 (40)	

Abbreviations: HR-HPV (High-risk Human Papillomavirus), RT (radiotherapy), CTX, (chemotherapy).

Supplementary Table 2. Differentially expressed proteins between HPV+ and HPV - OSCC samples after Gene Ontology enrichment analysis, and miRNA prediction using samples in TCGA.

Gene	Protein	<i>p</i> value	Log2 ratio	miRNA fold change
<i>Up-regulated proteins</i>				
RACK1	Receptor of activated protein C kinase 1	0.044	0.61	-
CAD	CAD protein	0.019	1.99	-
RPL14	60S ribosomal protein L14	0.002	1.12	1.72
RPL29	60S ribosomal protein L29	0.048	0.68	-
EIF4A2	Eukaryotic initiation factor 4A-II	0.038	0.94	1.90
HNRNPF	Heterogeneous nuclear ribonucleoprote	0.021	0.77	-
SF3B3	Splicing factor 3B subunit 3	0.029	1.52	-
VAR5	Valine-tRNA ligase	0.019	1.66	-
DYNC1H1	Cytoplasmic dynein 1 heavy chain	0.001	1.49	-1.42
LRPPRC	Leucine-rich PPR motif-containing protein	0.042	1.02	3.11
CKAP4	Cytoskeleton-associated protein 4	0.038	1.50	2.00
COPS3	COP9 signalosome complex subunit 3	0.023	1.60	2.40
S100A8	Protein S100-A8	0.004	1.80	1.97
<i>Down-regulated proteins</i>				
RPL23	60S ribosomal protein L23	0.039	-0.99	-
RPS11	40S ribosomal protein S11	0.023	-1.85	-
RPS24	40S ribosomal protein S24	0.037	-0.975	-
EIF4A3	Eukaryotic initiation factor 4A-III	0.004	-2.03	-
NDRG1	NDRG1	0.001	-2.24	5.86
EIF4G2	Eukaryotic translation initiation factor	0.008	-1.14	3.11
PLP2	Proteolipid protein 2	0.012	-1.77	1.47
SERPINA1	Alpha-1-antitrypsin	0.009	-4.20	1.74
A2M	Alpha-2-macroglobulin	0.004	-4.47	1.85
HP1BP3	Heterochromatin protein 1-binding protein	0.042	-1.04	2.58
SON	SON	0.016	-1.52	-
PPP1R13L	RelA-associated inhibitor	0.015	-1.67	-
YWHAH	14-3-3 protein eta	0.017	-1.73	-

Supplementary Table 3. Enriched biological processes p-value.

<i>Differential expressed proteins</i>		
Term	p-value	Adjusted p-value
Viral process	4.09	0.01
Cellular protein metabolic process	3.58	0.01
Viral gene expression	2.38	0.01
Viral transcription	2.71	0.01
Protein targeting to ER	0.01	0.01
SRP-dependent cotranslational protein targeting to membrane	8.41	0.01
Cotranslational protein targeting to membrane	1.04	0.01
Nuclear-transcribed mRNA catabolic process	4.22	0.01
Nuclear-transcribed mRNA catabolic process, nonsense-mediated decay	7.97	0.01
<i>HPV (+) exclusive proteins</i>		
Term	P-value	Adjusted P-value
Gene expression	3.27	0.01
Nuclear export	2.10	0.01
Neutrophil degranulation	1.22	0.01
Neutrophil activation involved in immune response	1.39	0.01
Neutrophil mediated immunity	1.58	0.01
mRNA transport	5.10	0.01
mRNA-containing ribonucleoprotein complex export from nucleus	3.50	0.01
mRNA export from nucleus	5.58	0.01
RNA export from nucleus	1.61	0.01
RNA processing	3.90	0.01
<i>HPV(-) exclusive proteins</i>		
Term	P-value	Adjusted P-value
Negative regulation of blood coagulation	1.74	8.88
Receptor-mediated endocytosis	1.15	6.53
Humoral immune response mediated by circulating immunoglobulin	4.66	2.97
Complement activation, classical pathway	3.78	2.75
Regulation of protein processing	8.60	7.32
Regulation of acute inflammatory response	2.48	2.53
Regulation of protein activation cascade	1.95	9.98
Regulation of humoral immune response	5.40	9.18
Regulation of immune effector process	6.57	8.39
Regulation of complement activation	2.40	6.14

Supplementary Table 4. Correlation between S100A8 expression and clinicopathological features.

<i>Variable</i>	<i>Category</i>	<i>S100A8</i>		<i>p</i>
		<i>Low</i>	<i>High</i>	
<i>Sex</i>	<i>Male</i>	75.8	76.9	<i>0.917</i>
	<i>Female</i>	24.2	23.1	
<i>Tobacco use</i>	<i>Yes</i>	83.9	90.5	<i>0.494</i>
	<i>No</i>	16.1	9.5	
<i>Alcohol use</i>	<i>Yes</i>	64.5	66.7	<i>0.873</i>
	<i>No</i>	35.5	33.3	
<i>Anatomical site</i>	<i>Tongue</i>	43.3	50	<i>0.816</i>
	<i>Floor m.</i>	33.3	25	
	<i>Other</i>	23.3	25	
<i>Tumor</i>	<i>T1-T2</i>	36.4	11.5	<i>0.030*</i>
	<i>T3-T4</i>	63.6	88.5	
<i>Node</i>	<i>N0</i>	0	0	<i>ND</i>
	<i>N1-N3</i>	100	100	
<i>Clinical stage</i>	<i>I-II</i>	24.2	0	<i>0.007*</i>
	<i>III-IV</i>	75.8	100	
<i>Histological classification</i>	<i>I</i>	60.6	72	<i>0.448</i>
	<i>II</i>	30.3	16	
	<i>III</i>	9.1	12	
<i>Surgical margins</i>	<i>Negative</i>	96.3	71.4	<i>0.015*</i>
	<i>Positive</i>	3.7	28.6	
<i>Recurrence</i>	<i>Yes</i>	48.5	26.9	<i>0.092</i>
	<i>No</i>	51.5	73.1	

* Statistically significant difference.