**Figure 1**

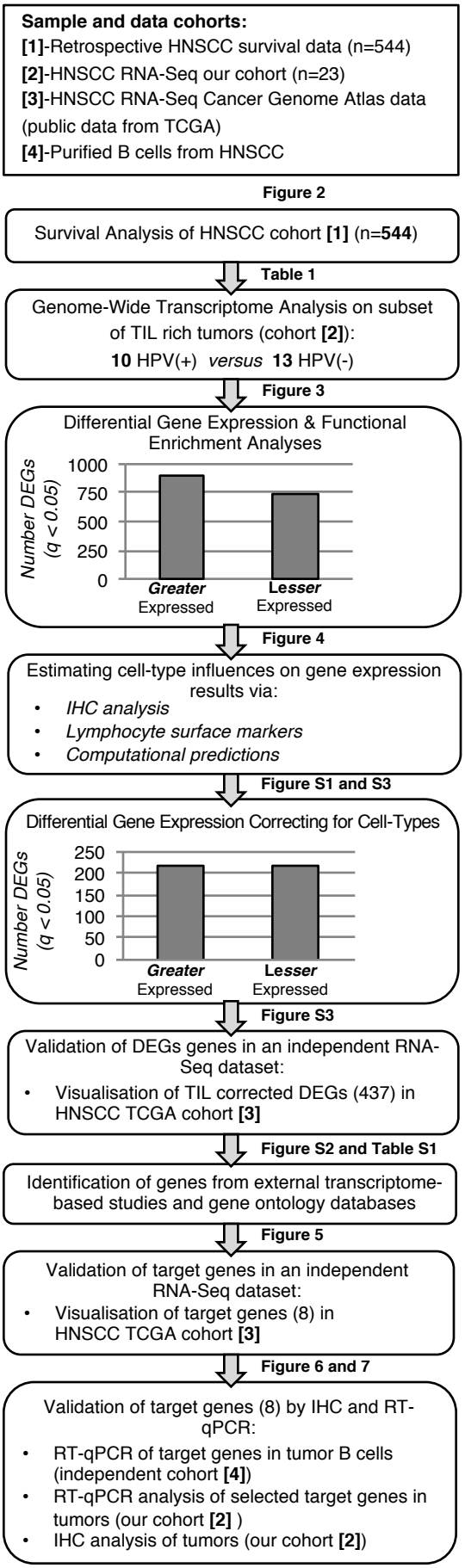
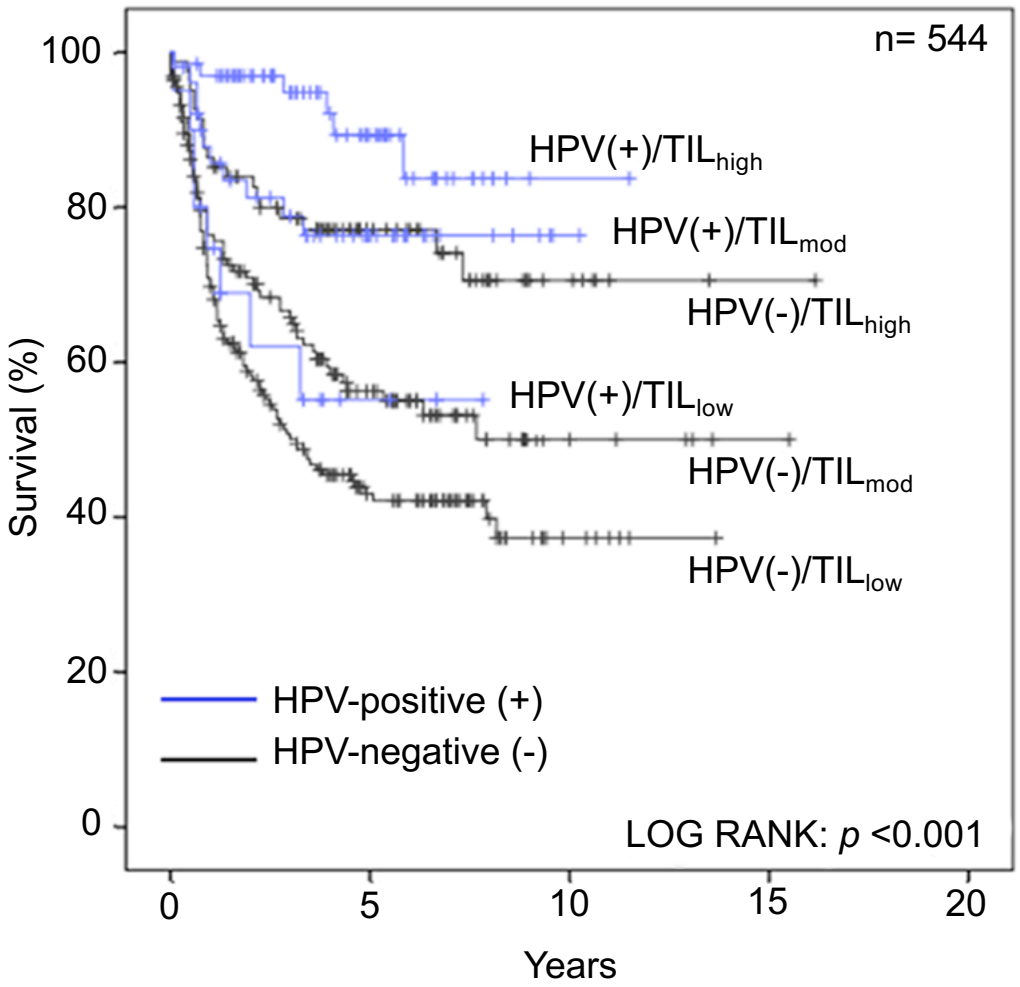

Sample and data cohorts:
[1]-Retrospective HNSCC survival data (n=544)
[2]-HNSCC RNA-Seq our cohort (n=23)
[3]-HNSCC RNA-Seq Cancer Genome Atlas data (public data from TCGA)
[4]-Purified B cells from HNSCC
Figure 2
Survival Analysis of HNSCC cohort [1] (n=544)
Table 1
Genome-Wide Transcriptome Analysis on subset of TIL rich tumors (cohort [2]):
10 HPV(+) versus 13 HPV(-)
Figure 3
Differential Gene Expression & Functional Enrichment Analyses
Number DEGs (q < 0.05)
1000
750
500
250
0
Greater Expressed
Lesser Expressed
Figure 4
Estimating cell-type influences on gene expression results via:
IHC analysis
Lymphocyte surface markers
Computational predictions
Figure S1 and S3
Differential Gene Expression Correcting for Cell-Types
Number DEGs (q < 0.05)
250
200
150
100
50
0
Greater Expressed
Lesser Expressed
Figure S3
Validation of DEGs genes in an independent RNA-Seq dataset:
Visualisation of TIL corrected DEGs (437) in HNSCC TCGA cohort [3]
Figure S2 and Table S1
Identification of genes from external transcriptome-based studies and gene ontology databases
Figure 5
Validation of target genes in an independent RNA-Seq dataset:
Visualisation of target genes (8) in HNSCC TCGA cohort [3]
Figure 6 and 7
Validation of target genes (8) by IHC and RT-qPCR:
RT-qPCR of target genes in tumor B cells (independent cohort [4])
RT-qPCR analysis of selected target genes in tumors (our cohort [2] )
IHC analysis of tumors (our cohort [2])

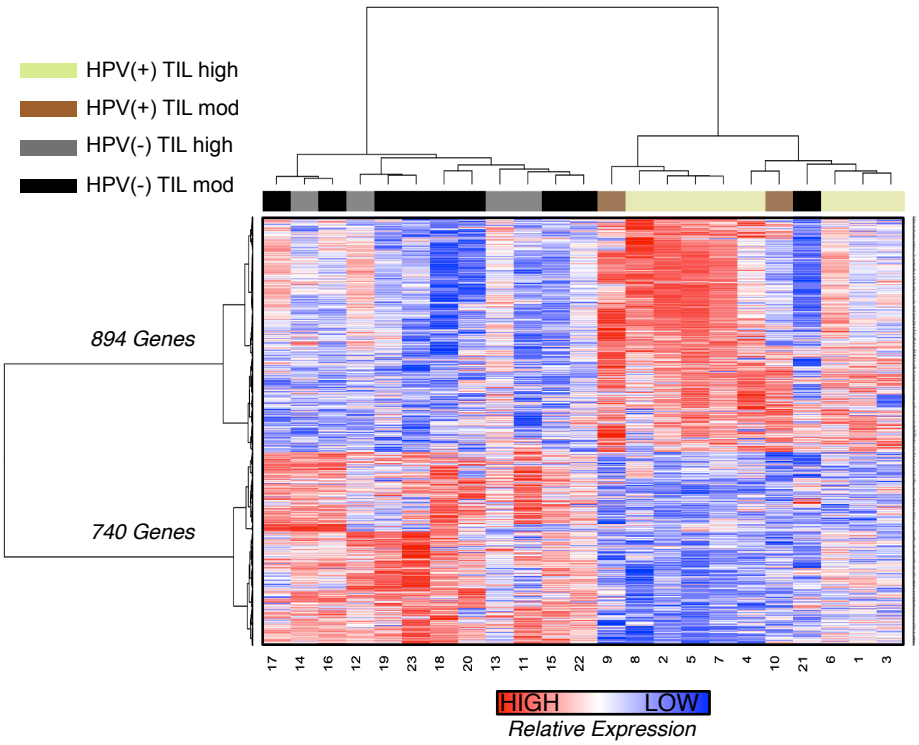
**Figure 2**




| | | | | |
|---|---|---|---|---|
| HPV(+)/TIL$_{high}$ | 61 | 26 | 1 | |
| HPV(+)/TIL$_{mod}$ | 51 | 21 | 1 | |
| HPV(+)/TIL$_{low}$ | 20 | 4 | | |
| HPV(-)/TIL$_{high}$ | 81 | 33 | 7 | 1 |
| HPV(-)/TIL$_{mod}$ | 134 | 47 | 6 | 1 |
| HPV(-)/TIL$_{low}$ | 192 | 49 | 6 | |

**Figure 3**

A


HPV(+) TIL high
HPV(+) TIL mod
HPV(-) TIL high
HPV(-) TIL mod
894 Genes
740 Genes
17 14 16 12 19 23 18 20 13 11 15 22 9 8 2 5 7 4 10 21 6 1 3
HIGH
LOW
Relative Expression

B

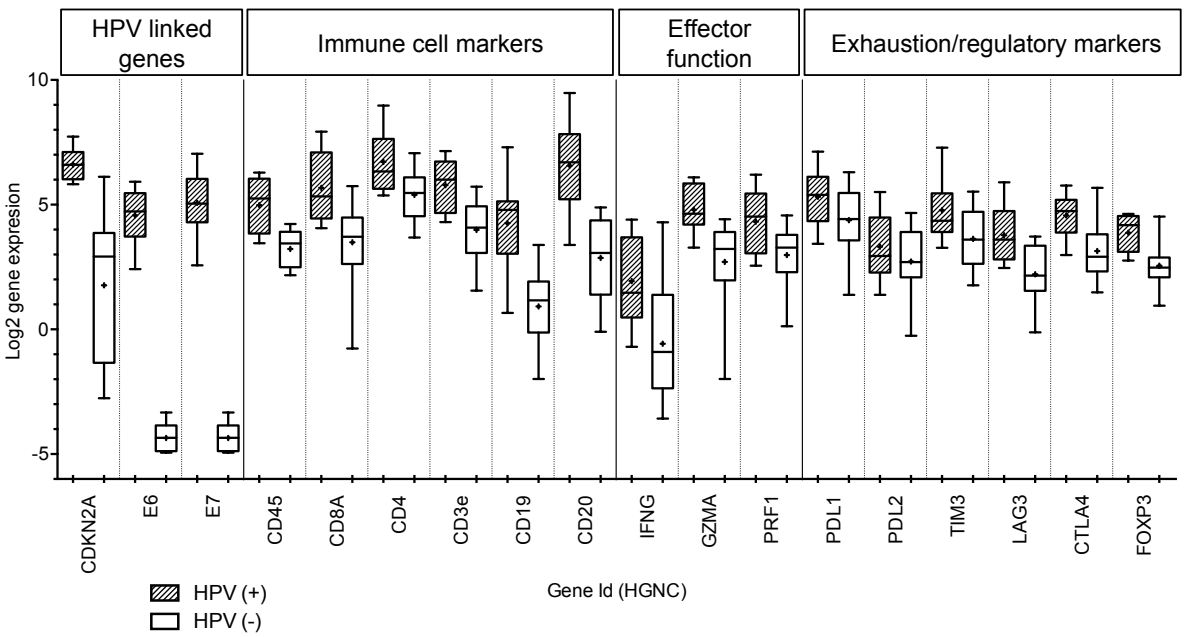

HPV linked genes
Immune cell markers
Effector function
Exhaustion/regulatory markers
Log2 gene expresion
10
5
0
-5
CDKN2A
E6
E7
CD45
CD8A
CD4
CD3e
CD19
CD20
IFNG
GZMA
PRF1
PDL1
PDL2
TIM3
LAG3
CTLA4
FOXP3
HPV (+)
HPV (-)
Gene Id (HGNC)

**Figure 4**

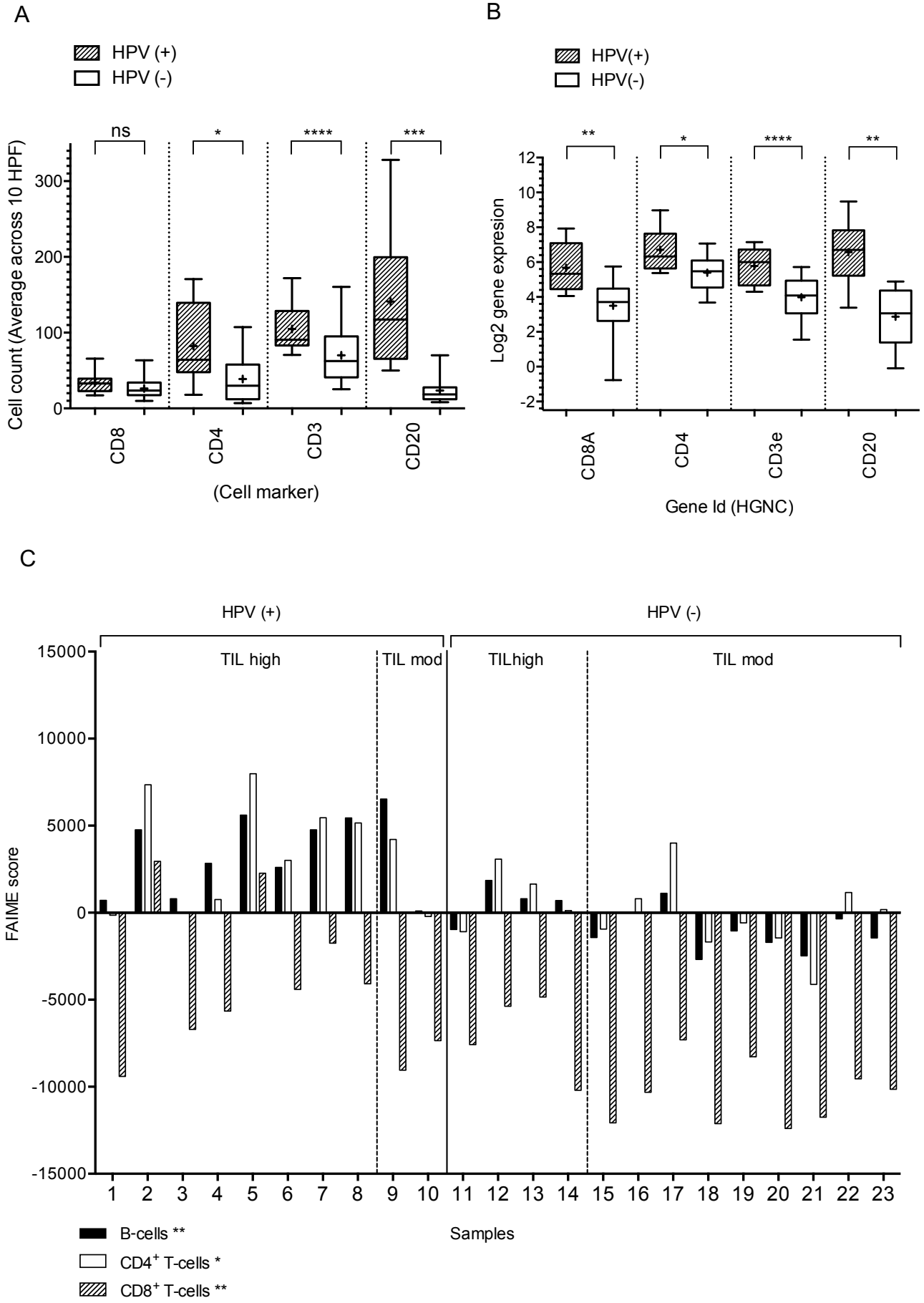

A
HPV (+)
HPV (-)
ns
*
****
***
Cell count (Average across 10 HPF)
300
200
100
0
CD8
CD4
CD3
CD20
(Cell marker)
B
HPV(+)
HPV(-)
**
*
****
**
Log2 gene expresion
12
10
8
6
4
2
0
-2
CD8A
CD4
CD3e
CD20
Gene Id (HGNC)
C
HPV (+)
HPV (-)
TIL high
TIL mod
TILhigh
TIL mod
15000
10000
5000
0
-5000
-10000
-15000
FAIME score
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
Samples
B-cells **
CD4+ T-cells *
CD8+ T-cells **

**Figure 5**

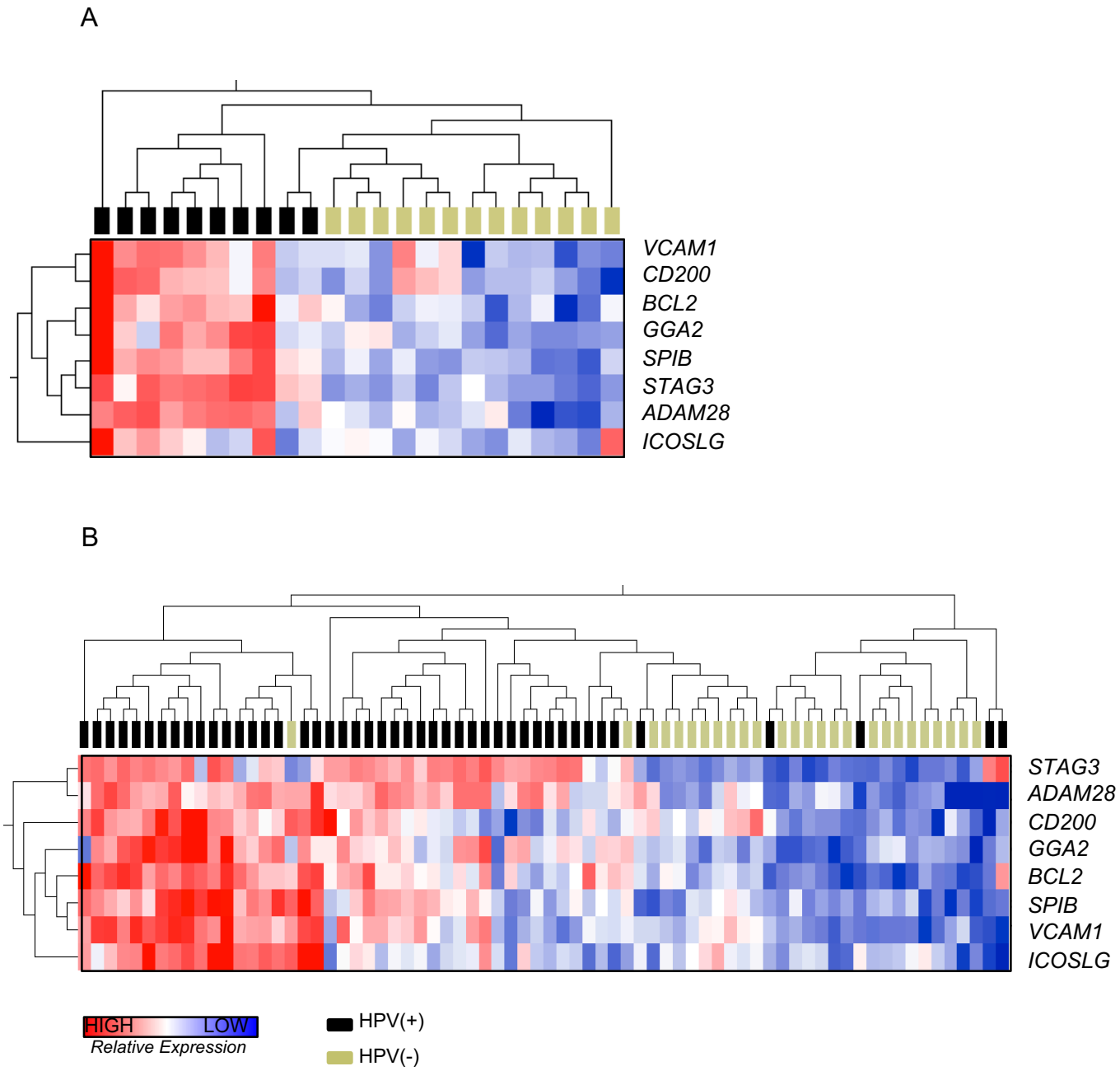
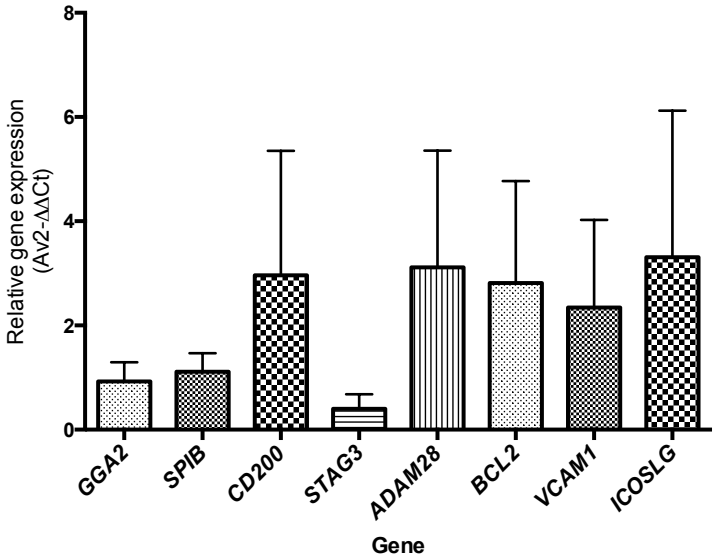

A
VCAM1
CD200
BCL2
GGA2
SPIB
STAG3
ADAM28
ICOSLG
B
STAG3
ADAM28
CD200
GGA2
BCL2
SPIB
VCAM1
ICOSLG
HIGH
LOW
Relative Expression
HPV(+)
HPV(-)

**Figure 6**


Relative gene expression
(Av2-ΔΔCt)
8
6
4
2
0
GGA2
SPIB
CD200
STAG3
ADAM28
BCL2
VCAM1
ICOSLG
Gene

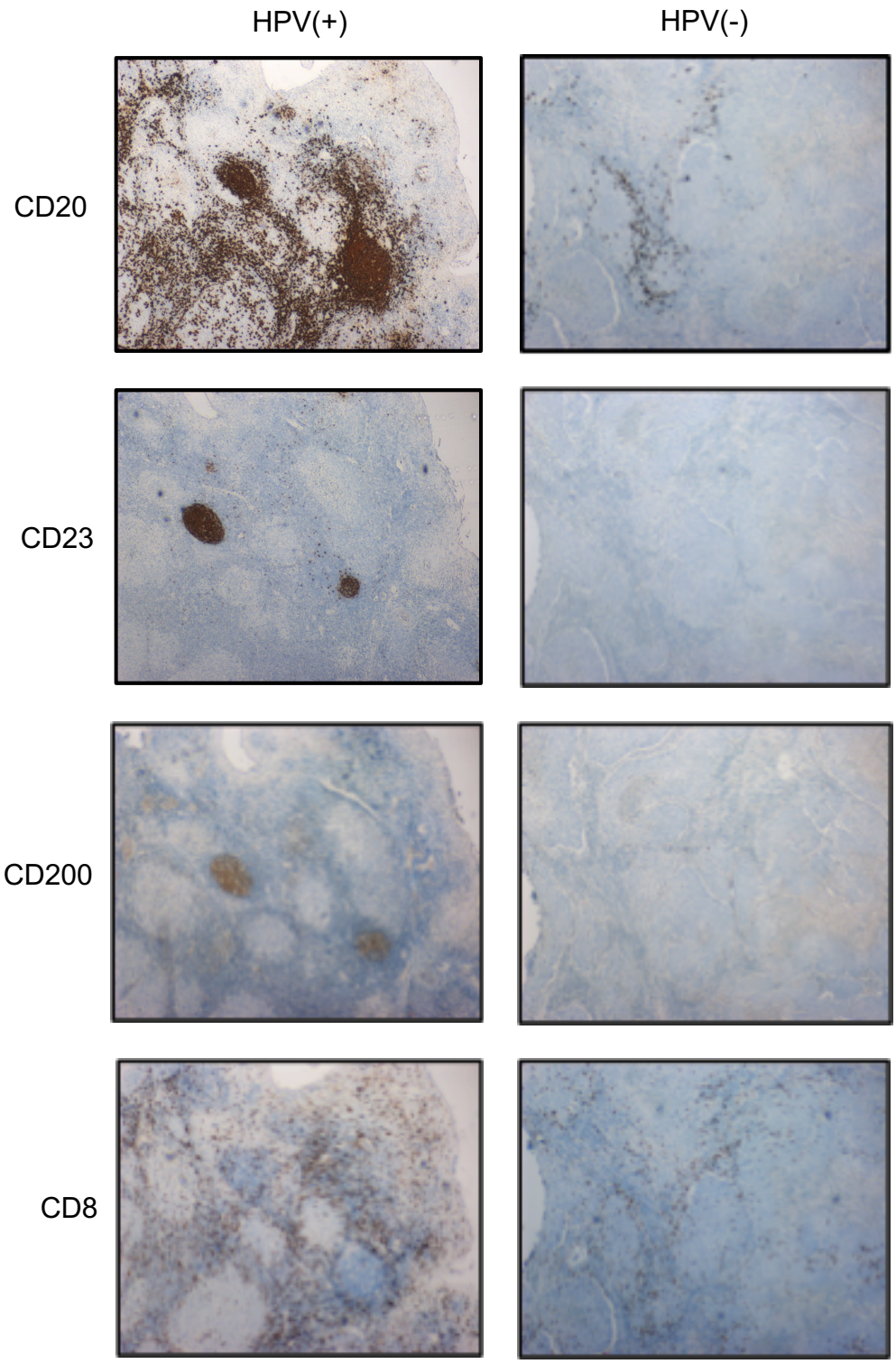



**Figure 7**