**Supplementary Methods**

**Supplementary Methods S1, Histology and immunohistochemistry**

TIL status was scored on frozen tumor sections that had been stained with H&E and viewed under low-power magnification (x2.5 objective) as described previously [1]; TILhigh: diffuse, present in >80% of tumor/stroma; TILmod: patchy, present in 20–80% of tumor/stroma; TILlow: weak/absent, present in <20% of tumor/stroma. Data regarding the percentage tumor cells, tumor grade and pattern of invasion were also recorded. Furthermore, IHC was performed on FFPE tumor sections against CD3, CD4, CD8 and CD20 (all from Novocastra, Milton Keynes, UK). TILs were quantified using a Zeiss AxioCam MRc5 microscope (Zeiss, Cambridge, UK) and Zeiss Axiovision software (version 4.8.1.0; Zeiss) in an average of 10 high-power (x400) fields across representative areas of each tumor to allow for intratumoral heterogeneity; an average intratumoral TIL score per high-power field was calculated. Additionally, IHC was performed against the antigenic targets, CD200 (Sigma-Aldrich Company Ltd., Gillingham, UK) and CD23 (Abcam, Cambridge, UK). HPV status was evaluated by IHC against p16 (CINtec, Roche, Burgess Hill, UK) and scored as HPV(+) (>50% tumor cells positive) or HPV(-) (<50% tumor cells positive); confirmation was by evaluation of E6 and E7 RNA transcript levels from the RNA-Seq data (Table 1).

**Supplementary Methods S2, RNA-Seq**

RNA quality was assessed using the Agilent 2100 Bioanalyser (Agilent Technologies UK Ltd., Stockport, UK); an average RNA quality number (RIN) of 8.51±0.90 was observed across all tumor samples. Total RNA was converted into a library for sequencing on the HiSeq 2000 (Illumina Inc., San Diego, USA) using the TruSeq™ stranded mRNA Sample Preparation Kit (Illumina Inc.). Briefly, poly-A mRNA was purified from total RNA (100ng) using the Poly(A) Purist Mag Kit (Life Technologies Ltd., Paisley, UK), according to the manufacturer’s instructions. The mRNA was then amplified and converted into cDNA, which was purified and used to construct libraries that were hybridized to the flow cell for single end (SE 35bp) sequencing.

**Supplementary Methods S3, RNA-Seq data analysis**

The quality of raw SE read data in FASTQ files was assessed and reads of low quality were trimmed or removed. SE reads were then mapped to the human genome (hg19) using TopHat (version 2.0.9) [2] and, following the removal of multi-mapping reads, converted to gene-specific read counts for 23,368 annotated genes using HTSeq-count (version 0.5.4) [3]. Non-specific filtering of count data was performed using the Bioconductor package EdgeR (version 3.4.2) [4, 5] such that genes with less than 2 read counts per million in 25% of tumor samples were excluded from further analysis. The remaining 14,528 genes were subject to normalization using the TMM method [6] to account for differences in library size from sample to sample. Unsupervised clustering of samples was performed following variance stabilizing transformation of TMM normalized data and illustrated as a heatmap.

DEGs between HPV(+) and HPV(-) groups were identified with a FDR adjusted *p-*value <0.05 (i.e., *q*-value <0.05) and a fold change of >2 or <-2 using EdgeR [4]. Fold change was calculated in EdgeR as the log2 of geometric mean of intensities; a positive and a negative fold change represents genes that were expressed to a greater or lesser extent, respectively, in HPV(+) versus HPV(-) tumors. *q*-values were obtained from differential expression test in EdgeR using the generalized linear model likelihood ratio test and adjusted for multiple testing using the Benjamini and Hochberg method to control the FDR. This package models the negative binomial distribution and implements general linear models to identify DEGs. EdgeR was also used to identify DEGs while adjusting for covariates associated with varying proportions of lymphocyte subsets in each tumor sample as reflected in the expression of CD19 (B-cells) and CD4 and CD8A (T-cells) e.g. R-script used in EdgeR for the covariate adjustment was: design <model.matrix (~adjustv\_CD19+adjustv\_CD4+adjustv\_CD8+Group).

**Supplementary Methods S4, B-cell sorting and RT-qPCR**

Tumor-infiltrating B-cells were isolated from HPV(+) tumors using a combination of mechanical and enzymatic dissociation. The tumor tissue was cut into small fragments using a scalpel. Tumor fragments were then incubated at 37oC for 15 minutes in an orbital shaker with 1-2mL RPMI 1640 medium (Gibco, Fisher Scientific UK Ltd., Loughborough, UK) containing 20 units/mL Liberase DL (Roche Diagnostics Ltd., Burgess Hill, UK) and 800 units/mL DNase I (Sigma-Aldrich Co. Ltd., Gillingham, UK). The tumor cell lysate was then passed through a 70μm filter with ice-cold RPMI 1640 medium and centrifuged at 1500rpm for 7 minutes. Cells were re-suspended in MACS buffer (1xPBS containing 2mM EDTA (pH 8.0) and 0.5% BSA) and the volume adjusted to give a concentration of <10x106 cells/mL. Cells were incubated with 10μL FcR block (Miltenyi Biotec Ltd., Bisley, UK) per 100μL of cell suspension. The B-cells (CD19+ and CD20+) were then stained with a cocktail of fluorescently conjugated antibodies (see below) at 4oC for 30 minutes: anti-CD45 FITC-conjugated (clone HI30); anti-CD4 PE-conjugated (clone RPA-T4); anti-CD3 PE-Cy7-conjugated (clone SK7); anti-CD8 PerCP-Cy5.5-conjugated (clone SK1); anti-HLA-DR APC-conjugated (clone L243); anti-CD14 APC-H7-conjugated (clone MφP9); anti-CD19 PerCP-Cy5.5-conjugated; anti-CD20 PerCP-Cy5.5-conjugated. One-thousand to 50,000 B-cells were sorted into ice-cold TRIzol LS reagent (Ambion®, Fisher Scientific UK Ltd.) at a flow rate of <2000 events/second on a BD FACSAria™ (BD Biosciences). The time from arrival of the tumor in the laboratory to processed, sorted B-cell was <3 hours.

RNA isolation from sorted B-cells was performed using the Direct-zol™ RNA MiniPrep system (ZYMO Research Co., Irvine, USA). RT was performed on 1.5ng of RNA using SuperScript® III First-Strand Synthesis System (Invitrogen, Fisher Scientific UK Ltd.). qPCR was performed for selected genes using TaqMan Gene Expression Assays (Life Technologies Ltd.), according to the manufacturer’s instructions: *GGA2* (Human Hs00370910\_m1), *ADAM28* (Human Hs00248020\_m1), *STAG3* (Human Hs00429370\_m1), *CD200* (Human Hs01033303\_m1), *SPIB* (Human Hs00162150\_m1), *ICOSLG* (Hs00323621), *BCL2* (Hs01048932\_g1) and *VCAM1* (Hs01003372\_m1). Analysis of RT-qPCR data was performed using the comparative Ct method (2-ΔΔCt method) using an internal control (*Actin*) and displayed as relative gene expression levels against a control sample [7]. RT-qPCR was reported in accordance with Minimum Information for Publication of Quantitative Real-Time PCR Experiments (MIQE) [8].

**Supplementary Methods S5, Functional analysis of individual microarray expression (FAIME) method**

The FAIME method [9] was adapted to generate a score for a large number of tissue and cell types present in each tumor sample. Marker gene sets whose expression was associated with different tissue and cell types, including lymphocyte subsets (B-cells, NK cells and CD4+ and CD8+ T-cells), were accrued from the following resources: CTen [10], IRIS, [11],HeamAtlas [12], Palmer *et al.* [13], Grigoryev *et al.* [14]and Whitney *et al*.[15]. Particular attention was paid to gene expression markers of lymphocyte origin; a marker for a particular type of lymphocyte (e.g., a B-cell) needed to be expressed in that lymphocyte as confirmed in at least two of the resources and could not be expressed in another lymphocyte type (e.g., an NK or CD4+ or CD8+ T-cell). A FAIME score was then calculated for each tumor sample, for each cell type, by producing a weighted ranking of the genes in each sample and then determining the ranking of the marker genes for a particular cell type as compared to the genes not associated with that cell type. Finally, a student’s t-test was used to assess whether the FAIME scores for a particular cell type were significantly different (*q*-value <0.05) between HPV(+) and HPV(-) tumors. In a separate group level assessment, the marker gene sets for each tissue and cell type significantly over-represented for DEGs (Bonferroni corrected *p*-value <0.05) were identified using a hypergeometric test.

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