

**Supplementary Figure S1.** Bar graph that represents the expression of most upregulated genes (*AQP5*, *CD109*, *CLDN18*, *GP2*, *NTSR1*, *TMS4F4*, and *VNN1*) comparing samples from *BRAF* wt and mut COAD patients.

**Supplementary Figure S2.** Bar graph indicating the expression of most upregulated genes (*AQP5*, *CD109*, *CLDN18*, *GP2*, *NTSR1*, *TMS4F4*, and *VNN1*) comparing colorectal *BRAF* wt and *BRAF* mut cell lines.

**Supplementary Figure S3.** Heatmap indicating the Rho and Spearmen's p-value of the correlation between the expression of upregulated genes (*CD74*, *FCGR2B*, *HLA-DMA*, *HLA-DMB*, *HLA-DOA*, *HLA-DPA1*, *HLA-DPB1*, *HLA-DQA1*, *HLA-DQB1*, *HLA-DRA*, *HLA-DRB1*, *HLA-DRB5*, and *LAG3*) and the infiltration level of some immune populations (CD8+ T cells, CD4+ T cells and myeloid dendritic cells (DC) in COAD (n=458) and READ (n=166).

**Supplementary Figure S4.** Dot plot showing the expression in READ (n=166) of upregulated genes (*CD74*, *FCGR2B*, *HLA-DMA*, *HLA-DMB*, *HLA-DOA*, *HLA-DPA1*, *HLA-DPB1*, *HLA-DQA1*, *HLA-DQB1*, *HLA-DRA*, *HLA-DRB1*, *HLA-DRB5*, and *LAG3*) in the Y axes and the infiltration level of some immune cells (CD8+ T, CD4+ T, and myeloids dendritic cells) in the X axes. The blue regression line shows the positive correlation and Rho and Spearmen's p-value data are presented in red.

**Supplementary Figure S5.** Heatmap indicating the Rho and Spearmen's p-value of the correlation between the expression of upregulated genes (*CD74*, *FCGR2B*, *HLA-DMA*, *HLA-DMB*, *HLA-DOA*, *HLA-DPA1*, *HLA-DPB1*, *HLA-DQA1*, *HLA-DQB1*, *HLA-DRA*, *HLA-DRB1*, *HLA-DRB5*, and *LAG3*) and the infiltration level of some immune population (CD8+ T cells, CD4+ T cells, myeloid dendritic cells, macrophages, and myeloid derived supressor cells (MDSC) in COAD (n=458).

**Supplementary Figure S6.** Bar graph that represents the expression of CD74 signature in relation to the status of MSI-H, comparing samples from CRC MSI low (0) and CRCMSI high (1). Mann-Whitney statistical p-value ( $p=3.6E-06$ ) was performed with a  $\pm 95\%$  confidence interval.

**Supplementary Figure S7.** Bar graph that represents the expression of CD74 signature in each CRC subtypes (CMS1, CMS2, CMS3 and CMS4). Kruskal-Wallis statistical p-value was calculated ( $p=9.8E-28$ ) with a  $\pm 95\%$  confidence interval.

**Supplementary Figure S8.** Dot plot showing the expression in COAD (n=458) (A) and in READ (n=166) (B) of most upregulated genes (*AQP5*, *CD109*, *CLDN18*, *GP2*, *NTSR1*, *TMS4F4*, and *VNN1*) in the X axes and PD1 or PD(L)1 in the Y axes. The blue regression line shows the positive correlation and Rho and Spearmen's p-value data are presented in red.

**Supplementary Figure S9.** Heatmap representing the Rho and Spearmen's p-value of the correlation between the expression of most upregulated genes (*AQP5*, *CD109*, *CLDN18*, *GP2*, *NTSR1*, *TMS4F4*, and *VNN1*) and the infiltration level of some immune populations (CD8+ T cells, CD4+ T cells, myeloids dendritic cells, macrophages, and myeloid derived supresor cells) in COAD (n=458) and READ (n=166).

**Supplementary Figure S10.** Table that indicates the association between gene expression and tumor mutational burden where CD74 signature (in yellow) refers to the combined expression of: *CD74*, *FCGR2B*, *HLA-DMA*, *HLA-DMB*, *HLA-DOA*, *HLA-DPA1*, *HLA-DPB1*, *HLA-DQA1*, *HLA-DQB1*, *HLA-DRA*, *HLA-DRB1*, *HLA-DRB5*, and *LAG3*, while *AQP5* signature (in green) refers to the combined expression of: *AQP5*, *CD109*, *CLDN18*, *GP2*, *NTSR1*, *TMS4F4*, and *VNN1* genes.