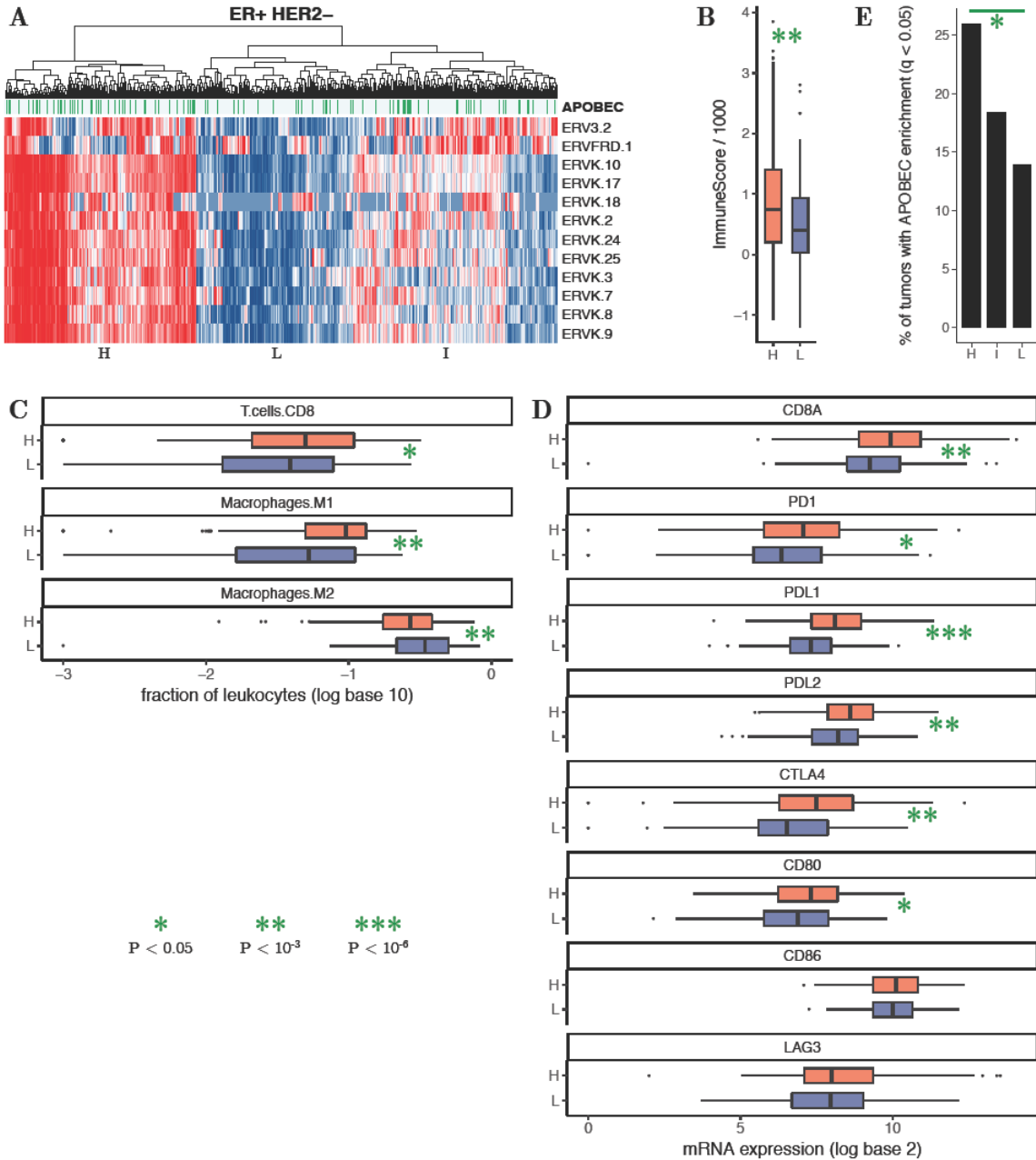
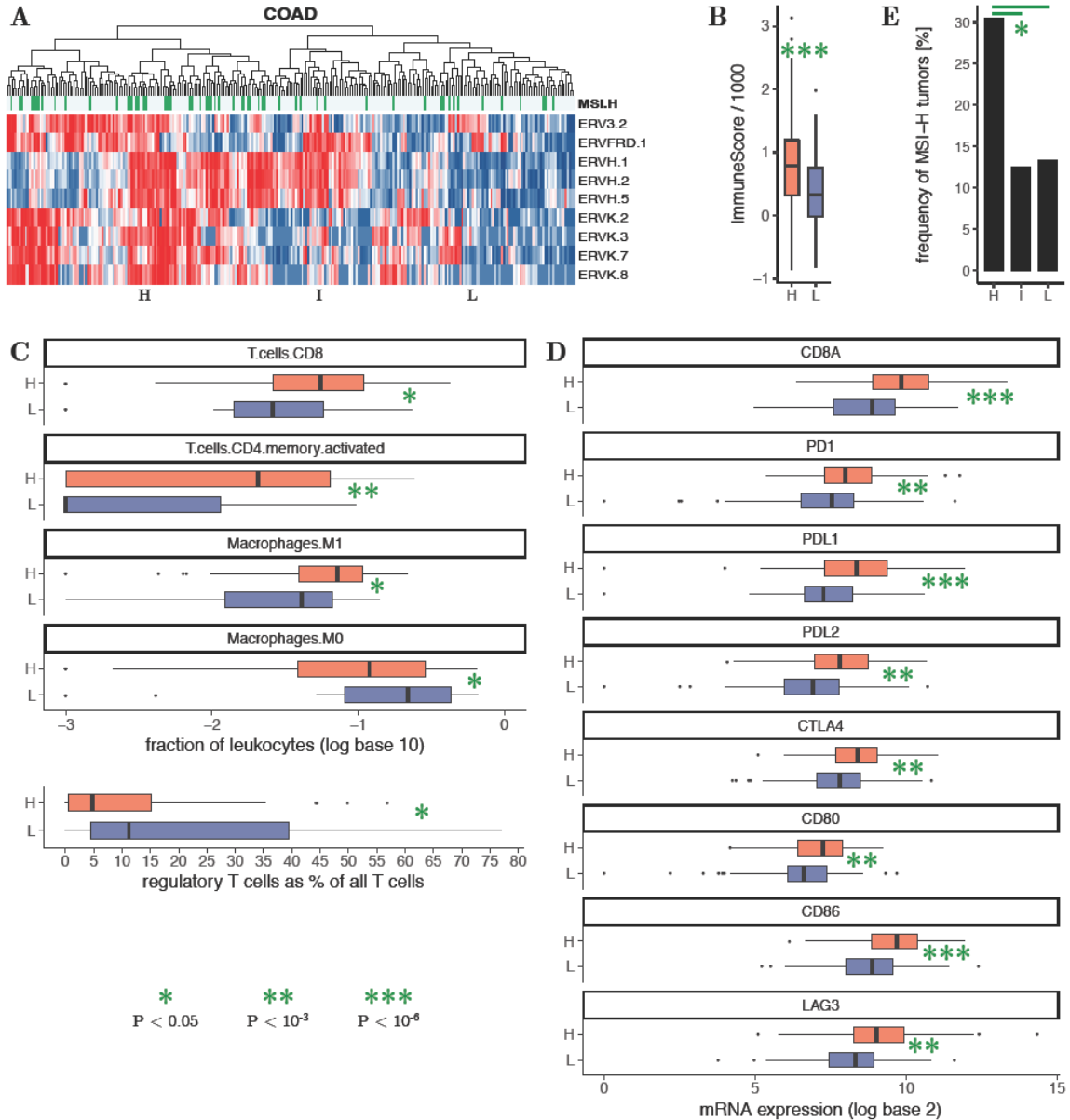


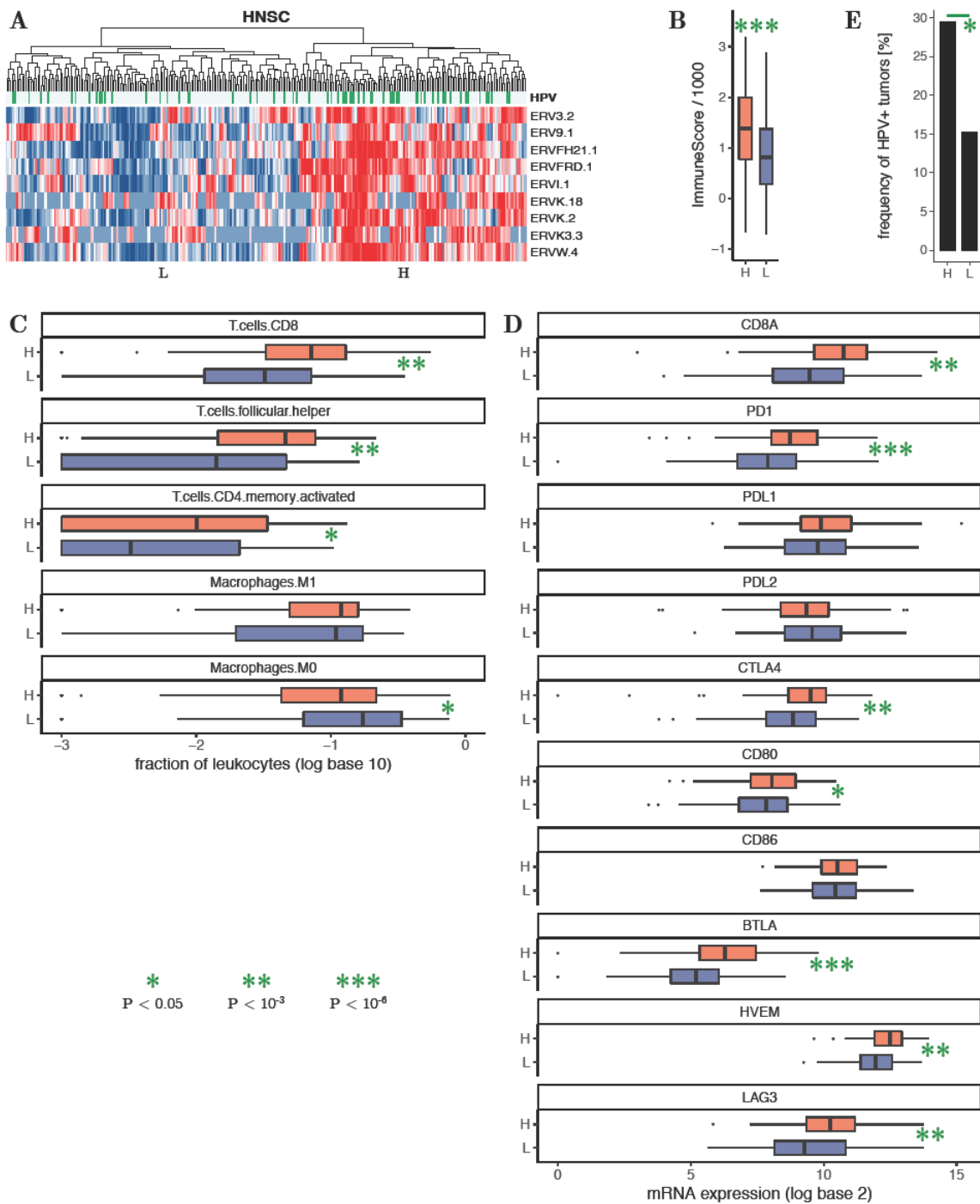
SUPPLEMENTARY FIGURES



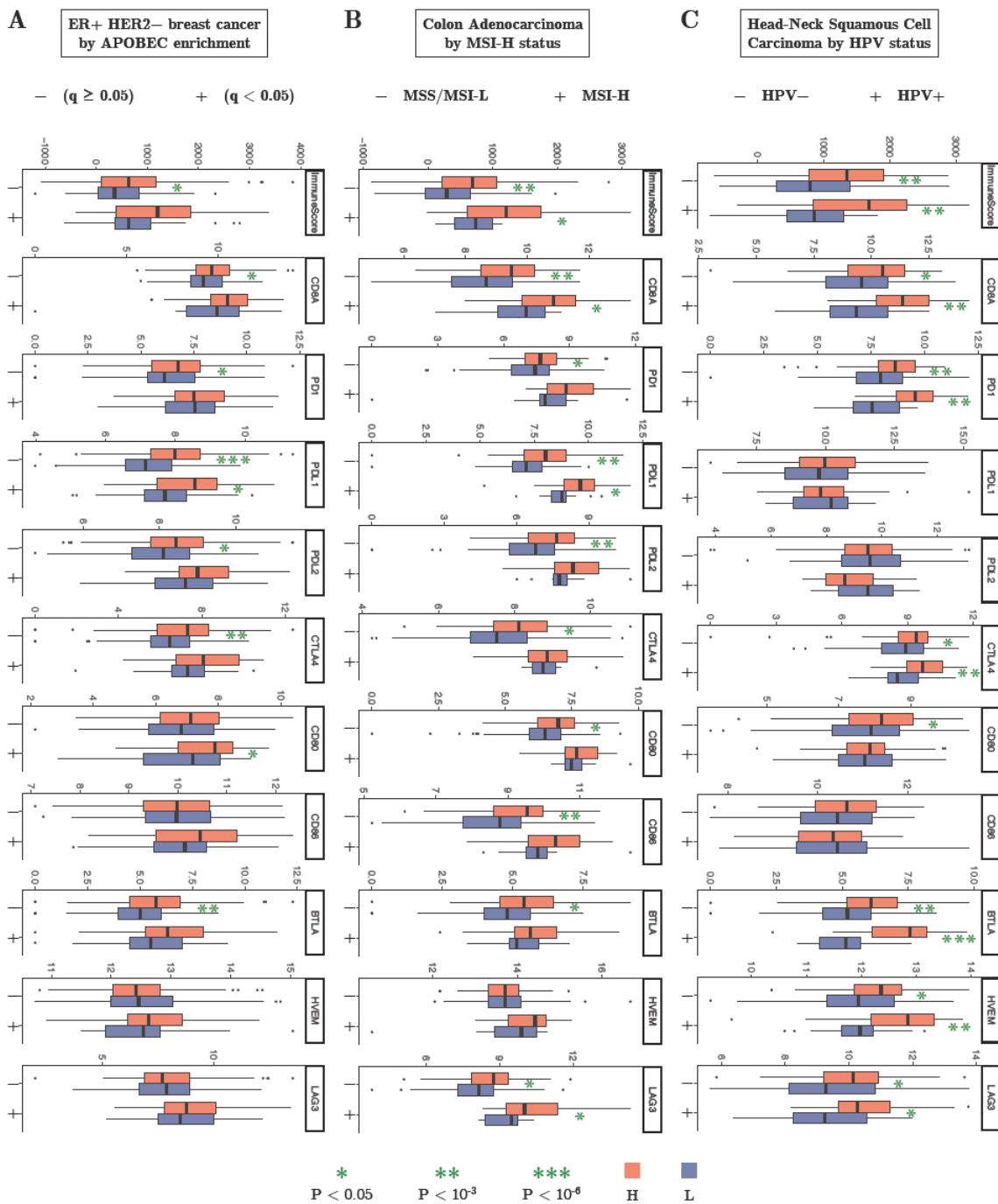
Supplementary Figure 1. Expression of π ERVs define subtypes with differential immune checkpoint activation in ER+/HER2- breast cancer. [A] Hierarchical clustering of tumors (columns) by expression (percentile) of π ERVs (rows) stratifies tumors into three subtypes (H/I/L). Comparison of [B] overall immune infiltration in tumor (“ImmuneScore”) and [C] fractional composition of tumor infiltrating leukocytes, and [D] mRNA expression of *CD8A* (cytotoxic T-cell marker) and immune checkpoint genes between π ERV-high and π ERV-low subtypes. [E] Percent of tumors with APOBEC mutagenesis in the three subtypes. Number of samples: [B & D] 226 H and 185 L, [C] 152 H and 123 L. P-values reported in bar plots and boxplots are from Fisher’s exact test and Wilcoxon rank-sum test respectively (all two-sided).



Supplementary Figure 2. Expression of π ERVs define subtypes with differential immune checkpoint activation in colon adenocarcinoma. [A] Hierarchical clustering of tumors (columns) by expression (percentile) of π ERVs (rows) stratifies tumors into three subtypes (H/I/L). Comparison of [B] overall immune infiltration in tumor (“ImmuneScore”) and [C] fractional composition of tumor infiltrating leukocytes and percentages of regulatory T-cells among all T-cells, and [D] mRNA expression of *CD8A* (cytotoxic T-cell marker) and immune checkpoint genes between π ERV-high and π ERV-low subtypes. [E] Frequency of MSI-H tumors in the three subtypes. Number of samples: [B & D] 128 H and 97 L, [C] 68 H and 29 L. P-values reported in bar plots and boxplots are from Fisher’s exact test and Wilcoxon rank-sum test respectively (all two-sided).



Supplementary Figure 3. Expression of π ERVs define subtypes with differential immune checkpoint activation in head-neck squamous-cell carcinoma. [A] Hierarchical clustering of tumors (columns) by expression (percentile) of π ERVs (rows) stratifies tumors into two subtypes (H/L). Comparison of [B] overall immune infiltration in tumor (“ImmuneScore”) and [C] fractional composition of tumor infiltrating leukocytes, and [D] mRNA expression of *CD8A* (cytotoxic T-cell marker) and immune checkpoint genes between π ERV-high and π ERV-low subtypes. [E] Frequency of HPV+ tumors in the two subtypes. Number of samples: [B & D] 131 H and 170 L, [C] 119 H and 143 L. P-values reported in bar plots and boxplots are from Fisher’s exact test and Wilcoxon rank-sum test respectively (all two-sided).



Supplementary Figure 4. π ERV expression is an independent predictor of immune checkpoint activation. π ERV-high and π ERV-low subtypes have differential immune checkpoint activation independently of [A] APOBEC enrichment status in ER+/HER2- breast cancer, [B] MSI-H status in colon cancer, and [C] HPV status in head-neck squamous-cell cancer. Number of samples: [A] - (165 H, 155 L), + (58 H, 25 L); [B] - (89 H, 84 L), + (39 H, 13 L); [C] - (91 H, 144 L), + (38 H, 26 L). P-values are from two-sided Wilcoxon rank-sum test.