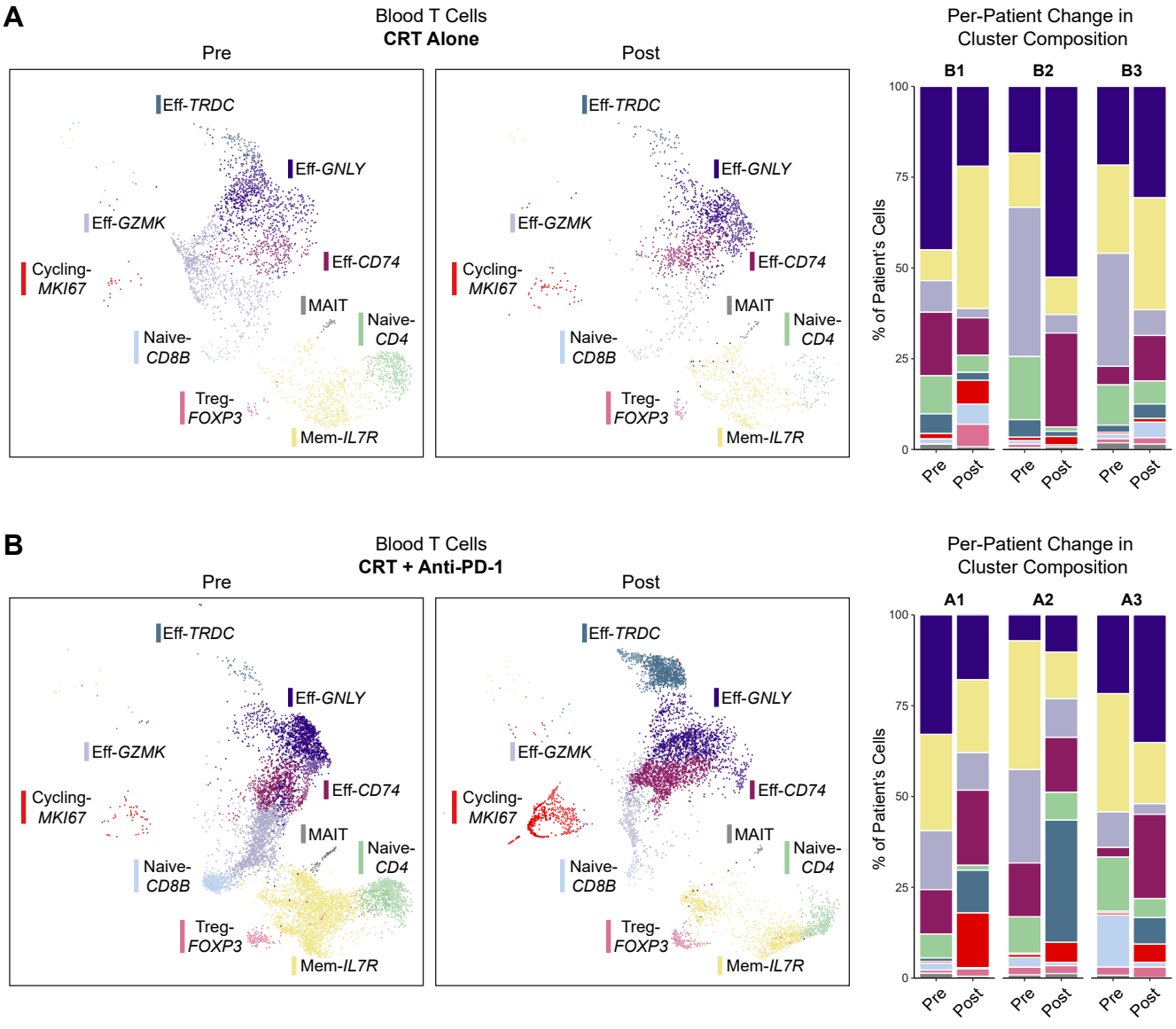
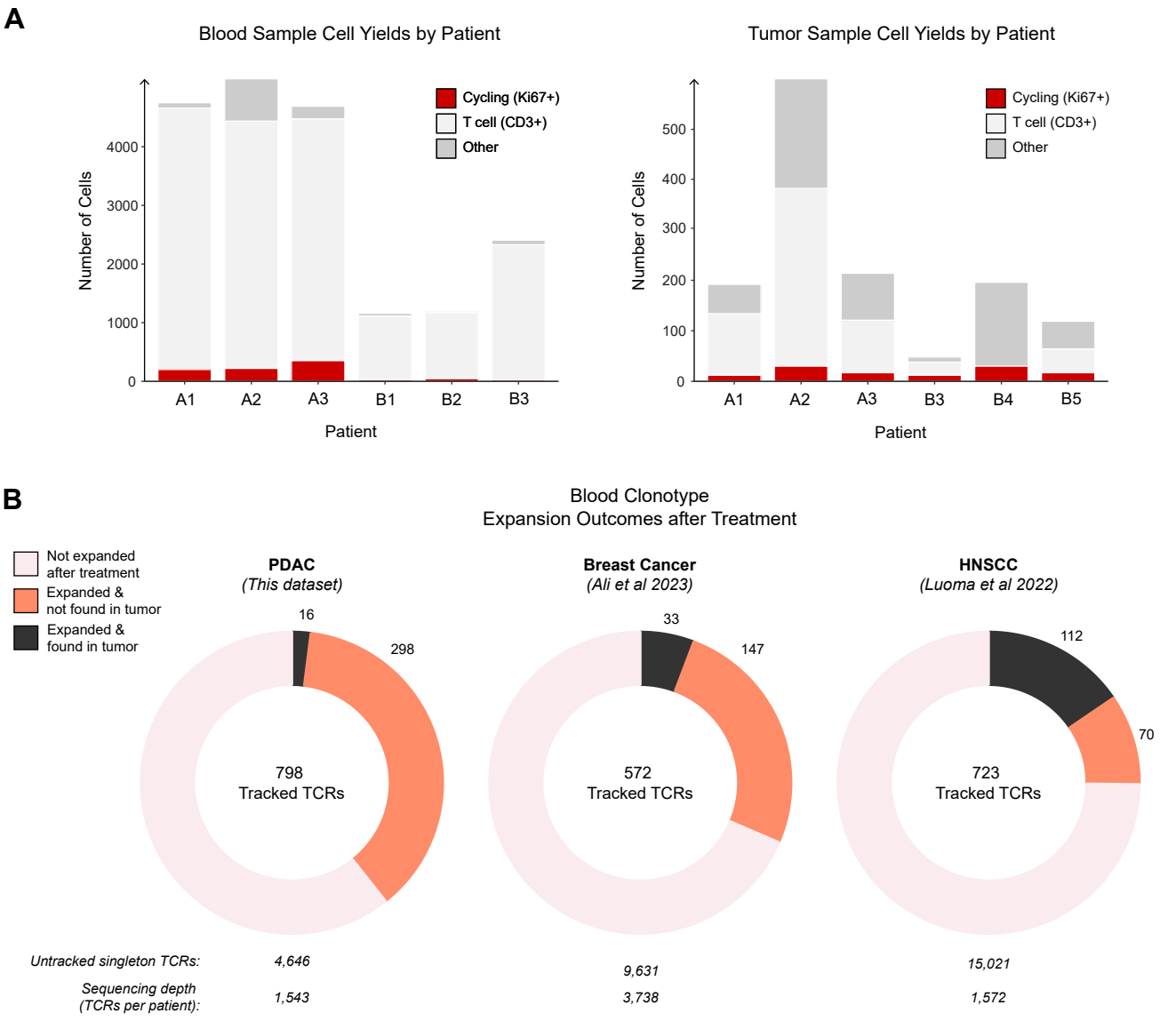
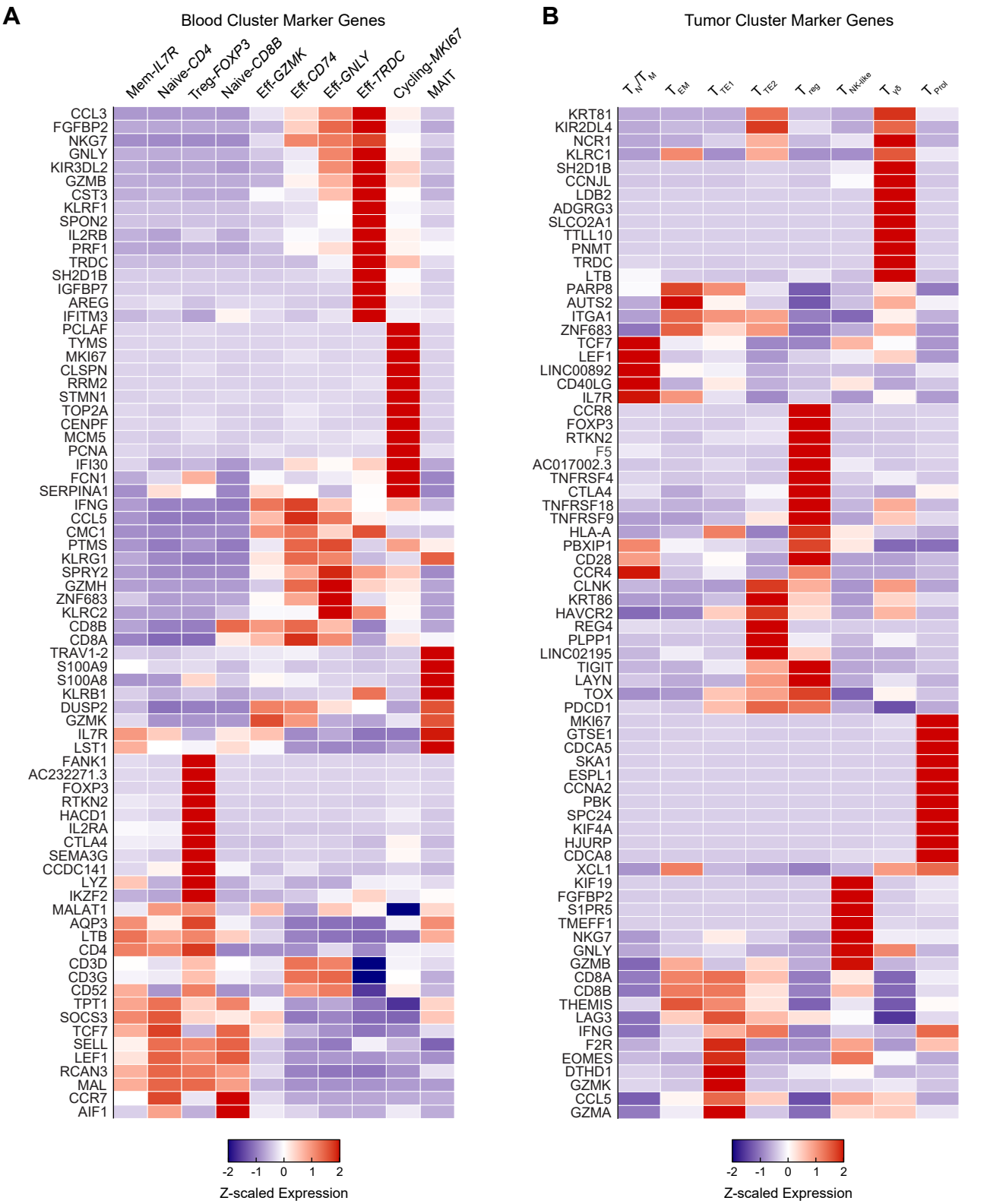


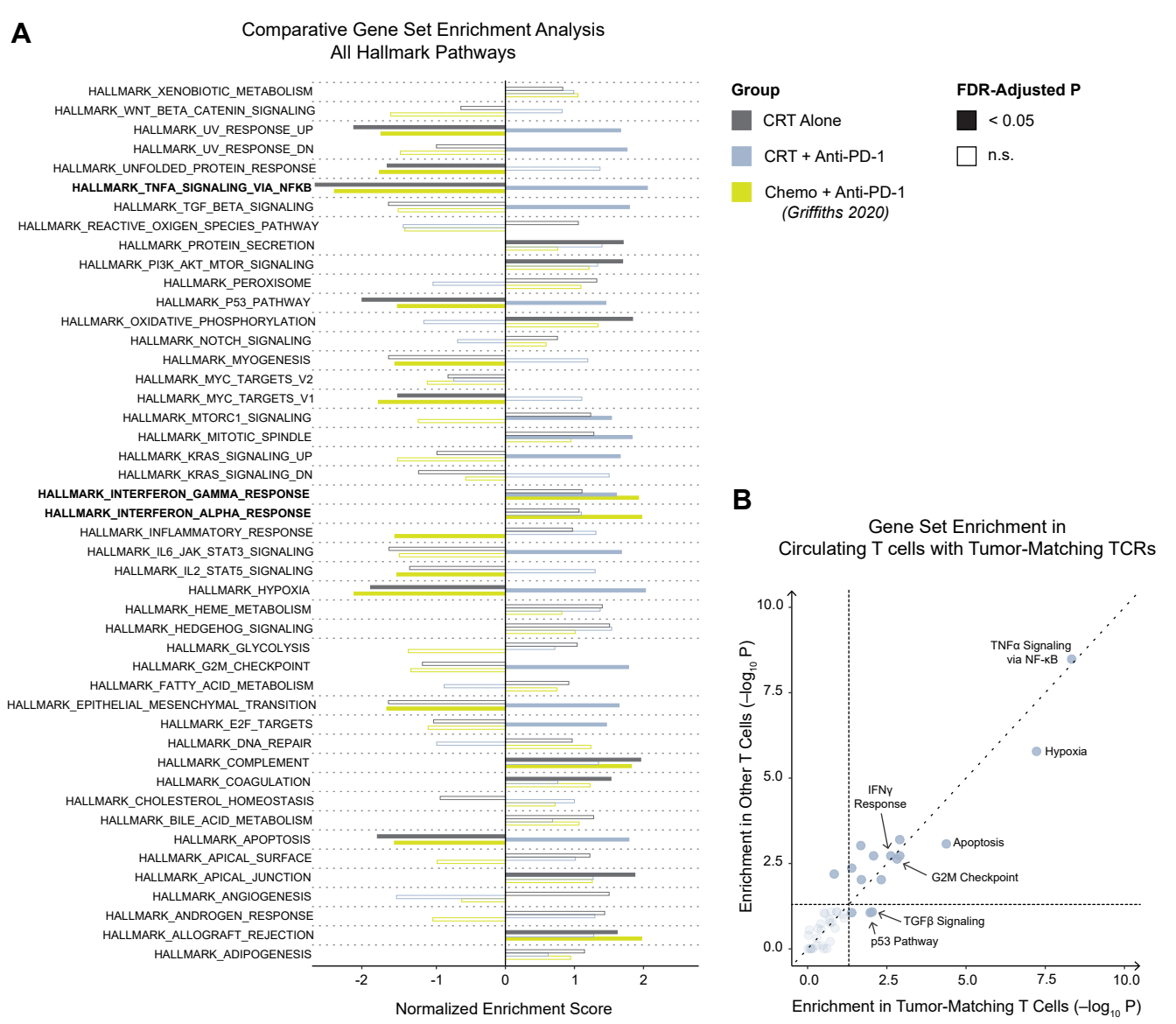
Supplementary Figure 1: Neoadjuvant PD-1 blockade changes the transcriptional phenotype of circulating T cells in PDAC patients. (A) UMAP of circulating T cells colored by unsupervised clustering before (left) and after treatment (right) with standard-of-care neoadjuvant CRT. (B) UMAP of circulating T cells colored by unsupervised clustering before (left) and after treatment (right) with neoadjuvant anti-PD1 in addition to CRT.



Supplementary Figure 2: Neoadjuvant PD-1 blockade stimulates T cell expansion in PDAC patients. (A) Bar plot showing the total number of cells recovered from each patient's blood (left) or tumor (right) samples that passed quality checks and were included in the analysis; colors denote notable cell subsets. (B) Donut plots showing the number and proportion of circulating clonotypes that expanded after PD-1 blockade in our pancreatic cancer dataset (left), in a dataset of metastatic breast cancer patients treated with anti-PD1 and a CDK4/6 inhibitor (center), and in a dataset of anti-PD1-treated head & neck squamous cell carcinoma patients (right). Clonotypes that were also encountered in the tumor are colored separately from those that were only observed in circulation; pre-treatment singleton TCRs that were not detected in the post-treatment sample were excluded.



Supplementary Figure 3: Sequenced blood and tumor cells exhibit distinct phenotypes captured by clustering analysis. Heatmap showing the average expression within each cluster of the top 75 most variable genes among (A) blood T cells and (B) tumor-infiltrating cells. Each row is centered on the global expression mean and scaled by the standard deviation, and the resulting z-scores are shown.



Supplementary Figure 4: Lack of response to neoadjuvant PD-1 correlates with NF-κB activation and a relatively restrained upregulation of interferon-response genes. (A) GSEA of all 50 hallmark gene sets applied to the list of treatment-induced differentially expressed genes (DEGs) in each group of patients. (B) Scatterplot of GSEA scores conducted separately for the treatment-induced DEGs within known tumor-matching T cell clones compared to all other T cells; FDR-adjusted P values were used for plotting, with the horizontal and vertical dashed lines demarcating the significance cutoff of 0.05.