Supplemental Figures for

Peripheral blood immune cell dynamics reflect anti-tumor immune responses and predict clinical response to immunotherapy

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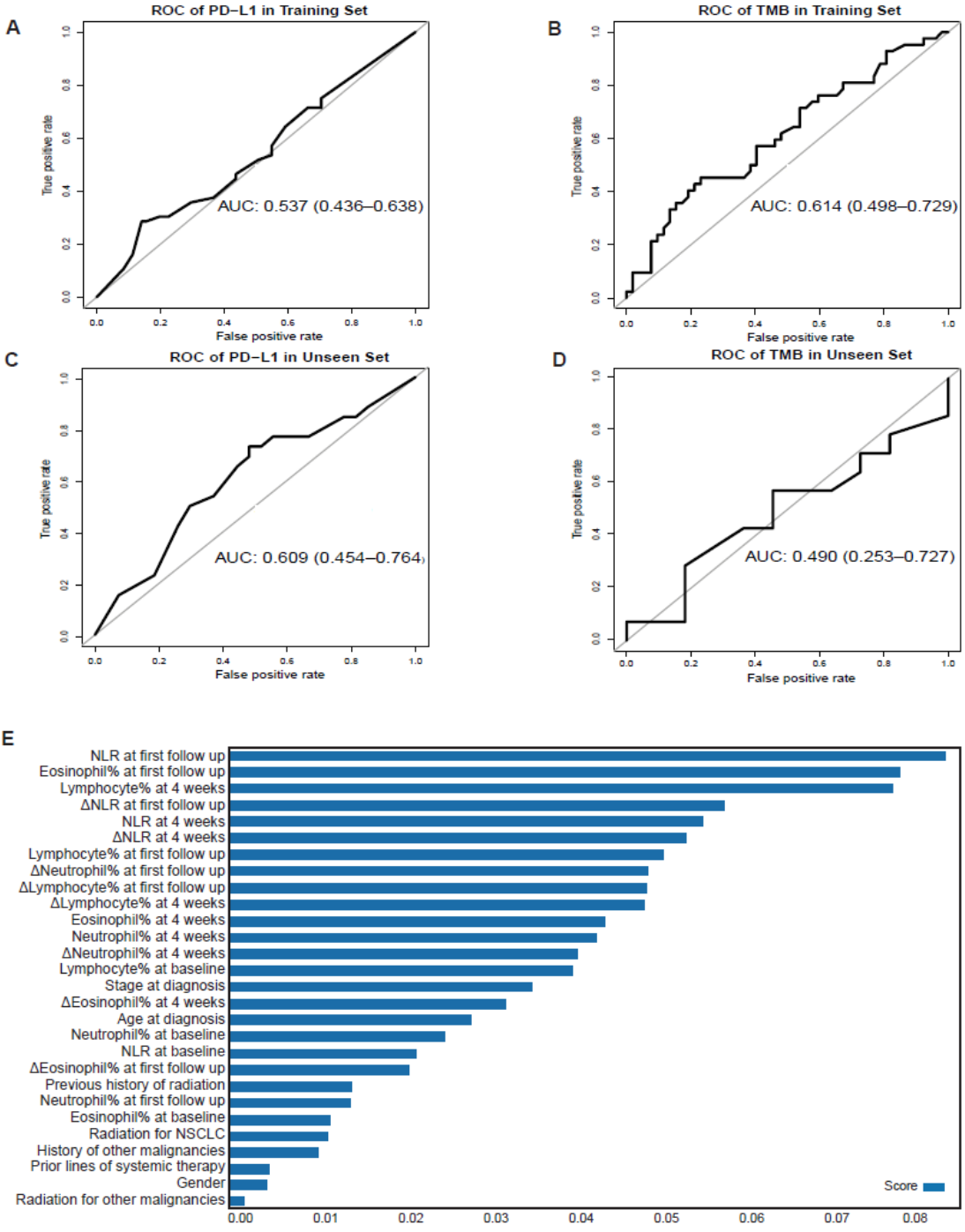
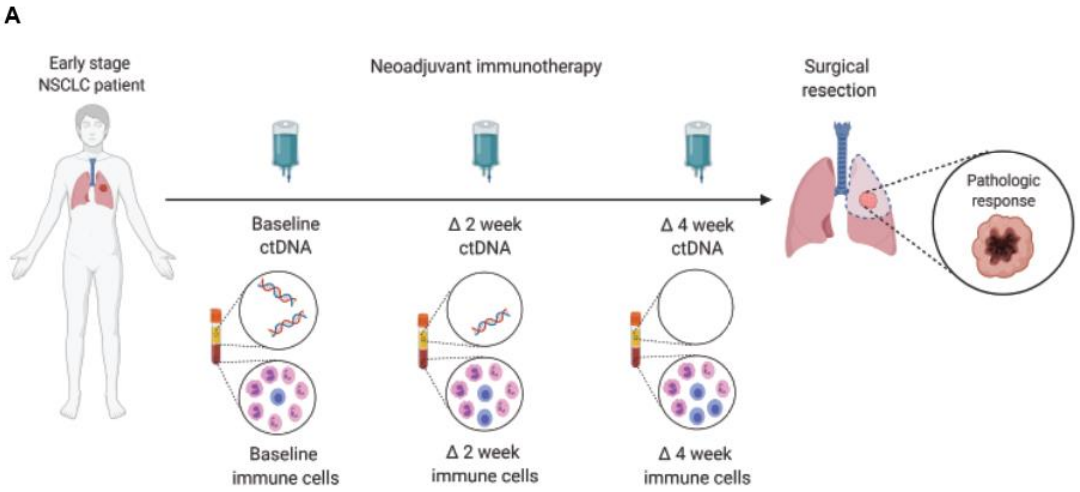
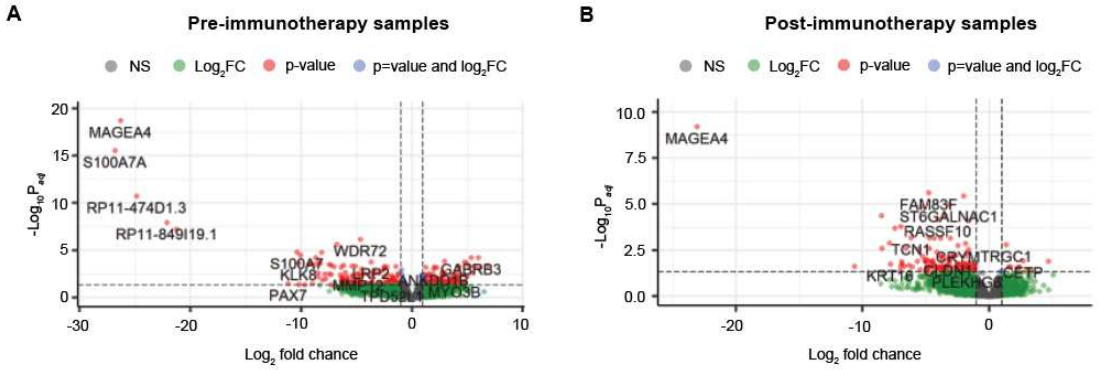


Supplemental figure S1: Predictive models in metastatic NSCLC cohort. (A, B) Receiver operator curve (ROC) for predicting durable clinical benefit using (A) PD-L1 and (B) TMB in the training set. (C, D) ROC for

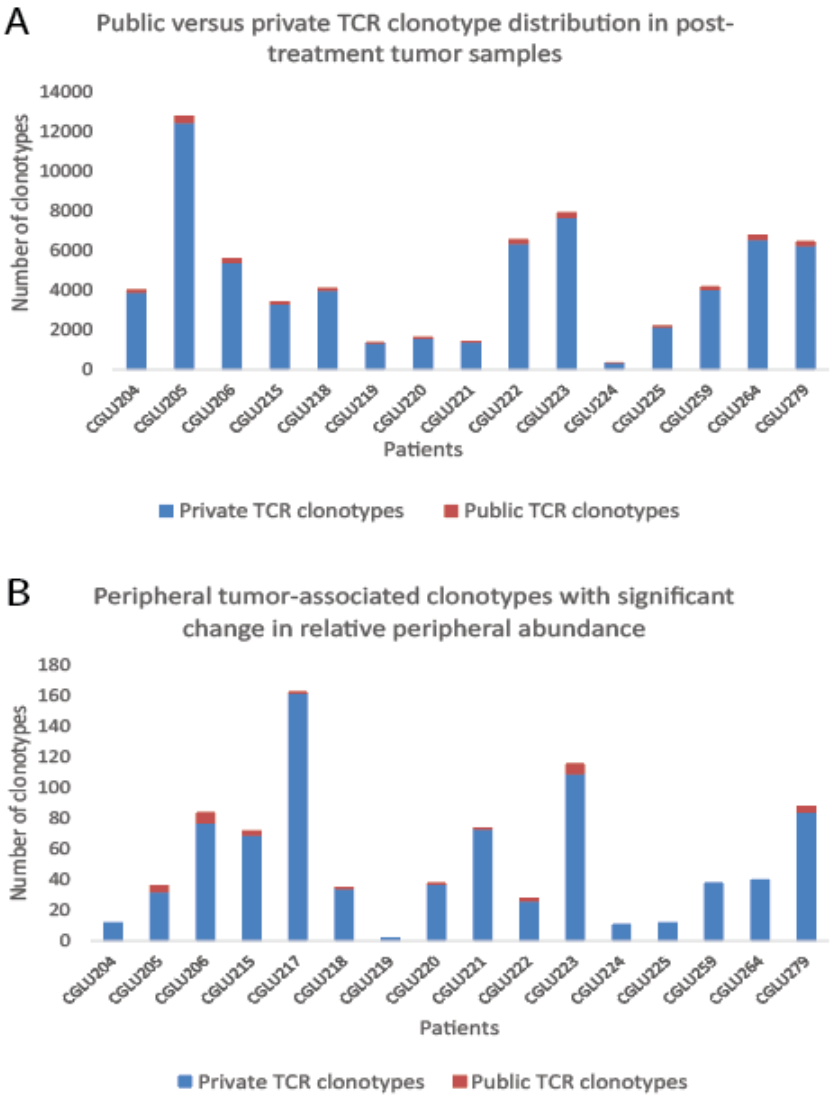
predicting durable clinical benefit using (C) PD-L1 and (D) TMB in the unseen testing set. (E) XGBoost embedded feature selection revealed important features for predicting durable clinical benefit, which were consistent with a separate SHAPley feature importance analysis shown in Figure 1.
Abbreviations: AUC: Area under receiver operator curve, NLR: Neutrophil-lymphocyte ratio, NSCLC: Non-small cell lung cancer, TMB: Tumor mutation burden, XGBoost; eXtreme gradient boosting



Supplemental figure S2: Study schema for early stage NSCLC cohort. Sample collection schema for the 26 patients with early stage NSCLC treated with neoadjuvant immunotherapy followed by definitive resection.
Abbreviations: NSCLC: Non-small cell lung cancer, ctDNA; circulating tumor DNA



Supplemental figure S3: Differential gene expression analysis in pre- and post-immunotherapy tumor samples from patients with and without NLR decrease. (A, B) Volcano plots presenting -$\log_{10}$(pvalue) vs. $\log_2$FC of differential gene expression analysis between tumors from patients with a peripheral blood NLR decrease versus no NLR decrease in (A) pre-immunotherapy and (B) post-immunotherapy tumor samples. The effect size is defined as $\log_2$FC, where FC is the fold change obtained by differential testing of gene expression in post- vs pre-ICI tumors. $\text{Log}_2\text{FC} > 0$ (right side of each graph) indicates increased expression in patients with a decrease in NLR, while $\log_2\text{FC} < 0$ (left side of graph) indicates increased expression in patients without an NLR decrease. Each dot represents a single gene, differential expression of genes shown in grey indicates $p \geq 0.05$, and differential expression of genes shown in blue indicates $p < 0.05$. Green dots indicate an absolute value of log2(FC) > 2. Genes in red have both $p < 0.05$ and $|\log2(FC)| > 2$. Abbreviations: ICI; Immune checkpoint inhibition, NLR; Neutrophil-lymphocyte ratio, Log2FC; standard error of the log2FoldChange estimate, NS; non-significant



Supplemental figure S4: Distribution of private and public intratumoral TCR clones among patients that received immune checkpoint blockade in the neoadjuvant setting. (A) The number of private (only identified in a single patient, shown in blue) and public (identified in more than one patient, shown in red) T-cell receptor clonotypes found in the post-treatment tumor sample from patients in the early stage NSCLC cohort. The majority of clonotypes found in each patient's tumor are private. (B) Focusing on peripheral blood clonotypes with significant changes in relative abundance (FDR < 0.05) that were also identified in matched tumor samples, we show the fraction of public versus private clonotypes from each patient. The vast majority of peripheral tumor-associated clonotypes with significant change in their relative abundance during immune checkpoint blockade were private (only identified in a single patient).