SUPPLEMENTAL FIGURES

Clinical benefit from immunotherapy in patients with small cell lung cancer is associated with tumor capacity for antigen presentation

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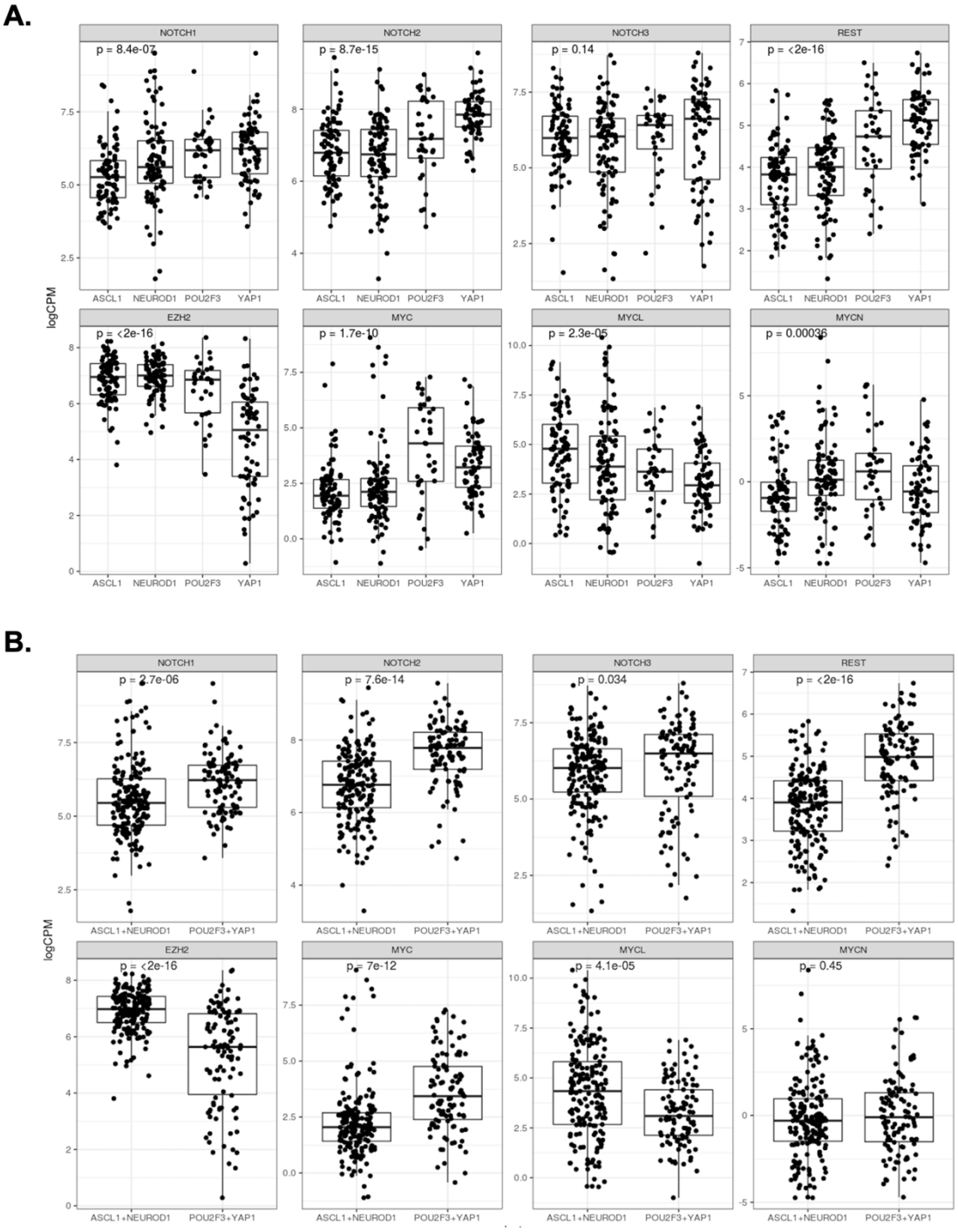
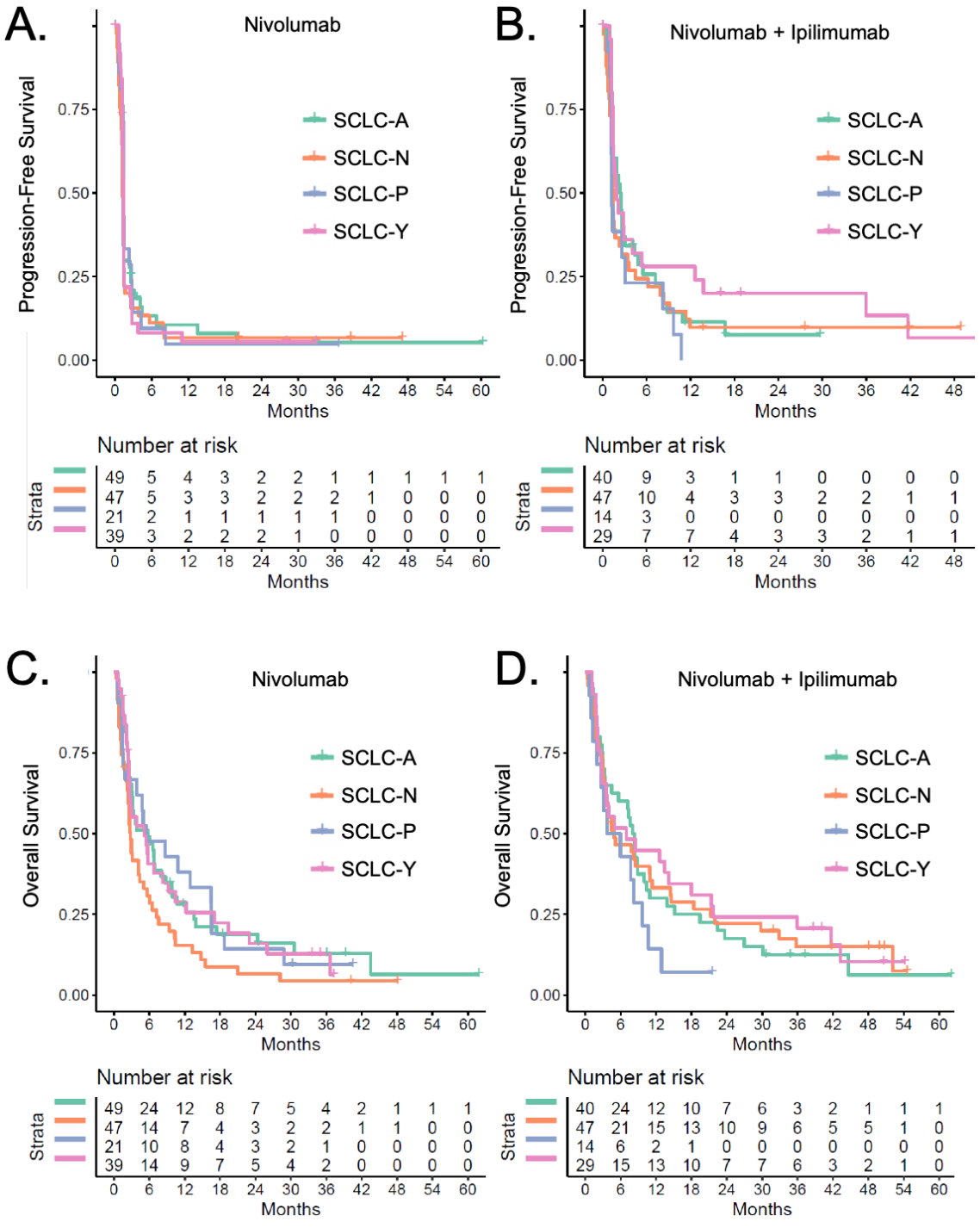
Supplemental Figure S1



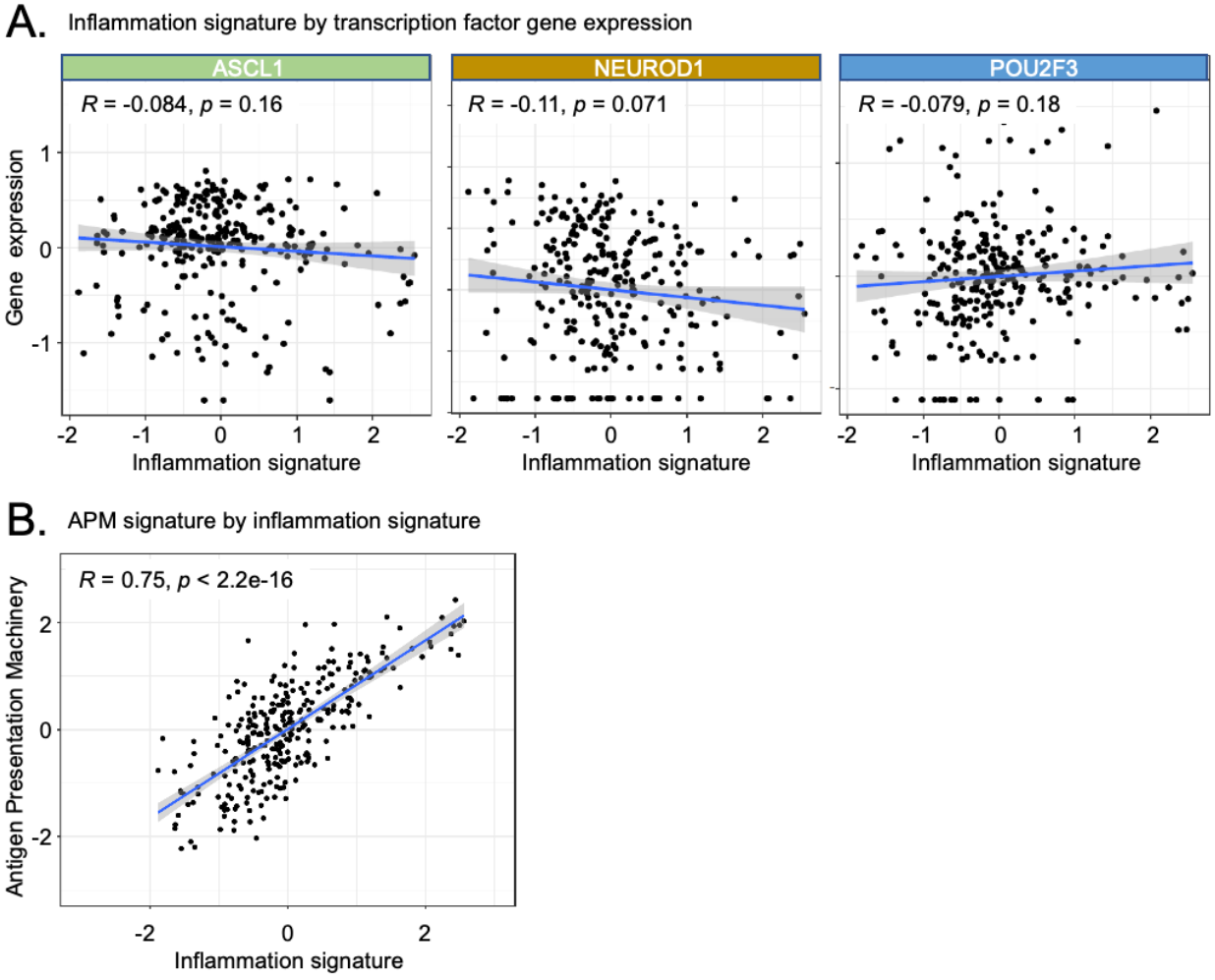
Supplemental Figure S1. Differential expression of factors implicated in neuroendocrine-high vs. -low SCLC. Log scale relative gene expression for NOTCH and MYC family members, REST, and EZH2 are shown (**A.**) by subtype or (**B.**) clustered neuroendocrine-high (ASCL1 + NEUROD1) vs. -low (POU2F2+YAP1). CPM = counts per million.

Supplemental Figure S2



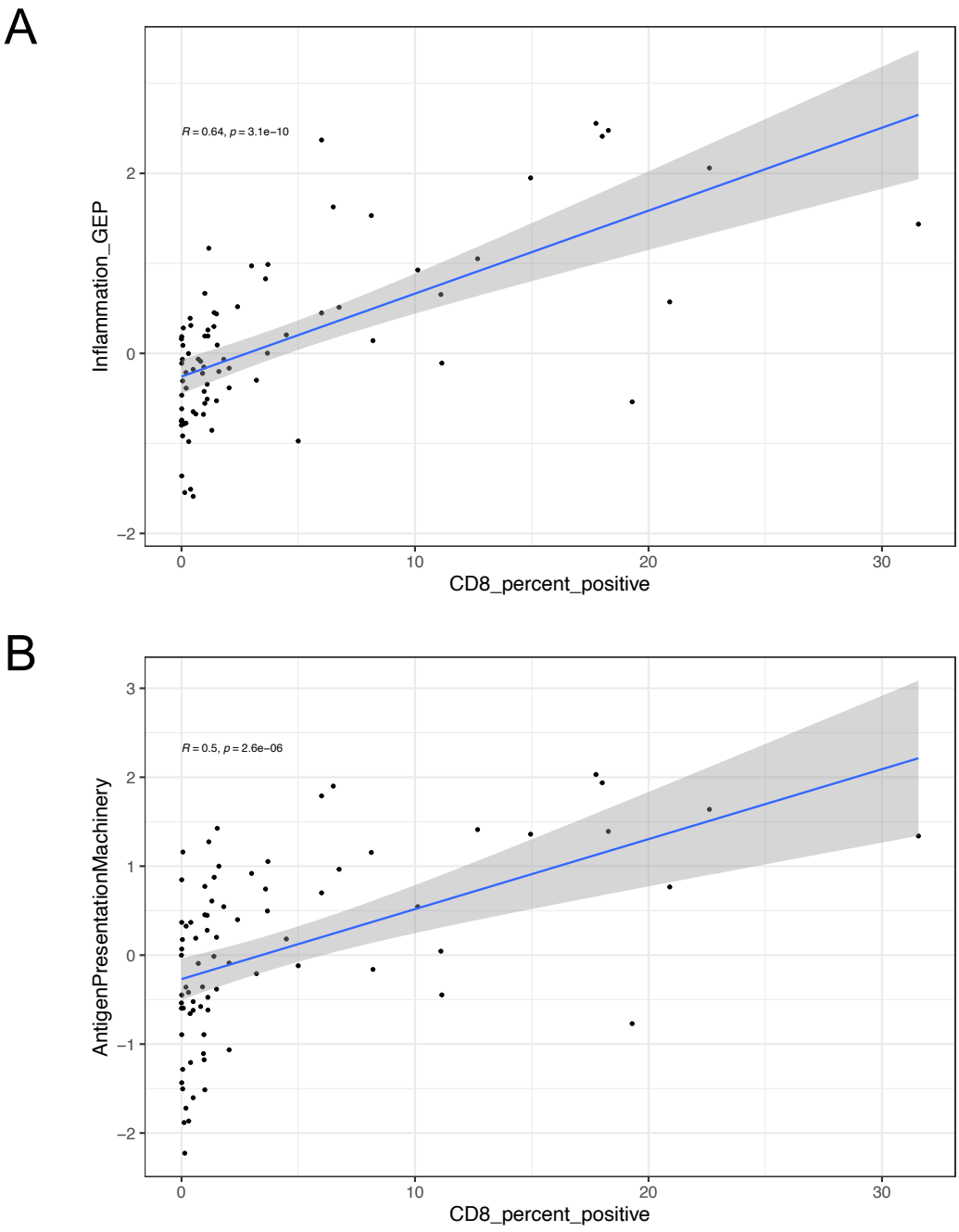
Supplemental Figure S2. Assessment of clinical outcome by subtype. Kaplan-Meier curves of progression-free (**A, B**) and overall (**C, D**) survival among all 286 SCLC patients enrolled on CheckMate 032 whose tumors were assessed by RNASeq. Outcomes are shown by study arm: nivolumab only (**A, C**) and nivolumab plus ipilimumab (**B, D**). No statistically significant differential outcome is seen based on subtype assignment.

Supplemental Figure S3



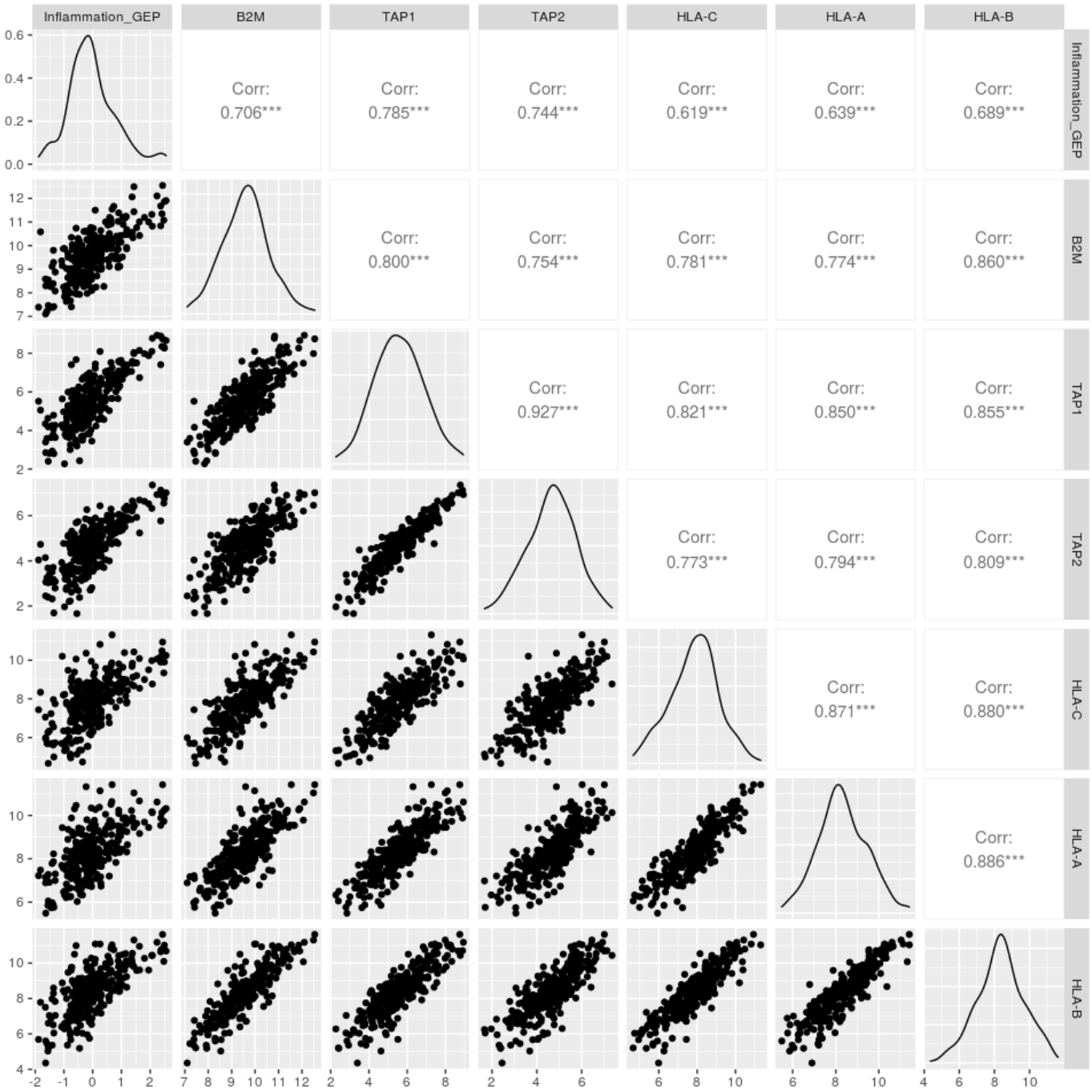
Supplemental Figure S3. Inflammation signature associations with expression of key transcription factors and antigen presentation machinery. A. Correlation between inflammation signature with gene expression of subtype-defining transcription factors ASCL1, NEUROD1, or POU2F3. None of these factors demonstrate a significant association with inflammation. Linear correlations are shown with shaded area reflecting 95% confidence intervals. **B.** Correlation between antigen presentation machinery gene signature and inflammation signature.

Supplemental Figure S4



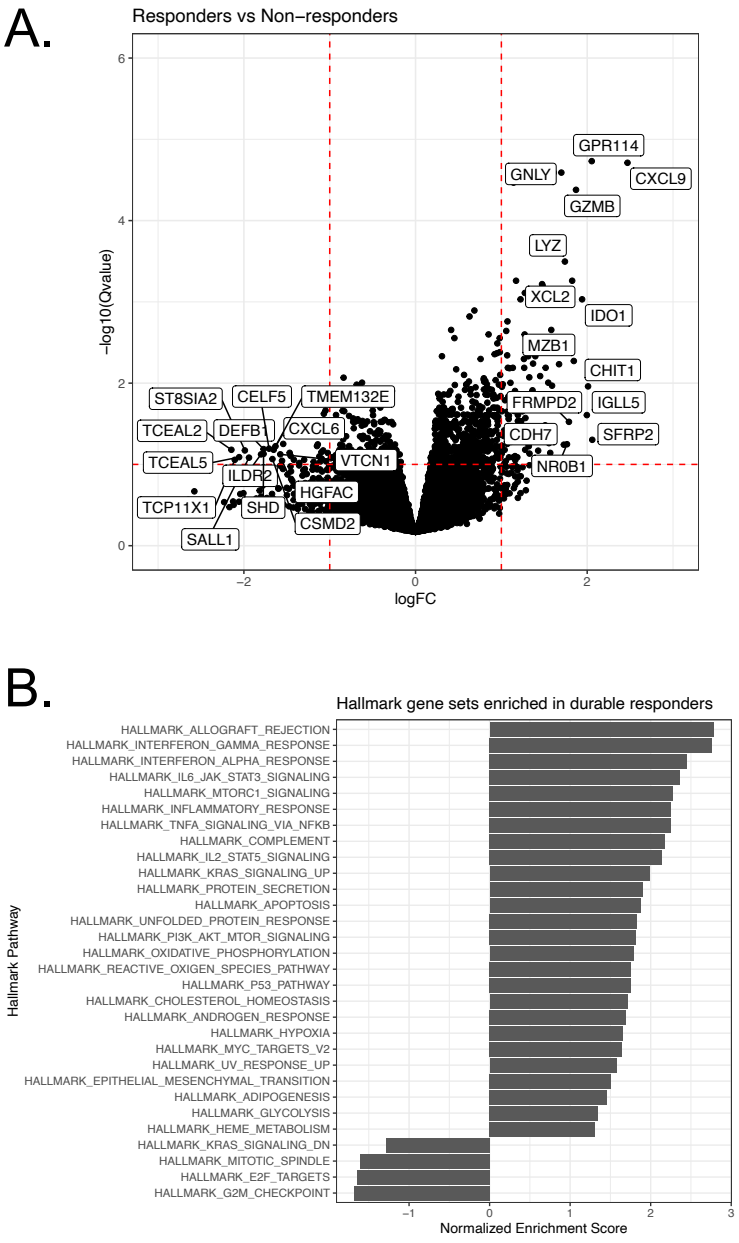
Supplemental Figure S4. Tumor CD8 infiltration as a correlate of inflammation and antigen presentation. A. Correlation between tumor CD8 percent positivity by immunohistochemistry and inflammation gene signature. **B.** Correlation between CD8 percent positivity and antigen presentation machinery gene signature.

Supplemental Figure S5



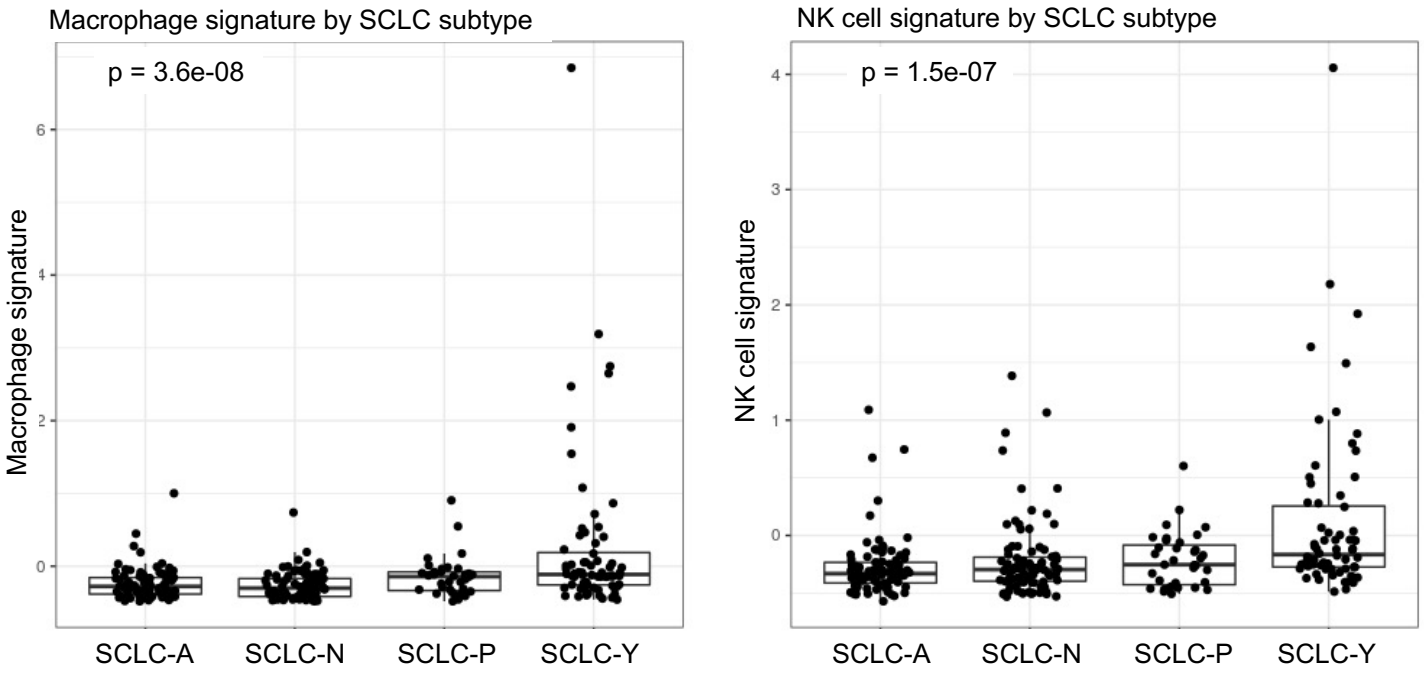
Supplemental Figure S5. Correlation among genes comprising the antigen presentation signature. Pairwise correlations of gene expression of HLA-A, HLA-B, HLA-C, B2M, TAP1, and TAP2 are shown in the boxes to the lower left, together with correlation of each individual gene with the Inflammation gene expression profile. Boxes at upper right indicate strength of correlation.

Supplemental Figure S6



Supplemental Figure S6. Individual gene and Hallmark gene set associations with durable benefit. A. Volcano plot of gene expression associated with durable benefit from ICB, defined as progression-free survival of ≥ 6 months. Positive association with durable benefit on the X axis (log fold-change) is to the right of 0; negative association to the left. Y axis represents negative log of adjusted p value, with a significance threshold set at 1.0. **B.** Hallmark gene sets associated with durable benefit. Gene sets positively correlating with durable benefit are indicated by bars to the right of 0; gene sets negatively correlating are to the left. Bar length reflects strength of association.

Supplemental Figure S7



Supplemental Figure S7. Enrichment of macrophage and NK cell signatures in SCLC-Y. Gene expression signatures reflective of macrophage and NK cells are significantly enriched in tumors classified here as SCLC-Y.