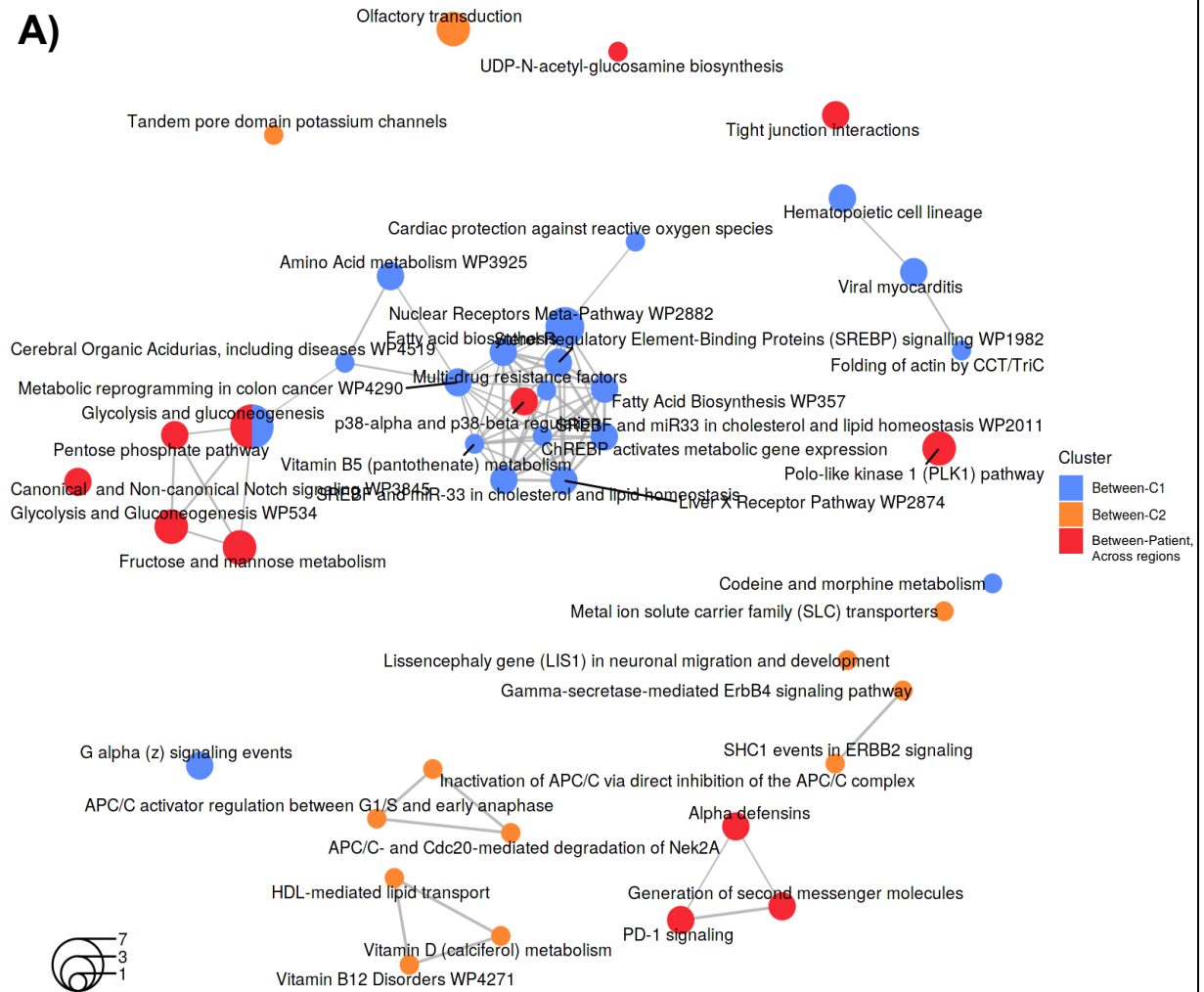
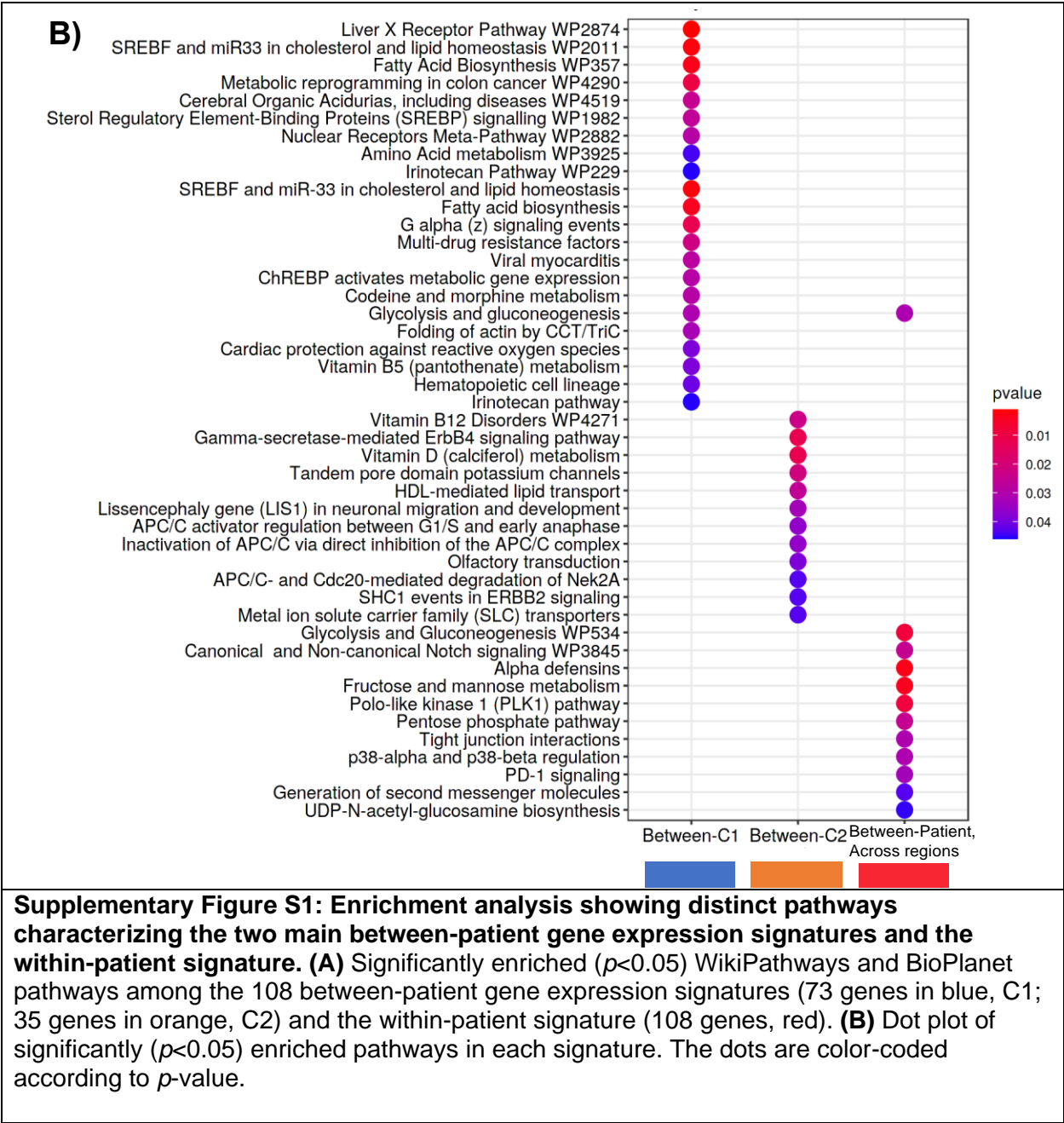
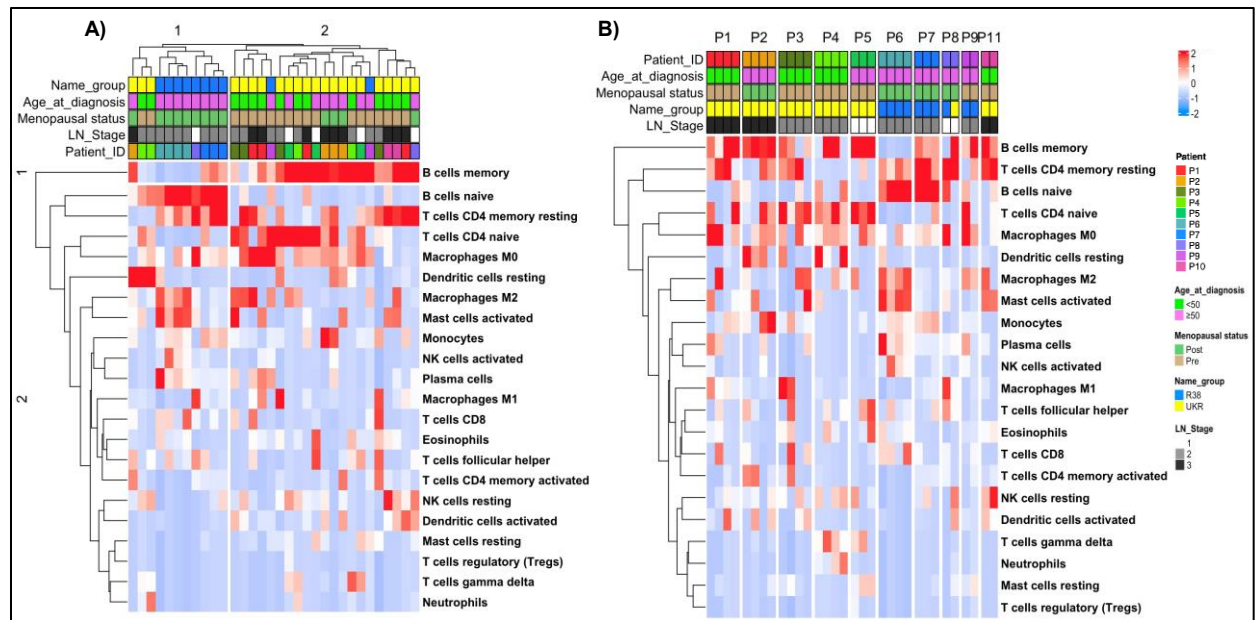


A)

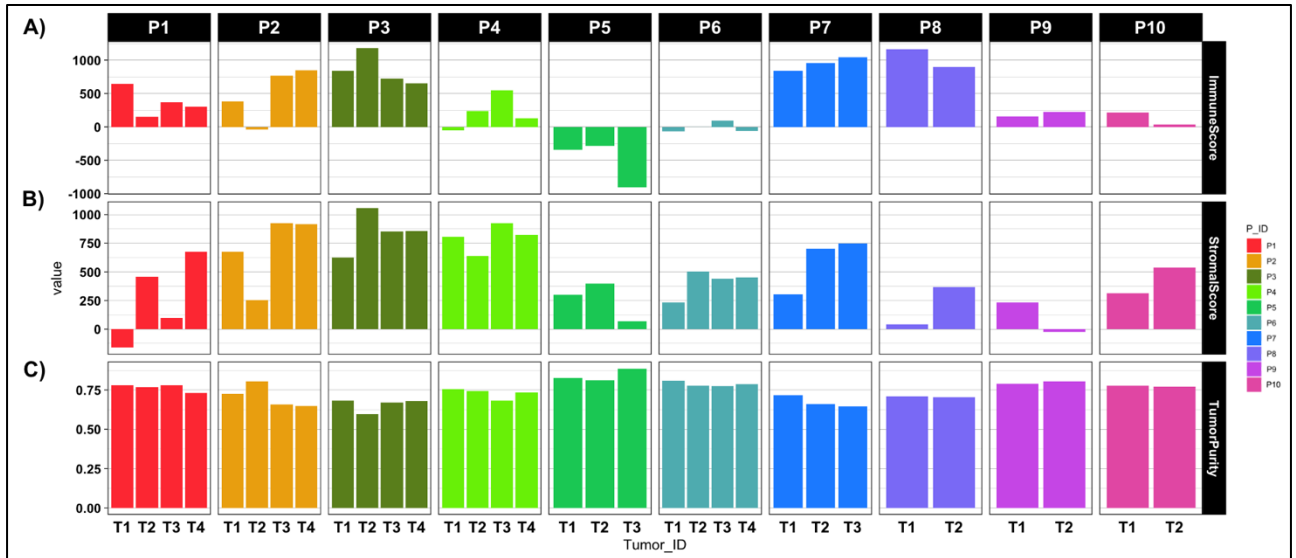




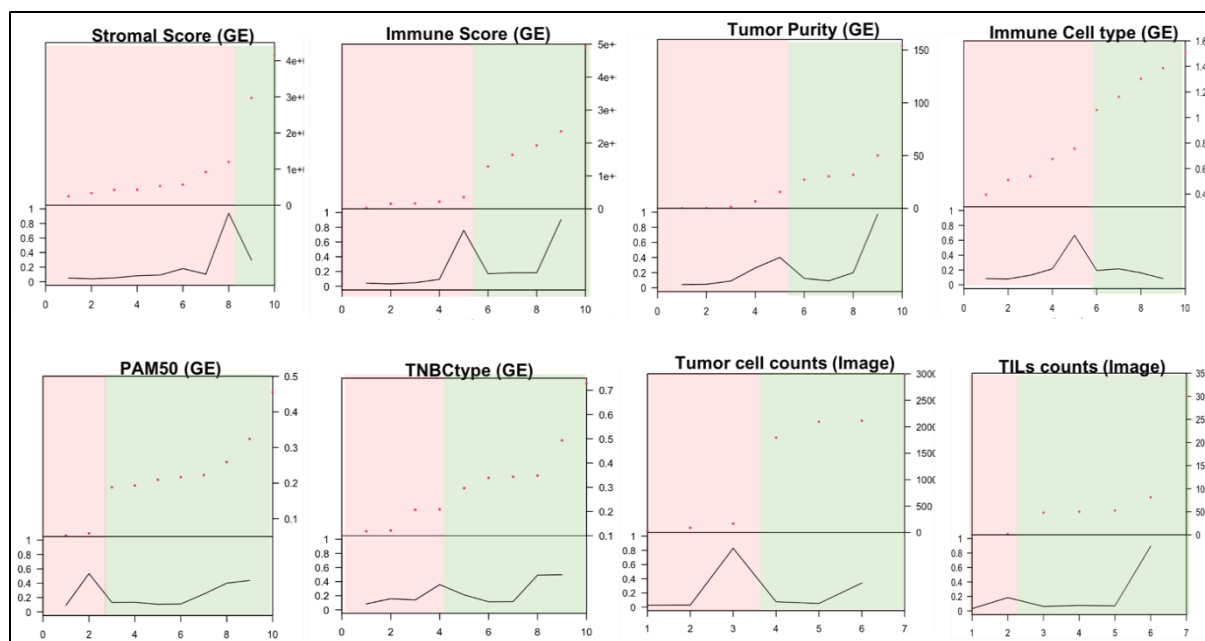
Supplementary Figure S1: Enrichment analysis showing distinct pathways characterizing the two main between-patient gene expression signatures and the within-patient signature. (A) Significantly enriched ($p < 0.05$) WikiPathways and BioPlanet pathways among the 108 between-patient gene expression signatures (73 genes in blue, C1; 35 genes in orange, C2) and the within-patient signature (108 genes, red). **(B)** Dot plot of significantly ($p < 0.05$) enriched pathways in each signature. The dots are color-coded according to p -value.



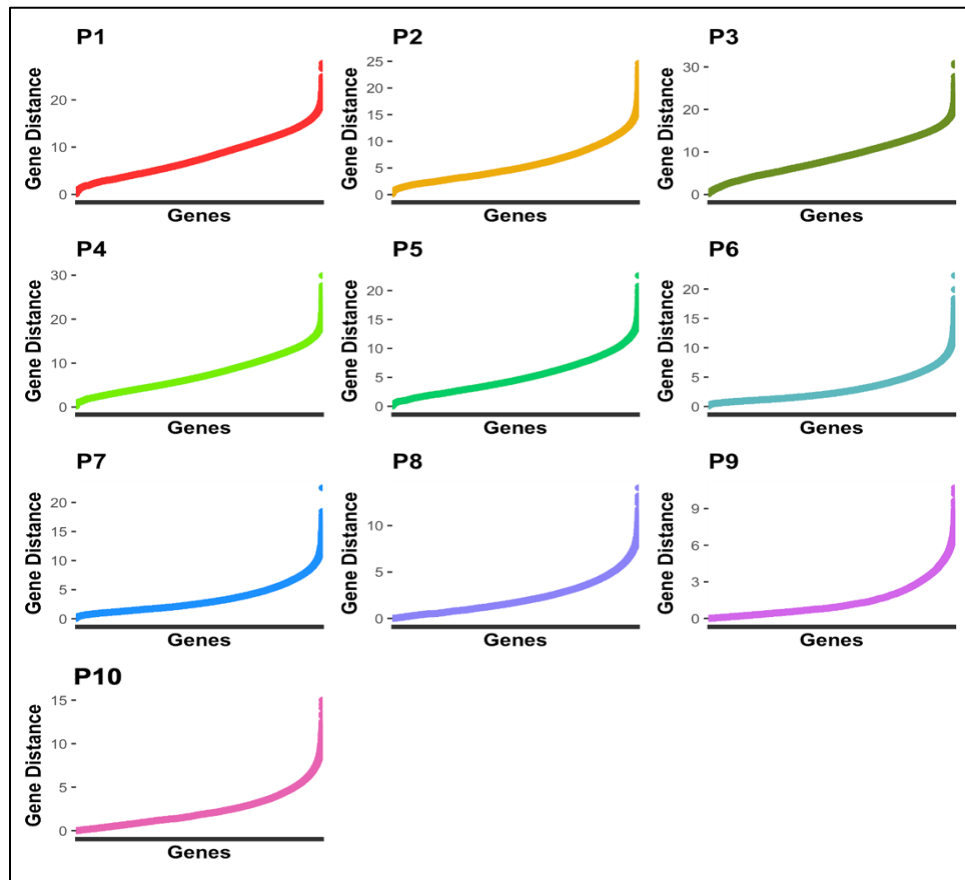
Supplementary Figure S2: Immune signatures differ among different regions of the same tumor. Heatmaps of gene expression-derived abundance scores (column scaled, complete linkage with Euclidean distance) for 22 immune cell types, with patient-level molecular and tumor characteristics highlighted. **(A)** Unsupervised clustering resulted in two sample clusters (denoted by 1 and 2). **(B)** Sample-supervised, patient-ordered clustering.



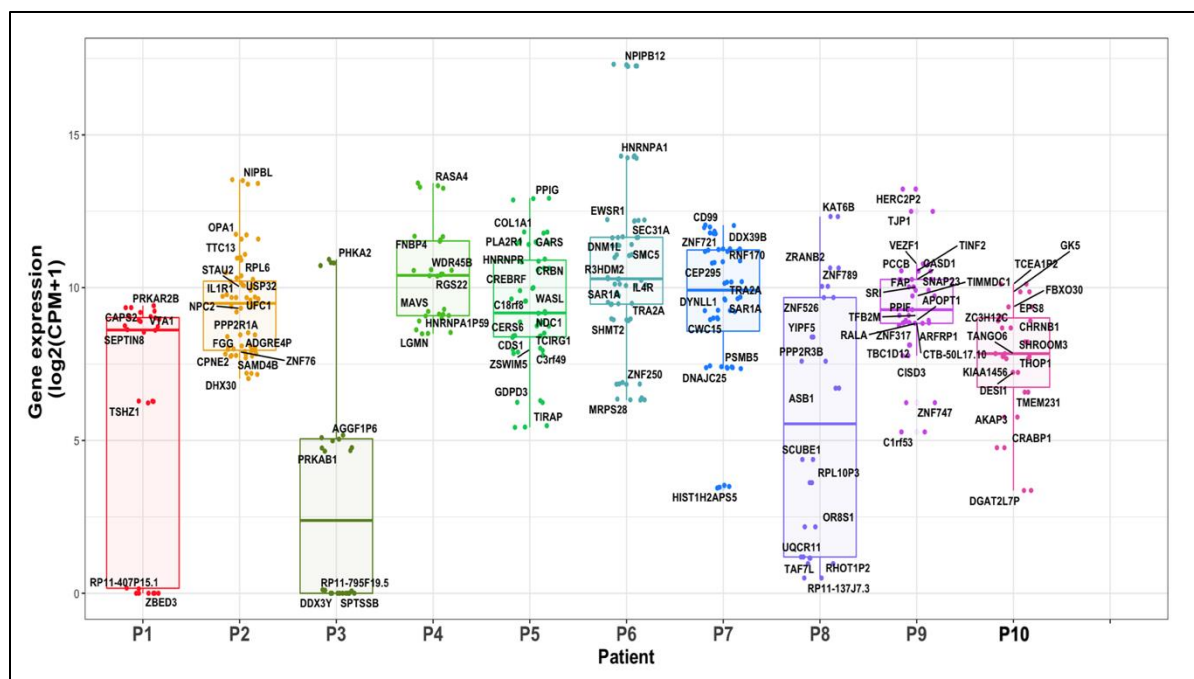
Supplementary Figure S3: Regional intratumoral heterogeneity in gene expression-derived immune, stromal, and tumor purity scores. Bar charts showing predicted gene expression-derived immune (A), stromal (B) and tumor purity (C) scores.



Supplementary Figure S4: Divergence analysis for regional variation in gene expression-derived and imaging-derived features. Plots of posterior means (above horizontal line) and posterior probabilities (below horizontal line) from Bayesian changepoint analysis applied to pairwise (among regions, within patients) Euclidean distances for each feature. Each red dot represents a patient. Patients to the right of the identified changepoint are categorized as divergent (green), and to the left, as convergent (pink).



Supplementary Figure S5: Distributions of regional intratumoral heterogeneity in gene expression. Scatter plots of ordered individual gene-level expression differences based on pairwise (among regions) Euclidean distance (denoted by gene distance) for each patient.



Supplementary Figure S6: The distribution of intratumoral region heterogeneity low variability gene signatures by patient. The boxplots shows that low-variability gene signatures are mostly expressed among all regions in each patient, only with the exception of a few non-coding genes (e.g., RP11) in certain patients (P1, P2, P8).