Supplementary Tables and Figures

PDAC Lymph node (Figure 2):

Pattern ⟶	1	2	3	4	5	6	7	8	9	10
sigmaOpt	13.2	5	5.8	10.6	9.2	4.4	10.6	9.6	4.2	10
threshOpt	1	1	1.1	1	1	1	1.1	1.1	1	1.2

PanIN (Figure 3):

Pattern ⟶	1	2	3	4	5	6	7	8	9	10
sigmaOpt	5	4.6	5	4.8	3	8.8	4.6	5	3.6	7
threshOpt	1.6	1	1.3	1.4	1.6	1.1	1.4	1.2	1	1.3

Breast cancer with low-res CoGAPS (Figure 4):

Pattern ⟶	1	2	3	4	5
sigmaOpt	4.2	4.8	3.8	4.4	4
threshOpt	2.1	1.3	1.6	1.5	2.2

Breast cancer with high-res CoGAPS (Figure 5):

Pattern ⟶	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
sigmaOpt	4.2	4.2	4.6	7.4	5	7.6	5	6.4	4.6	5.2	4	7.8	4.6	4.6	4	4.4
threshOpt	1	2.3	2.6	2.4	1.7	1.5	3	2.8	1	1.2	2.6	1.2	2.9	2.8	1.4	2

Breast Cancer with STdeconvolve (Figure S4):

Pattern →	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
sigmaOpt	4.2	4.8	5	4.8	4.6	3.8	4.4	4.6	6.4	4.2	6.4	5	5.8	4.4	3.6	5.2	5.2	4.2	4.2	4.6
threshOpt	2.7	2.1	2.1	2.4	1.8	1.9	1.3	2.8	2.2	2.7	1.5	1.4	1.2	2.3	1.9	2.1	2.3	1.3	2.5	1.2

HCC (Figure 6):

Pattern ⟶	1	2	3	4	5	6	7	8	9
sigmaOpt	15.4	9	8.2	24.4	25.2	23.6	15.8	9.2	20.6
threshOpt	1.5	1.3	1.3	1.5	1.3	1.1	1.3	1	1.2

Table S1. SpaceMarkers optParam values for spatial patterns related to Figures 2 to 6.

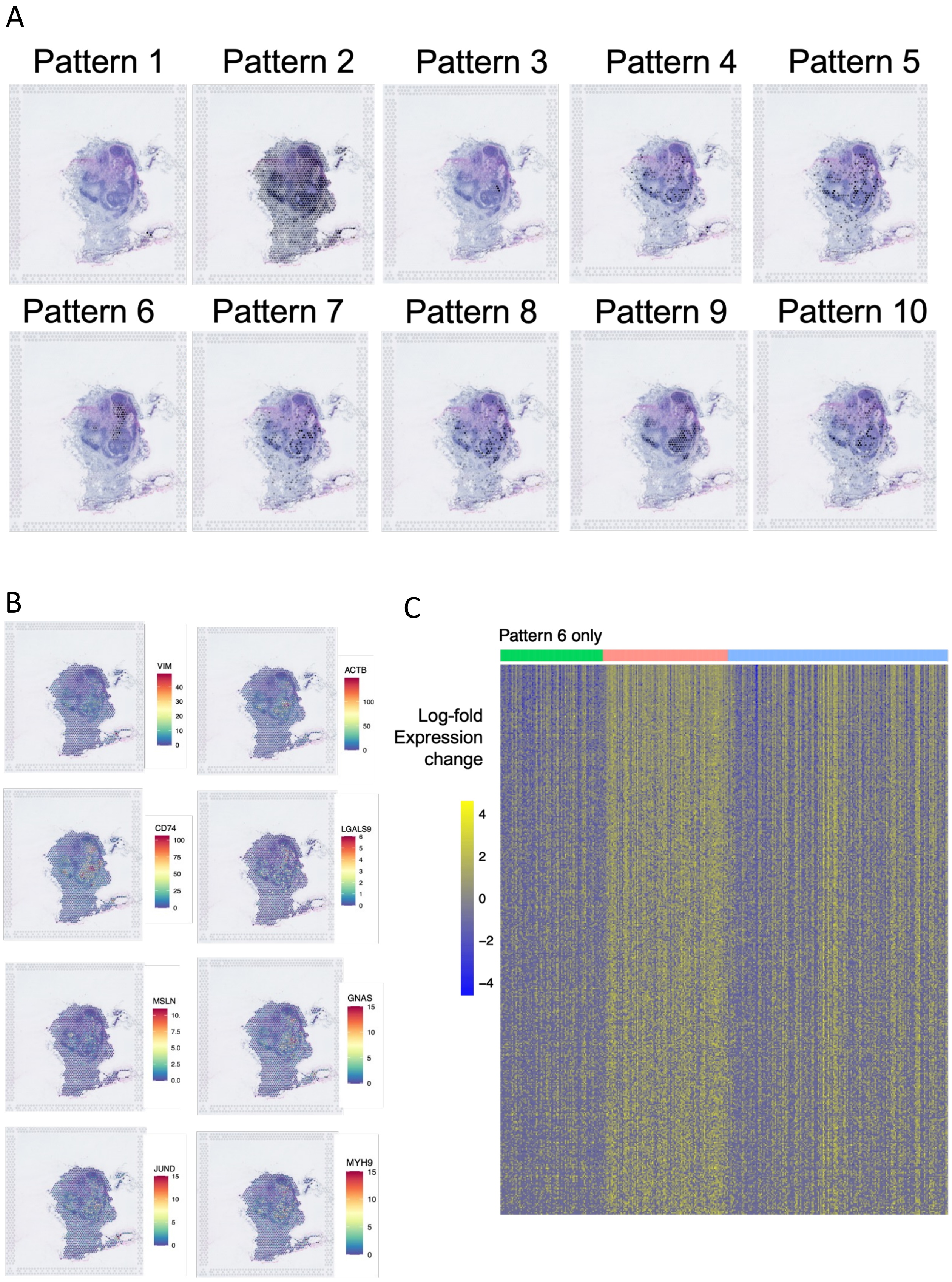

Figure S1. continued on the next page.

Figure S1. (continued) Analysis of lymph node tissue with metastatic PDAC (Related to Figure 2).
A. Intensity maps of CoGAPS patterns identified in the lymph tissue. Pattern 6 shows high activity levels in the region annotated as metastatic PDAC and Pattern 9 shows high activity levels in the region associated with the surrounding immune cells.

B. Spatial expression profile of the genes with expression box plots in Figure 2C. shows higher expression on the interface of the metastatic PDAC and immune cells.

C. Expression heatmap of top 500 genes identified as SpaceMarkers in the regions with Pattern 6 and Pattern 9 interacting compared to regions with exclusive influence from Pattern 6 and Pattern 9 respectively. Complete gene list provided in Table S2.

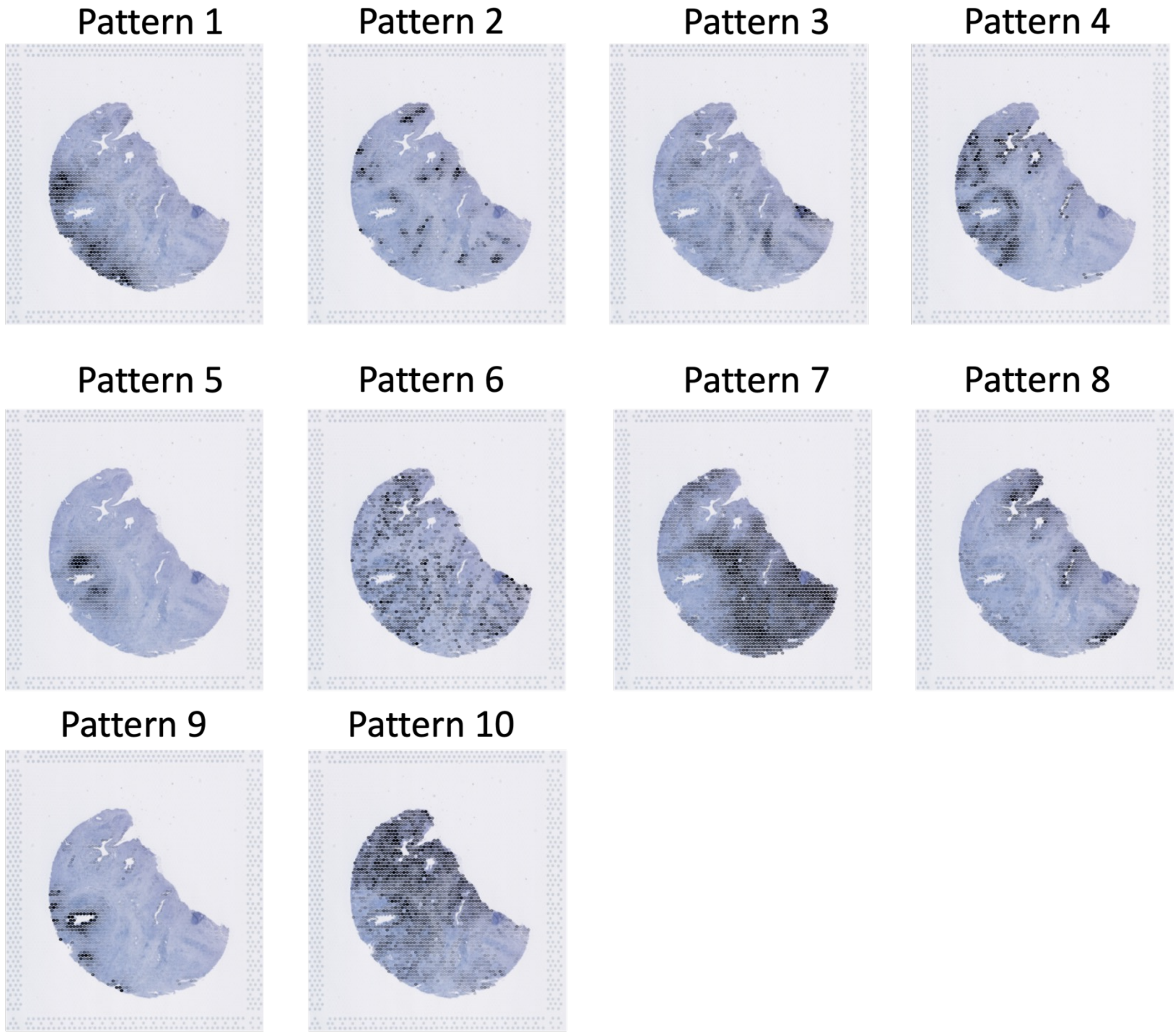

Figure S2. continued on the next page.

Figure S2. (continued) Analysis of PanIN tissue (Related to Figure 3).
Intensity maps of CoGAPS patterns identified in the PanIn tissue. Pattern 6 shows high activity levels in the region annotated as stroma, Pattern 9 shows high activity levels in the region associated with neoplasia, and Pattern 5 showsn high activity levels in the regions with acinar cells.

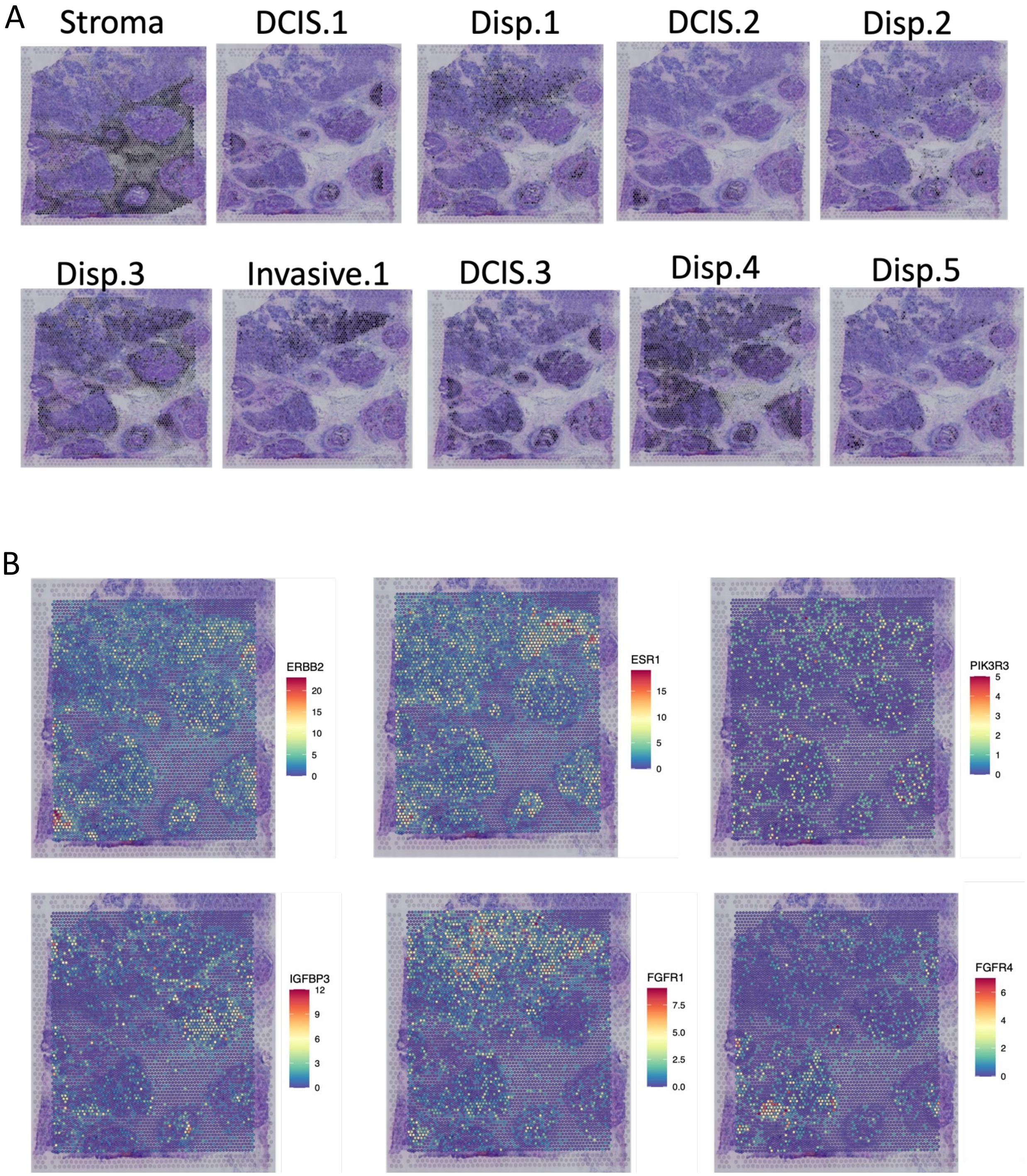

Figure S3. continued on the next page.

Figure S3. (continued) Analysis of high dimensional CoGAPS factorization of the breast cancer tissue (Related to Figure 5).

A. Spatial intensity plots of CoGAPS patterns not shown in Figure 5.

B. Spatial expression heatmap of select genes demonstrating the heterogeneity in the tissue sample. Whereas *ERBB2*, *ESR1* and *PIK3R3* are universally associated with all DCIS and Invasive lesions, *FGFR1* (Invasive.2), *IGFBP3* (DCIS.5) and *FGFR4* (DCIS.6) are associated with patterns associated with specific lesions.

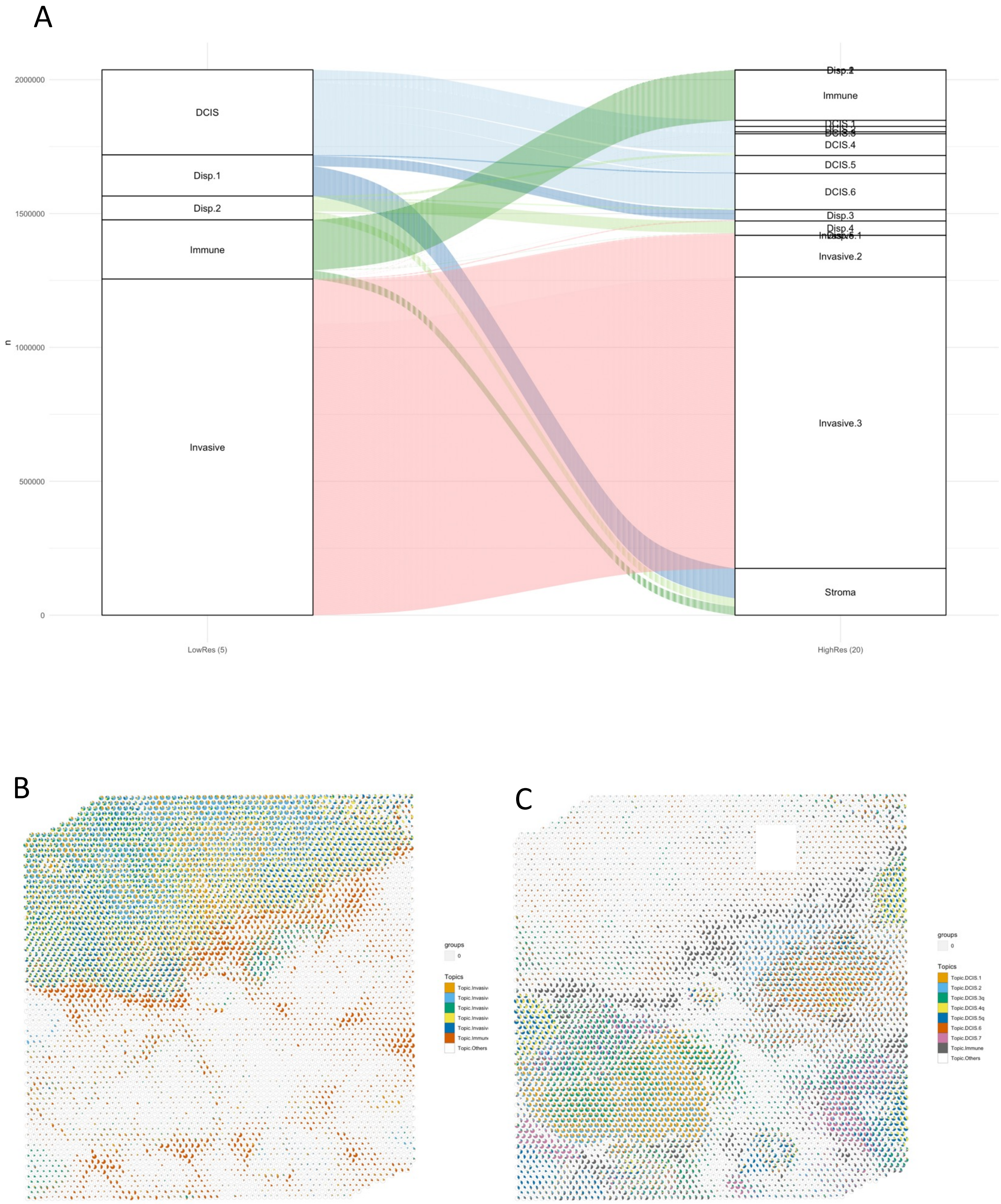

Figure S4. continued on the next page.

Figure S4. (continued) Additional analysis related to the breast cancer sample (Related to Figure 5).
A. Alluvial plot showing the most dominant pattern associated with each spot using low-resolution and all 16 high-resolution CoGAPS respectively.

B. Scatterpie plot showing cell populations in the invasive carcinoma region and immune cells identified using STdeconvolve.(see Supplementary File 4B for the associated SpaceMarkers output)

C. Scatterpie plot showing cell populations in the DCIS lesions and immune cells identified using STdeconvolve. (see Supplementary File 4B for the associated SpaceMarkers output)

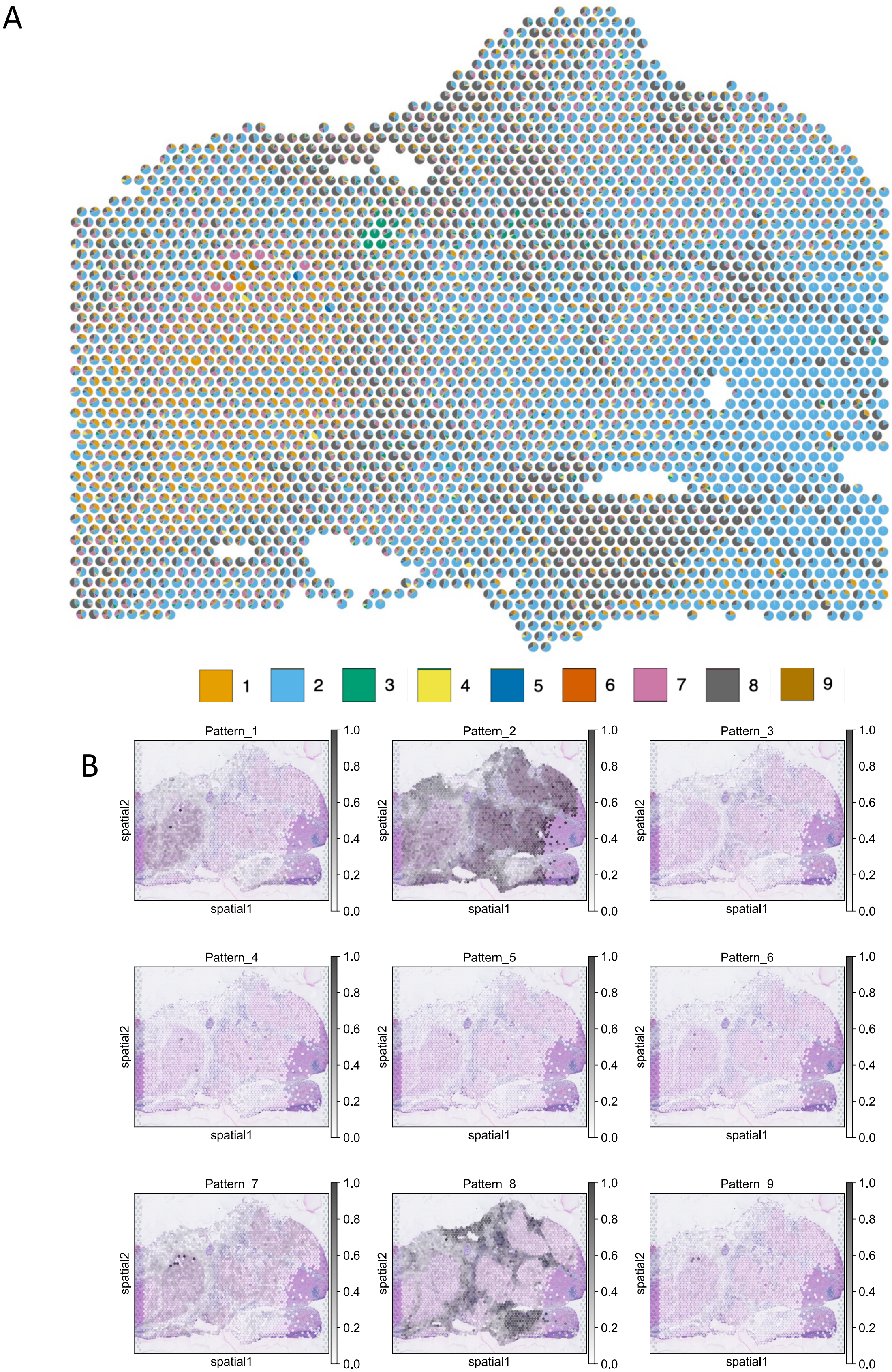

Figure S5. continued on the next page.

Figure S5. (continued) (CoGAPS learned spatial patterns from HCC tumor sample. Related to Figure 6) .
A. Scatterpie visualization showing the relative activity levels of all 9 patterns in each spot shows Patterns 1, 2, and 8 being the dominant patterns in the tissue.

B. Spatial intensity plots of individual patterns normalized to sum to 1 in each spot also shows that Pattern 1, 2, and 8 explain most of the gene signature in the tissue.

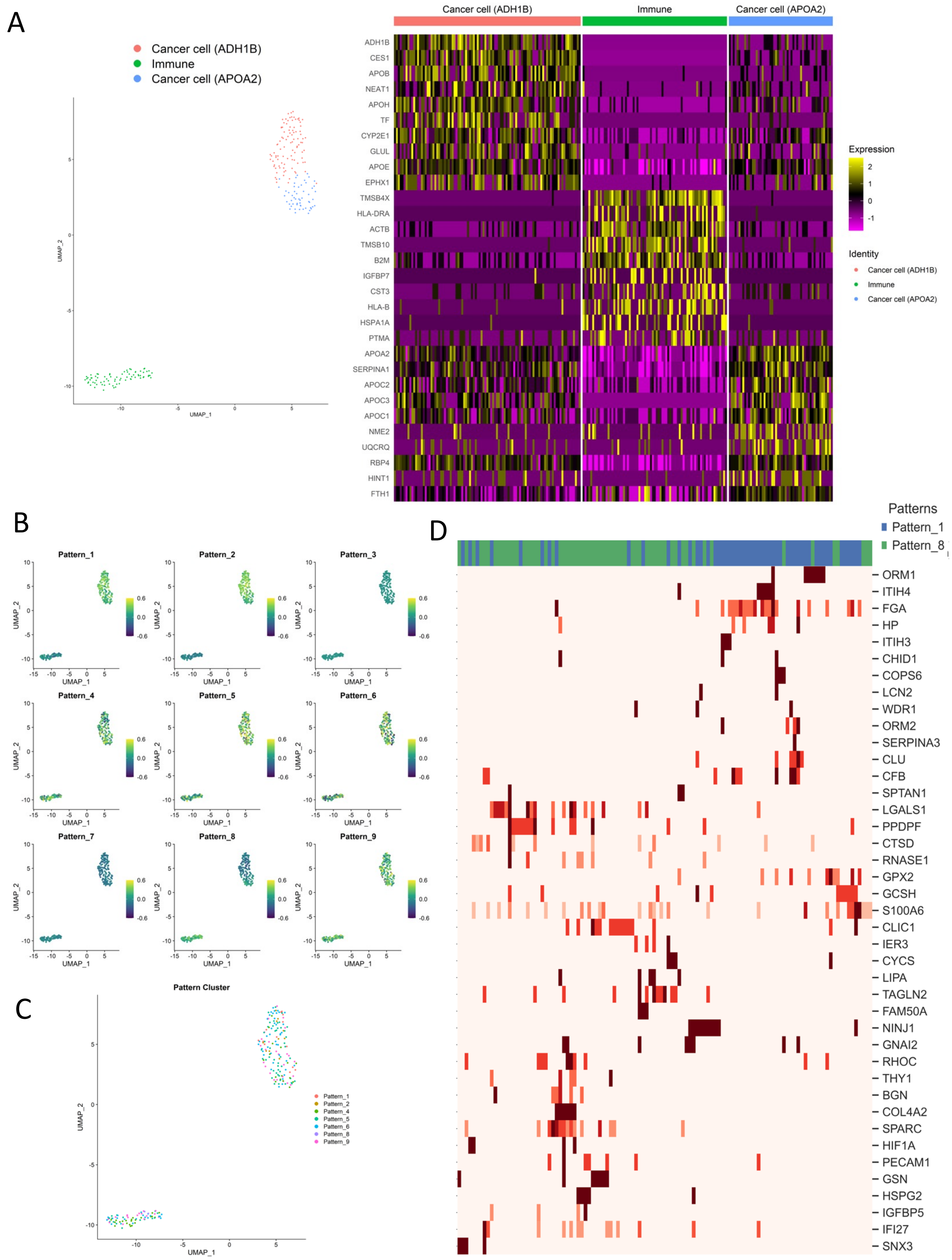

Figure S6. continued on the next page.

Figure S6. (continued) Analysis of SpaceMarkers in matched scRNAseq data (Related to Figure 6).

A. Unsupervised clustering of the scRNAseq data, using Seurat, reveals two distinct tumor cell clusters and an immune cell cluster. Expression heatmap of select cancer and immune markers shows heterogeneity in the sample.

B. UMAP plots showing projections of the spatial patterns learned in Figure S5 onto the scRNAseq data using ProjectR transfer learning.

C. Each cell in the scRNAseq data is associated with the pattern with the highest projection in the cell as seen in panel B. However, since Patterns 1, 2, and 8 are dominant in the matched ST data, we assign cells to those three patterns as shown in Figure 6A.

D. Expression heatmap of SpaceMarkers associated with interactions between Pattern 1 and Pattern 8 provide the spatial context of the individual cells.