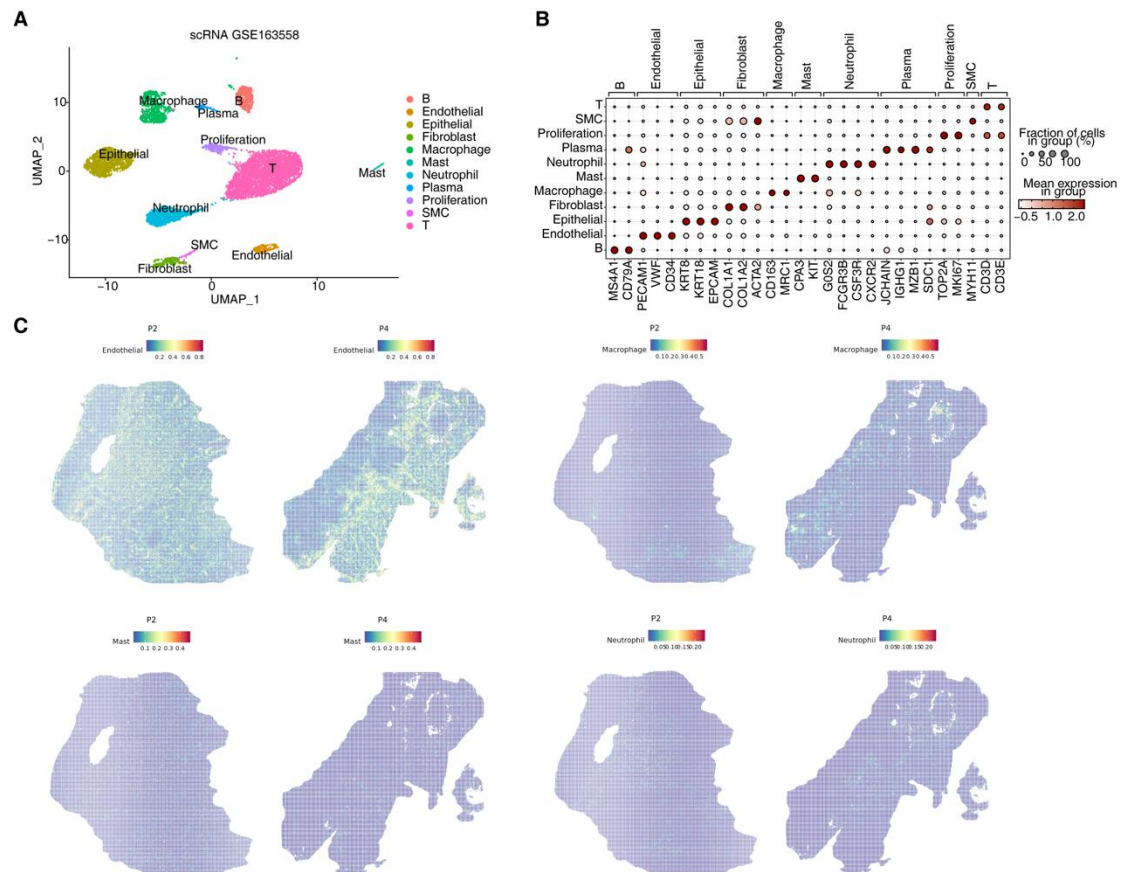
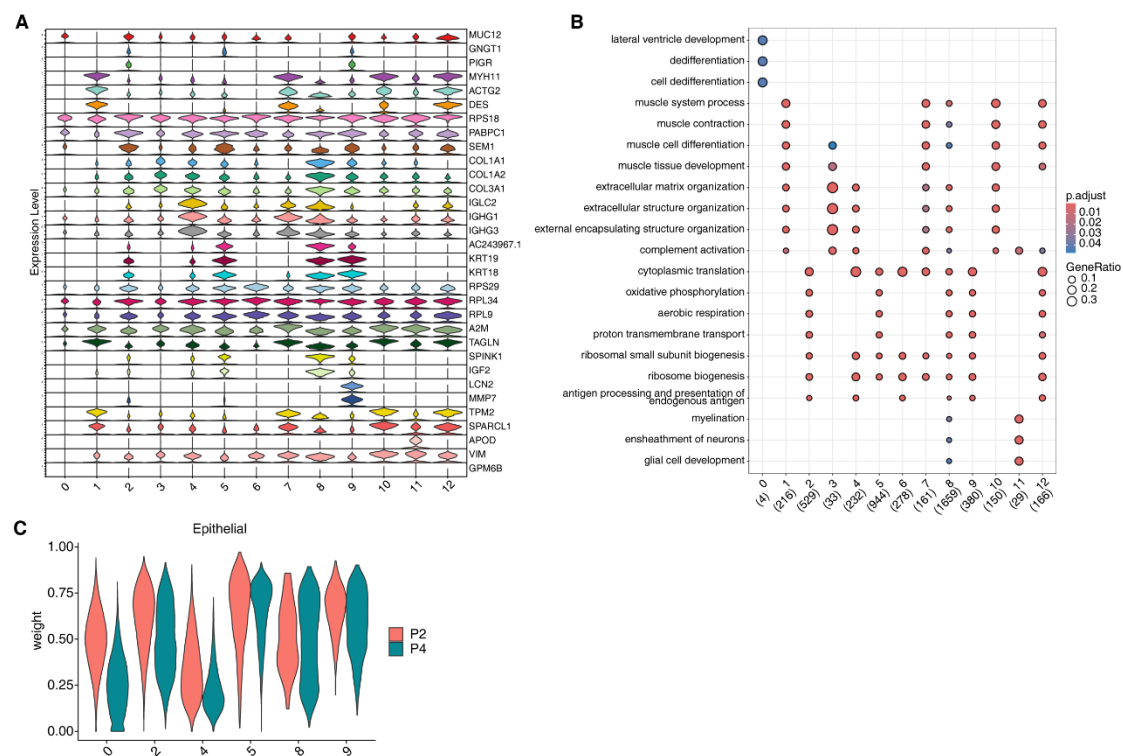
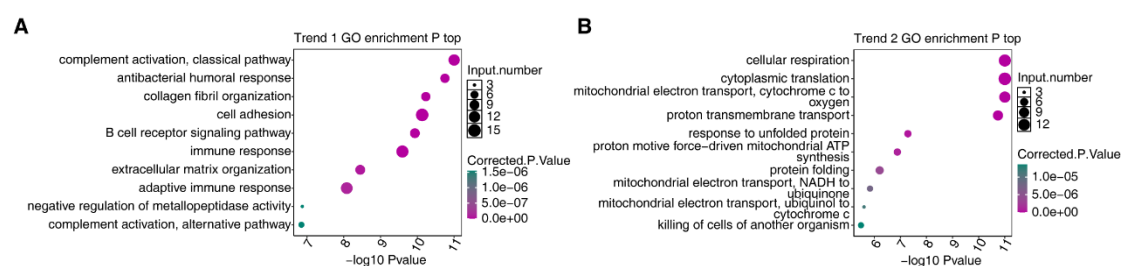




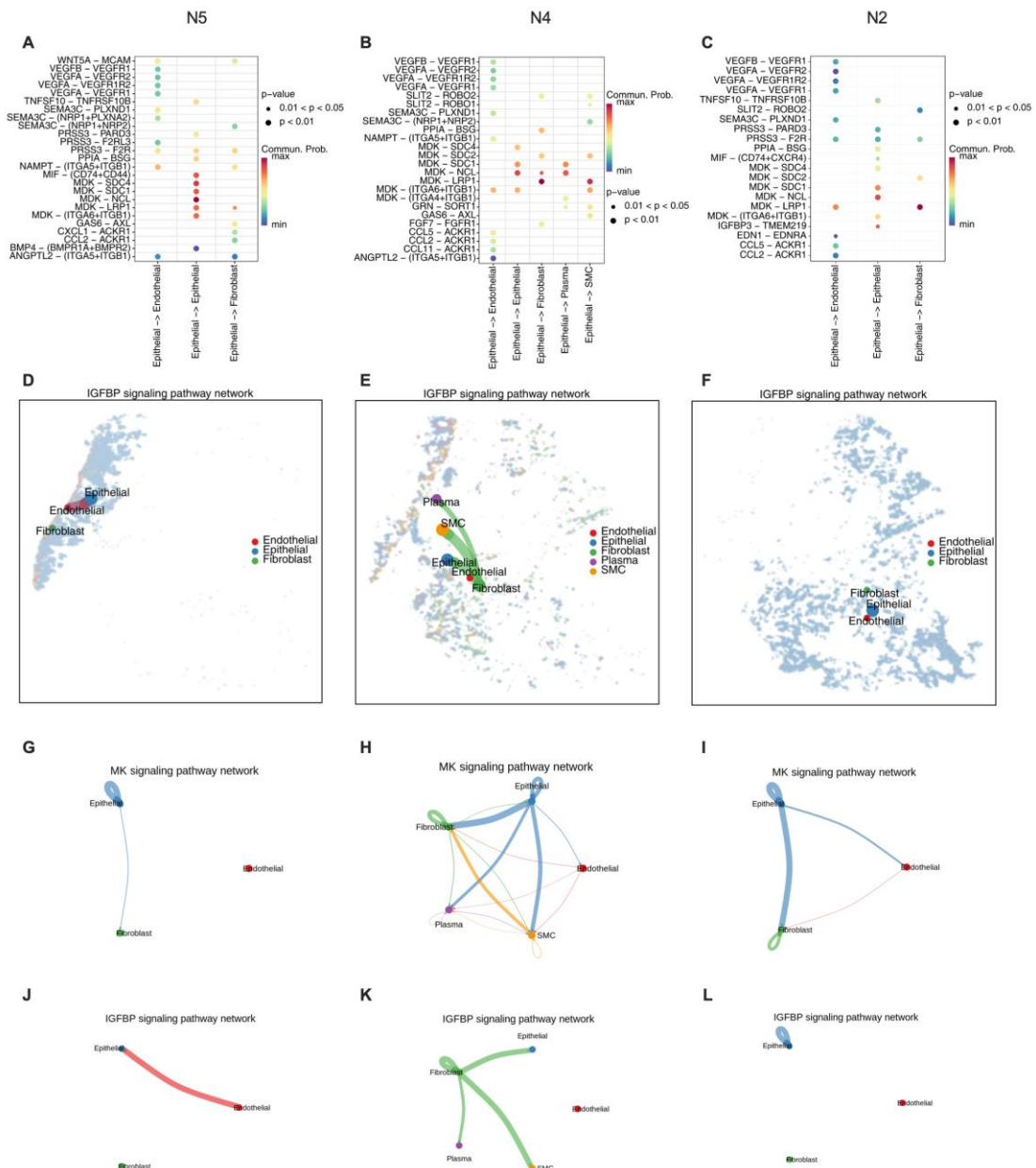
Supplementary Figure 1 Cellular composition and spatial architecture of advanced gastric cancer (related to Figure 1). A: UMAP visualization of reference scRNA-seq dataset (GSE163558), showing clustering and annotation of 10 major cell types: epithelial cells, fibroblasts, endothelial cells, T cells, B cells, plasma cells, macrophages, mast cells, neutrophils, and smooth muscle cells; B: Dot plot showing marker genes for each identified cell type. Dot size represents the percentage of cells expressing the gene within the cell type, and color intensity denotes average expression level; C: Spatial distribution of endothelial cells, macrophages, mast cells, and neutrophils in P2 and P4 tissue sections, with color scales representing the predicted cell type proportion per spot (range as shown).



Supplementary Figure 2 Identification and characterization of spatial niches via BANKSY algorithm (related to Figure 2). A: Violin plots showing expression levels of the top three marker genes for each niche (0–12); B: Bubble plot illustrating the most enriched Gene Ontology biological process terms for each niche. Dot size represents the gene ratio, and color indicates the adjusted P value; C: Violin plots showing epithelial cell weight scores for selected niches (0, 2, 4, 5, 8, 9) in P2 and P4 samples.

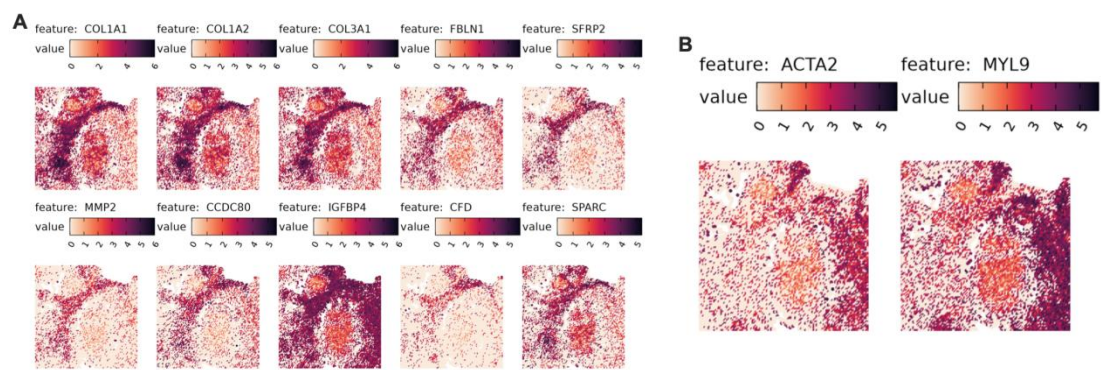


Supplementary Figure 3 Spatial functional profiling of distinct niches in advanced gastric cancer (related to Figure 3). A and B: Most enriched Gene Ontology biological process terms for Trend 1 and Trend 2. Dot size represents the number of input genes, and color indicates adjusted P value.

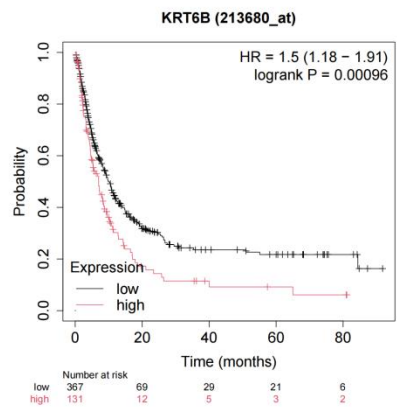


Supplementary Figure 4 Niche-specific intercellular communication in sample P2 (related to Figure 4). A-C: Bubble plots showing significant inferred ligand-receptor interactions in which tumor epithelial cells act as senders in N5, N4, and N2, respectively. Dot size indicates the significance level, and color indicates communication probability; D-F: Spatial interaction networks of the IGFBP signaling pathway in N5, N4, and N2, respectively. The background indicates the spatial distribution of major cell types within each niche; nodes denote cell types, and edges indicate inferred ligand-receptor interactions; G-I: Simplified network plots of the MK

signaling pathway in N5, N4, and N2, respectively, shown without spatial background;
 J-L: Simplified network plots of the IGFBP signaling pathway in N5, N4, and N2, respectively, shown without spatial background.



Supplementary Figure 5 Spatial expression patterns of fibroblast-associated markers surrounding N9 (related to Figure 5). A: Spatial expression heatmaps of the top 10 marker genes of fibroblasts surrounding N9 (*COL1A1*, *COL1A2*, *COL3A1*, *FBLN1*, *SFRP2*, *MMP2*, *CCDC80*, *IGFBP4*, *CFD*, and *SPARC*); B: Spatial heatmaps of *ACTA2* and *MYL9* showing relatively low expression in fibroblasts surrounding N9.



Supplementary Figure 6 Kaplan-Meier analysis of recurrence-free survival in patients stratified by KRT6B expression level.

Supplementary Table 1 Clinical and pathological features of spatial transcriptomic samples

Patient ID	Age	Sex	Tumor Location	pT Stage	pN Stage	Tumor Stage	Differentiation	Lauren Type
P2	68	M	Antrum	T3	N0	II A	Moderate to poor	Mixed
P4	56	F	Antrum	T3	N2	IIIA	Moderate	Intestinal

The tumor staging was determined according to the AJCC 8th edition staging system

Supplementary Table 2 Clinical and pathological features of the gastric cancer cohort used for immunohistochemistry validation

Patient ID	Age	Sex	Tumor Location	Tumor Stage	Differentiation	Lauren Type	KRT6B IHC Score (Tumor)	KRT6B IHC Score (Adjacent Normal)
Z001	59	F	Proximal	IIIA	Moderately to poorly	Mixed	300	210
Z002	71	M	Distal	IV	Moderately to poorly	Mixed	300	220
H004	77	M	Distal	IIIA	Moderately to well	Intestinal	170	260
H006	51	F	Distal	IIIA	Poorly	Diffuse	300	280
Z007	55	F	Distal	IIIC	Poorly	Diffuse	300	200
H008	48	F	Distal	IIIB	Poorly	Diffuse	280	220
H009	60	F	Distal	IIIA	Poorly	Diffuse	300	140
H010	66	M	Proximal	IIIA	Moderately to poorly	Intestinal	200	210
Z012	52	M	Distal	IIIC	Mucinous	Mixed	300	270
Z013	57	M	Distal	I B	Mucinous	Diffuse	260	300
H014	56	M	Proximal	IIIC	Moderately	Intestinal	240	200
H015	68	M	Distal	I B	Poorly	Intestinal	240	130
H016	56	M	Distal	II B	Poorly	Intestinal	200	270
H017	54	M	Proximal	IIIA	Moderately to well	Intestinal	250	300
H018	66	M	Distal	II A	Moderately to well	Intestinal	140	200
H019	68	M	Distal	I B	Poorly	Diffuse	200	200
H020	78	M	Distal	IIIA	Poorly	Mixed	300	200
H021	59	M	Proximal	IIIA	Mucinous	Diffuse	200	200
H022	52	F	Distal	I A	Poorly	Diffuse	300	200
H023	73	M	Distal	I A	Moderately to well	Intestinal	200	300
H024	52	M	Distal	IIIB	Poorly	Diffuse	200	100
H025	68	M	Proximal	IV	Poorly	Diffuse	180	100
H026	64	M	Distal	IIIB	Poorly	Diffuse	230	220
H027	61	M	Distal	II B	Poorly	Diffuse	200	200
H028	67	M	Distal	IIIA	Moderately to poorly	Intestinal	140	200
H029	64	M	Proximal	IIIB	Poorly	Mixed	300	300
H031	76	M	Distal	IIIB	Poorly	Diffuse	300	200
H032	47	M	Distal	II B	Moderately to poorly	Mixed	300	200
H033	68	F	Distal	II B	Moderately to well	Intestinal	300	300
H034	69	F	Distal	I A	Moderately to well	Intestinal	200	300

H036	69	M	Distal	I B	Moderately to well	Intestinal	300	300
H037	54	M	Distal	I A	Moderately to poorly	Diffuse	300	200
H038	56	M	Proximal	IIIA	Poorly	Diffuse	200	100
H039	73	F	Distal	I B	Moderately to well	Intestinal	200	30
H040	58	F	Distal	IIIA	Moderately to poorly	Diffuse	200	200
H041	45	M	Distal	I A	Moderately to poorly	Intestinal	200	140
H042	60	M	Distal	II B	Poorly	Intestinal	200	150
H044	69	M	Proximal	II A	Moderately to poorly	Intestinal	300	300
H045	69	F	Distal	IIIB	Poorly	Mixed	300	300
H046	70	M	Distal	I A	Moderately to poorly	Mixed	300	300
H047	72	M	Proximal	IIIA	Moderately to poorly	Intestinal	40	140
H048	55	M	Proximal	IIIB	Moderately to well	Intestinal	240	130
H049	69	F	Distal	I B	Moderately	Intestinal	200	200
H050	45	F	Distal	II B	Moderately	Mixed	250	130
H051	60	M	Distal	IIIA	Moderately to poorly	Mixed	300	160
H052	70	M	Distal	IIIA	Poorly	Diffuse	300	200
H053	59	M	Distal	IV	Moderately to poorly	Mixed	300	240
L054	59	M	Proximal	II A	Moderately to poorly	Intestinal	200	160
L056	67	M	Proximal	I B	Moderately	Intestinal	300	200
L057	56	M	Proximal	IIIA	Moderately	Intestinal	220	170
L059	50	M	Proximal	II B	Moderately	Intestinal	200	100
L060	74	M	Distal	IIIC	Moderately to poorly	Intestinal	140	200
L061	52	M	Proximal	II B	Moderately	Intestinal	220	230

Tumor staging was based on the AJCC 8th edition.

Supplementary Table 3 Dominant cell type and spot counts for each BANKSY-defined spatial niche

[illegible]

The KRT6B sequence information used to construct the KRT6B-over expressing lentivirus

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