SUPPLEMENTARY TABLES AND FIGURES

Table S1: Clinical and pathological information on the patients whose BC samples (A1, B1, C1 and D1) were used for the spatial analysis.

Table S2: Clinical and pathological information on the patients whose BC samples (N=75) were used for the validation analysis.

Table S3: Gene expression signatures of the individual cell populations used in the present study.

Table S4: The relationship between EMILIN1 expression and clinico-pathological variables in the cohort of 75 patients with BC. P-values were calculated using the $\chi 2$ test.

Figure S1: Epithelial and fibroblast populations in the newly generated BC single-cell atlas. (**A**) InferCNV analysis of epithelial cancer cells. (**B**) Gene expression analysis of individual CAF subpopulations.

Figure S2: Analysis of individual CAF subpopulation gene expression signatures (**Table S3**) in CAF cells from (**A**) Kieffer et al. and (**B**) Wu et al. datasets.

Figure S3-S12: Spatial distribution of different cellular populations in BC samples (patients A1-D1, present study; patients 1160920F, 1124423F, CID4290, CID44971, CID4465 and CID4535 from Wu et al. dataset). Labels TGFb, IFNab and IFNg refer to TGFβ, IFNαβ and IFNγ respectively.

Figure S13: Spatial distribution of selected GO processes in the remaining eight BC samples. Shown are the following GO processes: ECM Structural Organization, Wound Healing, TGF-β Receptor Signaling, Regulation of Immune System, Macrophage Activation, and T-Cell Activation. In some samples, some GO processes were not significantly enriched and are not shown.

Figure S14: Histological annotation of BC samples (Reference tissue) and estimation of highly proliferative regions (S+G2M), actively cycling cancer cells and two immune populations (macrophages and CD8$^+$ T cells) in the remaining eight BC samples.

Figure S15: Correlation analysis for all cancer cell populations in the BC atlas, highly proliferative regions (S+G2M) and two immune populations (macrophages and CD8$^+$ T cells).

Figure S16: Gene ontology analysis of the top 5 significantly enriched biological processes in the indicated CAF subpopulations. No significant enrichment was found for Acto-myCAFs.

Figure S17: Box plots showing the patient-wise statistical analysis of *EMILIN1* expression in CD8$^+$ cells/TGFβ+ regions in the indicated ten BC samples.

Figure S18: (**A**) Brightfield image showing the histological structure and cell nuclei of the IF staining from the **Figure 5A**. (**B**) Low- and high-power views of the multiplexed immunofluorescence analysis displaying the localization of EMILIN1, Ki-67 and CD8 in representative BC samples (N=7). Histological structure and cell nuclei are shown using brightfield imaging.

Figure S1

A

ECM-myCAF

Detox-iCAF

IL-iCAF

TGFβ-myCAF

Wound-myCAF

IFNγ-iCAF

IFNαβ-myCAF

Acto-myCAF

B

ECM-myCAF

Detox-iCAF

IL-iCAF

TGFβ-myCAF

Wound-myCAF

IFNγ-iCAF

IFNαβ-myCAF

Acto-myCAF

Figure S2

Figure S3

B1
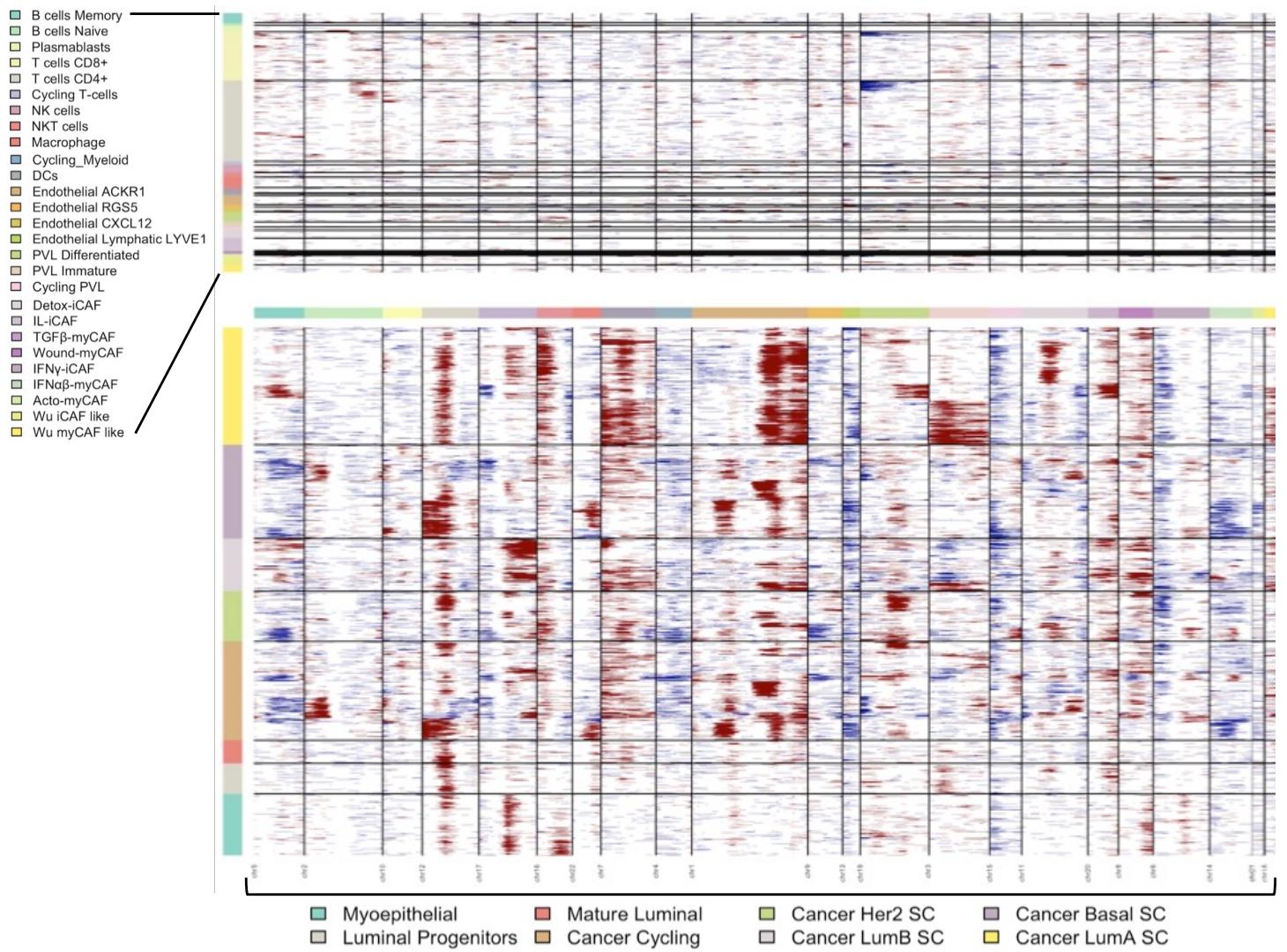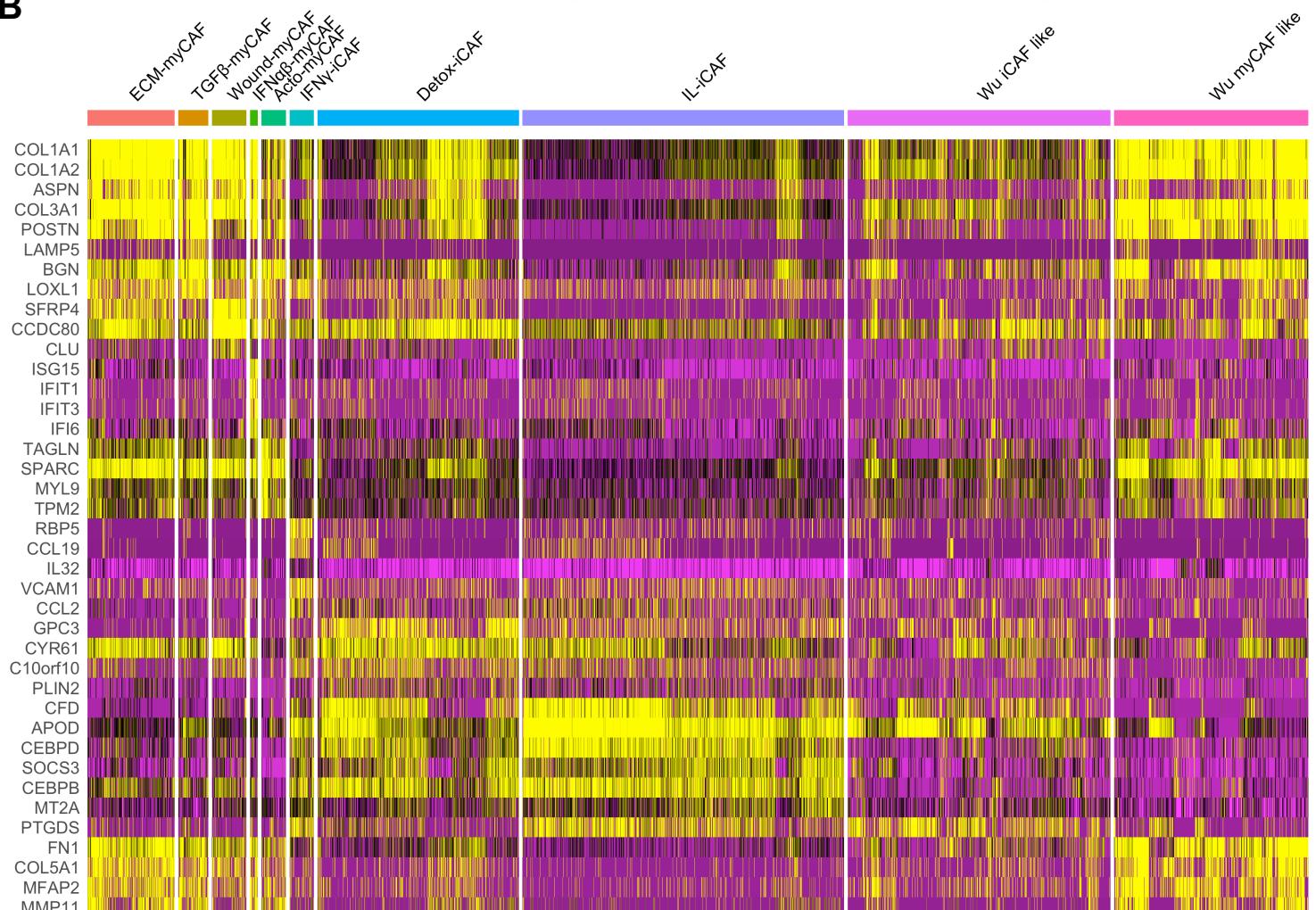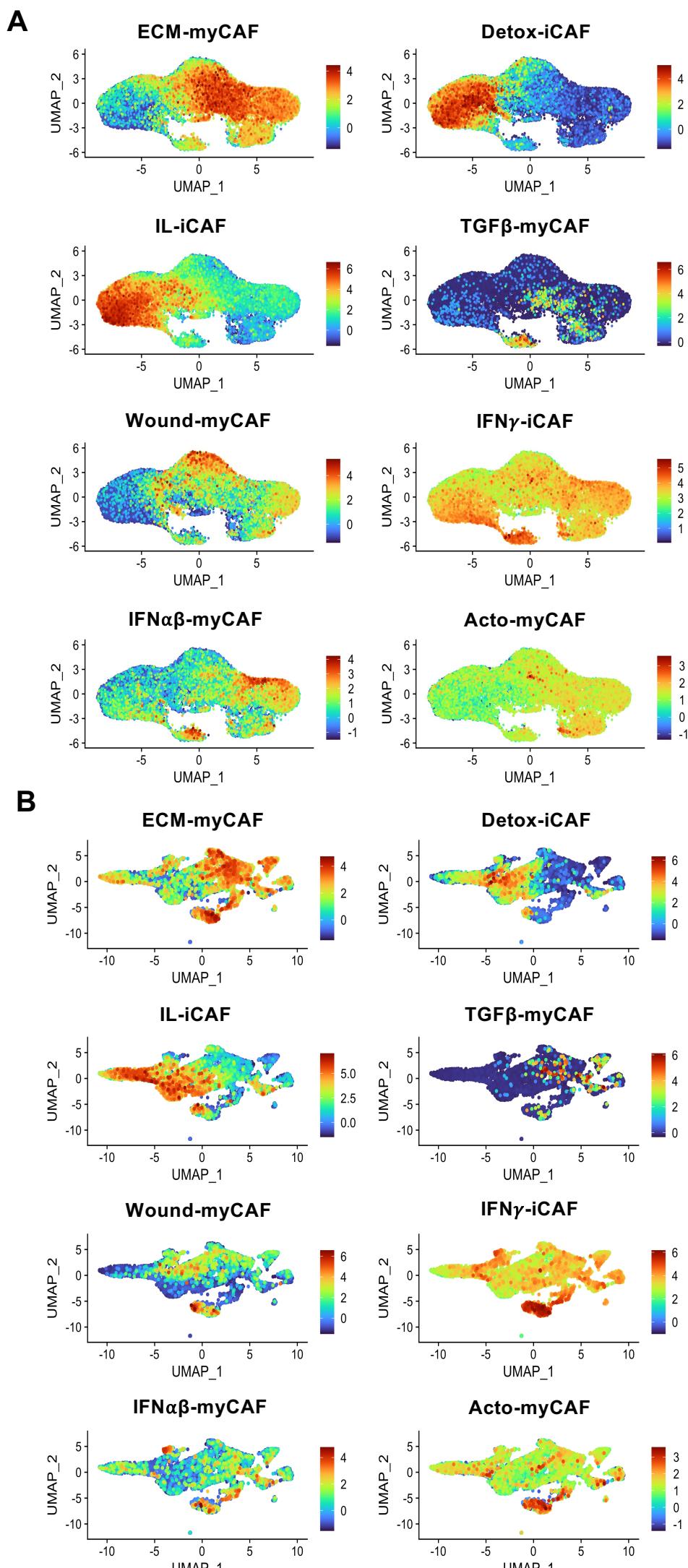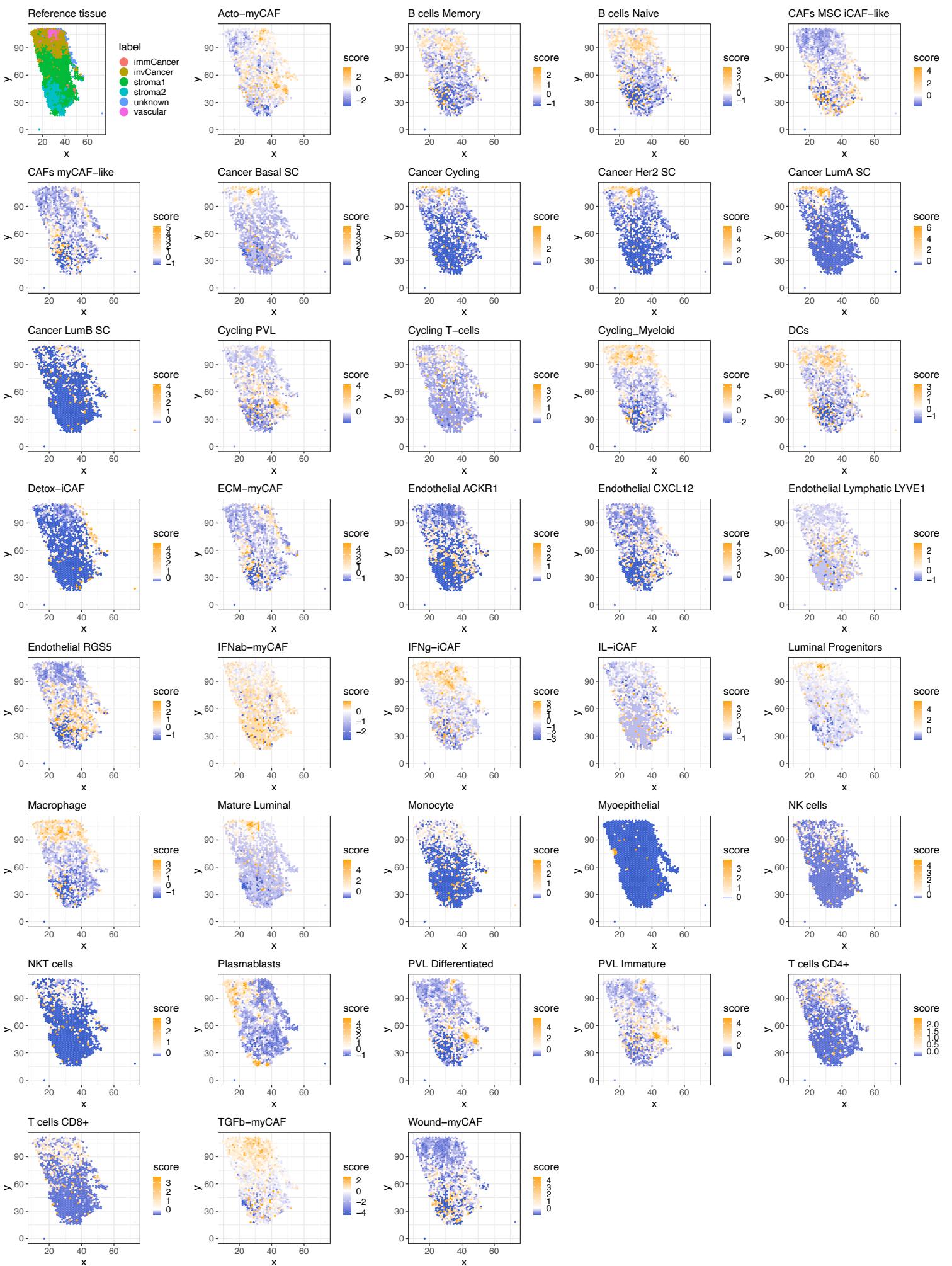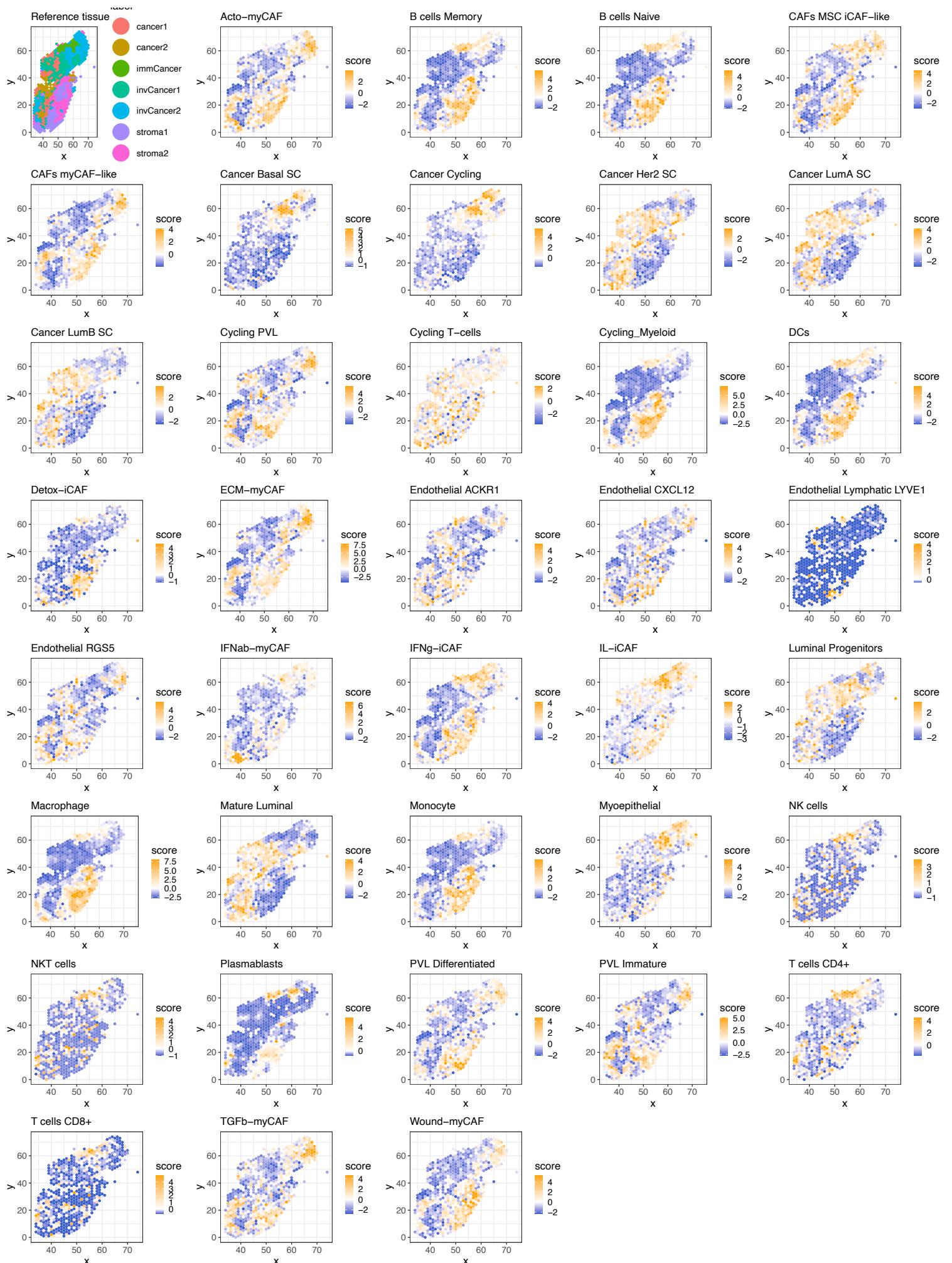
Figure S4

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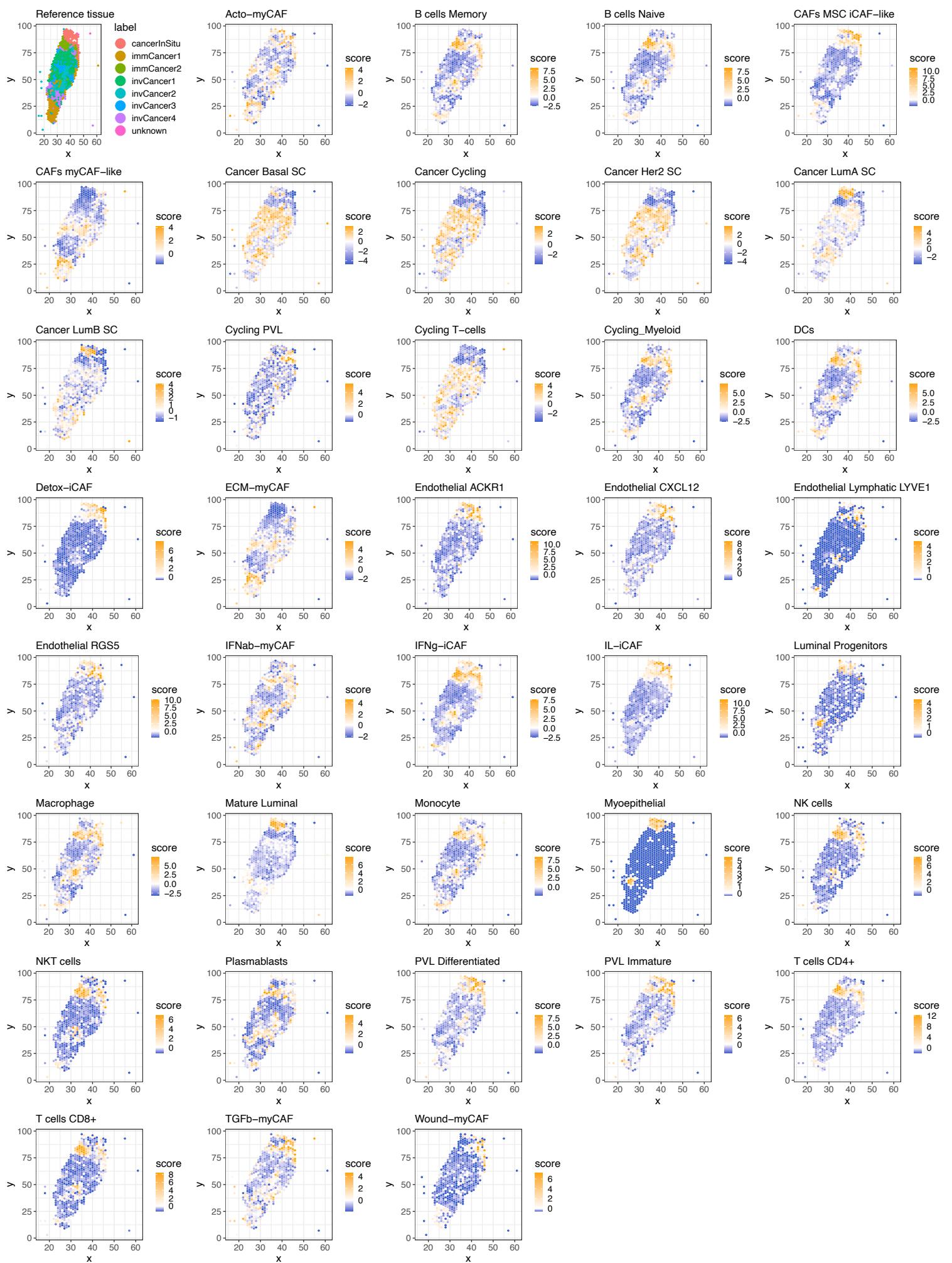
Figure S5

D1

Figure S6

1160920F

Figure S7

1124423F
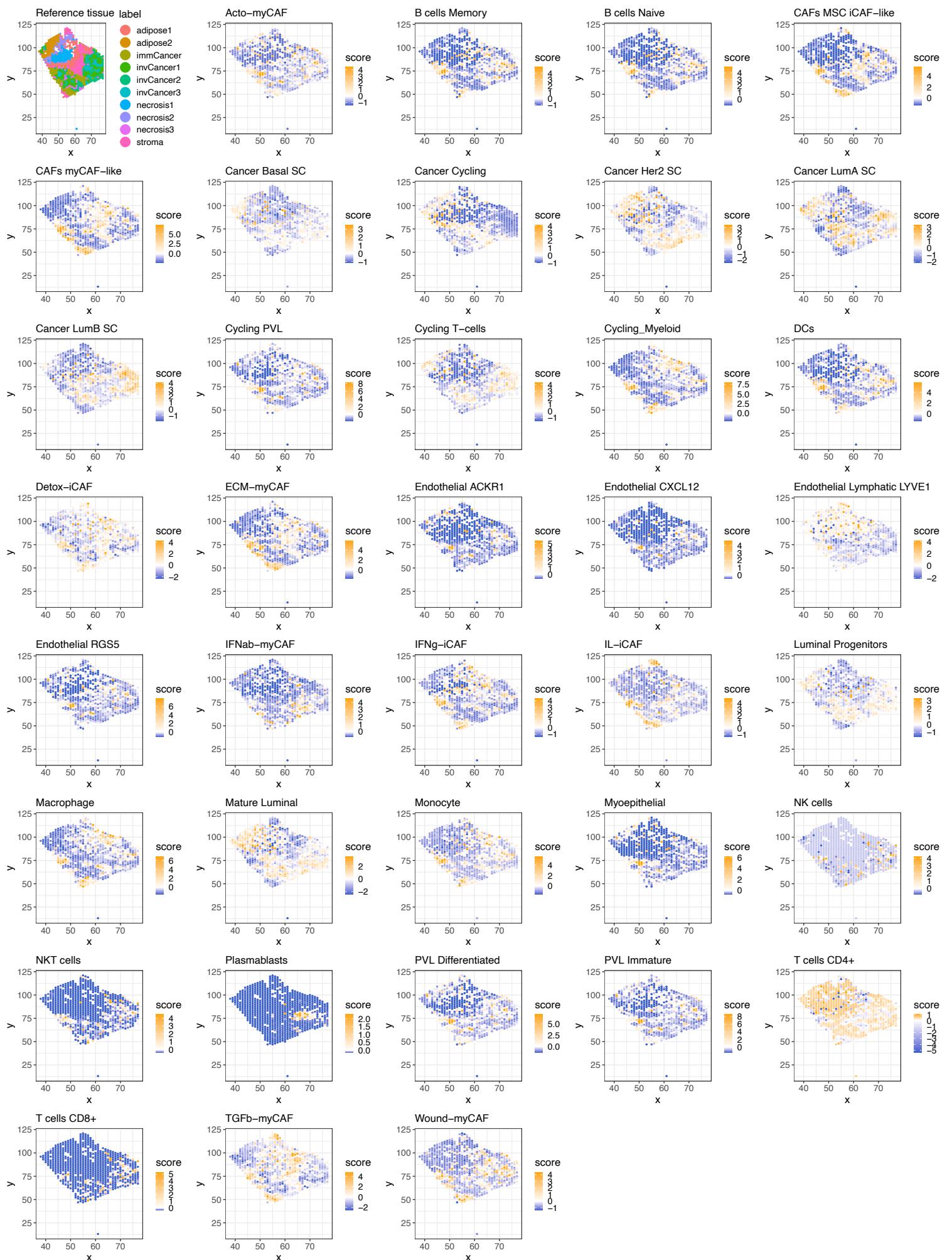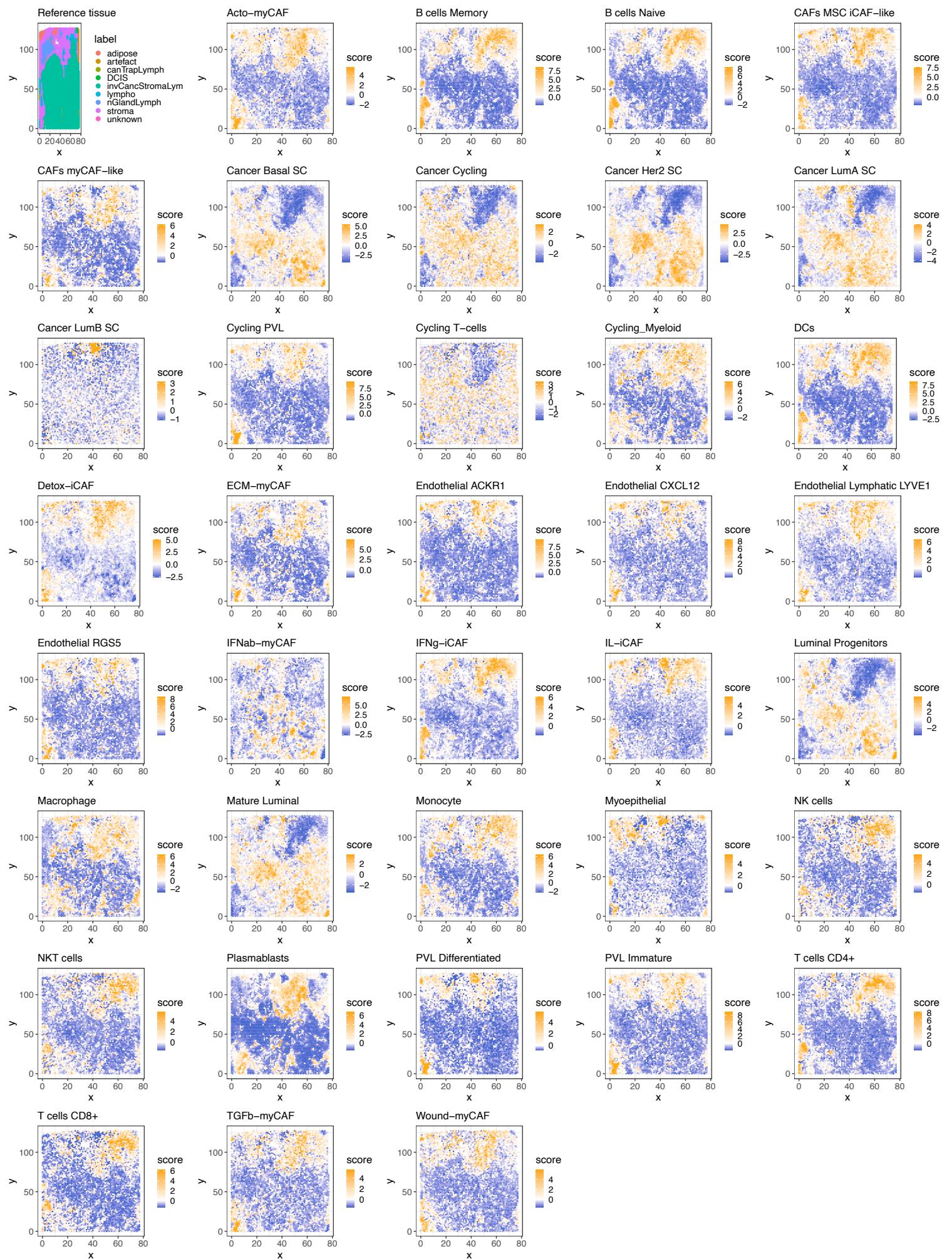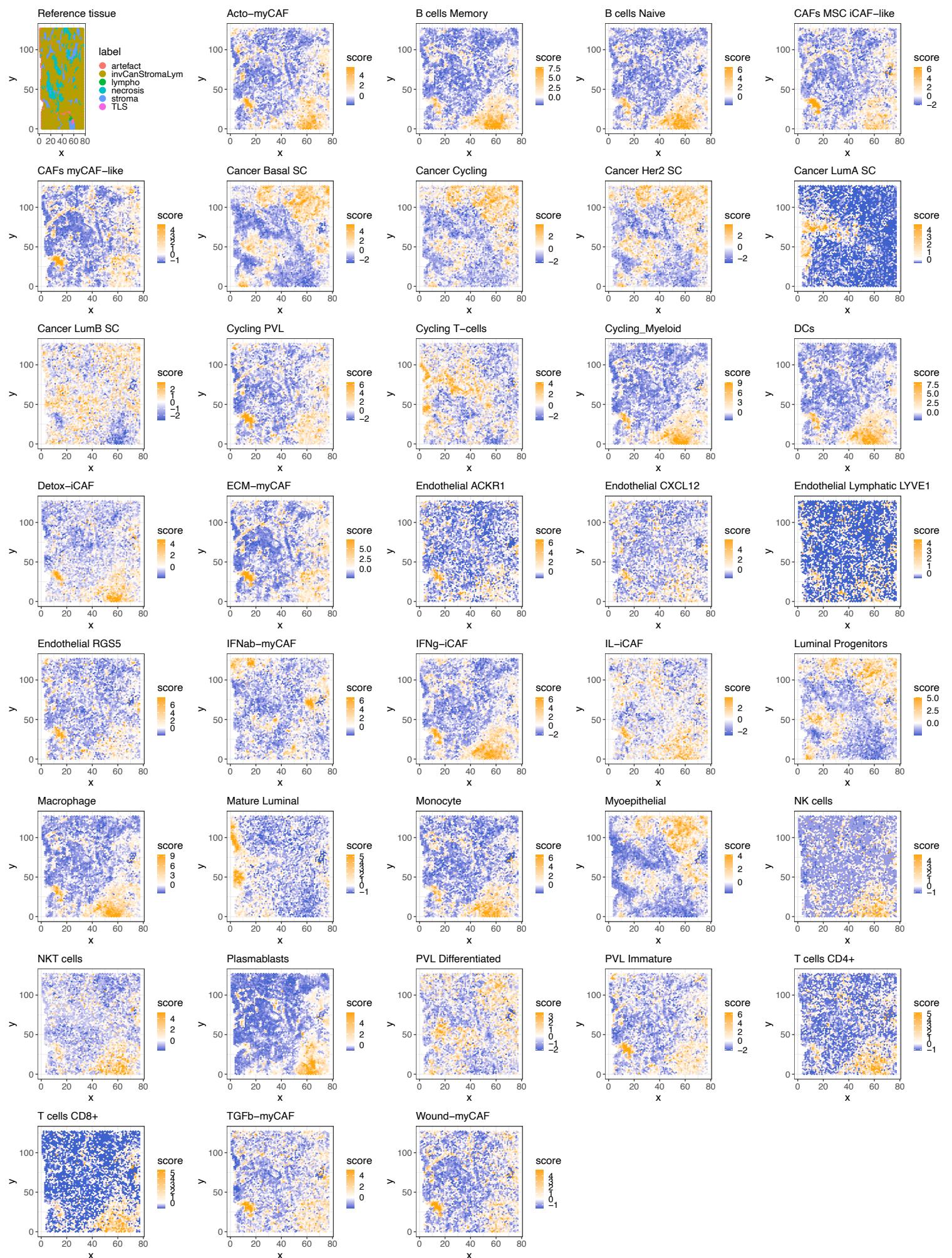
Figure S8

CID4290
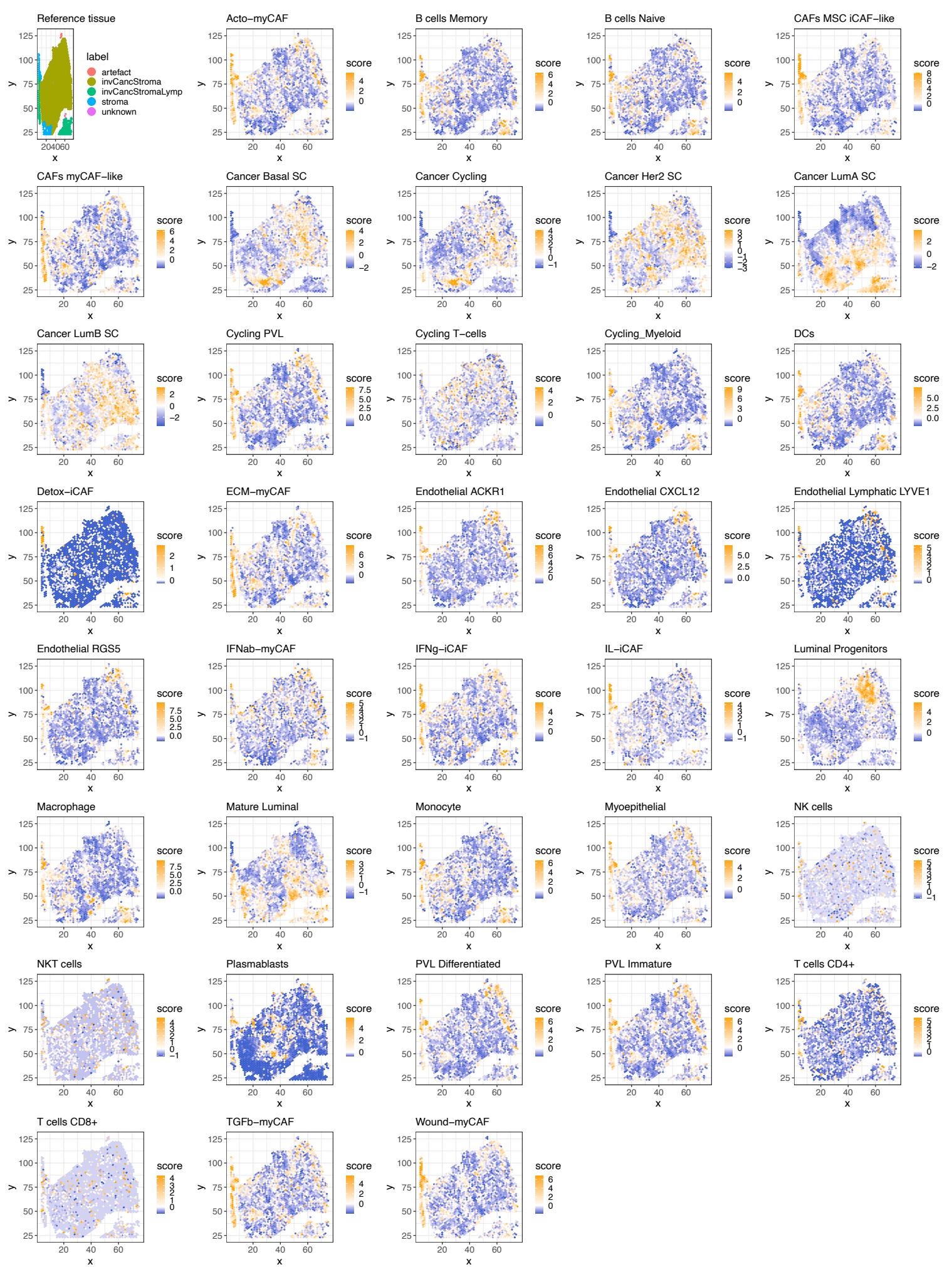
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CID44971
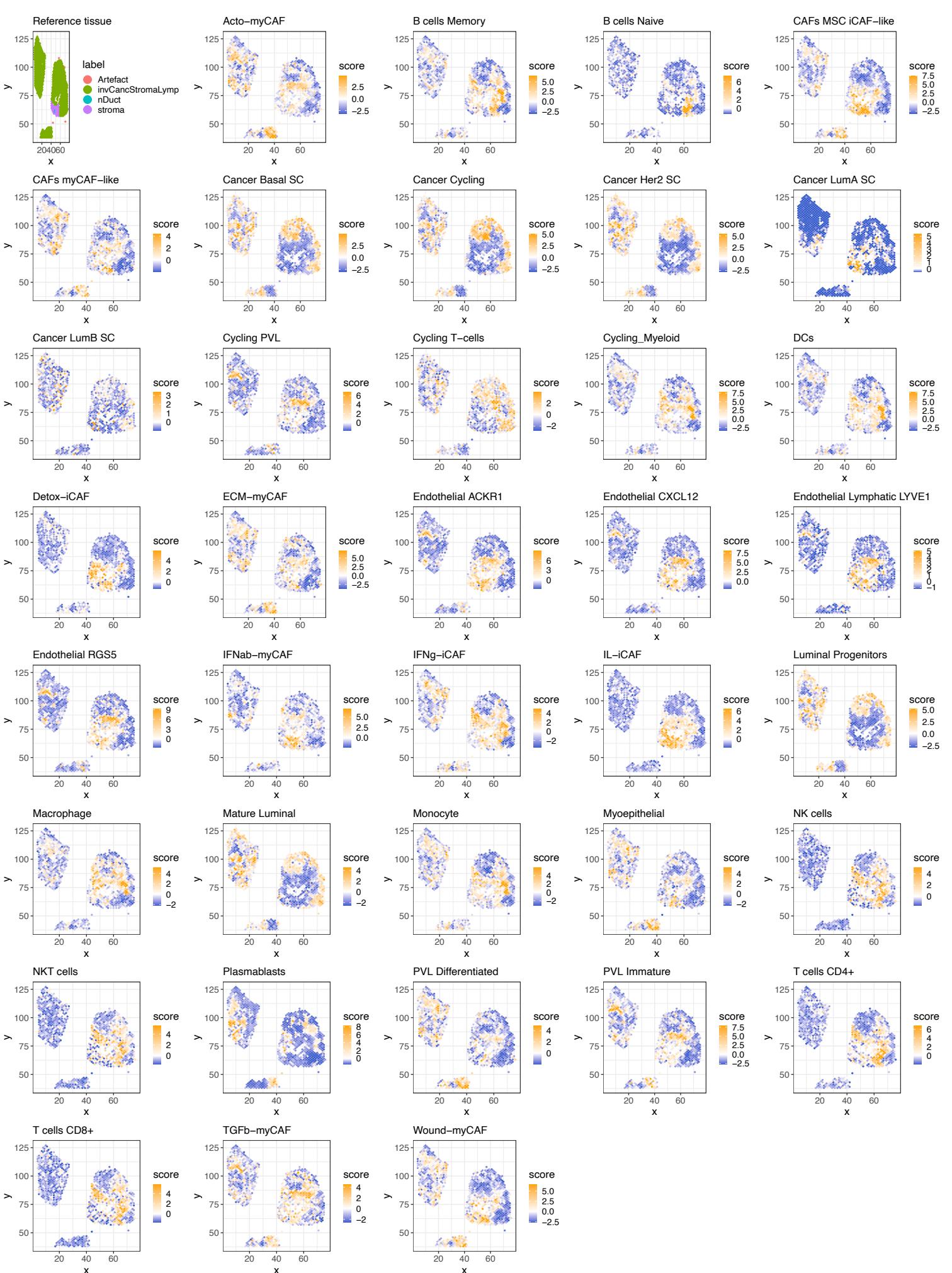
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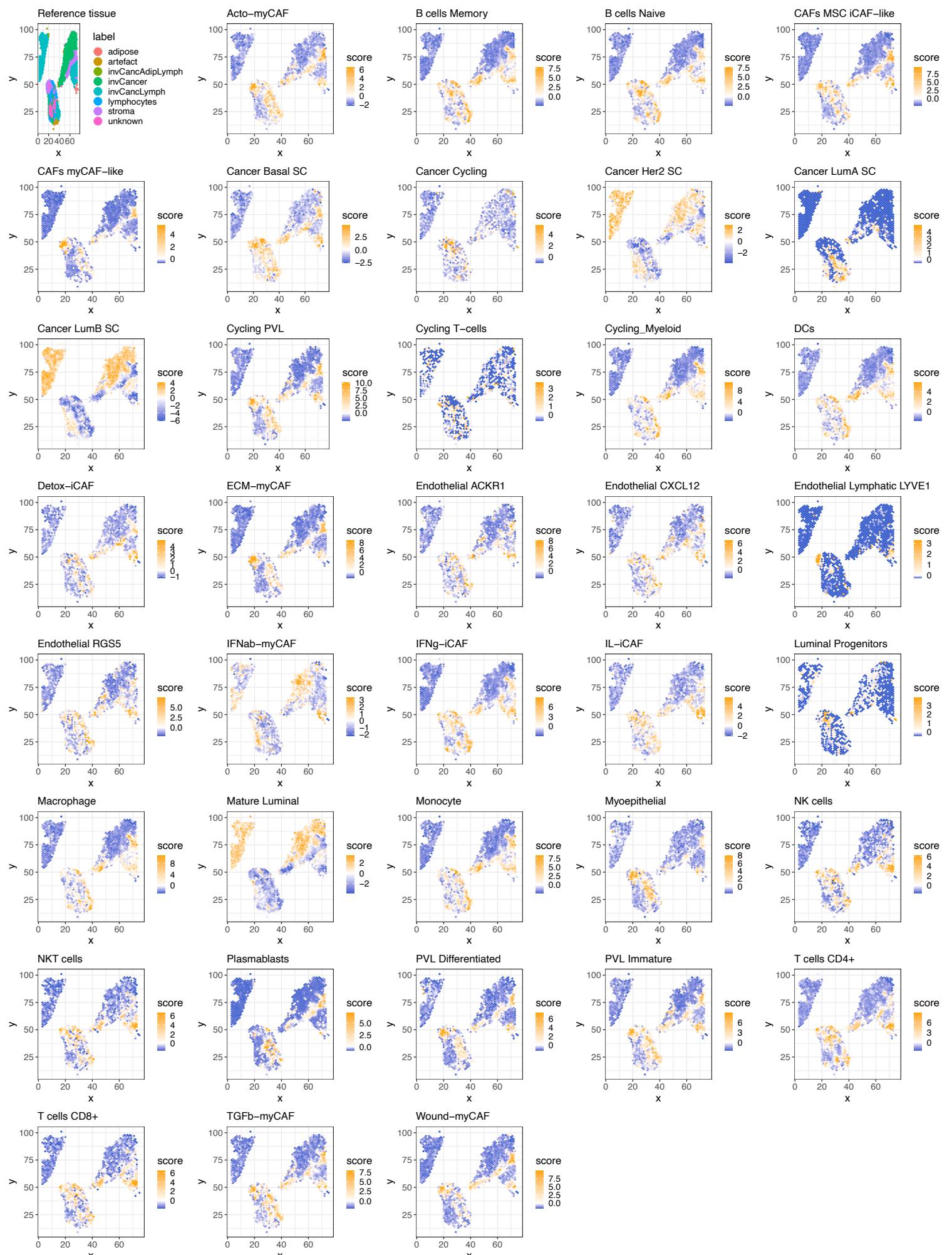
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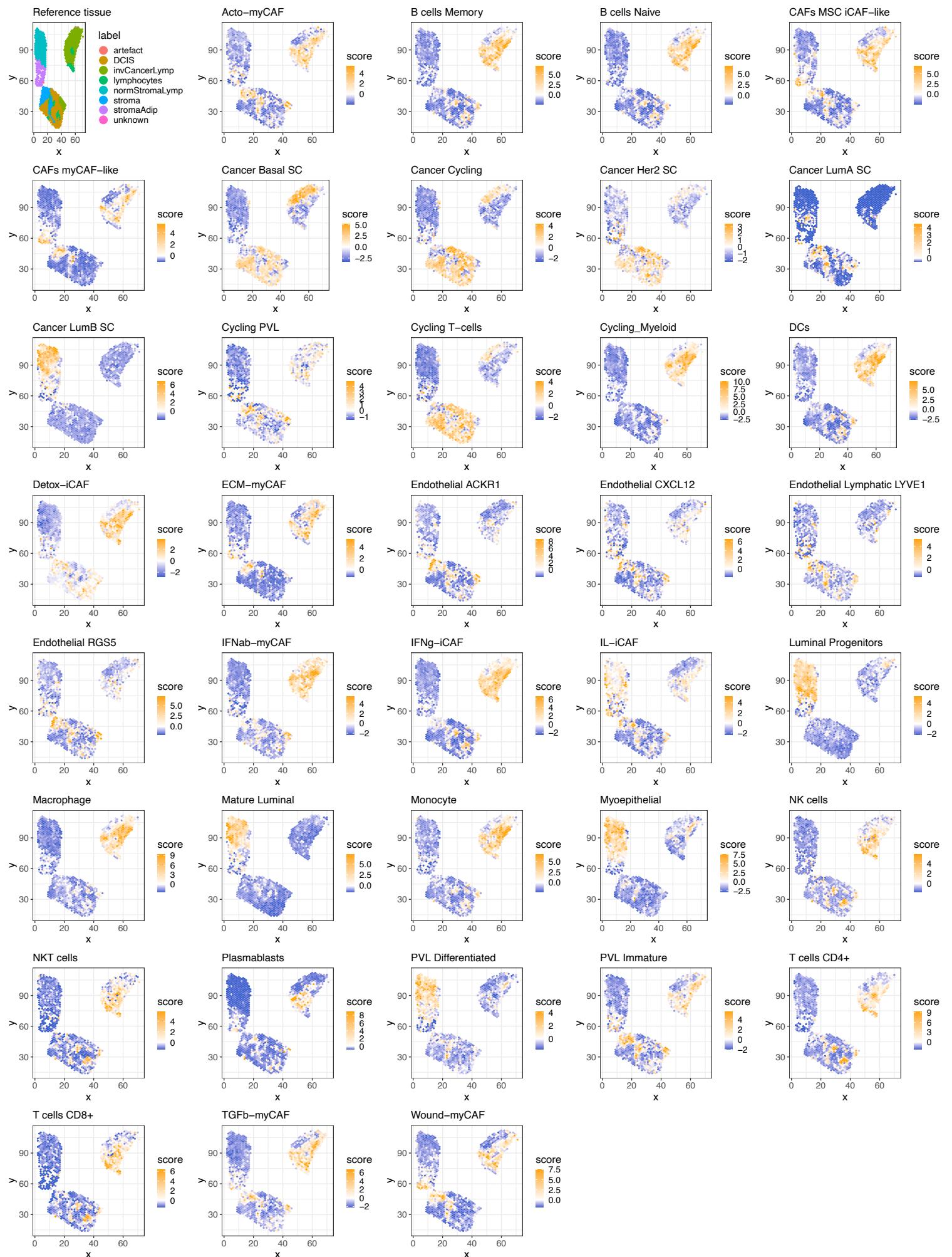
Figure S12

A1

ECM Structure Org.   Wound Healing   TGFβ-Receptor Sig.

B1
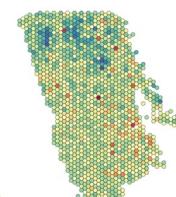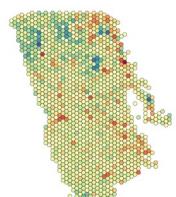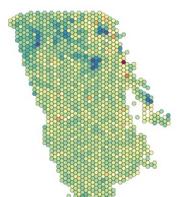
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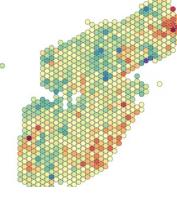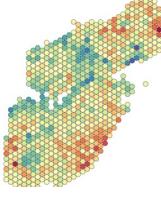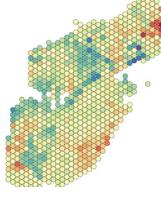
Reg. of Immune System   Macrophage Activ.   T-Cell Activ.

D1

ECM Structure Org.   Wound Healing   TGFβ-Receptor Sig.

Reg. of Imm. System   Macrophage Activ.   T-Cell Activ.

P1142243F

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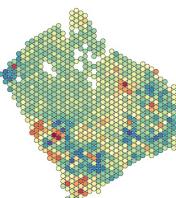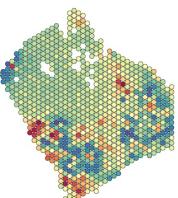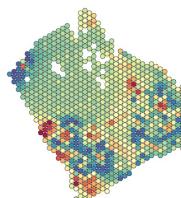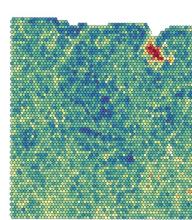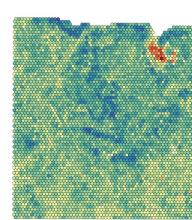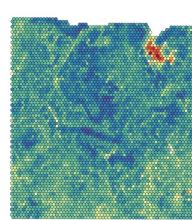
Reg. of Imm.System   T-Cell Activ.

CID4290

ECM Structure Org.   Wound H.   TGFβ-R Sig.

Reg. of Imm. System   Macrophage A.   T-Cell A.
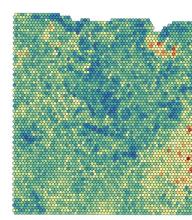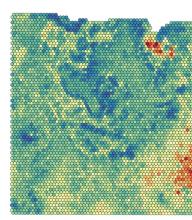
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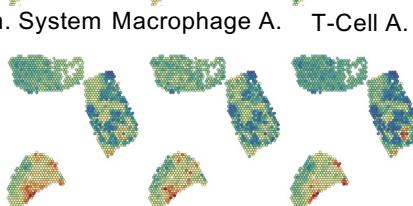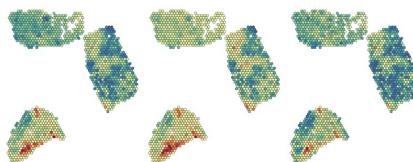
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CID4465

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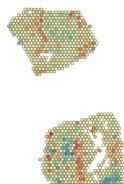
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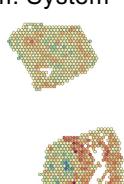
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ECM Structure Org.   Wound H.   TGFβ-R Sig.

Reg. of Imm. System   Macrophage A.   T-Cell A.

Figure S13
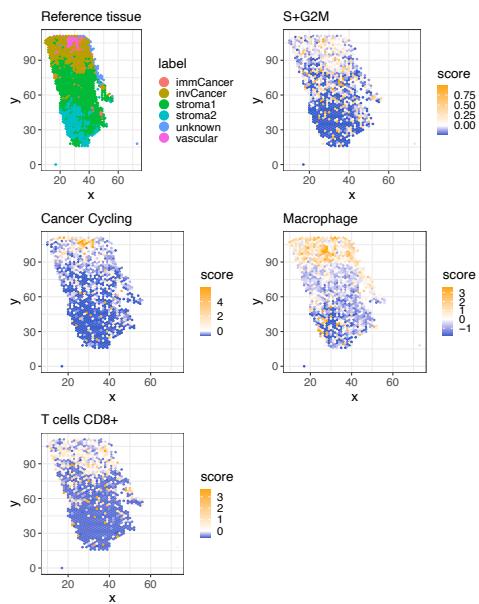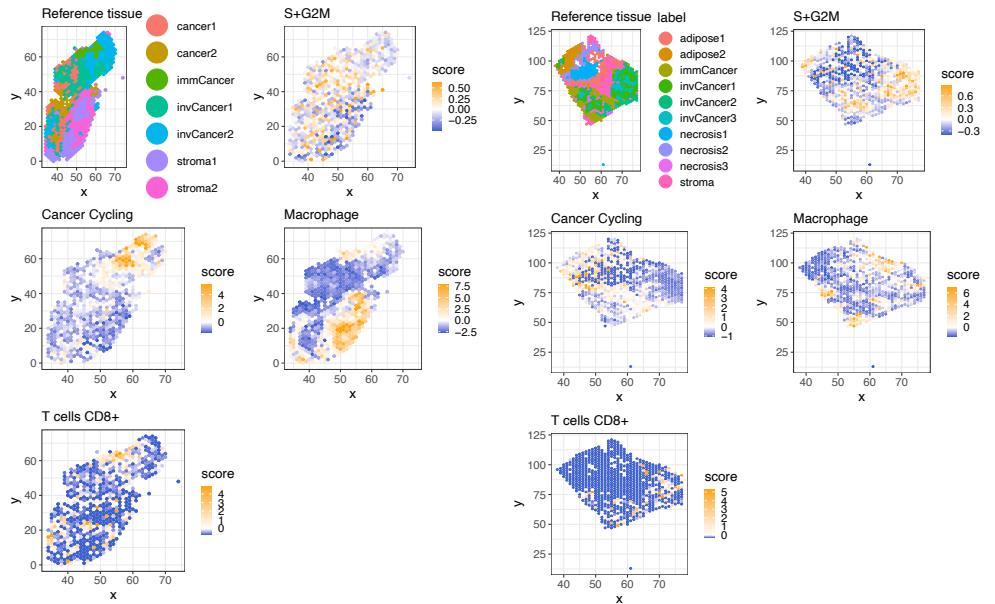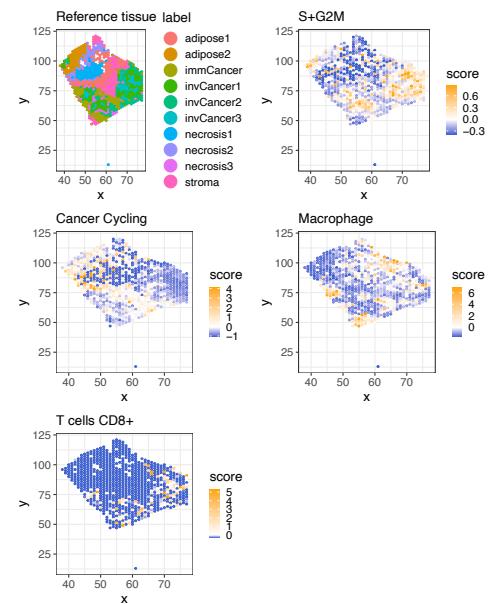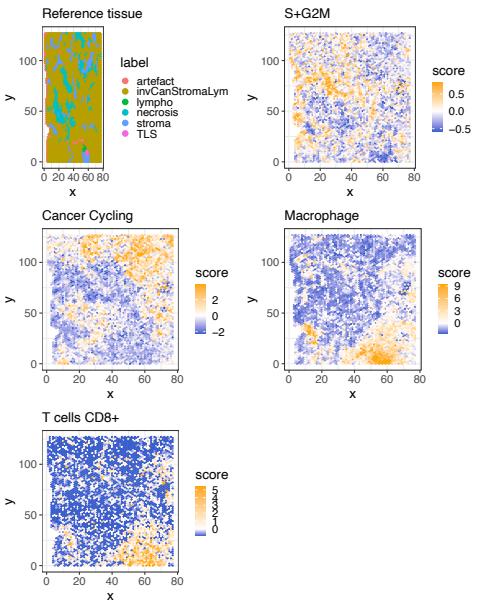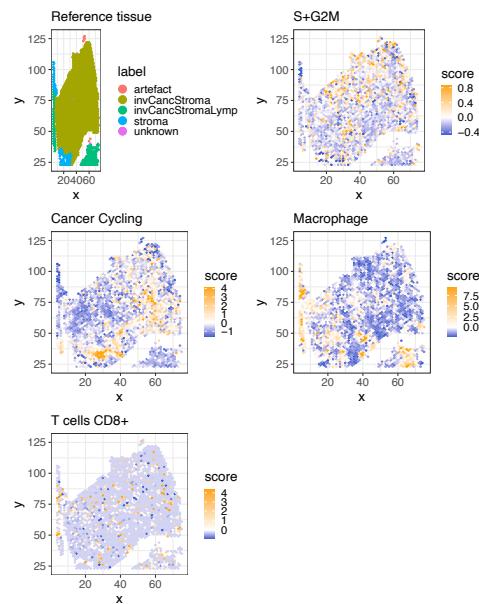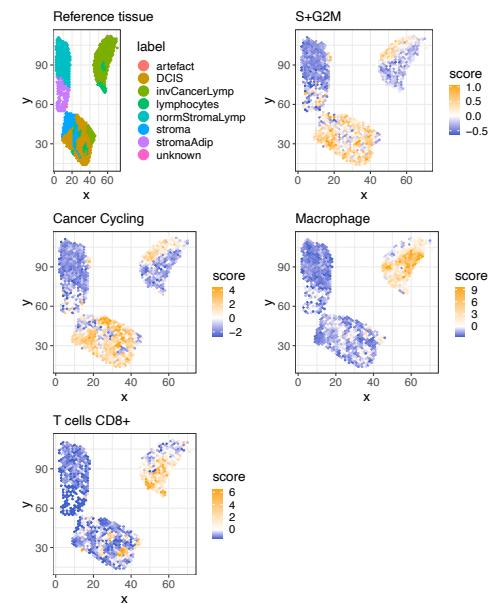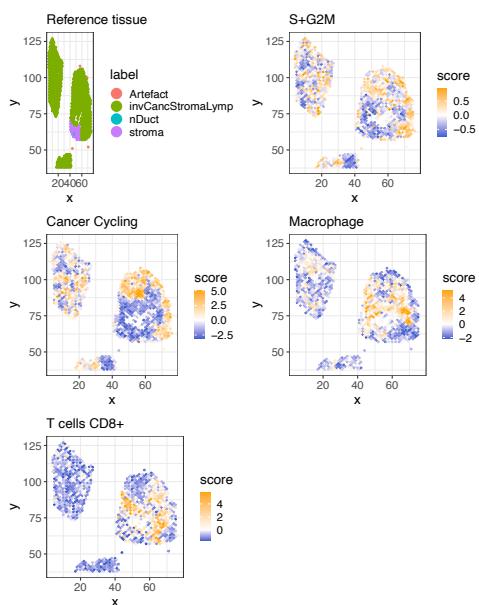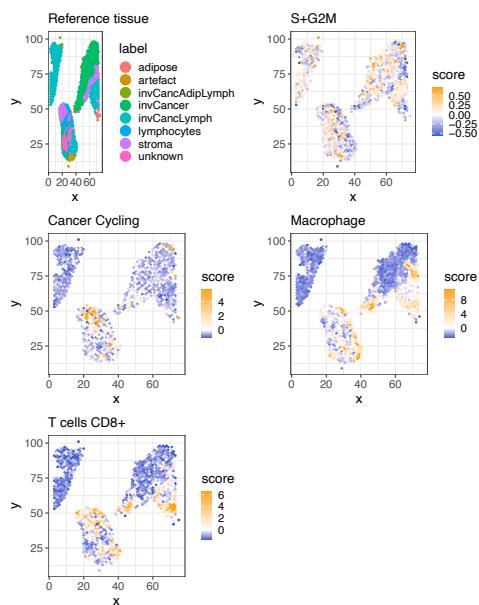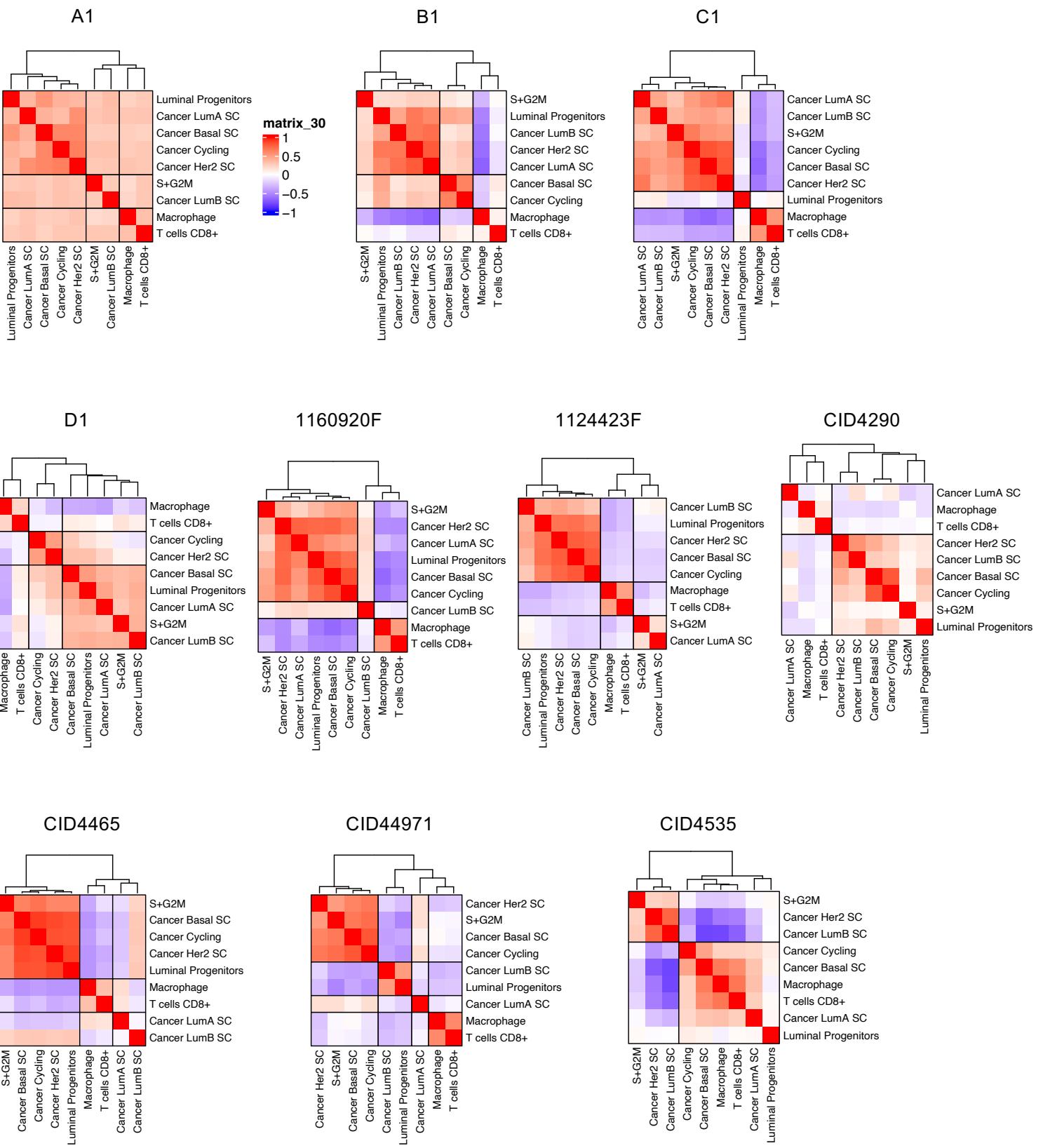
Figure S14

Figure S15

Figure S16

Figure S17

A

EMILIN1-TGFBI-CD8

Bright-field image

low

high

100 μm

100 μm

Tumor

Tumor

100μm

B

EMILIN1-Ki67-CD8

EMILIN1-Ki67-CD8

200 μm

50μm

Stroma

Tumor

Tumor

Stroma

Stroma

200μm

50μm
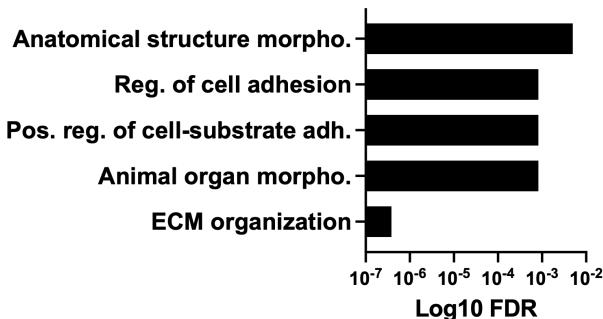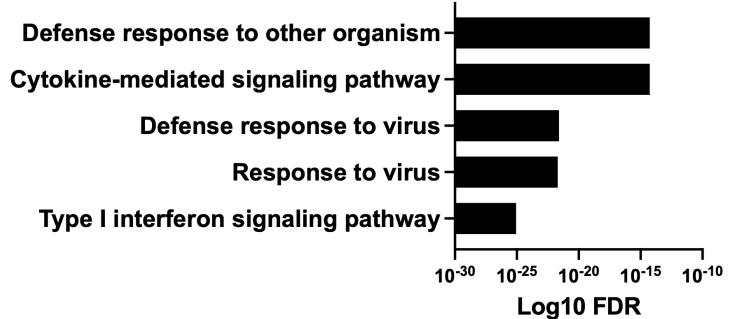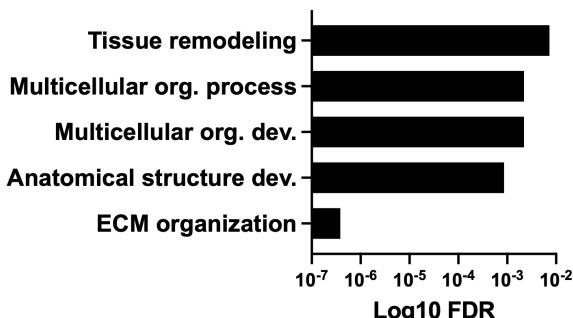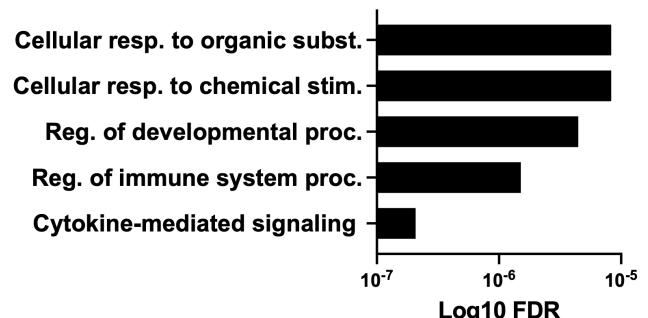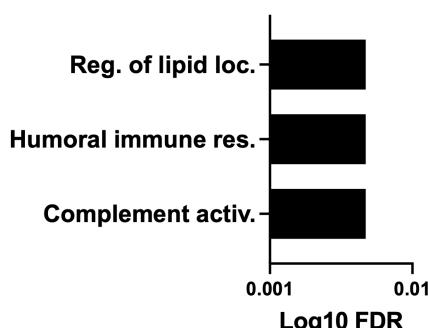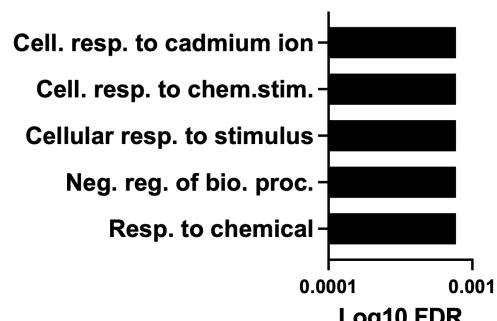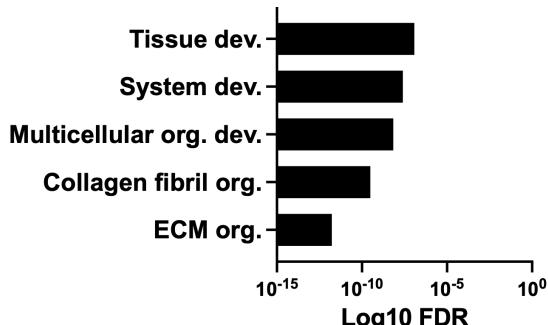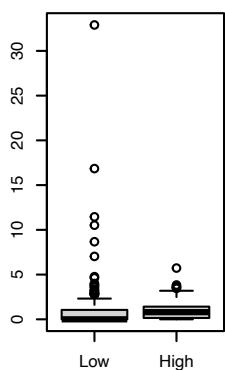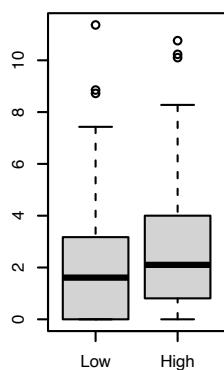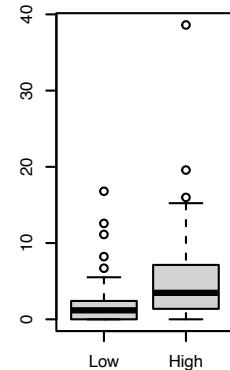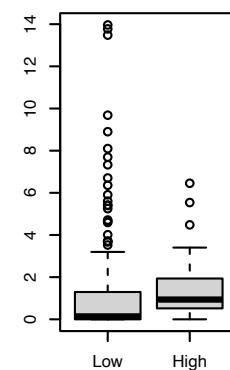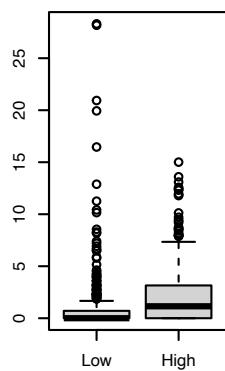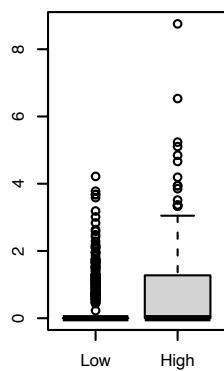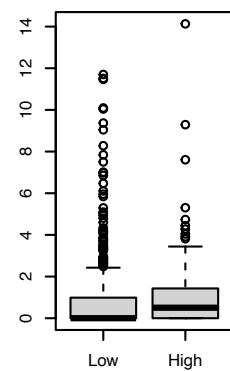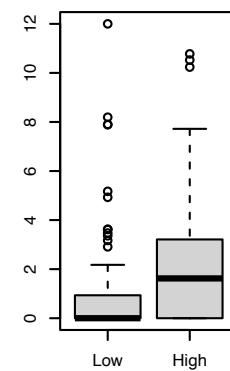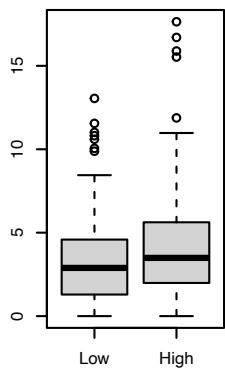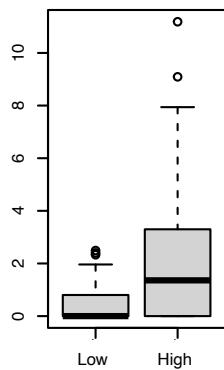
Figure S18

Table S1: Clinicopathological factors of 4 spatial transcriptomic cases

Patient	A1	B1	C1	D1
Age	89	79	52	56
Histological subtype	IDC	IDC	IDC	IDC
ER	1%>	1%>	1%≦	1%≦
PgR	10%>	10%>	10%≦	10%≦
HER2	3+	1+	3+	2+ (FISH negative)
T factor	T2	T2	T1c	T3
N factor	3a	0	0	0
M factor	0	0	0	0
SBR Grade	3	3	3	3
Stage (UICC 8th)	IIIC	IIA	I	IIB
Ki-67 （%）	12−17	7--15	unknown	27-32
Lymphatic invasion	1+	0	1+	1+
Vascular invasion	1+	0	1+	0

Table S2: Clinical features of 75 case strong validation cohort

Factors	Number
Age	
<60	34
60≦	41
Histologic subtype	
IDC	59
ILC	6
Others	10
T factor	
T1	38
T2-4	37
N factor	
N0	47
N1-3	28
M factor	
0	75
1	0
Nuclear Grade	
1	11
2	10
3	54
Stage	
I	34
II-III	41
ER	
1%≦	39
1%>	36
PgR	
10%≦	25
10%>	50
HER2	
0	2
1+	34
2+	6
3+	33
Lymphatic invasion	
0	35
1	29
2	10
3	1
Vascular invasion	
0	50
1	24
2	1
3	0
EMILIN	
Low	18
High	57

Table S3: Gene signatures for individual cell subpopulations

Endothelial ACKR1	Endothelial RGS5	Endothelial CXCL12	Endothelial Lymphatic LYVE1	Wu iCAF-like	Wu myCAF-like	ECM-myCAF	Detox-iCAF	IL-iCAF	TGFβ-myCAF
ACKR1	FABP4	IGFBP3	CCL21	APOD	COL1A1	POSTN	CFD	APOD	CST1
PLVAP	PLVAP	FABP4	MMRN1	DCN	COL1A2	FN1	ADH1B	MT2A	LAMP5
VWF	RBP7	CLDN5	PROX1	PTGDS	COL3A1	COL1A1	GPC3	RASD1	HOPX
AQP1	COL4A1	RAMP2	SDPR	CFD	LUM	ACTA2	C10orf10	MT1A	BGN
SPARCL1	HSPG2	SLC9A3R2	CLDN5	LUM	SFRP2	SFRP2	GPX3	IRF1	LOXL1
RAMP3	RAMP2	PLPP1	ECSCR.1	C1S	POSTN	POSTN	C3	PDK4	TIMP1
RAMP2	COL4A2	A2M	RAMP2	CXCL12	MMP11	CTHRC1	APOC1	MT1M	F2R
ENG	GNG11	CAV1	FABP4	C3	CTHRC1	SPARC	MT1M	CEBPD	IGFBP7
FABP4	EGFL7	GNG11	GNG11	SFRP2	FN1	TAGLN	EFEMP1	KLF4	EDNRA
PECAM1	A2M	CLEC14A	EGFL7	CXCL14	SPARC	COL3A1	SOD2	SOCS3	NREP
SPRY1	IGFBP7	RBP7	TFPI	CCDC80	CXCL14	COL5A2	MGP	PTGDS	TGFB3
EGFL7	VWF	C10orf10	NRP2	MFAP4	DCN	MMP11	SFRP1	ZFP36L2	POSTN
IGFBP7	SPARCL1	TM4SF1	AKAP12	FBLN1	COL6A3	SDC1	LEPR	JUNB	MMP3
CLDN5	CALCRL	ID1	EFEMP1	GSN	BGN	COL5A1	C7	ITM2A	RAMP1
NPDC1	AQP1	EGFL7	TFF3	CTSK	COL6A2	GJB2	CXCL12	RGMA	MMP11
EMCN	ESAM	CXCL12	PPFIBP1	SERPINF1	COL6A1	SERPINH1	IL6	GSN	COL10A1
IGFBP4	CD36	CAV1	CAV1	RARRES2	CTGF	VCAN	CXCL2	ADIRF	MGP
PRCP	PLPP1	PECAM1	RCAN1	C1R	AEBP1	COL10A1		BTG2	ELN
HSPG2	RAMP3	IFI27	FABP5	IGF2	COL5A2	THY1		CFD	CXCL14
GNG11	SPARC	ICAM2	CD9	CYR61	VCAN	TPM1		CXCL12	COMP
					CTSK				

Wound-myCAF	IFNγ-iCAF	IFNαβ-myCAF	Acto-myCAF	myCAF	iCAF	CAFs1	CAFs4	PVL Differentiated	PVL Immature
SFRP4	B2M	ISG15	ATP5E	COL1A2	SOD2	MMP2	MCAM	ACTA2	CCL19
CCDC80	CCL19	IFI6	PLP2	TAGLN	CXCL12	MFAP5	MEF2C	TAGLN	RGS5
FBLN1	VCAM1	MX1	OST4	BGN	PLA2G2A	LAMA2	MOCS1	MYL9	IGFBP7
OGN	HLA-B	OAS1	SERF2	TPM2	MCL1	SFRP4	PTP4A3	TPM2	NDUFA4L2
PTGER3	CD74	IFI44L	SMYD3	IGFBP7	S100A10	LUM	NRIP2	NDUFA4L2	CCL2
SFRP2	RBP5	RSAD2	MFAP5	MMP11	S100A4	PDGFRA	MYH11	SOD3	CCL21
DHRS3	CLSTN3	IFIT1	DIO2	CST1	ABL2	LRRC15	PARM1	ADIRF	COL18A1
PDGFRL	C3	LY6E	IGFBP7	ACTA2	CXCL1	GREM1	CDH6	MYH11	CALD1
CLU	TYMP	IGFBP7	HOPX	POSTN	CXCL2	SFRP2	GJA4	RGS5	LHFP
SMOC2	IL32	IFIT3	PPIC	CTHRC1	PTX3	KIAA1462	CACNB2	RERGL	THY1
IGFBP6	PGF	IFI27	HCFC1R1	CALD1	HAS1	CCL11		IGFBP7	CPE
MFAP5	CTSH	IFITM3	IGKC	INHBA	FBLN2	CXCL12		CALD1	MYL9
CYR61	PSME2	MX2	CTTN	GRP		CXCL13		SPARCL1	SPARC
CD9	CYP1B1	IFI44	SPARC			CXCL14		MT1M	COL4A1
COL1A2	BIRC3	STAT1	CDKN2A					C11orf96	TAGLN
CTGF	PTGDS	CXCL10	TAGLN					PPP1R14A	STEAP4
WISP2	APOE	IFIT2	TGFB3					MFGE8	ACTA2
COL8A1	CXCL9		PALLD					PLAC9	COL4A2
PRSS23	CCL2		IFI27					DSTN	TIMP1
CITED2	CXCL10		IGHM					PTP4A3	IGFBP5

Cycling PVL	B cells Memory	B cells Naive	Plasmablasts	T cells CD8+	T cells CD4+	NK cells	Cycling T-cells	NKT cells	Macrophage
NDUFA4L2	MS4A1	CD79A	IGKV3-15	CCL4	IL7R	GNLY	HIST1H4C	GNLY	C1QB
RGS5	CD79A	TCL1A	IGHG1	CCL5	LTB	XCL1	STMN1	NKG7	C1QA
THY1	CD83	MS4A1	IGKV1-5	CD8A	CD2	XCL2	HMGB2	GZMB	C1QC
COL4A1	CD37	CD37	IGKV3-20	CCL4L2	CXCR4	AREG	TYMS	FGFBP2	APOE
COL4A2	BANK1	LINC00926	IGKV3-11	IFNG	TRAC	KLRD1	MKI67	PRF1	APOC1
MYLK	HLA-DRA	HLA-DRA	IGKV1-9	NKG7	IL32	NKG7	CXCL13	KLRD1	SPP1
SDC2	CD74	CD79B	IGKC	XCL1	CD3E	TRDC	TUBB	GZMH	TYROBP
COL18A1	HLA-DQB1	VPREB3	IGLV2-14	GZMA	CD3D	KLRC1	HMGN2	GZMA	FTL
ACTA2	VPREB3	BANK1	IGKV4-1	CD8B	CREM	GZMB	TUBA1B	CST7	CD68
BGN	HLA-DQA1	IGHD	IGLV3-25	XCL2	ICOS	CTSW	RRM2	KLRB1	CXCL8
MYL9	IGHM	FCER2	IGLV1-40	CST7	TNFAIP3	KLRB1	PTTG1	KLRF1	CCL3
COL1A1	CD79B	HVCN1	IGLV1-44	GZMK	BIRC3	CD7	CENPF	MYOM2	CTSB
TAGLN	HLA-DPB1	HLA-DPB1	IGHV6-1	ZNF683	KLRB1	CCL5	CORO1A	FCGR3A	FCER1G
TPM2	HLA-DPA1	FCMR	IGLC2	CD69	CYTIP	CD69	NUSAP1	PLAC8	LYZ
SPARC	IRF8	IGHV3-23	IGLV1-51	GZMB	TSC22D3	IL2RB	TOP2A	CCL5	MS4A6A
CALD1	HLA-DRA1	CD74	IGHV3-23	GZMH	CCR7	GZMA	HIST1H1E	SPON2	HLA-DRA
IGFBP7	ARHGAP24	LAPTM5	IGLV3-21	CTSW	BTG1	CCL4	PFN1	HOPX	AIF1
TIMP1	ADAM28	IGLV3-21	IGLC3	RP11-291B21.2	TRBC2	DUSP2	HMGB1	CD247	RNASE1
LGALS1	LINC00926	NCF1	IGLV1-47	CD7	RGS1	CMC1	H2AFZ		HLA-DRB1
TUBA1B	IGHA1	CD83		CD3E	SPOCK2				CCL3L3

Monocyte	Cycling_Myeloid	DCs	Myoepithelial	Luminal Progenitors	Mature Luminal	Cancer Cycling	Cancer Her2 SC	Cancer LumB SC	Cancer Basal SC	Cancer LumA SC
LYZ	C1QB	HLA-DPB1	KRT14	KRT15	SCGB3A1	CD24	CD24	SLC39A6	S100A8	SCGB2A2
IL1B	C1QC	HLA-DRA	KRT17	LTF	AZGP1	S100A8	MUCL1	DHRS2	SAA1	SCGB1D2
G0S2	C1QA	HLA-DPA1	MYLK	PTN	PIP	S100A9	CALML5	AGR3	RARRES1	PIP
TYROBP	LYZ	HLA-DQA1	KRT5	MMP7	MGP	MUCL1	MIEN1	COX6C	MGST1	ELF3
FCN1	AIF1	HLA-DQB1	TAGLN	MGP	XBP1	STMN1	KRT7	H2AFJ	MGP	SCGB2A1
AIF1	TYROBP	HLA-DRB1	ACTG2	CXCL2	TFF1	S100A2	DBI	AGR2	CALML5	AGR2
PLAUR	FCER1G	CD74	DST	TACSTD2	C8orf4	UBE2C	ERBB2	TSPAN13	EPCAM	AZGP1
LST1	CD68	HLA-DRB1	ACTA2	SLPI	STC2	MGST1	MGST1	ANKRD30A	S100A2	TFF1
FCER1G	MS4A6A	HLA-DRB5	CSRP1	SFRP1	AREG	HIST1H4C	KRT19	STC2	CSTB	S100A14
S100A9	SPP1	CST3	CNN1	CLDN4	KRT18	KRT19	GRB7	STARD10	CD24	CLDN3
CXCL8	APOC1	IRF8	C2orf40	SAA1	KRT8	KRT18	SPINT2	MAGED2	MARCKSL1	ANKRD30A
HLA-DRA	HLA-DRA	PLAC8	FBXO32	TM4SF1	MAFF	TUBB	SLPI	MLLT4	LDHB	KRT19
SERPINA1	HLA-DPA1	LILRA4	MT1X	MAFF	CLDN4	TK1	EPCAM	AZGP1	GAPDH	CALML5
C15orf48	TUBA1B	HLA-DQA2	SFN	CCL28	WFDC2	EPCAM	SERINC2	S100A8	TPD52L1	EFNA1
HLA-DPB1	HLA-DRB5	LYZ	MT1E	CRYAB	TM4SF1	RARRES1	RARRES1	XBP1	PERP	KRT8
HLA-DPA1	HMGN2	CD83	KRT23	WFDC2	EFHD1	HMGA1	FABP7	KRT19	ARMT1	MUC1
BCL2A1	GPX1	LGALS2	CRYAB	KRT23	ANKRD30A	IDH2	S100A8	FXYD3	CCND1	AGR3
MS4A6A	CTSB	IRF7	MT2A	GABRP	TFF3	CKS1B	CLDN3	CRABP2	S100A9	
EREG	FTL	GZMB	TPM2	RCAN1	SERPINA1	CENPF	S100A9	CCND1	S100A6	
CXCL2	APOE	AREG	EGR1	KRT7	MUCL1	AIM1	RP11-206M11.7	CCND1		
				NDRG2		CKB	KRT8	KRT8		
							ATG5	MRPS30		

Table S4: EMILIN and clinicopathological factors for 75 breast cancer patients.

Factors	EMILIN		P-value
	Low n=18	**High** n=57	
Age			
<60	10	24	0.3176
60≦	8	33	
T factor			
T1	9	29	0.9483
T2-4	9	28	
N factor			
N0	9	38	0.2025
N1-3	9	19	
Stage			
I	6	28	0.2407
II-III	12	29	
ER			
Positive	10	29	0.7291
Negative	8	28	
PgR			
Positive	5	20	0.5663
Negative	13	37	
HER2			
Positive	9	26	0.7451
Negative	9	31	
Subtype			
Luminal	4	16	0.8702
Luminal HER2	6	14	
HER2	3	12	
Triple negative	5	15	
Ki-67 (n=70)*			
< 20%	1	20	0.0126
≥ 20%	16	33	

*Ki-67 data were not available for 5 cases.