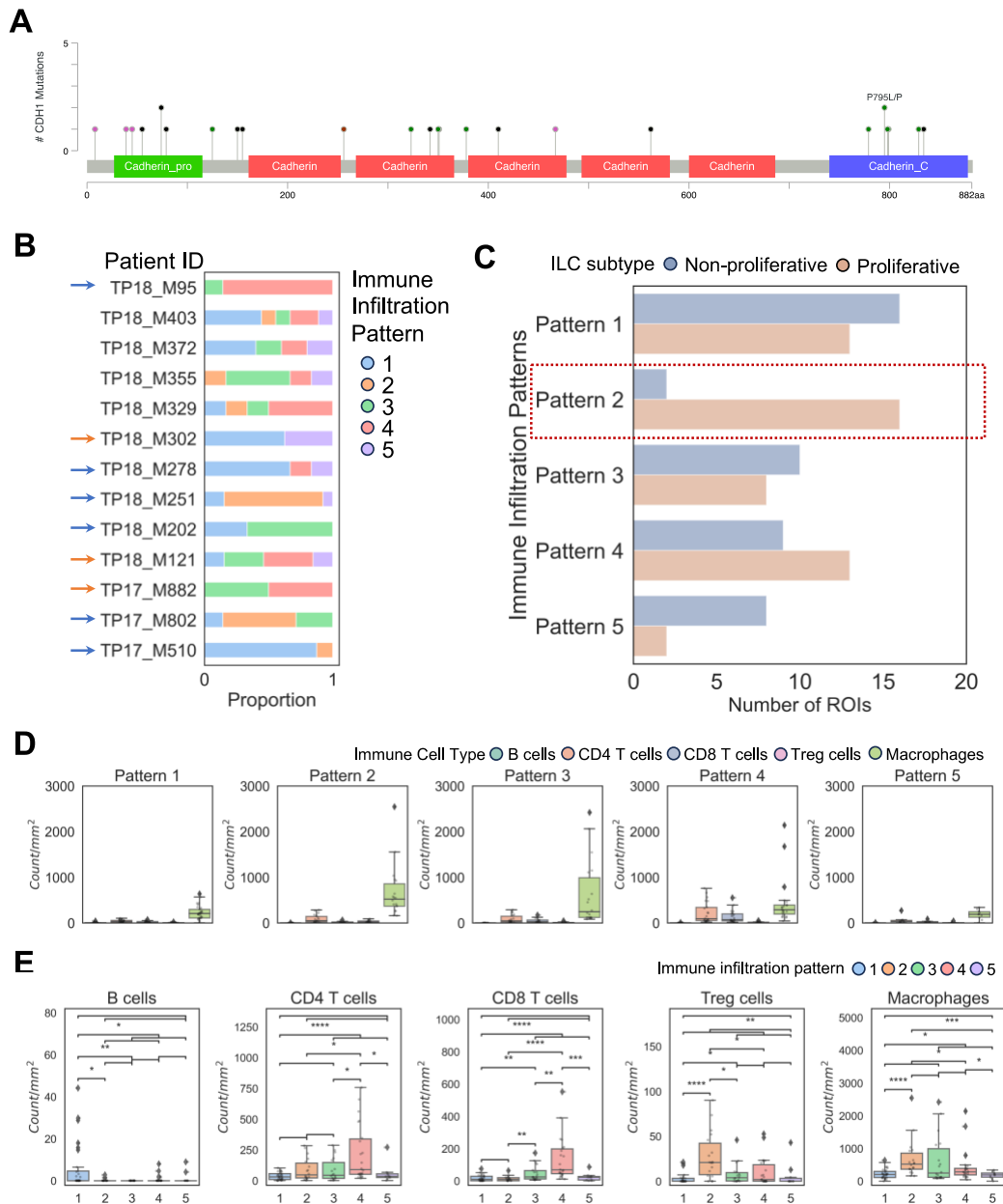


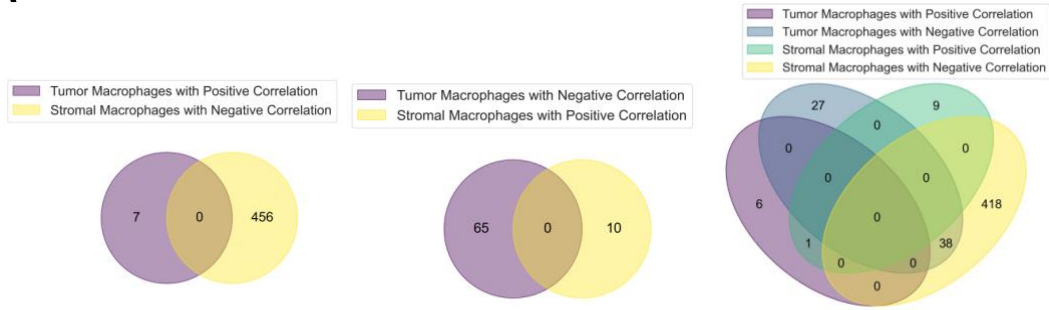
1 Supplementary Figures



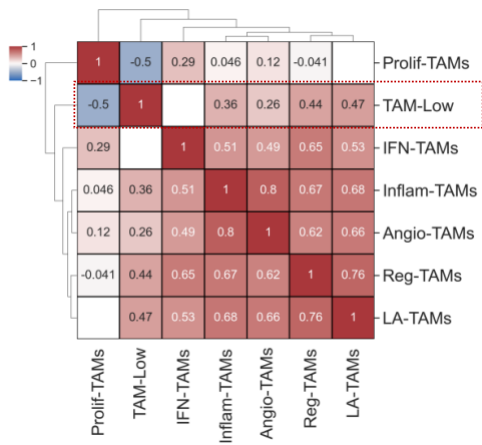
2 3 **Supplementary Figure 1. CDH1 mutation, ILC subtypes, and immune infiltration patterns**

4 A. Short variants of CDH1 detected from RNA-seq. B. Distribution of immune infiltration patterns among patient
5 tumors. Blue arrows, patient with 1 dominant immune pattern. Orange arrows, patients with 2 dominant immune
6 patterns. C. Number of immune infiltration patterns among ROIs in proliferative and non-proliferative ILC tumors. E.
7 Tumor region immune cell infiltration (number/mm²) among immune infiltration patterns, showing each pattern
8 per panel. ****p<0.0001, ***p<0.001, **p<0.01, *p<0.05, comparison (horizontal brackets) with no label, p≥0.05.
9 F. Tumor region immune cell infiltration (number/mm²) among immune infiltration patterns, showing each immune
10 cell type per panel.
11

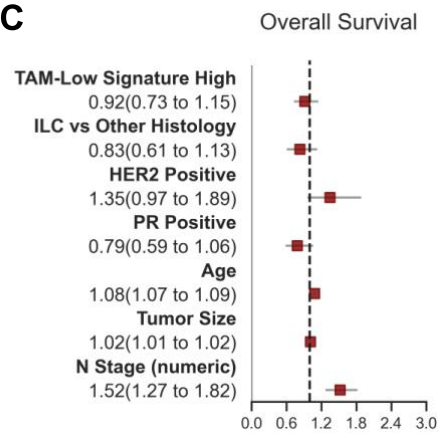
A



B



C



12

13 **Supplementary Figure 2. TAM-Low signature and clinical associations**

14 A Number of overlapped genes with expression positively or negatively correlated to stromal or tumor region
 15 macrophage infiltration (number/mm²). B. Spearman correlation (FDR<0.05) between TAM-Low and other TAM
 16 subtype signatures in SCAN-B ER+ tumors (N=2,776). C. Hazard ratio of overall survival of TAM-Low signature and
 17 demographic-clinical variables in SCAN-B ER+ tumors (N=2,750, excluding entries with missing data in any of the
 18 regression covariates) from multivariate Cox regression.

19

20 **Supplementary Tables**

21 **Supplementary Table 1. Clinical information and computed PAM50 and ILC subtypes from RNA-seq**

Sample ID	Age at diagnosis	Race	Postmenopausal	Pathological grade	Pathological stage	Ki67	ER	PR	HER2	ER IHC score*	ILC Subtype	PAM50
TP17_M605	39	White	No	1	1A	65	+	+	-	140	Non-proliferative	Normal
TP18_M403	67	White	Yes	1	1A	1	+	-	-	140	Non-proliferative	Normal
TP17_M383	41	White	No	3	3C	3	+	+	-	NA	Proliferative	Her2
TP18_M202	56	White	Yes	2	1A	15	+	+	-	225	Non-proliferative	Normal
TP18_M355	61	Other	Yes	2	1A	5	+	+	-	260	Non-proliferative	Normal
TP17_M510	44	White	No	2	1A	15	+	+	-	240	Proliferative	LumB
TP17_M802	47	White	No	2	1A	25	+	+	NA	195	Proliferative	LumA
TP17_M882	57	White	Yes	2	3A	35	+	+	-	300	Proliferative	LumB
TP18_M329	57	White	Yes	2	1B	8	+	+	-	300	Proliferative	Basal
TP17_M378	40	Other	No	3	2A	30	+	+	-	270	Proliferative	LumB
TP17_M384	57	White	Yes	1	2A	5	+	+	-	225	Proliferative	LumA
TP17_M559	66	White	Yes	2	1A	5	+	+	-	260	Non-proliferative	LumA
TP18_M121	50	White	Yes	2	2A	65	+	+	-	230	Non-proliferative	Normal
TP18_M278	75	White	Yes	1	1A	20	+	+	-	179	Non-proliferative	Normal
TP18_M302	56	White	Yes	2	1A	2	+	+	-	290	Non-proliferative	Normal
TP18_M372	62	White	Yes	2	1A	10	+	+	-	290	Proliferative	LumA
TP18_M95	68	White	Yes	2	1A	15	+	+	-	260	Proliferative	LumB
TP18_M251	74	White	Yes	2	1B	12	+	+	-	255	Proliferative	LumB
TP17_M622	79	White	Yes	2	2B	15	+	+	-	200	Proliferative	Basal
TP17_M899	37	White	No	2	2A	2	+	+	-	260	Proliferative	Normal
TP17_M901	45	White	No	2	1A	3	+	+	NA	75	Non-proliferative	Normal

22
 23 *ER IHC score: histochemical score of ER staining, corresponding to sum of tumor cell proportion multiplied by
 24 staining reactivity (<50, negative; 50-100: weakly positive; 101-200: moderately positive; 201-300: strongly
 25 positive). +, positive; -, negative; NA, not available. LumA, luminal A; LumB, luminal B; Basal, basal-like; normal,
 26 normal-like.

27 **Supplementary Table 2. CDH1 mutations identified from RNA-seq from chromosome 16**

Sample ID	Start Position	End Position	Reference Allele	Variant Allele	Protein Change	dbSNP147
A1_S12	68768474	68768474	C	T	Other	.
A1_S12	68801811	68801811	C	T	A102V	rs786202689
A1_S12	68812177	68812177	C	T	Q351*	.
A1_S12	68813423	68813423	G	C	L416F	rs772622537
A1_S12	68829742	68829742	C	T	P795L	.
A1_S12	68829743	68829743	C	T	P795P	.
C2_S13	68783696	68783696	A	G	Other	.
C2_S13	68812076	68812076	C	T	Other	.
C2_S13	68822260	68822260	C	T	Other	.
C2_S13	68833349	68833352	TGAC	-	D834Mfs*11	.
D2_S14	68741164	68741164	A	G	Other	.
D2_S14	68741165	68741165	G	T	Other	.
D2_S14	68772926	68772926	-	A	Other	.
D2_S14	68811819	68811819	C	T	T323I	.
D2_S14	68812174	68812174	C	T	L350F	.
D2_S14	68822210	68822210	C	T	Q641*	rs587782750
E2_S15	68819342	68819342	C	T	S543F	rs148400889
H2_S16	68744554	68744554	C	T	Other	rs7200690
H2_S16	68746891	68746891	A	G	Other	.
H2_S16	68763554	68763554	C	A	Other	.
H2_S16	68774984	68774984	A	G	Other	.
H2_S16	68811631	68811631	C	T	Other	.
H2_S16	68813403	68813403	G	T	E410*	.
H2_S16	68823538	68823538	T	C	A692A	rs1801552
K2_S17	68808403	68808403	C	T	Other	.
K2_S17	68808743	68808743	C	T	G194G	rs786202924
K2_S17	68823538	68823538	T	C	A692A	rs1801552
Q2_S18	68737469	68737469	C	T	Other	rs3743674
Q2_S18	68738383	68738383	C	T	H45H	.
Q2_S18	68775895	68775895	C	T	Other	.
Q2_S18	68801740	68801741	CA	-	T79Rfs*14	.
Q2_S18	68812145	68812145	C	T	T340M	rs61747631
Q2_S18	68819396	68819397	AC	-	T562Sfs*25	.
Q2_S18	68823440	68823440	-	T	D662*	rs730881653
Q2_S18	68828142	68828142	C	T	Other	.
R1_S21	68753598	68753598	A	G	Other	.

R1_S21	68773143	68773143	A	G	Other	.
R1_S21	68809340	68809340	A	G	Other	.
R1_S21	68809342	68809342	A	G	Other	.
R1_S21	68812124	68812125	TC	-	Other	.
R1_S21	68823538	68823538	T	C	A692A	rs1801552
S2_S19	68801879	68801879	C	A	P125T	.
S2_S19	68823538	68823538	T	C	A692A	rs1801552
S2_S19	68829750	68829750	C	T	L798F	.
S2_S19	68829756	68829756	C	T	R800C	rs587782162
T2_S20	68755191	68755191	A	G	Other	.
T2_S20	68757954	68757954	A	G	Other	.
T2_S20	68815595	68815595	C	T	T467T	.
T2_S20	68822234	68822234	C	T	Other	.
T2_S20	68823538	68823538	T	C	A692A	rs1801552
T2_S20	68829693	68829693	C	T	R779W	.
T2_S20	68834203	68834203	C	T	Other	.
O_10_S8	68742490	68742490	C	T	Other	.
O_10_S8	68751036	68751036	C	T	Other	.
O_10_S8	68801726	68801726	C	T	R74*	.
O_10_S8	68812259	68812259	C	T	T378I	.
O_10_S8	68819417	68819417	C	T	T568I	rs786202712
O_11_S9	68808485	68808485	G	-	R150Kfs*65	.
O_11_S9	68811990	68811990	-	A	Other	rs148398896
O_11_S9	68811991	68811991	-	A	Other	rs33945588
O_11_S9	68813274	68813274	C	T	Other	.
O_11_S9	68813293	68813293	C	T	Other	.
O_11_S9	68819200	68819200	C	G	Other	rs9934882
O_11_S9	68822185	68822185	C	T	H632H	rs33969373
O_11_S9	68823538	68823538	T	C	A692A	rs1801552
O_11_S9	68833284	68833284	C	G	Other	rs139757930
O_11_S9	68833484	68833484	C	T	G878G	rs2229044
O_11_S9	68833553	68833553	C	T	Other	rs1801026
O_12_S10	68808493	68808493	-	AG	D155Efs*61	.
O_12_S10	68823538	68823538	T	C	A692A	rs1801552
O_12_S10	68833336	68833336	C	T	S829F	.
O_13_S11	68757182	68757182	A	G	Other	.
O_13_S11	68813336	68813336	C	T	N387N	rs111266450
O_13_S11	68829708	68829708	C	T	R784C	rs775922721
O_1_S1	68737469	68737469	C	T	Other	rs3743674

O_1_S1	68765268	68765268	A	G	Other	.
O_1_S1	68800033	68800033	-	A	Other	rs34387170
O_1_S1	68823538	68823538	T	C	A692A	rs1801552
O_4_S2	68821949	68821949	G	C	Other	rs34582129
O_4_S2	68822268	68822268	C	T	Other	.
O_4_S2	68823538	68823538	T	C	A692A	rs1801552
O_4_S2	68829754	68829754	C	T	P799L	.
O_4_S2	68833844	68833844	C	T	Other	.
O_5_S3	68737469	68737469	C	T	Other	rs3743674
O_5_S3	68795504	68795505	TT	-	Other	.
O_5_S3	68823538	68823538	T	C	A692A	rs1801552
O_5_S3	68831161	68831161	C	T	Other	.
O_6_S4	68738365	68738365	C	T	F39F	.
O_6_S4	68759192	68759192	A	G	Other	.
O_6_S4	68812147	68812148	TA	-	T342Pfs*7	.
O_6_S4	68823538	68823538	T	C	A692A	rs1801552
O_7_S5	68737439	68737439	C	T	L8L	.
O_7_S5	68737464	68737464	G	A	Other	.
O_7_S5	68737469	68737469	C	T	Other	rs3743674
O_7_S5	68738411	68738411	G	-	V55*	.
O_7_S5	68738413	68738413	T	A	Other	.
O_7_S5	68753972	68753972	G	A	Other	rs12926010
O_7_S5	68759633	68759633	G	A	Other	rs12448199
O_7_S5	68812127	68812127	C	T	Other	rs201227194
O_7_S5	68823386	68823386	T	C	Other	rs2276330
O_7_S5	68823538	68823538	T	C	A692A	rs1801552
O_8_S6	68737339	68737339	C	T	Other	.
O_8_S6	68745790	68745790	A	G	Other	rs13335476
O_8_S6	68810351	68810351	C	T	Other	.
O_8_S6	68823538	68823538	T	C	A692A	rs1801552
O_8_S6	68824887	68824887	C	T	Other	.
O_9_S7	68745270	68745270	C	T	Other	.
O_9_S7	68768613	68768613	T	G	Other	rs12448448
O_9_S7	68771354	68771354	A	G	Other	.
O_9_S7	68771356	68771356	A	G	Other	.
O_9_S7	68801726	68801726	C	T	R74*	.
O_9_S7	68810276	68810276	-	TTC	N256_D257insS	.
O_9_S7	68819200	68819200	C	G	Other	rs9934882
O_9_S7	68822185	68822185	C	T	H632H	rs33969373

O_9_S7	68822260	68822260	C	T	Other	.
O_9_S7	68823538	68823538	T	C	A692A	rs1801552
O_9_S7	68824608	68824608	G	T	Other	.
O_9_S7	68824971	68824971	A	C	Other	rs74025315
O_9_S7	68824974	68824974	C	T	Other	.
O_9_S7	68824984	68824984	G	T	Other	.
O_9_S7	68833484	68833484	C	T	G878G	rs2229044
O_9_S7	68833553	68833553	C	T	Other	rs1801026
O_9_S7	68834120	68834120	C	T	Other	rs33956791

28 Somatic SNVs and indels in CDH1 identified from RNA-seq using GATK v4 MuTect2 pipeline. Truncating mutations
29 were marked in red.
30
31
32

Supplementary Table 3. TAM-Low signature and Marker genes of TAM subtypes derived from literature

TAM-Low signature	<p>AASS, ABCA10, ABCA6, ABCA8, ABCA9, ABCC9, ABI3BP, ABT1, ACOT9, ADAM22, ADAM33, ADAMTS1, ADAMTS3, ADAMTS5, ADAMTS9, ADD1, ADD3, ADGRA2, ADGRD1, ADGRL2, AKAP12, AKAP13, AKAP6, ALDH1A1, ALX4, AMOTL1, AMOTL2, ANGPTL1, ANK2, ANKRD11, ANKRD20A12P, ANTXR2, ANXA1, ANXA8, ARHGAP10, ARHGAP6, ARHGEF25, ARID5B, ATP10D, ATP11A, ATP8B2, AXL, BACH1, BACH2, BAG2, BBS2, BCHE, BHLHE22, BICC1, BICD2, BMP1, BNC2, BNIP2, BOC, BRD7, C14orf37, C1S, CACHD1, CACNA1G, CAPN6, CAV1, CAV2, CCDC80, CCDC82, CCL18, CCND2, CD163L1, CD34, CD99, CDH5, CDK11A, CDK6, CEBPB-AS1, CEP112, CEP85L, CES1, CFDP1, CFH, CFI, CHD9, CHL1, CHRDL1, CLCA4, CLEC12A, CLEC4G, CLIC2, CLIP4, CLMP, CNGA1, CNRIP1, COL14A1, COL16A1, COL21A1, COPZ2, CPE, CPNE8, CRCP, CRISPLD2, CRYBG3, CSPG4, CTSG, CTSK, CYP2U1, CYTH3, DAAM2, DAB2, DCBLD2, DCDC2C, DCN, DDR2, DDX19B, DDX60L, DENND2C, DHRS3, DHX38, DIAPH2, DKK2, DLX5, DNAJB4, DNAJC18, DNAJC8, DNM1, DNM3, DOK4, DOK6, DPT, DPYSL2, DPYSL3, DUS2, DZIP1, EBF3, ECM2, EFEMP2, EGFR, EHBP1, EHD2, ELN, EMILIN2, EMP1, EPDR1, ERC1, F13A1, FAM126A, FAM133CP, FAM180A, FAM49A, FAS, FAT4, FBLN1, FBLN2, FBLN5, FCGR2C, FCGRT, FES, FEZ1, FGD5P1, FGFR1OP2, FIGLA, FKBP9, FLNA, FLNC, FLRT2, FOXP2, FRMD3, FRRS1, FSTL1, GAS1, GAS7, GBTG1, GDF10, GEM, GFPT2, GIT2, GLG1, GLI1, GLI2, GLIPR2, GLS, GNG11, GOLGA8R, GOLIM4, GOPC, GPNMB, GRAP, GRID1, GRID2, GRIP2, GSN, HEG1, HERC3, HIF3A, HMCN1, HNMT, HNRNP, HRH1, HSPB6, HTR2A, ID1, ID3, IFI44, IGF1, IGFBP4, IGFBP6, IGSF10, IL1R1, ILK, INVS, ISLR, IST1, ITSN1, IWS1, JAM3, JDP2, KCNB1, KCNJ12, KCNT1, KCNT2, KIAA1614, KLC1, KLHL2, KLHL33, LAMA2, LAMA4, LAMB1, LDB2, LEPR, LIMA1, LINC01279, LMNA, LMOD1, LOC653513, LONRF1, LOX, LOXL4, LPPR4, LRCH2, LRCH3, LRFN5, LRIG3, LRP1, LRP12, LRRK2, LTBP2, LTBP4, LUM, LUZP1, MAF, MAGI2-AS3, MAP1A, MAP1B, MAP3K3, MAP7D3, MBNL1, MCTP1, MEDAG, MEG3, MEGF6, MEIS2, MEOX2, METTL24, MFAP4, MGA, MICU3, MID1, MIR100HG, MIR24-1, MIR655, MIR99AHG, MMP16, MMP19, MMRN1, MOXD1, MPP6, MRAS, MRGPRF, MSN, MX2, MYL9, MYOM1, NEGR1, NEXN, NFATC3, NGDN, NID1, NIN, NMT2, NOM1, NR5A2, NRXN2, ODF3L1, OGN, OLFML1, OMD, OSR2, PALLD, PAPP, PARD3B, PCDH18, PCDH9, PCDHGC3, PCOLCE, PCSK5, PDE2A, PDE3A, PDE8A, PDGFRB, PDGFRL, PI16, PID1, PITPNB, PKD2, PKHD1L1, PLAC9, PLAGL1, PLBD1, PLEKHM2, PLS3, PLSCR4, PNMAL1, PODN, POU6F2, PPFIBP1, PRDM5, PRELID2, PRELP, PREX2, PRKD1, PRKG1, PROS1, PRR5, PRRX1, PRRX2, PTGER2, PTGFR, PTGIS, PTPRH, PTRF, PTX3, PVRL3, RASA3, RASSF1, RBMS2, RBMS3, RBMX2, RBPJ, RCN3, RECK, RFTN2, RFX6, RGL1, RGS6, RNF216, ROCK2, ROR1, RPS6KA2, RUNX1T1, RYR3, SACS, SAMD4A, SCARA5, SCN3A, SEC23A, SEMA3D, SERPINE2, SERPING1, SFRP2, SFRP4, SH3BP5, SH3D19, SH3PXD2B, SHE, SHOX2, SKIDA1, SLC23A2, SLC25A27, SLFN11, SLIT2, SLIT3, SMAD9, SNED1, SNORD112, SNORD114-12, SNORD114-14, SNORD114-18, SNX1, SNX18, SNX29P2, SOCS5, SOD3, SPAG9, SPARCL1, SPOCK1, SPRY1, SRSF4, ST6GALNAC3, STAB2, STAC, STARD9, STEAP4, STX12, STX1B, STXPB1, SYNE1, SYT11, SZRD1, TACC1, TBKBP1, TBX15, TBX18, TCEAL2, TCEAL5, TCF4, TCF7L2, TERF2IP, TFPI, THSD7B, TIMP2, TLE4, TLL1, TLN1, TMEM117, TMEM119, TMEM130, TMEM200A, TNNT3, TNXB, TPM4, TRAM2, TRDN, TRPC1, TSHZ3, TSSC2, TTC7B, TUBB6, TWIST2, UACA, UBDT1, VASN, VCL, VIM, WASF2, WASF3, WBP5, WWTR1, XPNPEP2, ZBTB47, ZC3H18, ZCCHC24, ZEB1, ZFH4, ZFP90, ZNF354C, ZNF438, ZNF521, ZNF697, ZSCAN12, ACVR2A, ALDH1L2, COL5A3, COX19, DNASE1L3, EMX2, FNIP2, FOLR2, FOSB, GUCY1B3, KLF4, L1CAM, LILRB5, LYVE1, MRC1, PIM1, PNMAL2, RNASE1, RYR2, S100A6, SCN2B, SCN9A, SMCO4, SNAPC1, VTRNA2-1, YBX1, ZNF732</p>
Interferon-primed TAM (IFN-TAM)	<p>CASP1, CASP4, CCL2, CCL3, CCL4, CCL7, CCL8, CD274, CD40, CXCL2, CXCL3, CXCL9, CXCL10, CXCL11, IDO1, IFI6, IFIT1, IFIT2, IFIT3, IFITM1, IFITM3, IRF1, IRF7, ISG15, LAMP3, PDCD1LG2, TNFSF10, C1QA, C1QC, CD38, IL4I1, ISG15, TNFSF10, IFI44L</p>

Immune regulatory TAM (Reg-TAM)	CCL2, CD274, CD40, CD80, CD86, CHIT1, CX3CR1, HLA-A, HLA-C, HLA-DQA1, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB5, ICOSLG, IL10, ITGA4, LGALS9, MACRO, MRC1, TGFB2
Inflammatory cytokine-enriched TAM (Inflam-TAM)	CCL2, CCL3, CCL4, CCL5, CCL20, CCL3L1, CCL3L3, CCL4L2, CCL4L4, CXCL1, CXCL2, CXCL3, CXCL5, CXCL8, GOS2, IL1B, IL1RN, IL6, INHBA, KLF2, KLF6, NEDD9, PMAIP1, S100A8, S100A9, SPP1
Proangiogenic TAM (Angio-TAM)	ADAM8, AREG, BNIP3, CCL2, CCL4, CCL20, CD163, CD300E, CD44, CD55, CEBPB, CLEC5A, CTSB, EREG, FCN1, FLT1, FN1, HES1, IL1B, IL1RN, IL8, MAF, MIF, NR1H3, OLR1, PPARG, S100A8, S100A9, S100A12, SERPINB2, SLC2A1, SPIC, SPP1, THBS1, TIMP1, VCAN, VEGFA
Lipid-associated TAMs (lipid-associated TAM)	ACP5, AOPE, APOC1, ATF1, C1QA, C1QB, C1QC, CCL18, CD163, CD36, CD63, CHI3L1, CTSB, CTSD, CTSL, F13A1, FABP5, FOLR2, GPNMB, IRF3, LGALS3, LIPA, LPL, MACRO, MerTK, MMP7, MMP9, MMP12, MRC1, NR1H3, NRF1, NUPR1, PLA2G7, RNASE1, SPARC, SPP1, TFD2, TREM2, ZEB1
Proliferating TAM (Prolif-TAM)	CCNA2, CDC45, CDK1, H2AFC, HIST1H4C, HMGB1, HMGN2, MKI67, RRM2, STMN1, TOP2A, TUBA1B, TUBB, TYMS