

Supplementary Table 1. Correlations between the two CAF subtypes and clinical features in the TCGA cohort

		Total	CAF subtype (n, %)		P-value	FDR
			FA_L	FA_H		
Sex	Male	241 (64.2)	76 (60.8)	165 (66)	0.3608	0.4961
	Female	134 (35.8)	49 (39.2)	85 (34)		
Age	≤65 years	164 (43.7)	51 (40.8)	113 (45.2)	0.4358	0.4993
	>65 years	207 (55.2)	73 (58.4)	134 (53.6)		
	NA	4 (1.1)	1 (0.8)	3 (1.2)		
Race	Asian	74 (19.7)	31 (24.8)	43 (17.2)	0.0070	0.0193
	Black	11 (2.9)	7 (5.6)	4 (1.6)		
	White	238 (63.5)	67 (53.6)	171 (68.4)		
	NA	52 (13.9)	20 (16)	32 (12.8)		
Stage	Stage I	53 (14.1)	32 (25.6)	21 (8.4)	0.0003	0.0017
	Stage II	111 (29.6)	32 (25.6)	79 (31.6)		
	Stage III	150 (40)	47 (37.6)	103 (41.2)		
	Stage IV	38 (10.1)	9 (7.2)	29 (11.6)		
	NA	23 (6.2)	5 (4)	18 (7.2)		
T	T1	19 (5.1)	16 (12.8)	3 (1.2)	7.097e-05	0.0008
	T2	80 (21.3)	27 (21.6)	53 (21.2)		

	T3	168 (44.8)	53 (42.4)	115 (46)		
	T4	100 (26.7)	29 (23.2)	71 (28.4)		
	TX	8 (2.1)	0 (0)	8 (3.2)		
N	N0	111 (29.6)	45 (36)	66 (26.4)	0.2675	0.4204
	N1	97 (25.9)	31 (24.8)	66 (26.4)		
	N2	75 (20)	24 (19.2)	51 (20.4)		
	N3	74 (19.7)	20 (16)	54 (21.6)		
	NX	16 (4.3)	5 (4)	11 (4.4)		
	NA	2 (0.5)	0 (0)	2 (0.8)		
M	M0	330 (88)	112 (89.6)	218 (87.2)	0.6627	0.6627
	M1	25 (6.7)	7 (5.6)	18 (7.2)		
	MX	20 (5.3)	6 (4.8)	14 (5.6)	0.4539	0.4993
Therapy outcome	CR/PR	207 (55.2)	73 (58.4)	134 (53.6)		
	PD/SD	59 (15.7)	17 (13.6)	42 (16.8)		
	NA	109 (29.1)	35 (28)	74 (29.6)	0.0154	0.0339
Grade	G1	10 (2.7)	4 (3.2)	6 (2.4)		
	G2	137 (36.5)	57 (45.6)	80 (32)		
	G3	219 (58.4)	60 (48)	159 (63.6)		
	GX	9 (2.4)	4 (3.2)	5 (2)		

Molecular subtype	EBV	27 (7.2)	10 (8)	17 (6.8)	0.0013	0.0048
	MSI	61 (16.3)	24 (19.2)	37 (14.8)		
	GS	45 (12)	4 (3.2)	41 (16.4)		
	CIN	207 (55.2)	72 (57.6)	135 (54)		
	NA	35 (9.3)	15 (12)	20 (8)		
MSI_status	MSI-H	67 (17.9)	29 (23.2)	38 (15.2)	0.0265	0.0486
	MSS	252 (67.2)	72 (57.6)	180 (72)		
	MSI-L	56 (14.9)	24 (19.2)	32 (12.8)		

P-values were obtained using Fisher's exact test; FDR was corrected by the Benjamini & Hochberg methods. Bold values indicate statistical significance ($P < 0.05$) for both *P*-values and FDR. CR, complete response; FDR, false discovery rate; M, metastasis; N, lymph node; PD, progressive disease; PR, partial response; SD, stable disease; T, tumor. Epstein–Barr virus: EBV, microsatellite instable: MSI, genetically stable: GS, and chromosomal instability: CIN.

Supplementary Table 2. Correlations between the two CAF subtypes and clinical features in the GSE84437 cohort

		Total (n, %)	Subtypes (n, %)		P-value	FDR
			FA_L	FA_H		
Sex	Male	296 (68.4)	100(69.9)	196(67.6)	0.6612	0.8816
	Female	137 (31.6)	43(30.1)	94(32.4)		
Age	≤65 years	293 (67.7)	94(65.7)	189(65.2)	1	1
	>65 years	150 (32.3)	49(34.3)	101(34.8)		
T	T1	11 (2.5)	8(5.6)	3(1.0)	2.059e-05	8.236e-05
	T2	38 (8.8)	20(14.0)	18(6.2)		
	T3	92 (21.2)	39(27.3)	53(18.3)		
	T4	292 (67.5)	76(53.1)	216(74.5)		
N	N0	80 (18.5)	39(27.3)	41(14.2)	0.01126	0.0226
	N1	188 (43.4)	58(40.5)	130(44.8)		
	N2	132 (30.5)	38(26.6)	94(32.4)		
	N3	33 (7.6)	8(5.6)	25(8.6)		

P-values were obtained using Fisher's exact test; FDR was corrected by the Benjamini &

Hochberg methods. Bold values indicate statistical significance ($P < 0.05$) for both P -values and FDR. T: tumor; N, lymph node. FDR, false discovery rate.

Supplementary Table 3. Correlations between the two CAF subtypes and clinical features in the GSE26253 cohort

		Total	Subtype (n, %)		P -value	FDR
			FA_L	FA_H		
Sex	Male	152(35.2)	35(26.3)	117(39.1)	0.0119	0.0238
	Female	280(64.8)	98(73.7)	182(60.9)		
Age	≤65 years	390(90.3)	118(88.7)	272(91.0)	0.4840	0.4840
	>65 years	42(9.7)	15(11.3)	27(9.0)		
AJCC Stage	Stage I	68(15.7)	24(18.0)	44(14.7)	0.1096	0.1315
	Stage II	167(38.7)	59(44.4)	108(36.1)		
	Stage III	130(30.1)	30(22.6)	100(33.5)		
	Stage IV	67(15.5)	20(15.0)	47(15.7)		
Lauren	intestinal	139(32.2)	58(43.6)	81(27.1)	0.0028	0.0084
	diffuse	280(64.8)	71(53.4)	209(69.9)		
	mixed	13(3.0)	4(3.0)	9(3.0)		
Location	distal	226(52.3)	68(51.1)	158(52.8)	0.0593	0.0890
	mid	139(32.2)	45(33.9)	94(31.5)		
	cardia	54(12.5)	12(9.0)	42(14.0)		

	whole	13(3.0)	8(6.0)	5(1.7)		
Subgroup	MP	35(8.1)	0(0)	35(11.7)	1.601e-06	9.606e-06
	EP	397(91.9)	133(100.0)	264(88.3)		

P-values were obtained using Fisher's exact test; FDR was corrected by the Benjamini & Hochberg methods. Bold values indicate statistical significance ($P < 0.05$) for both *P*-values and FDR. FDR, false discovery rate; M-P, mesenchymal phenotype; E-P, epithelial phenotype; AJCC, American Joint Committee on Cancer.

Supplementary Table 4. Correlations between the two CAF subtypes and clinical features in the GSE66229 cohort

		Total	Subtype (n, %)		<i>P</i>	FDR
			FA_L	FA_H		
Sex	Male	199(66.3)	126(73.3)	73(57.0)	0.0043	0.0093
	Female	101(33.7)	46(26.7)	55(43.0)		
Age	≤65 years	172(57.3)	89(51.7)	83(64.8)	0.0253	0.0329
	>65 years	128(42.7)	83(48.3)	45(35.2)		
Stage	Stage I	30(10.0)	21(12.2)	9(7.0)	9.694e-05	0.0003
	Stage II	97(32.3)	71(41.3)	26(20.3)		
	Stage III	96(32.0)	43(25.0)	53(41.4)		
	Stage IV	77((25.7)	37(21.5)	40(31.3)		
T	T2	186(62.0)	129(75.0)	57(44.5)	8.4e-08	2.73e-07
	T3	91(30.3)	31(18.6)	60(46.9)		

	T4	21(7.0)	10(5.8)	11(8.6)		
	NA	2((0.7)	2(1.2)	0(0)		
N	N0	38(12.6)	25(14.5)	13(10.1)	0.1733	0.2048
	N1	131(43.7)	81(47.1)	50(39.1)		
	N2	80(26.7)	39(22.7)	41(32.0)		
	N3	51(17.0)	27(16.7)	24(18.8)		
M	M0	273(91.0)	163(94.8)	110(85.9)	0.0131	0.0213
	M1	27(9)	9(5.2)	18(14.1)		
Perineural invasion	(+)	88(29.3)	41(23.8)	47(36.7)	0.01575	0.0228
	(-)	159(53)	100(58.1)	59(46.1)		
	NA	53(17.7)	31(18.1)	22(17.2)		
Venous invasion	(+)	44(14.7)	29(16.9)	15(11.7)	0.2936	0.3181
	(-)	129(43.0)	73(42.4)	56(43.8)		
	NA	127(42.3)	70(40.7)	57(44.5)		
Lymphovascular invasion	(+)	205(68.3)	120(69.8)	85(66.4)	1	1
	(-)	73(24.3)	43(25.0)	30(23.4)		
	NA	22(7.3)	9(5.2)	13(10.2)		
MLH1 IHC	(+)	234(78.0)	124(72.1)	110(85.9)	0.0069	0.0128
	(-)	64(21.3)	46(26.7)	18(14.1)		

	NA	2(0.7)	2(1.2)	0(0)		
Lauren	diffuse	135(45.0)	52(30.2)	83(64.9)	9.708e-09	4.21E-08
	intestinal	146(48.7)	105(61.1)	41(32.0)		
	mixed	19((6.3)	15(8.7)	4(3.1)		
E-P phenotype	EP	216(72.0)	170(98.8)	46(35.9)	0	0
	MP	84(28.0)	2(1.2)	82(64.1)		
ACRG subtypes	TP53positive	79(26.3)	54(31.4)	25(19.5)	0	0
	TP53neg	107(35.7)	70(40.7)	37(28.9)		
	MSI	68(22.7)	47(27.3)	21(16.4)		
	EMT	46(15.3)	1(0.6)	45(35.2)		

P-values were obtained using Fisher's exact test; FDR was corrected by the Benjamini & Hochberg methods. Bold values indicate statistical significance ($P < 0.05$) for both *P*-values and FDR. FDR, false discovery rate; M-P, mesenchymal phenotype; E-P, epithelial phenotype; ACRG, Asian Cancer Research Group. T, tumor; M, metastasis; N, lymph node; MSI: microsatellite instable.

Supplementary Table 5. Correlations between the two CAF subtypes and clinical features in the GSE15459 cohort

		Total	Subtype (n, %)		<i>P</i> -value	FDR
			FA_L	FA_H		
Sex	Male	125(65.1)	40(71.4)	85(62.5)	0.2498	0.3123
	Female	67(34.9)	16(28.6)	51((37.5)		

Age	≤65 years	85(44.3)	22(39.3)	63(46.3)	0.4256	0.4256
	>65 years	107(55.7)	34(60.7)	73(53.7)		
Stage	Stage I	31(16.1)	15(28.8)	16(11.8)	0.0517	0.0862
	Stage II	29(15.1)	10(17.9)	19(14.0)		
	Stage III	72(37.5)	17(30.3)	55(40.4)		
	Stage IV	60(31.3)	14(25.0)	46(33.8)		
Lauren	intestinal	99(51.5)	39(69.6)	60(44.1)	7.948e-06	2.081e-06
	diffuse	75(39.1)	8(14.3)	67(49.3)		
	mixed	18(9.4)	9(16.1)	9(6.6)		
Subtype	Unstable	31(16.1)	5(9.0)	26(19.0)	8.325e-06	2.081e-06
	Proliferative	70(36.5)	34(70.7)	36(26.5)		
	Metabolic	40(20.8)	17(30.3)	23(17.0)		
	Invasive	51(26.6)	0(0)	51(37.5)		

P-values were obtained using Fisher's exact test; FDR was corrected by the Benjamini & Hochberg methods. Bold values indicate statistical significance ($P < 0.05$) for both *P*-values and FDR. FDR, false discovery rate.