Table SI. Distribution of hypoxic and normoxic CAFs across single-cell clusters.

Cluster	Hypoxic CAF counts	Normoxic CAF counts
1	2,520	144
2	1,425	601
3	1,529	253
4	1,387	23
5	1161	0
6	1095	0
7	1057	23
8	1045	20
9	894	149
10	725	189
11	303	546
12	465	250
13	38	571
14	54	549
15	11	261

CAF, cancer-associated fibroblast.

Table SII. Overlapping 59 genes that were upregulated in both hypoxic cancer-associated fibroblast and hypoxic HCT116 and HT29.

Gene name	Fold Change	Fold Change
SNORA29	742.34	660.167
SNORA7B	126.911	483.696
SNORA46	140.782	429.25
SNORA55	267.225	305.544
SLC2A3	983.099	112.657
KRT17	52.21	100.013
IFNL2	22.022	97.667
CA9	32.125	84.076
XAF1	24.903	76.619
NDRG1	1836.26	75.708
IFNL3	10.84	59.795
ANGPTL4	17.288	48.286
CREB5	15.479	43.58
CTGF	8.468	41.774
IFI27	13.459	40.478
ANKRD37	8.538	39.047
IFI44L	20.769	38.652
DUSP10	40.739	37.039
EDN2	238.164	32.916
TNFAIP3	19.486	30.364
IFITM1	30.086	29.854
ETS1	18.4	27.426
BCL6	9.863	27.221
KDM3A	31.055	25.521
GBP1	14.761	25.089
IL1RAP	30.713	24.107
PDK1	12.989	24.009
PFKFB4	28.44	23.408
PCAT6	32.217	20.981
RSAD2	15.765	20.141
CPEB2	22.972	20.054
EPSTI1	22.972	20.054

P4HA1	15.954	19.536
SUMO4	17.959	18.566
PAG1	13.152	18.378
BNIP3L	10.06	18.067
IFI16	24.382	17.802
HIST1H2AK	44.594	16.575
REC8	16.51	15.731
GPR146	8.992	15.496
DBP	11.36	15.036
MX1	32.945	14.48
SEPP1	8.573	13.824
ALDOC	108.415	13.791
MMP28	40.118	13.56
ABL2	23.483	13.502
KRT16	16.007	12.957
PTHLH	49.919	12.798
OAS2	8.496	12.626
CYP2E1	14.14	12.341
UCA1	13.088	12.239
TNNT2	12.096	12.147
PPP1R3B	18.833	11.875
PPFIA4	21.091	11.799
LMO7-AS1	43.98	11.637
HIST1H3E	10.636	11.599
RBM5-AS1	15.195	11.539
EGLN3	8.491	11.129
BHLHE40	25.594	10.999
LOC100507291	260.817	10.975
UBA7	12.122	10.934
NFATC2	16.093	10.715
HIST1H2BM	43.641	9.98
KLHL24	31.357	9.81
GEM	30.773	9.804
IL32	24.406	9.69
OVGP1	9.455	9.643
RNF103-CHMP3	15.636	9.614

DDIT3	21.247	9.532
CFB	22.435	9.441
CAND1.11	14.341	9.441
PLOD2	35.063	9.236
LRP1	9.409	9.089
NDUFA4L2	2008.541	8.975
AHNAK2	20.183	8.915
KRTAP5-2	10.465	8.864
TCP11L2	24.6	8.823
DUSP5	18.774	8.761
FERMT2	12.504	8.73
CREBRF	71.256	8.703
OPTN	9.589	8.681
ADM	54.172	8.554
ISG20	23.981	8.548
NDNF	38.713	8.518
RPS15AP10	16.642	8.392
C7orf61	8.357	8.392
LOC100129617	16.111	8.392
HIST2H2BE	14.648	8.287
MIR210HG	41.143	8.28
LSMEM1	9.571	8.095
BTG1	9.842	8.039

Gene name (59 genes)

SLC2A3

CA9

XAF1

ANGPTL4

CREB5

CTGF

IFI27

ANKRD37

DUSP10

TNFAIP3

KRT16

IFITM1

BCL6

KDM3A

GBP1

IL1RAP

PFKFB4

PCAT6

CPEB2

EPSTI1

P4HA1

GEM

SUMO4

PAG1

BNIP3L

IFI16

REC8

GPR146

DBP

ALDOC

MMP28

ABL2

FERMT2

Table SIII. Details of RAS mutations, including KRAS and NRAS.

	RAS mutation	
	Immature (n=10)	Mature (n=11)
KRAS, n		
G12D/G12V	6/3	2/4
G13A/G13D/G13R	0	1/2/1
K117N	0	1
NRAS, n		
Q61K	1	0

RAS, rat sarcoma oncogene; KRAS, Kirsten rat sarcoma viral oncogene homolog; NRAS, neuroblastoma RAS viral oncogene homolog.