

Table SI. Western blotting antibodies.

Antibody	Dilution	Cat. no.	Supplier
GAPDH	1:10,000	ab181602	Abcam
Goat anti-rabbit secondary	1:20,000	7076S	Cell Signaling Technology, Inc.
Goat anti-mouse secondary	1:20,000	sc-2357	Santa Cruz Biotechnology, Inc.
Phosphorylated p42/44 MAPK	1:2,000	4370S	Cell Signaling Technology, Inc.
p42/44 MAPK	1:2,000	4696S	Cell Signaling Technology, Inc.
E-cadherin	1:1,000	A20798	ABclonal Biotech Co., Ltd.
N-cadherin	1:500	A19083	ABclonal Biotech Co., Ltd.
Vimentin	1:1,000	A19607	ABclonal Biotech Co., Ltd.
MMP1	1:1,000	A22080	ABclonal Biotech Co., Ltd.
Fibronectin	1:500	ab2413	Abcam

Table SII. Primer sequences.

Target	Forward, 5'→3'	Reverse, 5'→3'
18S	GTAACCCGTTGAACCCATT	CCATCCAATCGGTAGTAGCG
CDH1	CGAGAGCTACACGTTACGG	GGGTGTCGAGGGAAAAATAGG
CDH2	TGGGAAATGGAACTTGATGGC	AGTTGCTAAACTTCACTGAAAGGA
VIM	TGTCCAAATCGATGTGGATGTTTC	TTGTACCATTCTTCTGCCTCCTG
MMP1	ATGCGAACAATCCCTTCTACC	TTTCCTCAGAAAGAGCAGCATCG
TGF-β1	GGCCAGATCCTGTCCAAGC	GTGGGTTTCCACCATTAGCAC
SMAD3	TGGACGCAGGTTCTCCAAAC	CCGGCTCGCAGTAGGTAAC
JUNB	ACGACTCATACACAGCTACGG	GCTCGGTTTCAGGAGTTTGTAGT
SLC20A1	TCCTTTGGTGGACTACCTATGG	CGGATGGTTTCGCTCACTTTG

CDH, Cadherin; VIM, Vimentin; SLC20A1, solute carrier family 20 member 1.

Table SIII. Clinical characteristic baseline for databases.

A, ICGC-ARGO baseline				
Clinical characteristic (%)	KRAS wild-type (n=351)	KRAS mutant (n=286)	Total (n=637)	P-value
Sex				0.112
Male	200 (57.0)	144 (50.3)	344 (54.0)	
Female	151 (43.0)	142 (49.7)	293 (46.0)	
Age, years				0.750
<50	81 (23.1)	70 (24.5)	151 (23.7)	
≥50	270 (76.9)	216 (75.5)	486 (76.3)	
CMS				<0.001
1	30 (8.5)	35 (12.2)	65 (10.2)	
2	157 (44.7)	70 (24.5)	227 (35.6)	
3	21 (6.0)	67 (23.4)	88 (13.8)	
4	105 (29.9)	64 (22.4)	169 (26.5)	
NA	38 (10.8)	50 (17.5)	88 (13.8)	
pT stage				0.223
1	27 (7.7)	16 (5.6)	43 (6.8)	
2	66 (18.8)	72 (25.2)	138 (21.7)	
3	233 (66.4)	179 (62.6)	412 (64.7)	
4	25 (7.1)	19 (6.6)	44 (6.9)	
pN stage				0.289
N0	224 (63.8)	194 (67.8)	418 (65.6)	
N+	127 (36.2)	92 (32.2)	219 (34.4)	
Metachronous metastasis				0.040
No	320 (91.2)	246 (86.0)	566 (88.9)	
Yes	31 (8.8)	40 (14.0)	71 (11.1)	
B, MSKCC				
Clinical characteristic (%)	KRAS wild-type (n=213)	KRAS mutant (n=144)	Total (n=357)	P-value
Sex				0.003
Male	137 (38.4)	70 (19.6)	207 (58.0)	
Female	76 (21.3)	74 (20.7)	150 (42.0)	
Age, years				0.060
<50	68 (19.0)	60 (16.8)	128 (35.9)	
≥50	145 (40.6)	84 (23.5)	229 (64.1)	
CMS				0.001
1	3 (0.8)	9 (2.5)	12 (3.4)	
2	20 (5.6)	5 (1.4)	25 (7.0)	

3	10(2.8)	15(4.2)	25(7.0)	
4	24(6.7)	8(2.2)	32(9.0)	
NA	156(43.7)	107(30.0)	263(73.7)	
Tumorlocation				0.675
Upper rectum	68(19.0)	43(12.0)	111(31.1)	
Middle rectum	96(26.9)	61(17.1)	157(44.0)	
Lower rectum	48(13.4)	38(10.6)	86(24.1)	
NA	1(0.3)	2(0.6)	3(0.8)	
ypT stage				0.991
0-Tis	42(11.8)	30(8.4)	72(20.2)	
1	12(3.4)	8(2.2)	20(5.6)	
2	50(14.0)	32(9.0)	82(23.0)	
3	42(11.8)	26(7.3)	68(19.0)	
4	4(1.1)	2(0.6)	6(1.7)	
NA	63(17.6)	46(12.9)	109(30.5)	
ypN stage				0.978
N0	109(30.5)	72(20.2)	181(50.7)	
N+	27(7.6)	18(5.0)	45(12.6)	
NA	77(21.6)	54(15.1)	213(59.7)	
Metachronousmetastasis				0.077
No	185(51.8)	115(32.2)	300(84.0)	
Yes	28(7.8)	29(8.1)	57(16.0)	

### C, Sidra-LUMCAC-ICAM

Clinicalcharacteristic (%)	KRASwild-type (n=147)	KRASmutant (n=77)	Total(n=224)	P-value
Sex				0.972
Male	76(33.9)	40(17.9)	116(51.8)	
Female	71(31.7)	37(16.5)	108(48.2)	
Age, years				0.776
<50	10(4.5)	4(1.8)	14(6.3)	
≥50	137(61.2)	73(32.6)	210(93.8)	
CMS				0.838
1	21(9.4)	9(4.0)	30(13.4)	
2	37(16.5)	17(7.6)	54(24.1)	
3	32(14.3)	15(6.7)	47(21.0)	
4	27(12.1)	16(7.1)	43(19.2)	
Mixed	30(13.4)	20(8.9)	50(22.2)	
Tumorlocation				0.079

Righthemicolon	66(29.5)	35(15.6)	101(45.1)	
Transversecolon	6(2.7)	9(4.0)	15(6.7)	
Lefthemicolon	75(33.5)	33(14.7)	108(48.2)	
pT stage				0.292
1	9(4.0)	4(1.8)	13(5.8)	
2	35(15.6)	11(4.9)	46(20.5)	
3	93(41.5)	58(25.9)	151(67.4)	
4	10(4.5)	4(1.8)	14(6.3)	
pN stage				<0.001
N0	129(57.6)	13(5.8)	142(63.4)	
N+	18(8.0)	64(28.6)	82(36.6)	
Metachronousmetastasis				0.091
No	129(57.9)	61(27.2)	190(84.8)	
Yes	18(8.0)	16(7.1)	34(15.2)	

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ICGC-ARGO, The International Cancer Genome Consortium Accelerating Research in Genomic Oncology; CMS, Consensus Molecular Subtypes; MSKCC, Memorial Sloan-Kettering Cancer Center; LUMC AC-ICAM, Leiden University Medical Center Atlas and Compass of Immune-Cancer-Microbiome interactions

Table SIV. Clinical characteristic baseline of databases.

A, ICGC-ARGOKRAS-MUTchemotherapy						
Clinical characteristic (%)	Before matching			After matching		
	Noadjuvant chemotherapy (n=171)	Adjuvant chemotherapy (n=115)	P-value	Noadjuvant chemotherapy (n=79)	Adjuvant chemotherapy (n=79)	P-value
Sex			0.074			0.750
Male	94 (55.0)	50 (43.5)		41 (51.9)	44 (55.7)	
Female	77 (45.0)	65 (56.5)		38 (48.1)	35 (44.3)	
Age, years			0.001			0.001
<50	30 (17.5)	40 (34.8)		9 (11.4)	28 (35.4)	
≥50	141 (82.5)	75 (65.2)		70 (88.6)	51 (64.6)	
pT stage			<0.001			.387
1	15 (8.8)	1 (0.9)		2 (2.5)	0 (0.0)	
2	58 (33.9)	14 (12.2)		9 (11.4)	9 (11.4)	
3	90 (52.6)	89 (77.4)		62 (78.5)	60 (75.9)	
4	8 (4.7)	11 (9.6)		6 (7.6)	10 (12.7)	
pN stage			<0.001			.868
N0	143 (83.6)	51 (44.3)		51 (64.6)	50 (63.3)	
N+	28 (16.4)	64 (55.7)		28 (10.4)	29 (12.5)	
B, ICGC-ARGOKRAS-WT CRC chemotherapy						
Clinical characteristic (%)	Before matching			After matching		
	Noadjuvant chemotherapy (n=226)	Adjuvant chemotherapy (n=175)	P-value	Noadjuvant chemotherapy (n=81)	Adjuvant chemotherapy (n=81)	P-value
Sex			>0.999			0.874
Male	130 (57.5)	101 (57.7)		48 (59.3)	46 (56.8)	
Female	96 (42.5)	74 (42.3)		33 (40.7)	35 (43.2)	
Age, years			0.009			0.167
<50	41 (18.1)	52 (29.7)		12 (14.8)	20 (24.7)	
≥50	185 (81.9)	123 (70.3)		69 (85.2)	61 (75.3)	
pT stage			<0.001			0.637
1	24 (10.6)	5 (2.9)		3 (3.7)	1 (1.2)	

2	70 (31.0)	13 (7.4)		5 (6.2)	8 (9.9)	
3	123 (54.4)	140 (80.0)		64 (79.0)	63 (77.8)	
4	9 (4.0)	17 (9.7)		9 (11.1)	9 (11.1)	
pN stage			<0.001			>0.999
N0	192 (85.0)	54(30.9)		51 (63.0)	51 (63.0)	
N+	34(15.0)	121(69.1)		30(27.0)	30(27.0)	
C, MSKCCKRAS-MUTchemotherapy						
Clinicalcharacteristic (%)	Beforematching			Aftermatching		
	Noadjuvantchemo(n=52)	Adjuvantchemo(n=24)	P-value	Noadjuvantchemo(n=24)	Adjuvantchemo(n=24)	P-value
Sex			0.344			>0.999
Male	20(26.3)	12(15.8)		12 (25.0)	12 (25.0)	
Female	32(42.1)	12(15.8)		12 (25.0)	12 (25.0)	
Age, years			0.715			0.562
<50	24(31.6)	10(13.2)		12(25.0)	10(20.8)	
≥50	28(36.8)	14(18.4)		12(25.0)	14(29.2)	
Tumorlocation			0.113			0.484
Upper rectum	22(28.9)	5(6.6)		8(16.7)	5(10.4)	
Middle rectum	18(23.7)	14(18.4)		10(20.8)	14(29.2)	
Lower rectum	12(15.8)	5(6.6)		6(12.5)	5(10.4)	
ypT stage			0.541			>0.999
0-Tis	16(21.1)	4(5.3)		4(8.3)	4(8.3)	
1	4(5.3)	4(5.3)		4(8.3)	4(8.3)	
2	17(22.4)	9(11.8)		9(18.8)	9(18.8)	
3	14(18.4)	7(9.2)		7(14.6)	7(14.6)	
4	1(1.3)	0 (0.0)		0 (0.0)	0 (0.0)	
ypN stage			0.708			0.731
N0	41(53.9)	18(23.7)		19(39.6)	18(37.5)	
N+	11(14.5)	6(7.9)		5(10.4)	6(12.5)	
D, MSKCCKRAS-WTchemotherapy						
Clinicalcharacteristic (%)	Beforematching			Aftermatching		
	Noadjuvantchemo(n=84)	Adjuvantchemo(n=32)	P-value	Noadjuvantchemo(n=32)	Adjuvantchemo(n=32)	P-value
Sex			0.270			0.200

Male	54(46.6)	17(14.7)		22(34.4)	17(26.6)	
Female	30(25.9)	15(12.9)		10(15.6)	15(23.4)	
Age, years			0.121			0.777
<50	34(29.3)	8(6.9)		9(14.1)	8(12.5)	
≥50	50(43.1)	24(20.7)		23(35.9)	24(37.5)	
Tumorlocation			0.855			0.855
Upper rectum	32(27.6)	14(12.1)		13(20.3)	14(21.9)	
Middle rectum	38(32.8)	13(11.2)		16(25.0)	13(21.3)	
Lower rectum	14(12.1)	5(4.3)		3(4.7)	5(7.8)	
ypT stage			0.512			0.750
0-Tis	23(19.8)	8(6.9)		8(12.5)	8(12.5)	
1	6(5.2)	3(2.6)		3(4.7)	3(9.4)	
2	28(24.1)	12(10.3)		13(20.34)	12(18.8)	
3	26(22.4)	7(6.0)		8(12.5)	7(10.9)	
4	1(0.9)	2(1.7)		0 (0.0)	2(3.1)	
ypN stage			0.120			0.708
N0	65(56.0)	29(25.0)		27(42.2)	29(45.3)	
N+	19(16.4)	3(2.6)		5(7.8)	3(4.7)	
E, Sidra-LUMCAC-ICAMKRAS-MUTCRCchemotherapy						
Clinicalcharacteristic (%)	Beforematching			Aftermatching		
	Noadjuvantchemo(n=60)	Adjuvantchemo(n=17)	P-value	Noadjuvantchemo(n=13)	Adjuvantchemo(n=13)	P-value
Sex			0.314			0.695
Male	33(42.9)	7(9.1)		7(26.9)	6(23.1)	
Female	27(35.1)	10(13.0)		6(23.1)	7(26.9)	
Age, years			0.210			>0.999
<50	2(2.6)	2(2.6)		1(3.8)	1(3.8)	
≥50	58(75.3)	15(19.5)		12(46.2)	12(46.2)	
Tumorlocation			0.005			0.760
Upper	24(31.2)	11(14.3)		8(30.8)	9(34.6)	
Middle	4(5.2)	5(6.5)		4(15.4)	3(11.5)	
Lower	32(41.6)	1(1.3)		1(3.8)	1(3.8)	
pT stage			0.888			>0.999

1	3(3.9)	1(1.3)		1(3.8)	1(3.8)	
2	8(10.4)	3(3.9)		3(11.5)	3(11.5)	
3	47(61.0)	11(14.3)		9(34.9)	9(34.9)	
4	2(2.6)	2(2.6)		0 (0.0)	0 (0.0)	
pN stage			<0.001			0.411
N0	4(5.2)	9(11.7)		3(11.5)	6(23.1)	
N+	56(72.7)	8(10.4)		10(38.5)	7(26.9)	
F, Sidra-LUMCAC-ICAMKRAS-WTCRCchemotherapy						
Clinicalcharacteristic (%)	Beforematching			Aftermatching		
	Noadjuvantchemo(n=111)	Adjuvantchemo(n=36)	P-value	Noadjuvantchemo(n=18)	Adjuvantchemo(n=18)	P-value
Sex			0.194			>0.999
Male	54(36.7)	22(15.0)		10(27.8)	10(27.8)	
Female	57(38.8)	14(9.5)		8(22.2)	8(22.2)	
Age, years			0.260			>0.999
<50	6(4.1)	4(2.7)		1(2.8)	1(2.8)	
≥50	105(71.4)	32(21.8)		17(47.2)	17(47.2)	
Tumorlocation			0.585			0.855
Righthemicolon	51(34.7)	15(10.2)		8(22.2)	9(25.0)	
Transversecolon	5(3.4)	1(0.7)		0 (0.0)	0 (0.0)	
Lefthemicolon	55(37.4)	20(13.6)		10(27.8)	9(25.0)	
pT stage			0.035			0.803
1	8(5.4)	1(0.7)		1(2.8)	1(2.8)	
2	30(20.4)	5(3.4)		4(11.1)	5(13.9)	
3	67(45.6)	26(17.7)		12(33.3)	11(30.6)	
4	6(4.1)	4(2.7)		1(2.8)	1(2.8)	
pN stage			<0.001			>0.999
N0	111(75.5)	18(12.2)		18(50.0)	18(50.0)	
N+	0 (0.0)	18(12.2)		0 (0.0)	0 (0.0)	

MUT, KRAS-mutant; KRAS-WT, KRAS-wildtype; ICGC-ARGO, The International Cancer Genome Consortium Accelerating Research in Genomic Oncology; MSKCC, Memorial Sloan-Kettering Cancer Center; LUMC AC-ICAM, Leiden University Medical Center Atlas and Compass of Immune-Cancer-Microbiome interactions