

Supplementary Table 1. Comparison of clinicopathological characteristics of patients with different *BRAF/KRAS/NRAS/PIK3CA* mutation status

Characteristics	All cases	<i>BRAF</i> status				<i>P</i> -value	<i>KRAS</i> status				<i>P</i> -value	<i>NRAS</i> status				<i>P</i> -value	<i>PIK3CA</i> status				<i>P</i> -value
	(N = 2271, n %)	Wide-type (N=2182)	Mutation (N=85)	NA (N=4)	Wide-type (N=1256)		Mutation (N=1014)	NA (N=1)	Wide-type (N=2182)	Mutation (N=78)		NA (N=11)	Wide-type (N=1740)	Mutation (N=88)	NA (N=443)						
Sex																					
Male	1361 (59.9)	1319 (60.4)	39 (45.9)	3 (75.0)	0.0223	791 (63.0)	569 (56.1)	1 (100.0)	0.0029	1307 (59.9)	47 (60.3)	7 (63.6)	0.967	1042 (59.9)	50 (56.8)	269 (60.7)	0.79				
Female	910 (40.1)	863 (39.6)	46 (54.1)	1 (25.0)		465 (37.0)	445 (43.9)	0	2	875 (40.1)	31 (39.7)	4 (36.4)		698 (40.1)	38 (43.2)	174 (39.3)					
Age (years)																					
≤50	288 (12.7)	280 (12.8)	8 (9.4)	1 (25.0)	0.495	151 (12.0)	138 (13.6)	0	0.492	280 (12.8)	8 (10.3)	1 (9.1)	0.748	231 (13.3)	12 (13.6)	46 (10.4)	0.256				
>50	1983 (87.3)	1902 (87.2)	77 (90.6)	3 (75.0)		1105 (88.0)	876 (86.4)	1 (100.0)		1902 (87.2)	70 (89.7)	10 (90.9)		1509 (86.7)	76 (86.4)	397 (89.6)					
Smoking status																					
No	1762 (77.6)	1695 (77.7)	65 (76.5)	2 (50.0)	0.402	948 (75.5)	813 (80.2)	1 (100.0)	0.0245	1693 (77.6)	59 (75.6)	10 (90.9)	0.524	1362 (78.3)	67 (76.1)	333 (75.2)	0.355				
Yes	509 (22.4)	487 (22.3)	20 (23.5)	2 (50.0)		308 (24.5)	201 (19.8)	0		489 (22.4)	19 (24.4)	1 (9.1)		378 (21.7)	21 (23.9)	110 (24.8)					
Drinking status																					
No	1848 (81.4)	1772 (81.2)	73 (85.6)	3 (75.0)	0.526	1017 (81.0)	830 (81.9)	1 (100.0)	0.772	1778 (81.5)	60 (76.9)	10 (90.9)	0.428	1425 (81.9)	70 (79.5)	353 (79.7)	0.511				
Yes	423 (18.6)	410 (18.8)	12 (14.1)	1 (25.0)		239 (19.0)	184 (18.1)	0		404 (18.5)	18 (23.1)	1 (9.1)		315 (18.1)	18 (20.5)	90 (20.3)					
Family history																					
No	1971 (86.8)	1886 (86.4)	81 (95.3)	4 (100.0)	0.0448	1091 (86.9)	879 (86.7)	1 (100.0)	0.92	1892 (86.7)	70 (89.7)	9 (81.8)	0.656	1512 (86.9)	73 (83.0)	386 (87.1)	0.551				
Yes	300 (13.2)	296 (13.6)	4 (4.7)	0		165 (13.1)	135 (13.3)	0		290 (13.3)	8 (10.3)	2 (18.2)		228 (13.1)	15 (17.0)	57 (12.9)					
Tumor location																					
Right colon	551 (24.3)	489 (22.4)	62 (72.9)	0	< 0.001	288 (22.9)	263 (25.9)	0	0.539	528 (24.2)	16 (20.5)	7 (63.6)	< 0.001	400 (23.0)	32 (36.4)	119 (26.9)	0.0221				
Left colon	1718 (75.6)	1691 (77.5)	23 (27.1)	4 (100.0)		967 (77.0)	750 (74.0)	1 (100.0)		1653 (75.8)	61 (78.2)	4 (36.4)		1339 (77.0)	56 (63.6)	323 (72.9)					
Liver	2 (0.1)	2 (0.1)	0	0		1 (0.1)	1 (0.1)	0		1 (0.05)	1 (1.3)	0		1 (0.1)	0	1 (0.2)					
Cancer nodules																					
No	1782 (78.5)	1710 (78.4)	68 (80.0)	4 (100.0)	0.541	1005 (80.0)	777 (76.6)	0	0.024	1715 (78.4)	58 (74.4)	9 (81.8)	0.646	1379 (79.3)	72 (81.8)	331 (74.7)	0.086				

Yes	489 (21.5)	472 (21.6)	17 (20.0)	0		251 (20.0)	2379 (23.4)	1 (100.0)		467 (21.4)	20 (25.6)	2 (18.2)		361 (20.7)	16 (18.2)	112 (25.3)	
Perineural invasion																	
No	1484 (65.3)	1418 (65.0)	63 (74.1)	3 (75.0)		834 (66.4)	650 (64.1)	0		1431 (65.6)	43 (55.1)	10 (90.9)		1086 (62.4)	52 (59.1)	346 (78.1)	
Yes	786 (34.6)	763 (35.0)	22 (25.9)	1 (25.0)	0.763	422 (33.6)	363 (35.8)	1 (100.0)	0.609	750 (34.4)	35 (44.9)	1 (9.1)	0.322	653 (37.5)	36 (40.9)	97 (21.9)	<0.001
NA	1 (< 0.01)	1 (0.05)	0	0		1 (0.1)	0	0		1 (0.05)	0	0		1 (0.1)	0	0	
Vascular invasion																	
No	1779 (78.3)	1722 (78.9)	53 (62.4)	4 (100.0)		965 (76.8)	813 (80.2)	1 (100.0)		1709 (78.3)	60 (76.9)	10 (90.9)		1336 (76.8)	73 (83.0)	370 (83.5)	
Yes	486 (21.4)	454 (20.8)	32 (37.6)	0	0.0046	286 (22.8)	200 (19.7)	0	0.247	467 (21.4)	18 (23.1)	1 (9.1)	0.85	398 (22.9)	15 (17.0)	73 (16.5)	0.0198
NA	6 (0.3)	1 (0.05)	0	0		1 (0.1)	0	0		1 (0.05)	0	0		1 (0.1)	0	0	
Tumor classification																	
poorly differentiated	226 (10.0)	190 (8.7)	35 (41.2)	1 (25.0)		147 (11.7)	79 (7.8)	0		215 (9.9)	7 (9.0)	4 (36.4)		162 (9.3)	8	56 (12.6)	
Moderately/well differentiated	1878 (82.6)	1840 (84.3)	36 (42.4)	2 (50.0)	<0.001	1037 (82.6)	840 (82.8)	1 (100.0)	<0.001	1803 (82.6)	69 (88.5)	7 (63.6)	0.0305	1452 (83.4)	72	354 (79.9)	0.293
NA	167 (7.4%)	152 (7.0)	14 (16.5)	1 (25.0)		95 (7.6)	729 (7.1)	0		164 (7.5)	3 (3.8)	0		126 (7.2)	8	33 (7.4)	
Stage																	
Tis	18 (0.8)	17 (0.8)	1 (1.2)	0		8 (0.6)	10 (1.0)	0		17 (0.8)	1 (1.3)	0		14 (0.8)	0	4 (0.9)	
I	305 (13.4)	296 (13.6)	8 (9.4)	1 (25.0)		180 (14.3)	125 (12.3)	0		295 (13.5)	8 (10.3)	2 (18.2)		228 (13.1)	15	62 (14.0)	
II	835 (36.8)	801 (36.7)	32 (37.6)	2 (50.0)	0.722	470 (37.4)	365 (36.0)	0	0.686	797 (36.5)	32 (41.0)	6 (54.5)	0.85	636 (36.6)	34	165 (37.2)	0.956
III	935 (41.2)	899 (41.2)	36 (42.4)	0		499 (39.7)	435 (42.9)	1 (100.0)		900 (41.2)	32 (41.0)	3 (27.3)		724 (41.6)	33	178 (40.2)	
IV	178 (7.8)	169 (7.7)	8 (9.4)	1 (25.0)		99 (7.9)	79 (7.8)	0		169 (7.7)	8 (10.3)	1 (9.1)		138 (7.9)	6	34 (7.7)	

Stage Tis: Carcinoma in situ.

Supplementary Table 2. Comparison of clinicopathological characteristics of patients with microsatellite instability/mismatch repair status

Characteristics	All cases (N = 2271, n%)	MSS (N = 2085)	MSI-L (N = 7)	MSI-H (N = 179)	P-value	Normal MMR IHC (N = 2092)	Abnormal MMR IHC (N = 179)	P-value
Sex								
Male	1361 (59.9)	1255 (60.2)	4 (57.1)	102 (57.0)	0.695	1260 (60.2)	101 (56.4)	0.319
Female	910 (40.1)	830 (39.8)	3 (42.9)	77 (43.0)		832 (39.8)	78 (43.6)	
Age category (years)								
<50	260 (11.4)	216 (10.4)	0 (0.0)	44 (24.6)	0.14	215 (10.3)	45 (25.1)	0.073
50~60	475 (20.9)	440 (21.1)	2 (28.6)	33 (18.4)		446 (21.3)	29 (16.2)	
60~70	783 (34.5)	740 (35.5)	3 (42.9)	40 (22.3)		740 (35.4)	43 (24.0)	
70~80	493 (21.7)	458 (22.0)	1 (14.3)	34 (19.0)		459 (21.9)	34 (19.0)	
≥80	260 (11.4)	231 (11.1)	1 (14.3)	28 (15.6)		232 (11.1)	28 (15.6)	
Stage								
Tis	18 (0.8)	17 (0.8)	0 (0.0)	1 (0.6)	<0.001	17 (0.8)	1 (0.8)	<0.001
I	305 (13.4)	287 (13.8)	2 (28.6)	16 (8.9)		286 (13.7)	19 (10.6)	
II	835 (36.8)	718 (34.4)	3 (42.9)	114 (63.7)		721 (34.5)	114 (63.7)	
III	935 (41.2)	891 (42.7)	2 (28.6)	42 (23.5)		895 (42.8)	40 (22.3)	
IV	178 (7.8)	172 (8.2)	0 (0.0)	6 (3.4)		173 (8.3)	5 (2.8)	
Tumor location								
Right colon	551 (24.3)	420 (20.1)	2 (28.6)	129 (72.1)	<0.001	422 (20.2)	129 (72.1)	<0.001
Left colon	1718 (75.6)	1663 (79.8)	5 (71.4)	50 (27.9)		1668 (79.7)	50 (27.9)	
Liver	2 (0.1)	2 (0.1)	0 (0.0)	0 (0.0)		2 (0.1)	0 (0.0)	
Family history								
No	1971 (86.8)	1823 (87.4)	5 (71.4)	143 (79.9)	0.008	1831 (87.5)	140 (78.2)	<0.001
Yes	300 (13.2)	262 (12.6)	2 (28.6)	36 (20.1)		261 (12.5)	39 (21.8)	

Perineural invasion

No	1484 (65.3)	1334 (64.0)	3 (42.9)	147 (82.1)	<0.001	1333 (63.7)	151 (84.4)	<0.001
Yes	786 (34.6)	750 (36.0)	4 (57.1)	32 (17.9)		758 (36.3)	28 (15.5)	
NA	1 (< 0.01)	1 (< 0.01)	0 (0.0)	0 (0.0)		1 (< 0.01)	0 (0.0)	

Tumor classification

Poorly differentiated	226 (10.0)	172 (8.2)	0 (0.0)	54 (30.1)	<0.001	173 (8.3)	53 (29.6)	<0.001
Moderately differentiated	1765 (77.7)	1666 (79.9)	7 (100.0)	92 (51.4)		1671 (79.9)	94 (52.5)	
Well differentiated	113 (5.0)	104 (5.0)	0 (0.0)	9 (5.0)		103 (4.9)	10 (5.6)	
NA	167 (7.3%)	143 (6.9)	0 (0.0)	24 (13.4)		145 (6.9)	22 (12.3)	

Vascular invasion

No	1779 (78.3)	1638 (78.6)	5 (71.4)	136 (76.0)	0.563	1642 (78.5)	137 (76.5)	0.444
Yes	486 (21.4)	441 (21.2)	2 (28.6)	43 (24.0)		444 (21.2)	42 (23.5)	
NA	6 (0.3)	6 (0.3)	0 (0.0)	0 (0.0)		6 (0.3)	0 (0.0)	

Cancer nodules

No	1782 (78.5)	1609 (77.2)	4 (57.1)	169 (94.4)	<0.001	1614 (77.2)	168 (93.9)	<0.001
Yes	489 (21.5)	476 (22.8)	3 (42.9)	10 (5.6)		478 (22.8)	11 (6.1)	

BRAF status

WT	2182 (96.1)	2033 (97.5)	7 (100.0)	142 (79.3)	<0.001	2043 (97.7)	139 (77.7)	<0.001
MT	85 (3.7)	48 (2.3)	0 (0.0)	37 (20.7)		45 (2.2)	40 (22.3)	
Unknown	4 (0.2)	4 (0.2)	0 (0.0)	0 (0.0)		4 (0.2)	0 (0.0)	

KRAS status

WT	1256 (55.3)	1130 (54.2)	4 (57.1)	122 (68.2)	0.01	1130 (54.0)	126 (70.4)	<0.01
MT	1014 (44.6)	954 (45.8)	3 (42.9)	57 (31.8)		961 (45.9)	53 (29.6)	
Unknown	1 (0.04)	1 (0.05)	0 (0.0)	0 (0.0)		1 (0.1)	0 (0.0)	

NRAS status

WT	2182 (96.1)	2008 (96.3)	7 (100)	167 (93.3)	0.18	2015 (96.3)	167 (93.3)	0.12
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MT	78 (3.4)	76 (3.6)	0	2 (1.1)		76 (3.6)	2 (1.1)	
Unknown	11 (0.5)	1 (0.05)	0	10 (5.6)		1 (0.05)	10 (5.6)	
PIK3CA status								
WT	1740 (76.6)	1617 (77.6)	6 (85.7)	117 (65.4)	0.24	1626 (77.7)	114 (63.7)	0.08
M	88 (3.9)	78 (3.7)	0 (0.0)	10 (5.6)		78 (3.7)	10 (5.6)	
Unknown	443 (19.5)	390 (18.7)	1 (14.3)	52 (29.1)		388 (18.5)	55 (30.7)	

MSI: Microsatellite instability; MSI-H: Microsatellite instability-high; MSI-L: Microsatellite instability-low; MSS: Microsatellite-stable; MMR: Mismatch repair; Stage Tis: Carcinoma in situ.