Figure S1. Genetic characteristics according to RAS status. (A) Proportion of patients presenting at least one mutation in the most frequently mutated genes, by RAS status. (B) Distribution of patients presenting an alteration in significant signaling pathways according to RAS status. Only pathways for which the Fisher tests were considered significant (P<0.05) are presented. WT, wild-type.

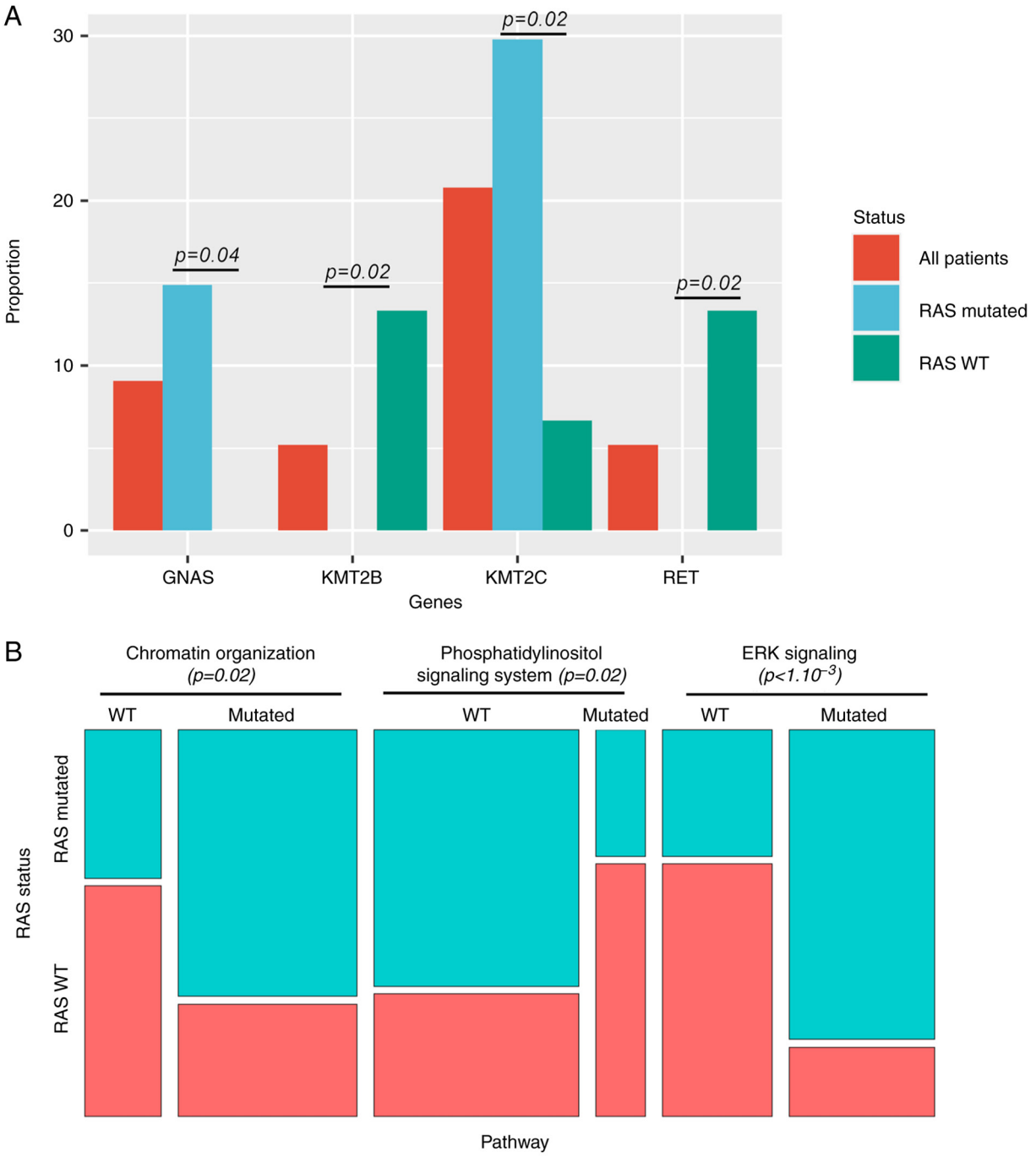

Figure S2. Gene mutation and overall survival. Kaplan Meier curves for genes with significantly different overall survival according to their mutation status, namely (A) PDGFRA, (B) SMAD4, (C) PTEN and (D) MYCN. HR, hazard ratio; WT, wild-type.

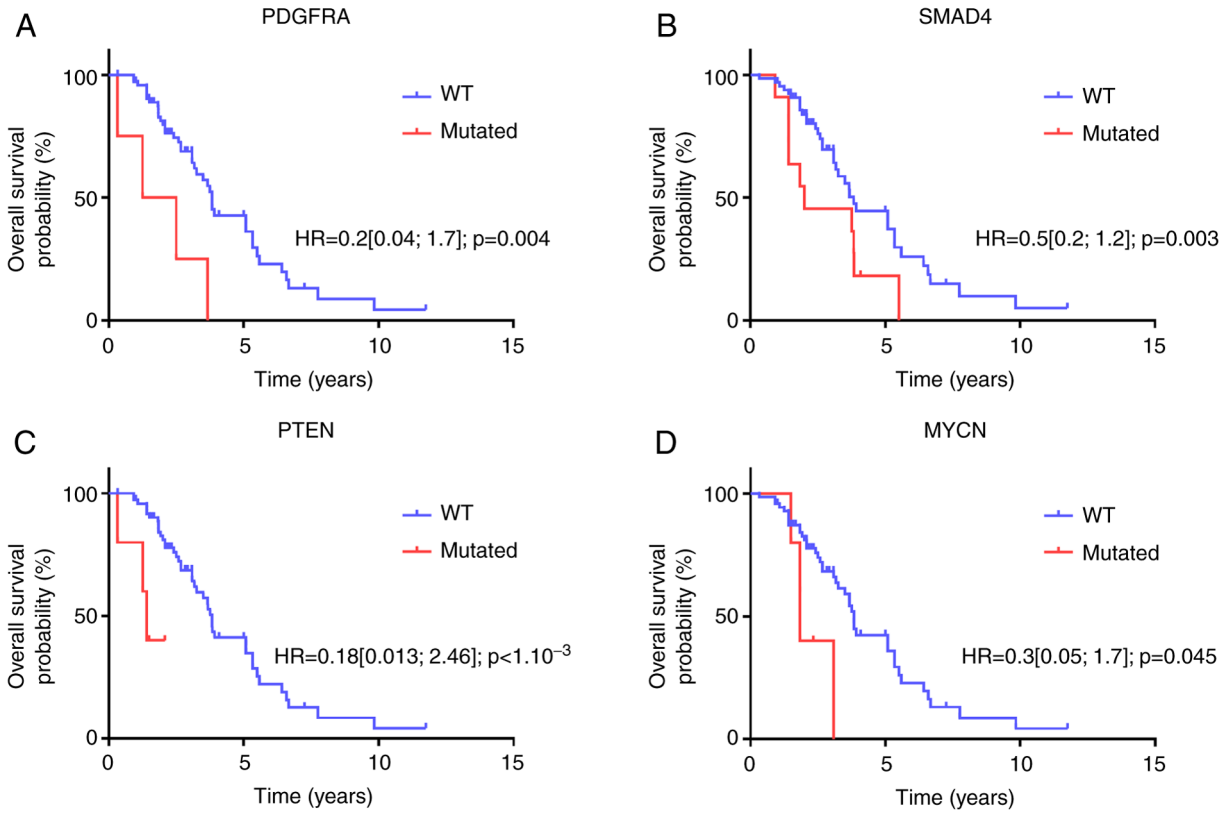

Table SI. Summary of clinical characteristics according to primary tumour side (right/left).

Variables	Whole population (n=77)	Right-sided group (n=27)	Left-sided group (n=50)	P-value
Sex, n (%)				>0.99
Male	50 (65)	18 (67)	32 (64)	
Female	27 (35)	9 (33)	18 (36)	
WHO, n (%)				>0.99
0	26 (34)	8 (31)	18 (36)	
1 and 2	25 (32)	8 (31)	17 (34)	
Age at diagnosis (years), median (IQR)	62 (11)	62 (9.5)	62 (12)	0.49
Age class at diagnosis, n (%)				0.83
≤60 years	34 (44)	11 (41)	23 (46)	
>60 years	43 (46)	16 (62)	27 (64)	
Metastasis, n (%)				0.62
Synchronous	50 (65)	19 (70)	31 (62)	
Metachronous	27 (35)	8 (31)	19 (38)	
Metastatic sites, n (%)				0.44
<2	43 (56)	13 (46)	30 (60)	
≥2	34 (44)	14 (54)	20 (40)	
Lung metastasis, n (%)				0.31
Absence	56 (73)	22 (81)	34 (68)	
Presence	21 (27)	5 (19)	16 (32)	
Liver metastasis, n (%)				0.82
Absence	23 (30)	9 (31)	14 (28)	
Presence	54 (70)	18 (69)	36 (72)	
Peritoneal metastasis, n (%)				0.001
Absence	53 (69)	13 (50)	40 (80)	
Presence	24 (31)	14 (50)	10 (20)	
Anti-EGFR, n (%)				0.17
Absence	47 (61)	20 (73)	27 (54)	
Presence	30 (39)	7 (27)	23 (46)	

IQR, interquartile range; WHO, World Health Organization.

Table SII. Summary of clinical characteristics according to metachronous/synchronous status.

Variables	Whole population (n=77)	Metachronous group (n=27)	Synchronous group (n=50)	P-value
Sex, n (%)				>0.99
Male	50 (65)	18 (67)	32 (64)	
Female	27 (35)	9 (33)	18 (36)	
WHO, n (%)				0.28
0	26 (34)	11 (41)	15 (30)	
1 and 2	25 (32)	6 (22)	19 (38)	
Age at diagnosis (years), median (IQR)	62 (11)	62 (10)	62 (13)	0.49
Age class at diagnosis, n (%)				0.83
≤60 years	34 (44)	11 (41)	23 (46)	
>60 years	43 (56)	16 (59)	27 (54)	
Primary tumour side, n (%)				0.63
Right-sided	27 (35)	8 (30)	19 (38)	
Left-sided	50 (65)	19 (70)	31 (62)	
Metastatic sites, n (%)				0.10
<2	47 (61)	19 (70)	24 (48)	
≥2	34 (39)	8 (30)	26 (52)	
Lung metastasis, n (%)				0.54
Absence	56 (73)	18 (67)	38 (76)	
Presence	21 (27)	9 (33)	12 (24)	
Liver metastasis, n (%)				$<1x10^{-3}$
Absence	23 (30)	17 (63)	6 (12)	
Presence	54 (70)	10 (37)	44 (88)	
Peritoneal metastasis, n (%)				1
Absence	53 (69)	19 (70)	34 (68)	
Presence	24 (31)	8 (30)	16 (32)	
Anti-EGFR, n (%)				0.61
Absence	47 (61)	18 (67)	29 (58)	
Presence	30 (39)	9 (33)	21 (42)	

IQR, interquartile range; WHO, World Health Organization.

Table SIII. Summary of clinical characteristics according to RAS mutational status.

Variables	Whole population (n=77)	RAS mutated (n=46)	RAS WT (n=31)	P-value
Sex, n (%)				0.20
Male	50 (65)	27 (59)	23 (74)	
Female	27 (35)	19 (41)	8 (26)	
WHO, n (%)				0.01
0	26 (34)	21 (46)	5 (16)	
1 and 2	25 (32)	9 (20)	16 (52)	
Age at diagnosis (years), median (IQR)	62 (11)	62 (11)	61 (12)	0.80
Age class at diagnosis, n (%)				>0.99
≤60 years	34 (44)	20 (43)	14 (45)	
>60 years	43 (56)	26 (57)	17 (55)	
Metastasis, n (%)				0.80
Synchronous	50 (65)	29 (63)	21 (68)	
Metachronous	27 (35)	17 (37)	10 (32)	
Metastatic sites, n (%)				0.50
<2	43 (56)	24 (52)	19 (61)	
≥2	34 (44)	22 (48)	12 (39)	
Lung metastasis, n (%)				0.30
Absence	56 (73)	31 (67)	25 (81)	
Presence	21 (27)	15 (33)	6 (19)	
Liver metastasis, n (%)				>0.99
Absence	23 (30)	14 (30)	9 (29)	
Presence	54 (70)	32 (70)	22 (71)	
Peritoneal metastasis, n (%)				0.60
Absence	53 (69)	33 (72)	20 (65)	
Presence	24 (31)	13 (28)	11 (35)	
Anti-EGFR, n (%)				$<1x10^{-3}$
Absence	47 (61)	42 (91)	5 (16)	
Presence	30 (39)	4 (9)	26 (84)	

IQR, interquartile range; WHO, World Health Organization; WT, wild-type.

Table SIV. Description of genomic characteristics according to MSI/MSS groups.

Variables	MSI (n=5), median (IQR)	MSS (n=72), median (IQR)	P-value
MSI score	1.1 (9.2)	0.1 (0.2)	0.023
TMB score	20.1 (20.1)	5.2 (2.7)	0.007
TMB without splicing regions score	21.8 (21.0)	5.4 (2.8)	0.007
HRD score	15.0 (0)	24.0 (13)	0.007
Ploidy	2.0 (0.2)	2.1 (0.5)	0.192
Deletions with LOH	8.0 (3.0)	2.0 (7.0)	0.242
Microdeletions	7.0 (6.0)	3.0 (4.0)	0.119
Neoantigens	15.0 (53.0)	11.0 (8.0)	0.016
Strong neoantigens	3.0 (15.0)	1.0 (2.0)	0.005

MSI, microsatellite instability; IQR, interquartile range; TMB, tumour mutation burden; HRD, homologous recombination deficiency; LOH, loss of heterozygosity; IQR, interquartile range.

Table SV. Description of mutations observed in genes differentially mutated in function of sidedness, synchronous or metachronous status, and KRAS mutated status.

Gene name	Sample name	HGVSc	Transcript	HGVSp	G/S
MYCN	N17-177	c.-77A>C	NM_005378	p.?	S
	N17-273	c.-183G>C	NM_005378	p.?	S
	N17-407	c.-127T>C	NM_005378	p.?	S
	N18-114	c.730A>C	NM_005378	p.Thr244Pro	S
	N18-154	c.*88G>A	NM_005378	p.?	S
PDGFRA	N16-10	c.2606A>T	NM_006206	p.Asp869Val	S
	N16-232	c.1495G>A	NM_006206	p.Val499Met	S
	N16-252	c.1432T>C	NM_006206	p.Ser478Pro	S
	N18-206	c.2153G>A	NM_006206	p.Arg718Gln	S
PTEN	N16-10	c.697C>T	NM_000314	p.Arg233*	S
	N18-20	c.802-2A>T	NM_000314	p.?	S
	N18-206	c.389G>A	NM_000314	p.Arg130Gln	S
	N18-54	c.802-1G>T	NM_000314	p.?	S
	N19-73	c.635-3C>A	NM_000314	p.?	S
SMAD 4	N16-02	c.1241T>A	NM_005359	p.Leu414Ter	S
	N16-129	c.1081C>T	NM_005359	p.Arg361Cys	S
	N17-145	c.725C>G	NM_005359	p.Ser242Ter	S
	N17-239	c.284A>G	NM_005359	p.Tyr95Cys	S
	N17-264	c.353C>T	NM_005359	p.Ala118Val	S
	N17-273	c.326T>G	NM_005359	p.Leu109Arg	S
	N17-382	c.1067C>T	NM_005359	p.Pro356Leu	S
	N17-411	c.1079A>T	NM_005359	p.Asp360Val	S
		c.1081C>T	NM_005359	p.Arg361Cys	S
	N18-20	c.388C>T	NM_005359	p.Pro130Ser	S
	N19-260	c.713_714insTG	NM_005359	p.Leu238PhefsTer4	S
		c.716del	NM_005359	p.Gln239ArgfsTer2	S
	R15-49	c.779dup	NM_005359	p.Tyr260Ter	S
AMER 1	20BM00593	c.1489C>T	NM_152424	p.Arg497Ter	S
	N16-139	c.1072C>T	NM_152424	p.Arg358Ter	S
	N17-350	c.1072C>T	NM_152424	p.Arg358Ter	S
	N17-361	c.519del	NM_152424	p.Phe173LeufsTer36	S
	N18-232	c.1591C>T	NM_152424	p.Arg531Ter	S
	N18-290	c.919dup	NM_152424	p.Asp307GlyfsTer17	S
	N18-335	c.1756C>T	NM_152424	p.Arg586Ter	S
	N19-260	c.1216_1217del	NM_152424	p.Leu406ArgfsTer34	S
	N19-73	c.1111G>T	NM_152424	p.Glu371Ter	S
CSF1R	N16-227	c.1132C>T	NM_005211	p.Arg378Cys	S
	N16-360	c.1845_1846del	NM_005211	p.Lys616AspfsTer9	S
	N17-361	c.641G>A	NM_005211	p.Arg214Gln	S
ERBB4	N18-134	c.149G>A	NM_005235	p.Arg50His	S
	N18-303	c.884-7T>A	NM_005235		S
	N19-18	c.884-7T>A	NM_005235		S
FUBP1	N18-19	c.60C>G	NM_003902	p.Gly20=	S
	N18-20	c.*98G>T	NM_003902	p.?	S
	N18-305	c.121-3_121-2del	NM_003902	p.?	S
	N19-147	c.*139_*141del	NM_003902	p.?	S
	N19-18	c.*115G>T	NM_003902	p.?	S
PTCH1	N17-273	c.2304C>T	NM_000264	p.Thr768=	G
		c.4310G>T	NM_000264	p.Cys1437Phe	S
	N17-361	c.1912C>T	NM_000264	p.Arg638Cys	S
	N18-12	c.4252G>A	NM_000264	p.Val1418Ile	S
	N18-19	c.3860A>C	NM_000264	p.His1287Pro	S
	N19-73	c.2680G>A	NM_000264	p.Asp894Asn	S
PTPRD	N16-227	c.5534+7_5534+8insACAGTT CAAGAATGGTAAGTT	NM_002839		S
	N17-361	c.4159G>A	NM_002839	p.Ala1387Thr	S
	N17-404	c.5439G>A	NM_002839	p.Val1813=	S
	N19-124	c.1722A>G	NM_002839	p.Gly574=	S

Table SV. Continued.

Gene name	Sample name	HGVSc	Transcript	HGVSp	G/S
SMARCB1	20BM00593	c.-53A>C	NM_003073	p.?	S
		c.*117T>G	NM_003073	p.?	S
		c.*123T>G	NM_003073	p.?	S
	N16-70	c.*117T>G	NM_003073	p.?	S
		c.*123T>G	NM_003073	p.?	S
	N17-234	c.*128T>G	NM_003073	p.?	S
	N18-12	c.-62C>G	NM_003073	p.?	S
	N18-19	c.-62C>G	NM_003073	p.?	S
	N18-303	c.*117T>G	NM_003073	p.?	S
	N19-260	c.*117T>G	NM_003073	p.?	S
		c.*123T>G	NM_003073	p.?	S
	R15-49	c.*314_*327del	NM_003073	p.?	S
KMT2C	20BM00593	c.1422T>C	NM_170606	p.Tyr474=	G
		c.11141A>C	NM_170606	p.Lys3714Thr	S
	N16-227	c.1005T>A	NM_170606	p.Pro335=	S
	N16-251	c.7825C>T	NM_170606	p.Arg2609Ter	S
	N16-252	c.10763C>T	NM_170606	p.Ser3588Leu	S
	N17-272	c.8064A>T	NM_170606	p.Lys2688Asn	S
	N17-273	c.14303A>G	NM_170606	p.Glu4768Gly	S
	N17-361	c.11093C>T	NM_170606	p.Thr3698Met	S
	N17-382	c.2518C>T	NM_170606	p.Pro840Ser	S
	N17-404	c.8390del	NM_170606	p.Lys2797ArgfsTer26	S
	N17-82	c.1184+10C>A	NM_170606		S
	N18-114	c.90A>C	NM_170606	p.Ala30=	S
	N18-12	c.162-6C>T	NM_170606		S
	N18-134	c.3434-8C>T	NM_170606		S
	N18-154	c.5694T>C	NM_170606	p.Tyr1898=	S
	N18-335	c.2459C>T	NM_170606	p.Thr820Ile	S
	N19-260	c.1050G>A	NM_170606	p.Pro350=	S
		c.1042G>A	NM_170606	p.Asp348Asn	S
TP53	20BM00586	c.584T>C	NM_000546	p.Ile195Thr	S
	N16-02	c.517G>C	NM_000546	p.Val173Leu	S
	N16-10	c.517G>A	NM_000546	p.Val173Met	S
	N16-232	c.524G>A	NM_000546	p.Arg175His	S
	N16-252	c.638G>T	NM_000546	p.Arg213Leu	S
	N16-264	c.755T>C	NM_000546	p.Leu252Pro	S
	N16-302	c.637C>T	NM_000546	p.Arg213Ter	S
	N16-306	c.993+1G>A	NM_000546		S
	N16-314	c.821T>G	NM_000546	p.Val274Gly	S
		c.770T>G	NM_000546	p.Leu257Arg	S
	N16-326	c.880G>T	NM_000546	p.Glu294Ter	S
		c.820G>C	NM_000546	p.Val274Leu	S
	N16-70	c.476C>G	NM_000546	p.Ala159Gly	S
	N17-145	c.577C>T	NM_000546	p.His193Tyr	S
	N17-193	c.814G>T	NM_000546	p.Val272Leu	S
	N17-234	c.844C>T	NM_000546	p.Arg282Trp	S
	N17-239	c.487T>C	NM_000546	p.Tyr163His	S
	N17-272	c.488A>G	NM_000546	p.Tyr163Cys	S
	N17-273	c.856G>T	NM_000546	p.Glu286Ter	S
		c.855G>T	NM_000546	p.Glu285Asp	S
	N17-298	c.536A>G	NM_000546	p.His179Arg	S
	N17-350	c.524G>A	NM_000546	p.Arg175His	S
	N17-354	c.638G>T	NM_000546	p.Arg213Leu	S
	N17-382	c.916C>T	NM_000546	p.Arg306Ter	S
	N17-404	c.818G>A	NM_000546	p.Arg273His	S
	N17-408	c.376-2A>T	NM_000546		S
	N17-430	c.402T>A	NM_000546	p.Phe134Leu	S
	N17-82	c.524G>A	NM_000546	p.Arg175His	S
	N18-114	c.639A>G	NM_000546	p.Arg213=	G

Table SV. Continued.

Gene name	Sample name	HGVSc	Transcript	HGVSp	G/S
		c.743G>A	NM_000546	p.Arg248Gln	S
	N18-12	c.818G>C	NM_000546	p.Arg273Pro	S
	N18-138	c.639A>G	NM_000546	p.Arg213=	G
		c.450_451del	NM_000546	p.Pro152AlafsTer28	S
		c.447C>G	NM_000546	p.Ser149=	S
	N18-143	c.859G>T	NM_000546	p.Glu287Ter	S
	N18-154	c.524G>A	NM_000546	p.Arg175His	S
	N18-19	c.639A>G	NM_000546	p.Arg213=	G
		c.743G>A	NM_000546	p.Arg248Gln	S
	N18-20	c.96+1G>T	NM_000546		S
	N18-204	c.994-1G>T	NM_000546		S
		c.764_766del	NM_000546	p.Ile255del	S
	N18-206	c.817C>T	NM_000546	p.Arg273Cys	S
	N18-232	c.637C>T	NM_000546	p.Arg213Ter	S
	N18-264	c.742C>T	NM_000546	p.Arg248Trp	S
	N18-290	c.734G>A	NM_000546	p.Gly245Asp	S
	N18-303	c.437G>A	NM_000546	p.Trp146Ter	S
	N18-305	c.586C>T	NM_000546	p.Arg196Ter	S
	N18-326	c.524G>A	NM_000546	p.Arg175His	S
	N18-53	c.639A>G	NM_000546	p.Arg213=	S
		c.481G>A	NM_000546	p.Ala161Thr	S
	N18-54	c.586C>T	NM_000546	p.Arg196Ter	S
	N19-147	c.515_522dup	NM_000546	p.Arg175LeufsTer2	S
	N19-18	c.396G>T	NM_000546	p.Lys132Asn	S
	N19-260	c.772G>T	NM_000546	p.Glu258Ter	S
	N19-325	c.621del	NM_000546	p.Asp207GlufsTer40	S
	N19-93	c.832C>T	NM_000546	p.Pro278Ser	S
	R15-49	c.437G>A	NM_000546	p.Trp146Ter	S
	R16-57	c.817C>T	NM_000546	p.Arg273Cys	S
GNAS	N16-10	c.465G>A	NM_000516	p.Glu155=	S
	N16-138	c.-37335C>T	NM_000516	p.?	G
		c.-37188T>C	NM_000516	p.?	S
	N16-227	c.393C>T	NM_000516	p.Ile131=	S
	N16-70	c.-36424_-36423del	NM_000516	p.?	S
		c.-36414C>T	NM_000516	p.?	S
	N17-145	c.-50970T>A	NM_000516	p.?	G
		c.-36154C>T	NM_000516	p.?	S
		c.602G>A	NM_000516	p.Arg201His	S
	N18-206	c.-37154C>A	NM_000516	p.?	S
	R15-49	c.-51672A>G	NM_000516	p.?	G
		c.-38396C>T	NM_000516	p.?	S
RET	N16-252	c.573G>C	NM_020975	p.Leu191=	S
	N17-234	c.1880-8A>C	NM_020975		S
	N18-232	c.2116G>A	NM_020975	p.Val706Met	S
	N18-326	c.2038G>A	NM_020975	p.Ala680Thr	S
KMT2B	N17-234	c.8037C>T	NM_014727	p.Arg2679=	S
	N17-404	c.2457+8T>C	NM_014727		S
	N18-138	c.3310C>T	NM_014727	p.Arg1104Trp	S
	N18-20	c.3325C>T	NM_014727	p.Arg1109Ter	S

HGVSc, Human Genome Variation Society coding sequence name; HGVSp, Human Genome Variation Society protein sequence name; G, germline; S, somatic.

Table SVI. Results of Enrichr analysis based on Kyoto Encyclopedia of Genes and Genomes pathways and genes differentially mutated in function of sidedness, synchronous or metachronous status, and KRAS mutated status.

Comparison	Name	P-value	Adjusted P-value	Odds ratio	Combined score
Metachronous or synchronous metastasis	Pancreatic cancer	0.000004186	0.0001395	138.33	1,713.00
	Thyroid cancer	0.0001189	0.001189	162.91	1,472.21
	Colorectal cancer	0.000006328	0.0001582	119.93	1,435.59
	Bladder cancer	0.0001463	0.001330	146.17	1,290.68
	Proteoglycans in cancer	0.000001199	0.00007398	80.38	1,095.91
	Endometrial cancer	0.0002937	0.002113	101.71	827.20
	Basal cell carcinoma	0.0003466	0.002113	93.35	743.75
	Central carbon metabolism in cancer	0.0003689	0.002113	90.38	714.41
	Mitophagy	0.0003689	0.002113	90.38	714.41
	Gastric cancer	0.00003294	0.0005890	67.96	701.43
Sidedness	Hepatocellular carcinoma	0.001433	0.04012	47.78	312.85
	Endometrial cancer	0.02013	0.07928	58.29	227.67
	Central carbon metabolism in cancer	0.02253	0.07928	51.90	196.84
	Melanoma	0.02493	0.07928	46.77	172.64
	p53 signaling pathway	0.02493	0.07928	46.77	172.64
	Inositol phosphate metabolism	0.02562	0.07928	45.48	166.66
	Glioma	0.02596	0.07928	44.86	163.80
	ErbB signaling pathway	0.02938	0.07928	39.50	139.34
	Small cell lung cancer	0.03210	0.07928	36.05	123.98
	Prostate cancer	0.03346	0.07928	34.54	117.35
KRAS status	Thyroid cancer	0.0001485	0.01004	142.54	1,256.48
	Endometrial cancer	0.0003664	0.01004	88.99	704.07
	Lysine degradation	0.0003792	0.01004	87.43	688.70
	Central carbon metabolism in cancer	0.0004602	0.01004	79.08	607.60
	Bacterial invasion of epithelial cells	0.0005962	0.01004	69.16	513.51
	Inositol phosphate metabolism	0.0005962	0.01004	69.16	513.51
	Colorectal cancer	0.0008042	0.01160	59.24	422.16
	Prostate cancer	0.001021	0.01194	52.36	360.55
	Phosphatidylinositol signaling system	0.001064	0.01194	51.27	351.00
	Leukocyte transendothelial migration	0.001358	0.01337	45.18	298.27

Only the top 10 pathways are displayed.