

Supplementary Tables

NOTCH gene alterations in metastatic colorectal cancer in the Nationwide Cancer Genome Screening Project in Japan (SCRUM-Japan GI-SCREEN)

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Supplementary Table 1 Target genes in the Oncomine™ Comprehensive Assay v3

Hotspot genes				Full-length genes			Copy-number genes		Gene fusions (inter- and intragenic)		
<i>AKT1</i>	<i>ESR1</i>	<i>KIT</i>	<i>PDGFRB</i>	<i>ARID1A</i>	<i>FBXW7</i>	<i>PTEN</i>	<i>AKT1</i>	<i>FGFR4</i>	<i>AKT2</i>	<i>FGFR2</i>	<i>NUTM1</i>
<i>AKT2</i>	<i>EZH2</i>	<i>KNSTRN</i>	<i>PIK3CB</i>	<i>ATM</i>	<i>MLH1</i>	<i>RAD50</i>	<i>AKT2</i>	<i>FLT3</i>	<i>ALK</i>	<i>FGFR3</i>	<i>PDGFRA</i>
<i>AKT3</i>	<i>FGFR1</i>	<i>KRAS</i>	<i>PIK3CA</i>	<i>ATR</i>	<i>MRE11</i>	<i>RAD51</i>	<i>AKT3</i>	<i>IGF1R</i>	<i>AR</i>	<i>FGR</i>	<i>PDGFRB</i>
<i>ALK</i>	<i>FGFR2</i>	<i>MAGOH</i>	<i>PPP2R1A</i>	<i>ATRX</i>	<i>MSH6</i>	<i>RAD51B</i>	<i>ALK</i>	<i>KIT</i>	<i>AXL</i>	<i>FLT3</i>	<i>PIK3CA</i>
<i>AR</i>	<i>FGFR3</i>	<i>MAP2K1</i>	<i>PTPN11</i>	<i>BAP1</i>	<i>MSH2</i>	<i>RAD51C</i>	<i>AXL</i>	<i>KRAS</i>	<i>BRCA1</i>	<i>JAK2</i>	<i>PRKACA</i>
<i>ARAF</i>	<i>FGFR4</i>	<i>MAP2K2</i>	<i>RAC1</i>	<i>BRCA1</i>	<i>NBN</i>	<i>RAD51D</i>	<i>AR</i>	<i>MDM2</i>	<i>BRCA2</i>	<i>KRAS</i>	<i>PRKACB</i>
<i>AXL</i>	<i>FLT3</i>	<i>MAP2K4</i>	<i>RAF1</i>	<i>BRCA2</i>	<i>NF1</i>	<i>RNF43</i>	<i>BRAF</i>	<i>MDM4</i>	<i>BRAF</i>	<i>MDM4</i>	<i>PTEN</i>
<i>BRAF</i>	<i>FOXL2</i>	<i>MAPK1</i>	<i>RET</i>	<i>CDK12</i>	<i>NF2</i>	<i>RB1</i>	<i>CCND1</i>	<i>MET</i>	<i>CDKN2A</i>	<i>MET</i>	<i>PPARG</i>
<i>BTK</i>	<i>GATA2</i>	<i>MAX</i>	<i>RHEB</i>	<i>CDKN1B</i>	<i>NOTCH1</i>	<i>SETD2</i>	<i>CCND2</i>	<i>MYC</i>	<i>EGFR</i>	<i>MYB</i>	<i>RAD51B</i>
<i>CBL</i>	<i>GNA11</i>	<i>MDM4</i>	<i>RHOA</i>	<i>CDKN2A</i>	<i>NOTCH2</i>	<i>SLX4</i>	<i>CCND3</i>	<i>MYCL</i>	<i>ERBB2</i>	<i>MYBL1</i>	<i>RAF1</i>
<i>CCND1</i>	<i>GNAQ</i>	<i>MED12</i>	<i>ROS1</i>	<i>CDKN2B</i>	<i>NOTCH3</i>	<i>SMARCA4</i>	<i>CCNE1</i>	<i>MYCN</i>	<i>ERBB4</i>	<i>NF1</i>	<i>RB1</i>
<i>CDK4</i>	<i>GNAS</i>	<i>MET</i>	<i>SF3B1</i>	<i>CHEK1</i>	<i>PALB2</i>	<i>SMARCB1</i>	<i>CDK2</i>	<i>NTRK1</i>	<i>ERG</i>	<i>NOTCH1</i>	<i>RELA</i>
<i>CDK6</i>	<i>H3F3A</i>	<i>MTOR</i>	<i>SMAD4</i>	<i>CREBBP</i>	<i>PIK3R1</i>	<i>STK11</i>	<i>CDK4</i>	<i>NTRK2</i>	<i>ESR1</i>	<i>NOTCH4</i>	<i>RET</i>
<i>CHEK2</i>	<i>HIST1H3B</i>	<i>MYC</i>	<i>SMO</i>	<i>FANCA</i>	<i>PMS2</i>	<i>TP53</i>	<i>CDK6</i>	<i>NTRK3</i>	<i>ETV1</i>	<i>NRG1</i>	<i>ROS1</i>
<i>CSF1R</i>	<i>HNF1A</i>	<i>MYCN</i>	<i>SPOP</i>	<i>FANCD2</i>	<i>POLE</i>	<i>TSC1</i>	<i>EGFR</i>	<i>PDGFRA</i>	<i>ETV4</i>	<i>NTRK1</i>	<i>RSPO2</i>
<i>CTNNB1</i>	<i>HRAS</i>	<i>MYD88</i>	<i>SRC</i>	<i>FANCI</i>	<i>PTCH1</i>	<i>TSC2</i>	<i>ERBB2</i>	<i>PDGFRB</i>	<i>ETV5</i>	<i>NTRK2</i>	<i>RSPO3</i>
<i>DDR2</i>	<i>IDH1</i>	<i>NFE2L2</i>	<i>STAT3</i>				<i>ESR1</i>	<i>PIK3CB</i>	<i>FGFR1</i>	<i>NTRK3</i>	<i>TERT</i>
<i>EGFR</i>	<i>IDH2</i>	<i>NRAS</i>	<i>TERT</i>				<i>FGF19</i>	<i>PIK3CA</i>			
<i>ERBB2</i>	<i>JAK1</i>	<i>NTRK1</i>	<i>TOP1</i>				<i>FGF3</i>	<i>PPARG</i>			
<i>ERBB3</i>	<i>JAK2</i>	<i>NTRK2</i>	<i>U2AF1</i>				<i>FGFR1</i>	<i>RICTOR</i>			
<i>ERBB4</i>	<i>JAK3</i>	<i>NTRK3</i>	<i>XPO1</i>				<i>FGFR2</i>	<i>TERT</i>			
<i>ERCC2</i>	<i>KDR</i>	<i>PDGFRA</i>					<i>FGFR3</i>				

Supplementary Table 2 Patient characteristics as a function of the presence of *NOTCH3* non-truncating and truncating variants

	<i>NOTCH3</i>		<i>P</i> value
	Non-truncating	Truncating	
	n = 103 N (%)	n = 17 N (%)	
Age			
Median, years (range)	60 (28-82)	64 (37-79)	0.69
Age			
< 65 years	65 (63.1)	9 (52.9)	0.43
≥ 65 years	38 (36.9)	8 (47.1)	
Gender			
Male	53 (51.5)	6 (35.3)	0.30
Female	50 (48.5)	11 (64.7)	
Primary site			
Right colon	50 (48.5)	5 (29.4)	0.19
Left colon, Rectum	53 (51.5)	12 (70.6)	
Unknown	0 (0.0)	0 (0.0)	
Histology			
Tubular adenocarcinoma	84 (81.6)	15 (88.2)	0.73
Non-tubular adenocarcinoma ^a	19 (18.4)	2 (11.8)	
Unknown	0 (0.0)	0 (0.0)	

^aPoorly differentiated, mucinous, and signet ring cell adenocarcinomas

P values were calculated using a two-sided Fisher's exact test, with the exception of those for age, which were calculated using the Mann-Whitney U test

Supplementary Table 3 Patient characteristics as a function of *NOTCH* amplification status

	<i>NOTCH1</i>			<i>NOTCH2</i>			<i>NOTCH3</i>		
	Non-amp n = 1145 N (%)	Amp (CN ≥ 4) n = 9 N (%)	<i>P</i> value	Non-amp n = 1144 N (%)	Amp (CN ≥ 4) n = 10 N (%)	<i>P</i> value	Non-amp n = 1149 N (%)	Amp (CN ≥ 4) n = 5 N (%)	<i>P</i> value
Age									
Median, years (range)	63 (23-88)	52 (30-76)	0.11	63 (23-88)	66.5 (44-74)	0.38	63 (23-88)	67 (35-69)	0.77
Age									
< 65 years	626 (54.7)	7 (77.8)	0.20	630 (55.1)	3 (30.0)	0.20	632 (55.0)	1 (20.0)	0.18
≥ 65 years	519 (45.3)	2 (22.2)		514 (44.9)	7 (70.0)		517 (45.0)	4 (80.0)	
Gender									
Male	622 (54.3)	6 (66.7)	0.52	623 (54.5)	5 (50.0)	1.00	625 (54.4)	3 (60.0)	1.00
Female	523 (45.7)	3 (33.3)		521 (45.5)	5 (50.0)		524 (45.6)	2 (40.0)	
Primary site									
Right colon	361 (31.5)	2 (22.2)	0.73	359 (31.4)	4 (40.0)	0.73	362 (31.5)	1 (20.0)	1.00
Left colon, Rectum	772 (67.4)	7 (77.8)		773 (67.6)	6 (60.0)		775 (67.4)	4 (80.0)	
Unknown	12 (1.0)	0 (0.0)		12 (1.0)	0 (0.0)		12 (1.0)	0 (0.0)	
Histology									
Tubular adenocarcinoma	1016 (88.7)	7 (77.8)	0.26	1014 (88.6)	9 (90.0)	1.00	1018 (88.6)	5 (100.0)	1.00
Non-tubular adenocarcinoma ^a	125 (10.9)	2 (22.2)		126 (11.0)	1 (10.0)		127 (11.1)	0 (0.0)	
Unknown	4 (0.3)	0 (0.0)		4 (0.3)	0 (0.0)		4 (0.3)	0 (0.0)	

Amp amplification, *CN* copy-number

^aPoorly differentiated, mucinous, and signet ring cell adenocarcinomas

P values were calculated using a two-sided Fisher's exact test, with the exception of those for age, which were calculated using the Mann-Whitney U test