

Table S1. Histopathological and molecular features of 49 colorectal adenomas from 14 MAP patients

MAP patients	<i>MUTYH</i> germline mutations		Age at diagnosis	Adenoma	Histological features	Site	Dysplasia	% Methylation		Mutation	
	DNA change	Protein						LINE-1	LI-MET	KRAS	NRAS
M1	c.1187G>A	p.G396D	51	A1	TB	Cecum	low	61.43	56.23	WT	WT
	c.1187insGG	p.G396GfsX12		A2	TB	NA	NA	63.20	62.50	WT	WT
				A3	TB	NA	NA	54.08	58.97	WT	WT
				A4	TBV	Right colon	low	56.25	N.A.	p.G12C	WT
M2	c.1187G>A	p.G396D	48	A1	TB	Sigma	low	75.33	67.33	WT	p.G12S
	c.1187insGG	p.G396GfsX12		A2	TBV	Sigma	low	66.60	69.57	WT	WT
				A3	TBV	Sigma	low	62.3	59.6	WT	WT
M3	c.1103delCC	p.P367QfsX160	79	A1	TB	Cecum	low	68.05	67.07	p.G12C	WT
	c.1187G>A	p.G396D		A2	TBV	Rectum	low	45.45	64.3	WT	p.G12C
				A3	TBV	Rectum	low	63.18	58.7	WT	WT
M4	c.536A>G	p.Y179C	47	A1	TB	Colon NOS	low	59.00	62.53	p.G12C	WT
	c.536A>G	p.Y179C		A2	TB	Colon NOS	low	61.05	59.80	p.G12C	WT
				A3	TBV	Colon NOS	low	61.45	60.87	p.G12C	WT
				A4	TB	Colon NOS	low	62.73	59.37	WT	p.G12V
M5	c.536A>G	p.Y179C	44	A1	TBV	Sigma	high	46.93	54.37	WT	WT
	c.536A>G	p.Y179C		A2	TB	Right colon	low	56.85	63.13	WT	WT
				A3	TBV	Right colon	high	55.98	57.2	WT	WT
				A4	TB	Right colon	low	62.15	53.4	WT	p.G12C
				A5	TB	Right colon	high	61.58	63.9	WT	WT
				A6	TB	Right colon	low	64.78	58.36	WT	WT
M6	c.536A>G c.1105G>T	p.Y179C p.E369X	42	A1	TBV	Colon NOS	low	51.63	59.17	p.G12C	WT
M7	c.312C>A c.325C>T	p.Y104X p.R109W	50	A1	TB	Right colon	low	54.97	59.36	WT	WT
M8	c.536A>G c.536A>G	p.Y179C p.Y179C	47	A1	TB	Sigma	low	59.88	60.86	p.G13D	WT
M9	c.1187insGG	p.G396GfsX12	40	A1	TBV	Rectum	low	53	59.9	p.G12C	WT
	c.1187insGG	p.G396GfsX12		A2	TB	Rectum	low	62.43	64.8	WT	WT
				A3	TBV	Rectum	low	69.28	64	WT	WT
				A4	TBV	Rectum	low	54.6	55.73	p.G12C	WT

				A5	TBV	Rectum	low	56.4	55.88	p.G12C	WT
				A6	TBV	Rectum	low	61.95	62.53	p.G12C	WT
				A7	TB	Rectum	low	61.2	62.63	p.G12C	WT
M10	692G>A c.1395_1397del GGA	p.R231H p.E466del.	43	A1	TB	Right colon	low	62.28	62	WT	WT
				A2	TB	Left colon	low	68.85	62.1	WT	WT
				A3	TB	Right colon	low	59.55	61.5	p.G12C	WT
				A4	TB	Right colon	low	73.2	68.36	WT	WT
				A5	TB	Rectum	low	64.95	65.73	WT	WT
				A6	TBV	Right colon	low	65.15	61.63	p.G12 A	WT
M12	c.733C>T c.1187G>A	p.R245C p.G396D	50	A1	TB	Right colon	low	71.2	63.96	p.G12C	WT
				A2	TBV	Rectum	low	70.61	63.4	p.K117 N	WT
				A3	TB	Right colon	low	65.1	63.5	p.G12C	WT
M14	c.494A>G c.1145G>A	p.E77X p.E393X	65	A1	TB	Colon NOS	low	52.05	52.93	WT	WT
				A2	TB	Colon NOS	low	60.07	53.4	WT	WT
M15	c.1187G>A c.1187G>A	p.G396D p.G396D	39	A1	TBV	NA	low	60.98	N.A.	WT	WT
				A2	TB	NA	low	51.5	54.2	WT	WT
M16	c.536A>G c.933 +3A>C	p.Y179C p.G264WfsX7	54	A1	TB	Hepatic flexure	low	60.23	56.9	WT	WT
				A2	TBV	Cecum	low	55.78	54.1	WT	WT
				A3	TB	Colon NOS	low	64.06	56.6	WT	WT
				A4	TB	Cecum	low	60.9	59	p.G12C	WT
				A5	TB	Colon NOS	low	58.55	57.7	WT	WT
				A6	TBV	Colon NOS	low	53.4	55.6	WT	WT

MAP, *MUTYH*-associated-polyposis; TB, tubular adenoma; TBV, tubulovillous adenoma; WT, wild type; NA, Not Available; NOS, Not Otherwise Specified.

Table S2. Histopathological and molecular features of 36 adenomas from 17 FAP/AFAP patients included in the study

FAP/AFAP patients	APC germline mutations		Age at diagnosis	Adenoma	Histological features	Site	Dysplasia	% Methylation		Mutation	
	DNA change	Protein						LINE-1	L1-MET	KRAS	NRAS
F1	c.3577_3578 delCA	p.Q1193VfsX14	29	A1	TB	Rectum	low	68.25	66.43	WT	WT
F2	c.505delATAGA	p.I169X	31	A1	TB	Sigma	low	54.10	58.80	WT	WT
				A2	TB	Rectum-Sigma	low	66.75	64.47	WT	WT
				A3	TB	Colon NOS	low	59.33	60.10	WT	WT
F3	c.505delATAGA	p.I169X	38	A1	TB	Right colon	low	60.33	61.53	WT	WT
F4	c.2524_2525 insA	p.D842EfsX74	37	A1	TB	Sigma	low	67.53	64.83	p.G12V	WT
				A2	TB	Right colon	low	63.43	NA	WT	WT
F5	c.4147_4148 delAT	p.M1383VfsX2	30	A1	TB	Left colon	NA	68.78	60.43	WT	WT
				A2	TBV	Left colon	low	60.40	53.83	p.G12S	WT
				A3	TBV	Sigma	low	64.03	61.60	p.G12V	WT
F6	Whole gene del.		48	A1	TBV	NA	low	67.33	61.47	p.G12D	WT
F7	c.2734delT	p.L912 YfsX3	21	A1	TB	Colon NOS	low	71.95	60.63	WT	WT
F8	c.2734delT	p.L912 YfsX3	23	A1	TB	Sigma	low	64.58	69.00	WT	WT
F9	c.677_684 delAGGACATAins TTTC	p.K226 IfsX66	61	A1	TBV	NA	low	62.75	62.60	p.G12V + p.A146P	WT
				A2	TBV	NA	low	59.8	NA	p.G12V	WT
F10	c.3495-3496insA	p.Y1166 IfsX1	19	A1	TB	Sigma	low	64.38	61.30	WT	WT
F11	c.745A>T	p.K249X	37	A1	TB	Rectum	low	66.50	62.77	WT	WT
F12	c.2626C>T	p.R876X	37	A1	TBV	Rectum-Sigma	high	53.53	NA	p.G13D	WT
F13	c.3926del5	p.E1309DfsX3	42	A1	TB	Left colon	low	60.73	61.2	WT	WT
				A2	TB	Left colon	low	61.88	63.07	p.G13C	WT

				A3	TB	Colon NOS	low	60.3	59.63	WT	WT
				A4	TBV	Colon NOS	low	57.83	58	WT	WT
				A5	TB	Colon NOS	low	60.13	58.93	WT	WT
				A6	TBV	Ampulla of Vater	low	65.5	61.53	WT	WT
				A7	TBV	Colon NOS	high	61.1	62.73	WT	WT
				A8	TB	Left colon	low	59.43	60.33	WT	WT
				A9	TB	Right colon	low	62.1	57.83	WT	WT
F14	c.4549_455 delCAGA	p.Q1517KfsX5	57	A1	TB	Duodenum	low	63.1	63.6	WT	WT
				A2	TB	Ampulla of Vater	low	65.38	63.03	WT	WT
				A3	TB	Ampulla of Vater	low	65.1	61.13	WT	WT
F15	t(5;7) (q22;p15)		33	A1	TB	Rectum	low	62.63	62.56	WT	WT
F16	c.637C>T	p.R213X	22	A1	TB	Rectum	low	70.18	67.3	NA	NA
				A2	TB	Right colon	low	72.98	68.13	WT	WT
				A3	TB	Left colon	low	70.25	64.8	WT	WT
				A4	TB	Rectum	low	61.1	68.06	WT	WT
F17	Exon 2del.		40	A1	TB	Sigma	low	62.95	68.3	WT	WT

FAP/AFAP, classical/attenuated adenomatous polyposis; TB, tubular adenoma; TBV, tubulovillous adenoma; WT, wild type; NA, Not Available; NOS, Not Otherwise Specified.

Table S3. Histopathological and molecular features of 24 sporadic colorectal adenomas from 21 patients included in the study

Sporadic patient	Age at diagnosis	Adenoma	Histological features	Site	Dysplasia	% Methylation		Mutation	
						LINE-1	L1-MET	KRAS	NRAS
S1	62	A1	TBV	Rectum-Sigma	high	66.53	65.13	p.G12D	WT
S2	66	A1	TB	Rectum	low	61.38	65.60	WT	WT
S3	66	A1	TBV	Sigma	low	59.48	62.37	WT	WT
S4	77	A1	TBV	Sigma	NA	60.88	63.03	WT	WT
S5	54	A1	TBV	Sigma	high	63.03	66.40	WT	WT
S6	82	A1	TBV	Sigma	low	62.03	65.67	WT	WT
S7	75	A1	TBV	Sigma	low	62.03	66.03	WT	WT
S8	72	A1	TBV	Sigma	low	59.05	66.37	p.G12V	WT
S9	61	A1	TBV	Rectum-Sigma	high	60.25	62.17	p.G12V	WT
S10	71	A1	TBV	Sigma	high	62.83	63.40	p.G12D	WT
S11	50	A1	TBV	Colon NOS	low	60.55	63.43	p.G12D	WT
S12	67	A1	TB	Colon NOS	low	62.4	61.2	WT	WT
S13	68	A1	TB	Ascending colon	low	60.05	59	WT	WT
S14	84	A1	TB	Hepatic flexure	low	63.13	62.9	WT	WT
S15	62	A1	TB	Ascending colon	low	63	62.1	WT	WT
S16	59	A1	TB	Colon NOS	low	60.38	62.23	WT	WT
		A2	TB	Colon NOS	low	60.73	62.56	WT	WT
		A3	TB	Colon NOS	low	61.06	62.06	WT	WT
S17	57	A1	TB	Sigma	low	62.75	60.08	WT	WT
		A2	TB	Left colon	low	60.07	60.36	WT	WT
S18	61	A1	TB	Colon NOS	low	67.3	68.6	WT	WT
S19	61	A1	TB	Ascending colon	low	62.9	67	p.G12A	WT
S20	73	A1	TB	Colon NOS	low	70	65.03	WT	WT
S21	74	A1	TB	Rectum-Sigma	low	69.23	65.07	WT	WT

Sporadic adenomas; TB, tubular adenoma; TBV, tubulovillous adenoma; WT, wild type; NA, Not Available; NOS, Not Otherwise Specified.

Table S4. . Molecular features of the 10 MAP adenocarcinomas found in 8 patients of our cohort; patients M1,M4,M6, M9, and M16 showed both adenomas and carcinomas whereas patients M11, M13, and M17 had only adenocarcinomas.

MAP patient	MUTYH germline mutations		Age at diagnosis	Adenocarcinoma	Site	% Methylation			Mutation		
	DNA change	Protein				LINE-1	L1-MET	KRAS	NRAS	BRAF	PI3KCA
M1	c.1187G>A c.1187insGG	p.G396D p.G396GfsX12	51	CRC	NA	58.70	57.73	p.G12C	WT	WT	p.Q546K
M4	c.536A>G c.536A>G	p.Y179C p.Y179C	47	CRC	Ascending colon	63.00	59.97	p.G12C	WT	WT	WT
				CRC	Ascending colon	59.55	59.54	p.G12C	WT	WT	WT
M6	c.536A>G c.1105G>T	p.Y179C p.E369X	42	CRC	Colon NOS	52.10	51.90	p.G12C	WT	WT	p.Q546K
M9	c.1186-1187 insGG c.1186-1187 insGG	p.G396GfsX12 p.G396GfsX12	40	CRC	Rectum	62.52	58.90	p.G12C	WT	WT	WT
				CRC	Right colon	65.23	61.47	p.G12V	WT	WT	WT
M11	c.1145G>A c.1145G>A	p.G382D p.G382D	47	CRC	Rectum	56.33	57.13	p.G12C	WT	WT	WT
M13	c.733C>T c.1187G>A	p.R245C p.G396D	57	CRC	Right colon	53.03	51.46	WT	WT	WT	WT
M16	c.536A>G c.933 +3A>C	p.Y179C p.G264WfsX7	54	CRC	Rectum	64.45	59.63	p.G12C	WT	WT	WT
M17	c.536A>G c.721C>T	p.Y179C p.R241W	41	CRC	Right colon	59.60	58.50	p.G12C	WT	WT	p. R38H

MAP, *MUTYH*-associated-polyposis; CRC, colorectal cancer; WT, wild type; NA, Not Available; NOS, Not Otherwise Specified.

Table S5. Fifteen samples of histologically normal colonic mucosa derived from healthy individuals used for LINE-1 and L1-*MET* methylation studies

Samples of normal colonic mucosa	Age of patients	Site
NM1	68	Right colon
NM2	57	Right colon
NM3	82	Left colon
NM4	57	Right colon
NM5	72	Rectum
NM6	60	Left colom
NM7	63	Left colon
NM8	71	Left colon
NM9	81	Left colon
NM10	56	Left colon
NM11	39	Left colon
NM12	45	Left colon
NM13	77	Righ colon
NM14	53	Left colon
NM15	64	Left colon

NM, normal mucosa.