

Supplementary Table S1. Germline mutation details for the 57 patients whose archival tumorous tissue specimens were included in this study.

Gene	Transcript	HGVS Mutation	HGVS Protein	No. of individuals with mutation
<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del (Mutation 1)	p.Pro579_Glu633del	28
<i>MLH1</i>	NM_000249.3	c.454-1G>A (Mutation 2)	p.Glu153Phefs*8	7
<i>MLH1</i>	NM_000249.3	c.1975C>T	p.Arg659*	2
<i>MLH1</i>	NM_000249.3	c.(207+1_208-1)_(453+1_454-1)del	p.Lys70_Thr151del	1
<i>MLH1</i>	NM_000249.3	c.1039-1G>A	p.(Thr347Lysfs*8)	1
<i>MLH1</i>	NM_000249.3	c.298C>T	p.(Arg100*)	1
<i>MLH1</i>	NM_000249.3	c.307-?_545+?del	p.(Ala103Valfs*9)	1
<i>MLH1</i>	NM_000249.3	c.320T>G	p.Ile107Arg	1
<i>MLH1</i>	NM_000249.3	c.543C>G	p.?	1
<i>MLH1</i>	NM_000249.3	c.546-2A>G	p.Arg182Serfs*6	1
<i>MSH2</i>	NM_000251.2	c.1552_1553_del	p.(Gln518Valfs*10)	2
<i>MSH2</i>	NM_000251.2	c.1807G>A	p.(Asp603Asn)	2
<i>MSH2</i>	NM_000251.2	c.696_697del	p.(Ser233Hisfs*22)	2
<i>MSH2</i>	NM_000251.2	c.1667_1671del	p.(Leu556Phefs*4)	1
<i>MSH2</i>	NM_000251.2	c.942+3A>T	p.(Val265_Gln314del)	1
<i>MSH6</i>	NM_000179.2	c.152-?_457+?del	p.?	1
<i>MSH6</i>	NM_000179.2	c.3013C>T	p.Arg1005*	1
<i>MSH6</i>	NM_000179.2	c.3195_3199del	p.(Asn1065Lysfs*13)	1
<i>MSH6</i>	NM_000179.2	c.3306del	p.Phe1104Leufs*11	1
<i>MSH6</i>	NM_000179.2	c.900dup	p.(Lys301Glufs*11)	1

Supplementary Table S2. Detailed characteristics of adenoma specimens (n = 68) collected from 57 Lynch syndrome patients.

		Germline mutation				Adenoma characteristics							Method(s) applied on the sample ⁸					
Patient ID	Sample ID	Age ¹	Gene	Transcript	HGVS Mutation	HGVS Protein	Dysplasia grade	Histology ²	Colonic region ³	Size (mm) ⁴	CIMP status	MSI status ⁵	MMR IHC ⁶	CRC diagnosed ⁷	Seq	TSG	CIMP	LINE-1
3	164Ad	45	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	VI	2-3	-	MSS?	+		x			x
5	165Ad		<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	high	TA	V		-	MSI	-(MLH1, PMS2)		x	x	x	x
6	247Ad	50	<i>MSH2</i>	NM_000251.2	c.1552_1553_del	p.(Gln518Valfs*10)	high	TA	VI	10	-	MSI	-(MSH2, MSH6)		x	x	x	x
12	670Ad	36	<i>MSH2</i>	NM_000251.2	c.1552_1553_del	p.(Gln518Valfs*10)	low	TA	V	small	-		+		x	x	x	x
13	671Ad	62	<i>MSH2</i>	NM_000251.2	c.1667_1671del	p.Leu556Phefs*4	high	TA	VI	10	-	MSI	-(MSH2, MSH6)		x	x	x	x
13	248Ad	59	<i>MSH2</i>	NM_000251.2	c.1667_1671del	p.Leu556Phefs*4	low	TA	I	2-3	-	MSS?	+		x	x	x	x
16	188Ad	68	<i>MSH6</i>	NM_000179.2	c.900dup	p.(Lys301Glufs*11)	low	TA	VI	small	-	MSI	-(MSH6)	metachronous (before)	x	x	x	x
16	187Ad	67	<i>MSH6</i>	NM_000179.2	c.900dup	p.(Lys301Glufs*11)	low	TA	IV	small	-	MSS	+	metachronous (before)	x	x	x	x
16	672Ad	70	<i>MSH6</i>	NM_000179.2	c.900dup	p.(Lys301Glufs*11)	low	TVA	V	small	-		+	metachronous (before)	x	x	x	x
17	250Ad	54	<i>MLH1</i>	NM_000249.3	c.546-2A>G	p.Arg182Serfs*6	low	TA	I	small	-	MSI	-(MLH1, PMS2)		x	x	x	x
17	249Ad	45	<i>MLH1</i>	NM_000251.2	c.546-2A>G	p.Arg182Serfs*6	low	TA	I		+	MSS?	+		x	x	x	x
18	100Ad	43	<i>MLH1</i>	NM_000249.3	c.454-1G>A	p.Glu153Phefs*8	high	TA	III	10	-	MSI	-(MLH1, PMS2)	synchronous - III	x	x	x	x
19	168Ad	64	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	I	<10	-	MSI	-(MLH1, PMS2)		x	x	x	x
19	169Ad	63	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	high	TVA	I	8	-	MSI	-(MLH1, PMS2)		x	x	x	x
21	674Ad	34	<i>MLH1</i>	NM_000249.3	c.320T>G	p.Ile107Arg	high	TA	II	20	-	MSI	-(MLH1, PMS2)	synchronous - II (ca in adenomate gradus 2)	x	x	x	x
21	675Ad	34	<i>MLH1</i>	NM_000249.3	c.320T>G	p.Ile107Arg	high	TA	III	7	-	MSI	-(MLH1, PMS2)		x	x	x	x
22	170Ad	31	<i>MLH1</i>	NM_000249.3	c.454-1G>A	p.Glu153Phefs*8	high	TA	VI	15	-	MSI	-(MLH1, PMS2)		x	x	x	x
24	251Ad	42	<i>MSH2</i>	NM_000251.2	c.696_697del	p.(Ser233Hisfs*22)	low	TA	VI	3	-	MSI	-(MSH2, MSH6)		x	x	x	x
26	171Ad	49	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	V	>10	-	MSI	-(MLH1, PMS2)		x	x	x	x
31	172Ad	56	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	I / III		-	MSS	-(MLH1, PMS2)			x	x	x
31	252Ad	48	<i>MLH1</i>	NM_000249.3	c.1975C>T	p.Arg659*	low	TA	I	3	-	MSI	-(MLH1)		x	x	x	x
31	253Ad	48	<i>MLH1</i>	NM_000249.3	c.1975C>T	p.Arg659*	high	TA	V	7	-	MSI	-(MLH1, PMS2)		x	x	x	x
31	173Ad	53	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	V		-	MSS			x	x	x	x
42	254Ad	66	<i>MLH1</i>	NM_000249.3	c.543C>G	p.?	low	TA	II	small	-	MSI	-(MLH1, PMS2)		x	x	x	x
42	255Ad	66	<i>MLH1</i>	NM_000249.3	c.543C>G	p.?	low	TA	I	small	-	MSI	-(MLH1, PMS2)		x	x	x	x
42	256Ad	66	<i>MLH1</i>	NM_000249.3	c.543C>G	p.?	low	TA	II	small	+	MSI	-(MLH1, PMS2)		x	x	x	x
42	257Ad	66	<i>MLH1</i>	NM_000249.3	c.543C>G	p.?	low	TA	III	4	-	MSI?	-(MLH1, PMS2)		x	x	x	x
44	258Ad	69	<i>MSH2</i>	NM_000251.2	c.1807G>A	p.(Asp603Asn)	low	TA	I	10	-	MSI	-(MSH2, MSH6)		x	x	x	x
45	259Ad	41	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	VI	small	-	MSS	+		x	x	x	x
46	190Ad	54	<i>MLH1</i>	NM_000249.3	c.454-1G>A	p.Glu153Phefs*8	high	TA	IV		-	MSI	-(MLH1, PMS2)	metachronous (before and after)		x	x	x
55	260Ad	38	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	II	5	-		-(MLH1)		x			x
60	099Ad	43	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	high	TVA	III	large	+	MSI	-(MLH1, PMS2)	metachronous (before); synchronous (region not known)		x	x	x
63	63Ad	62	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	III	6	-		-(MLH1, PMS2)					
65	151Ad	52	<i>MLH1</i>	NM_000249.3	c.307-?_545+?del	p.(Ala103Valfs*9)	low	TA	I	5	-		-(MLH1, PMS2)	metachronous (before)	x			x
68	193Ad	46	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	V	small	-		-(MSH2, MSH6)	metachronous (before)				x
69	101Ad	62	<i>MLH1</i>	NM_000249.3	c.454-1G>A	p.Glu153Phefs*8	low	TA	V	5	+	MSI	-(MLH1)	metachronous (before and after)	x	x	x	x
69	150Ad	74	<i>MLH1</i>	NM_000249.3	c.454-1G>A	p.Glu153Phefs*8	high	TVA	V	10	+	MSI	-(MLH1, PMS2)	metachronous (before)		x	x	x
73	148Ad	56	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	I	<10	-	MSS	+	metachronous (before and after)	x	x	x	x
73	677Ad	58	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	high	TA	I-II	3-4	-		+	metachronous (before); synchronous I-II (1-5cm from tumor)	x	x	x	x
74	261Ad	61	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	high	TVA	III	20	-		-(MLH1, PMS2)		x			x
76	679Ad	59	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	high	TA	III	7	-		-(MLH1, PMS2)					x
76	263Ad	50	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	high	TA	IV	<10	-	MSI	-(MLH1, PMS2)		x	x	x	x
76	264Ad	53	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	I	<5	-	MSS?	+		x	x	x	x
77	195Ad	38	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	IV-V	8	-	MSI	-(MLH1, PMS2)		x	x	x	x
82	106Ad		<i>MLH1</i>	NM_000249.3	c.454-1G>A	p.Glu153Phefs*8	low	TVA	I		-	MSI	-(MLH1, PMS2)	synchronous I	x	x	x	x
83	160Ad	68	<i>MSH2</i>	NM_000251.2	c.696_697del	p.(Ser233Hisfs*22)	low	TA	II		-	MSS	-(MSH2, MSH6)	metachronous (after)	x	x	x	x
83	83Ad	68	<i>MSH2</i>	NM_000251.2	c.696_697del	p.(Ser233Hisfs*22)	low	TA	I		-		+	metachronous (after)				
85	265Ad	36	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	high	TA	VI	10	-	MSI	-(MLH1, PMS2)		x	x	x	x
85	266Ad	36	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	VI	10	+	MSI	-(MLH1, PMS2)		x	x	x	x
87	680Ad	45	<i>MLH1</i>	NM_000249.3	c.454-1G>A	p.Glu153Phefs*8	low	TVA	III	25	-	MSI	-(MLH1, PMS2)		x	x	x	x
89	682Ad	52	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	high	TA	III	25	-		-(MLH1, PMS2)	synchronous II	x	x	x	x
90	684Ad	50	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	II	>10	-		-(MLH1, PMS2)		x	x	x	x
90	196Ad	47	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	III	6	-	MSI?	-(MLH1, PMS2)		x	x	x	x
95	268Ad	54	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	II	small	-	MSS	+		x	x	x	x
95	197Ad	63	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	III	2	-		+		x	x		x
98	270Ad	48	<i>MLH1</i>	NM_000249.3	c.1039-1G>A	p.(Thr347Lysfs*8)	high	TA	V	>10	-	MSI	-(MLH1, PMS2)		x	x	x	x
101	271Ad		<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	V	small	-	MSS	+		x	x	x	x
104	272Ad	74	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	high	TA	III	10	-	MSI	-(MLH1, PMS2)	metachronous (before)	x	x	x	x
108	685Ad	46	<i>MLH1</i>	NM_000249.3	c.298C>T	p.(Arg100*)	low	TA	III	>5	-	MSI	-(MLH1, PMS2)		x	x	x	x
112	686Ad	48	<i>MSH6</i>	NM_000179.2	c.3195_3199del	p.(Asn1065Lysfs*5)	high	TA	VI	20-30	-	MSS	+		x	x	x	x

116	687Ad	60	<i>MSH6</i>	NM_000179.2	c.152-?_457+?del	p.?	high	TVA	III	large	-	MSI	-(<i>MSH6</i>)	metachronous (before)	x	x	x	x
116	689Ad	60	<i>MSH6</i>	NM_000179.2	c.152-?_457+?del	p.?	low	TA	III	10-15	-		-(<i>MSH6</i>)	metachronous (before)	x	x	x	x
120	690Ad	26	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	III		-		+		x	x	x	x
122	691Ad	51	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	I	>10	-	MSI	-(<i>MLH1</i> , <i>PMS2</i>)		x	x	x	x
123	692Ad	64	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	III	<10	-	MSI	-(<i>MLH1</i> , <i>PMS2</i>)		x	x	x	x
123	693Ad	61	<i>MLH1</i>	NM_000249.3	c.1731+2247_1897-402del	p.Pro579_Glu633del	low	TA	IV	<10	-	MSS	+		x	x	x	x
124	694Ad	43	<i>MLH1</i>	NM_000249.3	c.(207+1_208-1)_(453+1_454-1)del	p.Lys70_Thr151del	low	TA	II				+					x
126	695Ad	49	<i>MSH2</i>	NM_000251.2	c.942+3A>T	p.(Val265_Gln314del)	low	TA	VI		-	MSI	-(<i>MSH2</i> , <i>MSH6</i>)		x	x	x	x

¹ Patient's age (years) at the time of biopsy.

² TA, tubular adenoma; TVA, tubulovillous adenoma.

³ I, cecum; II, ascending colon; III, transversum; IV, descending colon; V, sigmoid colon; V, rectum.

⁴ Size is given in numerical or verbal form, whichever was available.

⁵ Question mark after MSI or MSS status indicates that only one probe produced clearly interpretable result (for MSS?) or due to poor quality, the result was weakly interpretable (MSI?).

⁶ If immunohistochemistry was negative (i.e. protein expression was lost), lost MMR proteins are given in parentheses.

⁷ If the patient was diagnosed with colorectal cancer, timing of the diagnosis related to adenoma sample is given. Roman numerals indicate colonic location (please, see a footnote 3). Other relevant information available is given in parentheses.

⁸ CIMP, MS-MLPA for CIMP markers; LINE-1, MS-MLPA for LINE-1; Seq, Ion Torrent sequencing; TSG, MS-MLPA for selected candidate tumor suppressor genes.

Abbreviations: CIMP, CpG island methylator phenotype; CRC, colorectal cancer; HGVS, Human Genome Variation Society; IHC, immunohistochemistry; MMR, DNA mismatch repair; MSI, microsatellite instability; MSS, microsatellite stable.

Supplementary Table S3. Somatic non-synonymous mutations meeting our selection criteria (see Materials and Methods).

SampleID	Chr	Position (hg19)	Gene	HGVS protein	Ref/Alt	Cosmic Mutation ID (COSMIC v.71)	Quality	Depth	VAF	Sequence Ontology	<i>In silico</i> predictions ¹
101Ad	1	162724506	DDR2	p.Thr93Ile	C/T		49.8	298	0.07	missense_variant	1 of 6 Predicted as Damaging
101Ad	1	162724533	DDR2	p.Thr102Ile	C/T		107.9	301	0.10	missense_variant	6 of 6 Predicted as Damaging
260Ad	1	162724535	DDR2	p.Gln103Ter	C/T		70.3	303	0.08	stop_gained	2 of 6 Predicted as Damaging
685Ad	1	162724542	DDR2	p.Arg105His	G/A		1673.7	838	0.28	missense_variant	6 of 6 Predicted as Damaging
249Ad	1	162724575	DDR2	p.Pro116Leu	C/T		38.1	311	0.06	missense_variant	5 of 6 Predicted as Damaging
151Ad	1	162724598	DDR2	p.Arg124Trp	C/T	4024594,4024595	46.7	435	0.06	missense_variant	6 of 6 Predicted as Damaging
101Ad	1	162724610	DDR2	p.Arg128Cys	C/T		53.9	304	0.07	missense_variant	6 of 6 Predicted as Damaging
101Ad	1	162724611	DDR2	p.Arg128His	G/A		64.4	304	0.08	missense_variant	4 of 6 Predicted as Damaging
689Ad	1	162729617	DDR2	p.Gly235Ser	G/A		170.6	167	0.19	missense_variant	5 of 6 Predicted as Damaging
249Ad	1	162729669	DDR2	p.Pro252Leu	C/T		268.2	499	0.13	missense_variant	5 of 6 Predicted as Damaging
101Ad	1	162740123	DDR2	p.Thr442Ile	C/T		139.8	450	0.10	missense_variant	3 of 6 Predicted as Damaging
101Ad	1	162740131	DDR2	p.Leu445Phe	C/T		133.5	450	0.10	missense_variant	6 of 6 Predicted as Damaging
101Ad	1	162740140	DDR2	p.Pro448Ser	C/T		71.7	449	0.07	missense_variant	2 of 6 Predicted as Damaging
264Ad	1	162740174	DDR2	p.Ser459Phe	C/T		31.2	53	0.11	missense_variant	5 of 6 Predicted as Damaging
264Ad	1	162740224	DDR2	p.Pro476Ser	C/T		39.3	52	0.13	missense_variant	6 of 6 Predicted as Damaging
151Ad	1	162740245	DDR2	p.Glu483Ter	G/T		149.0	421	0.10	stop_gained	2 of 6 Predicted as Damaging
151Ad	1	162741831	DDR2	p.Lys508Glu	A/G		34.9	599	0.05	missense_variant	3 of 6 Predicted as Damaging
101Ad	1	162741847	DDR2	p.Ser513Asn	G/A		92.7	384	0.09	missense_variant	1 of 6 Predicted as Damaging
100Ad	1	162741910	DDR2	p.Gly534Glu	G/A		113.5	229	0.12	missense_variant	6 of 6 Predicted as Damaging
151Ad	1	162743259	DDR2	p.Val577Ile	G/A		149.8	382	0.11	missense_variant	6 of 6 Predicted as Damaging
101Ad	1	162743325	DDR2	p.Ala599Thr	G/A		60.9	602	0.06	missense_variant	2 of 6 Predicted as Damaging
249Ad	1	162743334	DDR2	p.Pro602Ser	C/T		63.1	663	0.06	missense_variant	4 of 6 Predicted as Damaging
101Ad	1	162743346	DDR2	p.Ala606Thr	G/A		92.9	601	0.07	missense_variant	6 of 6 Predicted as Damaging
100Ad	1	162745452	DDR2	p.Leu623Phe	C/T		37.4	443	0.05	missense_variant	4 of 6 Predicted as Damaging
151Ad	1	162745460	DDR2	p.Glu625Asp	G/T		33.1	265	0.06	missense_variant	5 of 6 Predicted as Damaging
100Ad	1	162745533	DDR2	p.Leu650Phe	C/T		37.1	445	0.05	missense_variant	3 of 6 Predicted as Damaging
249Ad	1	162745557	DDR2	p.Glu658Lys	G/A		103.2	352	0.09	missense_variant	5 of 6 Predicted as Damaging
260Ad	1	162748389	DDR2	p.Ser768Asn	G/A		156.1	570	0.09	missense_variant	6 of 6 Predicted as Damaging
260Ad	1	162748425	DDR2	p.Thr780Ile	C/T		75.4	569	0.07	missense_variant	3 of 6 Predicted as Damaging
260Ad	1	162748442	DDR2	p.Glu786Lys	G/A		122.2	567	0.08	missense_variant	4 of 6 Predicted as Damaging
261Ad	2	29445226	ALK	p.Glu1167Lys	C/T		86.3	266	0.10	missense_variant	6 of 6 Predicted as Damaging
151Ad	2	29445273	ALK	p.Thr1151Met	G/A	98478	36.4	699	0.05	missense_variant	5 of 6 Predicted as Damaging
260Ad	2	212288922	ERBB4	p.Pro942Ser	G/A	4090864,4090865	152.8	483	0.10	missense_variant	6 of 6 Predicted as Damaging
249Ad	2	212530054	ERBB4	p.Thr622Ile	G/A		52.4	427	0.06	missense_variant	4 of 6 Predicted as Damaging
249Ad	2	212530057	ERBB4	p.Cys621Tyr	C/T		97.3	429	0.08	missense_variant	6 of 6 Predicted as Damaging
689Ad	2	212530084	ERBB4	p.Arg612Gln	C/T	232263	194.0	154	0.21	missense_variant	2 of 6 Predicted as Damaging
101Ad	2	212530132	ERBB4	p.Gly59Asp	C/T		79.4	526	0.07	missense_variant	6 of 6 Predicted as Damaging
101Ad	2	212530136	ERBB4	p.Asp595Asn	C/T		110.9	526	0.08	missense_variant	2 of 6 Predicted as Damaging
260Ad	2	212530151	ERBB4	p.Val590Met	C/T		143.8	553	0.09	missense_variant	5 of 6 Predicted as Damaging
101Ad	2	212530153	ERBB4	p.Cys589Tyr	C/T		99.6	526	0.08	missense_variant	6 of 6 Predicted as Damaging
689Ad	2	212576808	ERBB4	p.Gly364Glu	C/T		166.4	1098	0.07	missense_variant	5 of 6 Predicted as Damaging
689Ad	2	212576809	ERBB4	p.Gly364Arg	C/T		58.4	1098	0.05	missense_variant	5 of 6 Predicted as Damaging
689Ad	2	212576820	ERBB4	p.Thr360Ile	G/A		252.5	1099	0.09	missense_variant	6 of 6 Predicted as Damaging
101Ad	2	212576847	ERBB4	p.Ser351Asn	C/T		185.4	1796	0.06	missense_variant	4 of 6 Predicted as Damaging
261Ad	2	212576868	ERBB4	p.Ser344Leu	G/A		77.3	468	0.07	missense_variant	2 of 6 Predicted as Damaging
689Ad	2	212576898	ERBB4	p.Cys334Tyr	C/T		58.7	1095	0.05	missense_variant	5 of 6 Predicted as Damaging
260Ad	2	212578301	ERBB4	p.Gly319Glu	C/T	272140	47.0	137	0.09	missense_variant	6 of 6 Predicted as Damaging
261Ad	2	212578301	ERBB4	p.Gly319Glu	C/T	272140	35.0	255	0.06	missense_variant	6 of 6 Predicted as Damaging
101Ad	2	212578340	ERBB4	p.Arg306His	C/T		90.9	1071	0.06	missense_variant	5 of 6 Predicted as Damaging
170Ad	2	212578340	ERBB4	p.Arg306His	C/T		195.0	350	0.13	missense_variant	5 of 6 Predicted as Damaging
689Ad	2	212587135	ERBB4	p.Cys289Tyr	C/T		74.5	391	0.08	missense_variant	6 of 6 Predicted as Damaging
101Ad	2	212587141	ERBB4	p.Ala287Val	G/A		76.2	1729	0.05	missense_variant	6 of 6 Predicted as Damaging
689Ad	2	212587172	ERBB4	p.His277Tyr	G/A		79.0	395	0.08	missense_variant	2 of 6 Predicted as Damaging
260Ad	2	212587208	ERBB4	p.Thr265Ala	T/C	1614290,3709393	70.3	220	0.10	missense_variant	2 of 6 Predicted as Damaging
151Ad	2	212652770	ERBB4	p.Ser179Leu	G/A		57.7	646	0.06	missense_variant	3 of 6 Predicted as Damaging
151Ad	2	212652788	ERBB4	p.Ser173Phe	G/A		57.5	647	0.06	missense_variant	4 of 6 Predicted as Damaging
101Ad	3	41266045	CTNNB1	p.Met14Ile	G/A		44.5	632	0.05	missense_variant	2 of 6 Predicted as Damaging
689Ad	3	41266073	CTNNB1	p.His24Tyr	C/T	5748	99.9	214	0.12	missense_variant	3 of 6 Predicted as Damaging
260Ad	3	41266079	CTNNB1	p.Gln26Ter	C/T		54.9	609	0.05	stop_gained	2 of 6 Predicted as Damaging
260Ad	3	41266089	CTNNB1	p.Ser29Phe	C/T	5694	54.9	609	0.05	missense_variant	3 of 6 Predicted as Damaging
260Ad	3	41266101	CTNNB1	p.Ser33Phe	C/T	5669	46.9	611	0.05	missense_variant	5 of 6 Predicted as Damaging
268Ad	3	41266124	CTNNB1	p.Thr41Ala	A/G	5664	42.1	660	0.05	missense_variant	5 of 6 Predicted as Damaging
674Ad	3	41266124	CTNNB1	p.Thr41Ala	A/G	5664	4643.3	812	0.54	missense_variant	5 of 6 Predicted as Damaging
270Ad	3	41266134	CTNNB1	p.Ser45del	C/T/-	33668,6128	5374.8	645	0.69	disruptive_inframe_deletion	
272Ad	3	41266136	CTNNB1	p.Ser45Pro	T/C	5663	6216.8	759	0.68	missense_variant	5 of 6 Predicted as Damaging
187Ad	3	41266137	CTNNB1	p.Ser45Phe	C/T	5667	2960.1	947	0.37	missense_variant	5 of 6 Predicted as Damaging
682Ad	3	41266137	CTNNB1	p.Ser45Phe	C/T	5667	2414.6	828	0.35	missense_variant	5 of 6 Predicted as Damaging
261Ad	3	41266143	CTNNB1	p.Ser47Asn	G/A	5712	64.4	74	0.16	missense_variant	3 of 6 Predicted as Damaging
169Ad	3	178936096	PIK3CA	p.Gln546His	G/T	24712,3205634	343.6	2332	0.08	missense_variant	3 of 6 Predicted as Damaging
260Ad	3	178938802	PIK3CA	p.Gln682Lys	C/A		40.5	322	0.06	missense_variant	2 of 6 Predicted as Damaging
101Ad	3	178938811	PIK3CA	p.Gly685Ser	G/A		39.9	401	0.06	missense_variant	4 of 6 Predicted as Damaging
249Ad	3	178938836	PIK3CA	p.Arg693His	G/A	327062,327063	30.6	384	0.05	missense_variant	5 of 6 Predicted as Damaging
101Ad	3	178938877	PIK3CA	p.Glu707Lys	G/A		62.8	399	0.07	missense_variant	5 of 6 Predicted as Damaging
260Ad	3	178938907	PIK3CA	p.Asp717Asn	G/A		48.8	326	0.07	missense_variant	2 of 6 Predicted as Damaging
260Ad	3	178938914	PIK3CA	p.Leu719Pro	T/C		144.9	325	0.12	missense_variant	6 of 6 Predicted as Damaging
247Ad	3	178938916	PIK3CA	p.Lys720Gln	A/C		55.9	75	0.15	missense_variant	2 of 6 Predicted as Damaging
684Ad	3	178938916	PIK3CA	p.Lys720Gln	A/C		142.8	80	0.26	missense_variant	2 of 6 Predicted as Damaging
689Ad	3	178938916	PIK3CA	p.Lys720Gln	A/C		131.1	86	0.23	missense_variant	2 of 6 Predicted as Damaging
258Ad	3	178938917	PIK3CA	p.Lys720Ile	A/T		34.1	234	0.06	missense_variant	6 of 6 Predicted as Damaging
689Ad	3	178952065	PIK3CA	p.Met1040Ile	G/A	25085	105.7	420	0.09	missense_variant	3 of 6 Predicted as Damaging
689Ad	3	178952090	PIK3CA	p.Gly1049Ser	G/A	1421012,777	103.0	412	0.09	missense_variant	3 of 6 Predicted as Damaging
689Ad	3	178952091	PIK3CA	p.Gly1049Asp	G/A	1421013,308548	103.0	412	0.09	missense_variant	3 of 6 Predicted as Damaging
689Ad	4	1806101	FGFR3	p.Ala376Thr	G/A		82.7	167	0.12	missense_variant	3 of 6 Predicted as Damaging
689Ad	4	1806186	FGFR3	p.Pro404Leu	C/T		41.6	158	0.08	missense_variant	3 of 6 Predicted as Damaging
260Ad	4	1808337	FGFR3	p.Pro701Ser	C/T		76.1	1041	0.05	missense_variant	5 of 6 Predicted as Damaging
260Ad	4	1808340	FGFR3	p.Val702Met	G/A		52.1	1041	0.05	missense_variant	5 of 6 Predicted as Damaging
151Ad	4	1808913	FGFR3	p.Ser784Phe	C/T		41.6	655	0.05	missense_variant	6 of 6 Predicted as Damaging
101Ad	4	1808942	FGFR3	p.Asp794Asn	G/A		39.9	896	0.05	missense_variant	6 of 6 Predicted as Damaging
249Ad	4	1808970	FGFR3	p.Ser803Asn	G/A		35.1	292	0.06	missense_variant	1 of 6 Predicted as Damaging

151Ad	4	153247288	FBXW7	p.Arg505His	C/T	133117,25812,287372,287373,287374,3127975	53,8	1194	0,05	missense_variant	4 of 6 Predicted as Damaging
261Ad	4	153247330	FBXW7	p.Gly491Asp	C/T		51,0	1311	0,05	missense_variant	5 of 6 Predicted as Damaging
151Ad	4	153247369	FBXW7	p.Ser478Phe	G/A		154,8	1182	0,09	missense_variant	5 of 6 Predicted as Damaging
670Ad	4	153249384	FBXW7	p.Arg465His	C/T	1149856,117308,117309,117310,22965	38,5	233	0,07	missense_variant	4 of 6 Predicted as Damaging
260Ad	4	153249388	FBXW7	p.Val464Met	C/T		68,5	656	0,06	missense_variant	5 of 6 Predicted as Damaging
261Ad	4	153249390	FBXW7	p.Thr463Ile	G/A		54,2	235	0,08	missense_variant	4 of 6 Predicted as Damaging
689Ad	4	153249390	FBXW7	p.Thr463Ile	G/A		166,5	345	0,12	missense_variant	4 of 6 Predicted as Damaging
261Ad	4	153249420	FBXW7	p.Cys453Tyr	C/T		48,1	238	0,08	missense_variant	5 of 6 Predicted as Damaging
689Ad	4	153249424	FBXW7	p.Glu452Lys	C/T		145,2	344	0,11	missense_variant	2 of 6 Predicted as Damaging
101Ad	4	153249441	FBXW7	p.Trp446Ter	C/T	1427742,1427743,1427744,1427745,1427746	86,3	678	0,07	stop_gained	2 of 6 Predicted as Damaging
100Ad	4	153249468	FBXW7	p.Gly437Glu	C/T	3940767,3940768,3940769,3940770,3940771	30,6	496	0,05	missense_variant	5 of 6 Predicted as Damaging
151Ad	4	153249471	FBXW7	p.Ser436Asn	C/T		85,2	352	0,09	missense_variant	5 of 6 Predicted as Damaging
689Ad	4	153258983	FBXW7	p.Arg278Ter	G/A	1173027,22971,327086,327087,327088	52,1	528	0,06	stop_gained	2 of 6 Predicted as Damaging
689Ad	7	55227987	EGFR	p.Gly485Asp	G/A		73,5	463	0,07	missense_variant	0 of 6 Predicted as Damaging
151Ad	7	55241647	EGFR	p.Pro699Ser	C/T	28600	54,5	936	0,05	missense_variant	5 of 6 Predicted as Damaging
689Ad	7	55241666	EGFR	p.Arg705Lys	G/A		230,3	256	0,17	missense_variant	5 of 6 Predicted as Damaging
689Ad	7	55241723	EGFR	p.Gly724Asp	G/A		135,6	252	0,13	missense_variant	5 of 6 Predicted as Damaging
695Ad	7	55241726	EGFR	p.Thr725Met	C/T	53264	7100,4	2628	0,40	missense_variant	5 of 6 Predicted as Damaging
261Ad	7	55241728	EGFR	p.Val726Met	G/A		36,4	223	0,07	missense_variant	6 of 6 Predicted as Damaging
260Ad	7	55242466	EGFR	p.Glu746Lys	G/A	13184	196,4	627	0,10	missense_variant	3 of 6 Predicted as Damaging
101Ad	7	55248990	EGFR	p.Ala763Val	C/T		40,7	718	0,05	missense_variant	4 of 6 Predicted as Damaging
249Ad	7	55248990	EGFR	p.Ala763Val	C/T		33,4	445	0,05	missense_variant	4 of 6 Predicted as Damaging
249Ad	7	55249002	EGFR	p.Ala767Val	C/T	26445	35,6	445	0,05	missense_variant	5 of 6 Predicted as Damaging
260Ad	7	55249019	EGFR	p.His773Tyr	C/T		67,8	289	0,08	missense_variant	2 of 6 Predicted as Damaging
100Ad	7	55249076	EGFR	p.Leu792Phe	C/T		31,3	275	0,06	missense_variant	4 of 6 Predicted as Damaging
100Ad	7	55249089	EGFR	p.Gly796Asp	G/A	133565	30,8	276	0,06	missense_variant	6 of 6 Predicted as Damaging
100Ad	7	55259533	EGFR	p.Ala864Val	C/T	219795	36,4	223	0,07	missense_variant	3 of 6 Predicted as Damaging
689Ad	7	55259535	EGFR	p.Glu865Lys	G/A	707337	49,7	93	0,12	missense_variant	4 of 6 Predicted as Damaging
151Ad	7	55259544	EGFR	p.Glu868Lys	G/A	214350	205,3	237	0,17	missense_variant	3 of 6 Predicted as Damaging
100Ad	7	55259550	EGFR	p.His870Tyr	C/T	53292	57,4	223	0,09	missense_variant	3 of 6 Predicted as Damaging
261Ad	7	116339628	MET	p.Pro164Ser	C/T		60,9	940	0,05	missense_variant	0 of 6 Predicted as Damaging
261Ad	7	116340177	MET	p.Ala347Thr	G/A		46,0	142	0,09	missense_variant	5 of 6 Predicted as Damaging
689Ad	7	116340189	MET	p.Pro351Ser	C/T		45,0	420	0,06	missense_variant	5 of 6 Predicted as Damaging
260Ad	7	116340210	MET	p.Asp358Asn	G/A		40,0	867	0,05	missense_variant	0 of 6 Predicted as Damaging
689Ad	7	116340210	MET	p.Asp358Asn	G/A		58,3	420	0,07	missense_variant	0 of 6 Predicted as Damaging
258Ad	7	116411990	MET	p.Thr1010Ile	C/T	707	13037,4	1992	0,59	missense_variant	4 of 6 Predicted as Damaging
260Ad	7	116423432	MET	p.Ser1254Asn	G/A		84,5	1908	0,05	missense_variant	4 of 6 Predicted as Damaging
256Ad	7	140453136	BRAF	p.Val600Glu	A/T	476	31,1	375	0,05	missense_variant	5 of 6 Predicted as Damaging
101Ad	7	140481402	BRAF	p.Gly469Glu	C/T	461	83,1	1632	0,05	missense_variant	6 of 6 Predicted as Damaging
261Ad	7	140481408	BRAF	p.Ser467Leu	G/A	27911	38,2	215	0,07	missense_variant	5 of 6 Predicted as Damaging
689Ad	7	140481408	BRAF	p.Ser467Leu	G/A	27911	238,8	382	0,14	missense_variant	5 of 6 Predicted as Damaging
151Ad	7	140481433	BRAF	p.Val459Met	C/T		137,0	573	0,09	missense_variant	3 of 6 Predicted as Damaging
260Ad	7	140481444	BRAF	p.Gly455Glu	C/T	1162152	86,0	430	0,08	missense_variant	3 of 6 Predicted as Damaging
260Ad	7	140481448	BRAF	p.Asp454Asn	C/T		108,4	430	0,09	missense_variant	3 of 6 Predicted as Damaging
249Ad	7	140481489	BRAF	p.Thr440Ile	G/A		46,7	754	0,05	missense_variant	2 of 6 Predicted as Damaging
101Ad	8	38282143	FGFR1	p.Glu305Lys	C/T		77,3	655	0,06	missense_variant	4 of 6 Predicted as Damaging
261Ad	8	38282146	FGFR1	p.Val304Met	C/T		147,0	78	0,27	missense_variant	5 of 6 Predicted as Damaging
101Ad	8	38282160	FGFR1	p.Ala299Val	G/A		81,8	656	0,07	missense_variant	2 of 6 Predicted as Damaging
151Ad	8	38282184	FGFR1	p.Gly291Glu	C/T		65,8	646	0,06	missense_variant	5 of 6 Predicted as Damaging
260Ad	8	38282188	FGFR1	p.Ala290Thr	C/T		228,1	455	0,13	missense_variant	5 of 6 Predicted as Damaging
151Ad	8	38282208	FGFR1	p.Pro283Leu	G/A		70,1	642	0,06	missense_variant	6 of 6 Predicted as Damaging
260Ad	8	38285875	FGFR1	p.Pro179Leu	G/A		121,1	121	0,18	missense_variant	4 of 6 Predicted as Damaging
101Ad	8	38285881	FGFR1	p.Thr177Ile	G/A		158,8	351	0,12	missense_variant	3 of 6 Predicted as Damaging
101Ad	8	38285945	FGFR1	p.Pro156Ser	G/A	3648909,3648910,3648911,3648912,3648913,36489	119,4	536	0,08	missense_variant	5 of 6 Predicted as Damaging
260Ad	9	139399351	NOTCH1	p.Arg1598Cys	G/A		100,2	360	0,09	missense_variant	5 of 6 Predicted as Damaging
689Ad	9	139399362	NOTCH1	p.Arg1594Gln	C/T	136758,136759	68,5	286	0,08	missense_variant	5 of 6 Predicted as Damaging
679Ad	9	139399363	NOTCH1	p.Arg1594Trp	C/T		6016,6	3414	0,36	missense_variant	6 of 6 Predicted as Damaging
151Ad	10	89685277	PTEN	p.Asp58Asn	G/A	1166806	41,0	985	0,05	missense_variant	4 of 6 Predicted as Damaging
100Ad	10	89685289	PTEN	p.Asn63fs	A/-	5811,5836,86071	1780,4	932	0,29	frameshift_variant	
689Ad	10	89711900	PTEN	p.Arg173His	G/A	5039	110,6	548	0,08	missense_variant	6 of 6 Predicted as Damaging
680Ad	10	89717672	PTEN	p.Arg233Ter	C/T	5154	5694,0	2112	0,35	stop_gained	2 of 6 Predicted as Damaging
261Ad	10	89717675	PTEN	p.Arg234Trp	C/T	5118	93,2	382	0,09	missense_variant	5 of 6 Predicted as Damaging
689Ad	10	89717681	PTEN	p.Asp236Asn	G/A		155,1	734	0,08	missense_variant	3 of 6 Predicted as Damaging
101Ad	10	89717727	PTEN	p.Gly251Asp	G/A	13981	101,5	1843	0,05	missense_variant	6 of 6 Predicted as Damaging
101Ad	10	89720805	PTEN	p.Thr319Ile	C/T		58,2	1020	0,06	missense_variant	4 of 6 Predicted as Damaging
101Ad	10	89720864	PTEN	p.Pro339Ser	C/T	23657	71,4	1022	0,05	missense_variant	5 of 6 Predicted as Damaging
689Ad	10	123258023	FGFR2	p.Ala554Val	G/A		103,9	641	0,07	missense_variant	4 of 6 Predicted as Damaging
261Ad	10	123258030	FGFR2	p.Leu552Phe	G/A		66,2	487	0,07	missense_variant	5 of 6 Predicted as Damaging
151Ad	10	123258033	FGFR2	p.Leu551Phe	G/A		51,7	1016	0,05	missense_variant	5 of 6 Predicted as Damaging
689Ad	10	123274745	FGFR2	p.Met392Ile	C/T		202,6	80	0,33	missense_variant	3 of 6 Predicted as Damaging
261Ad	10	123274752	FGFR2	p.Ala390Val	G/A		126,8	63	0,29	missense_variant	2 of 6 Predicted as Damaging
101Ad	10	123274773	FGFR2	p.Cys383Tyr	C/T	1346257,915493,915494,915495	34,3	604	0,05	missense_variant	6 of 6 Predicted as Damaging
100Ad	10	123274828	FGFR2	p.Gly365Arg	C/T		47,4	481	0,06	missense_variant	2 of 6 Predicted as Damaging
101Ad	10	123274830	FGFR2	p.Pro364Leu	G/A		60,9	601	0,06	missense_variant	4 of 6 Predicted as Damaging
249Ad	10	123279498	FGFR2	p.Leu312Phe	G/A		32,3	565	0,05	missense_variant	5 of 6 Predicted as Damaging
260Ad	10	123279507	FGFR2	p.Leu309Phe	G/A		140,9	409	0,10	missense_variant	4 of 6 Predicted as Damaging
689Ad	10	123279507	FGFR2	p.Leu309Phe	G/A		226,1	315	0,15	missense_variant	4 of 6 Predicted as Damaging
689Ad	10	123279618	FGFR2	p.Gly272Arg	C/T		52,9	200	0,09	missense_variant	5 of 6 Predicted as Damaging
260Ad	10	123279645	FGFR2	p.Pro263Ser	G/A		57,7	376	0,07	missense_variant	6 of 6 Predicted as Damaging
101Ad	10	123279650	FGFR2	p.Gly261Glu	C/T		89,9	503	0,08	missense_variant	6 of 6 Predicted as Damaging
101Ad	10	123279680	FGFR2	p.Arg251Gln	C/T	29828,3434789,3434790,3434791	44,4	501	0,06	missense_variant	5 of 6 Predicted as Damaging
674Ad	10	123279681	FGFR2	p.Arg251Ter	G/A	1346299,1346300,1346301,1346302	926,4	1002	0,18	stop_gained	2 of 6 Predicted as Damaging
670Ad	12	25378562	KRAS	p.Ala146Thr	C/T	1165198,19404	141,5	442	0,10	missense_variant	6 of 6 Predicted as Damaging
686Ad	12	25378562	KRAS	p.Ala146Thr	C/T	1165198,19404	5895,2	1381	0,45	missense_variant	6 of 6 Predicted as Damaging
695Ad	12	25378562	KRAS	p.Ala146Thr	C/T	1165198,19404	1344,3	1462	0,18	missense_variant	6 of 6 Predicted as Damaging
261Ad	12	25378586	KRAS	p.Gly138Arg	C/T		64,1	325	0,08	missense_variant	6 of 6 Predicted as Damaging
264Ad	12	25378586	KRAS	p.Gly138Arg	C/T		40,8	63	0,13	missense_variant	6 of 6 Predicted as Damaging
260Ad	12	25378618	KRAS	p.Thr127Ile	G/A		110,1	981	0,06	missense_variant	3 of 6 Predicted as Damaging
151Ad	12	25378622	KRAS	p.Asp126Asn	C/T		51,3	690	0,05	missense_variant	2 of 6 Predicted as Damaging
261Ad	12	25380274	KRAS	p.Glu62Lys	C/T	3459505,3459506	71,4	687	0,06	missense_variant	6 of 6 Predicted as Damaging
261Ad	12	25380279	KRAS	p.Gly60Asp	C/T	87290	62,8	689	0,06	missense_variant	6 of 6 Predicted as Damaging
689Ad	12	25380319	KRAS	p.Asp47Asn	C/T		50,1	779	0,05	missense_variant	3 of 6 Predicted as Damaging

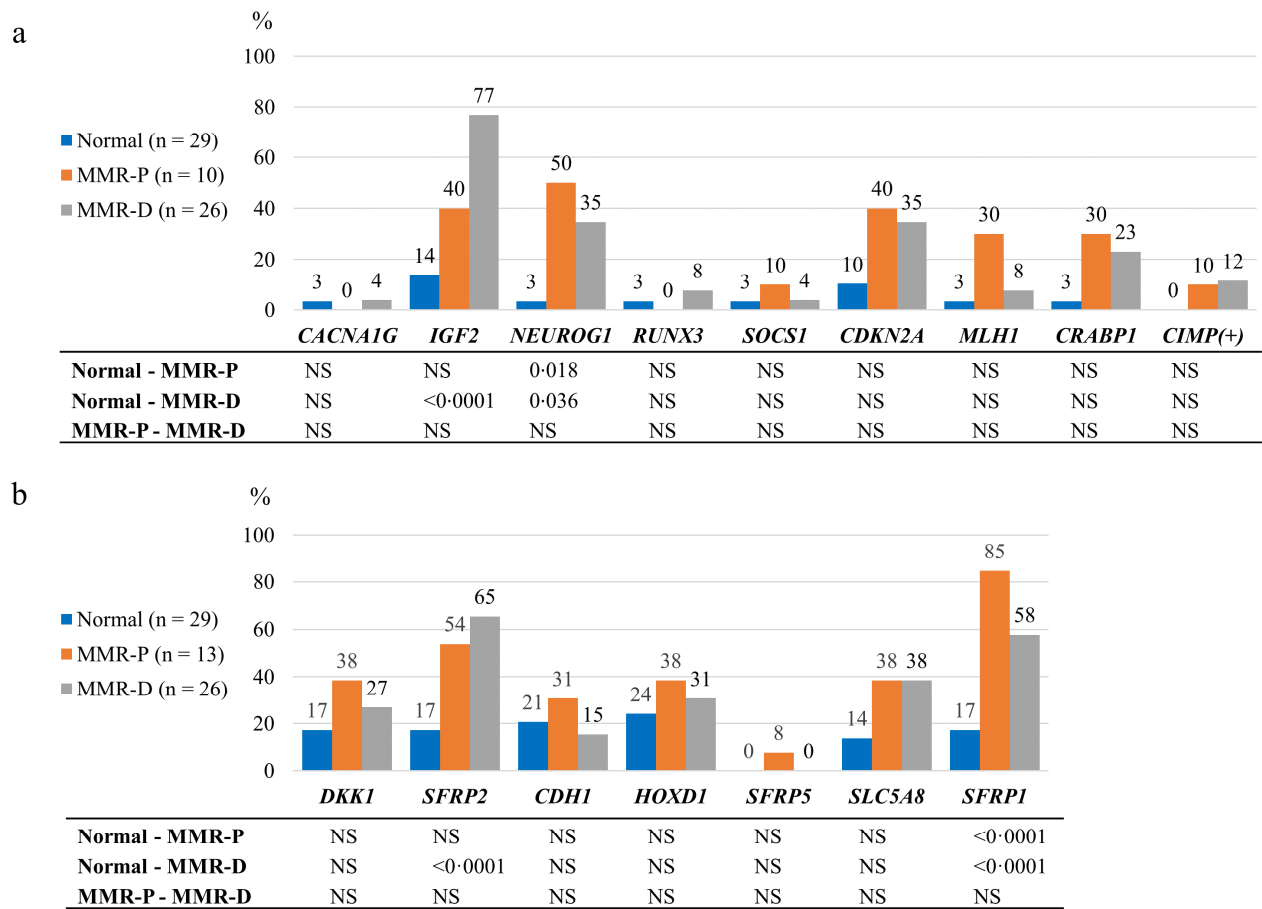
101Ad	12	25380325	KRAS	p.Val45Ile	C/T		80,9	2221	0,05	missense_variant	3 of 6 Predicted as Damaging
169Ad	12	25398281	KRAS	p.Gly13Asp	C/T	1140132,532	6422,7	2294	0,37	missense_variant	6 of 6 Predicted as Damaging
170Ad	12	25398281	KRAS	p.Gly13Asp	C/T	1140132,532	1497,0	687	0,29	missense_variant	6 of 6 Predicted as Damaging
171Ad	12	25398281	KRAS	p.Gly13Asp	C/T	1140132,532	1153,9	2641	0,14	missense_variant	6 of 6 Predicted as Damaging
270Ad	12	25398281	KRAS	p.Gly13Asp	C/T	1140132,532	52,8	809	0,05	missense_variant	6 of 6 Predicted as Damaging
106Ad	12	25398284	KRAS	p.Gly12Asp	C/T	1135366,521	1016,4	825	0,21	missense_variant	4 of 6 Predicted as Damaging
248Ad	12	25398284	KRAS	p.Gly12Asp	C/T	1135366,521	194,6	1555	0,07	missense_variant	4 of 6 Predicted as Damaging
249Ad	12	25398284	KRAS	p.Gly12Val	C/A	1140133,520	258,1	1316	0,08	missense_variant	4 of 6 Predicted as Damaging
260Ad	12	25398284	KRAS	p.Gly12Asp	C/T	1135366,521	41,8	951	0,05	missense_variant	4 of 6 Predicted as Damaging
264Ad	12	25398284	KRAS	p.Gly12Val	C/A	1140133,520	115,9	55	0,29	missense_variant	4 of 6 Predicted as Damaging
260Ad	12	25398300	KRAS	p.Val7Met	C/T	30620	71,2	944	0,06	missense_variant	6 of 6 Predicted as Damaging
249Ad	15	66727414	MAP2K1	p.Glu44Lys	G/A		30,9	382	0,05	missense_variant	6 of 6 Predicted as Damaging
260Ad	15	66727423	MAP2K1	p.Arg47Ter	C/T		44,2	400	0,06	stop_gained	2 of 6 Predicted as Damaging
101Ad	15	66727462	MAP2K1	p.Val60Met	G/A		36,4	531	0,05	missense_variant	5 of 6 Predicted as Damaging
151Ad	15	66727462	MAP2K1	p.Val60Met	G/A		103,0	492	0,08	missense_variant	5 of 6 Predicted as Damaging
101Ad	15	66727522	MAP2K1	p.Gly80Ser	G/A		30,2	526	0,05	missense_variant	4 of 6 Predicted as Damaging
689Ad	17	7573937	TP53	p.Ala364Thr	C/T	46361	59,6	559	0,06	missense_variant	2 of 6 Predicted as Damaging
260Ad	17	7573967	TP53	p.Gln354Ter	G/A	562344,562345	76,0	685	0,06	stop_gained	2 of 6 Predicted as Damaging
689Ad	17	7573970	TP53	p.Ala353Thr	C/T	45292	102,3	560	0,08	missense_variant	3 of 6 Predicted as Damaging
261Ad	17	7574008	TP53	p.Met340Thr	A/G		31,3	226	0,06	missense_variant	5 of 6 Predicted as Damaging
101Ad	17	7574030	TP53	p.Arg333Cys	G/A		158,1	959	0,08	missense_variant	6 of 6 Predicted as Damaging
261Ad	17	7574030	TP53	p.Arg333Cys	G/A		145,9	225	0,14	missense_variant	6 of 6 Predicted as Damaging
689Ad	17	7577021	TP53	p.Arg306Gln	C/T		182,4	178	0,19	missense_variant	6 of 6 Predicted as Damaging
689Ad	17	7577058	TP53	p.Glu294Lys	C/T	44127	113,8	178	0,14	missense_variant	1 of 6 Predicted as Damaging
680Ad	17	7577069	TP53	p.Arg290His	C/T	1386594,44017	489,7	1329	0,11	missense_variant	2 of 6 Predicted as Damaging
100Ad	17	7577091	TP53	p.Arg283Cys	G/A	10911	43,3	378	0,06	missense_variant	6 of 6 Predicted as Damaging
249Ad	17	7577094	TP53	p.Arg282Trp	G/A	10704,1636702,3378339,99925	35,6	382	0,06	missense_variant	6 of 6 Predicted as Damaging
689Ad	17	7577102	TP53	p.Gly279Val	C/A	46032	114,1	178	0,14	missense_variant	6 of 6 Predicted as Damaging
170Ad	17	7577103	TP53	p.Gly279Arg	C/T	44603	942,0	429	0,30	missense_variant	6 of 6 Predicted as Damaging
689Ad	17	7577112	TP53	p.Ala276Thr	C/T	44114	46,0	179	0,08	missense_variant	6 of 6 Predicted as Damaging
685Ad	17	7577121	TP53	p.Arg273Cys	G/A	10659,1645518,3355991,99933	1328,8	765	0,26	missense_variant	6 of 6 Predicted as Damaging
689Ad	17	7577142	TP53	p.Gly266Arg	C/T	10794,1559475,1645293,3388175	113,5	178	0,14	missense_variant	6 of 6 Predicted as Damaging
249Ad	17	7577532	TP53	p.Pro250Leu	G/A	10771,1646862,212111,212112,3378345	50,6	1251	0,05	missense_variant	6 of 6 Predicted as Damaging
249Ad	17	7577551	TP53	p.Gly244Ser	C/T	10941,1716873,3355992,984898,984900,984901	69,5	1250	0,05	missense_variant	6 of 6 Predicted as Damaging
689Ad	17	7577556	TP53	p.Cys242Trp	C/T	10646,251396,251397,251398,2744612,3403262	223,9	544	0,11	missense_variant	6 of 6 Predicted as Damaging
101Ad	17	7577599	TP53	p.Asp228Asn	C/T	44398	140,9	1613	0,06	missense_variant	4 of 6 Predicted as Damaging
671Ad	17	7578184	TP53	p.Pro222Leu	G/A	44606	4105,3	1848	0,30	missense_variant	5 of 6 Predicted as Damaging
100Ad	17	7578188	TP53	p.Glu221Lys	C/T	44853	41,5	879	0,05	missense_variant	6 of 6 Predicted as Damaging
151Ad	17	7578223	TP53	p.Arg209Lys	C/T	308314,308315,308316,308317,45995	62,3	928	0,05	missense_variant	1 of 6 Predicted as Damaging
151Ad	17	7578239	TP53	p.Glu204Lys	C/T	43990	62,7	925	0,05	missense_variant	1 of 6 Predicted as Damaging
151Ad	17	7578253	TP53	p.Gly199Glu	C/T	43989	90,0	924	0,06	missense_variant	6 of 6 Predicted as Damaging
101Ad	17	7578262	TP53	p.Arg196Gln	C/T	1386755,1386756,1386757,1386758,44599	42,3	992	0,05	missense_variant	6 of 6 Predicted as Damaging
260Ad	17	7578262	TP53	p.Arg196Gln	C/T	1386755,1386756,1386757,1386758,44599	136,2	853	0,07	missense_variant	6 of 6 Predicted as Damaging
101Ad	17	7578277	TP53	p.Pro191Leu	G/A	3890517,3890518,3890519,3890520,3890521,38905	571,3	988	0,06	missense_variant	6 of 6 Predicted as Damaging
261Ad	17	7578392	TP53	p.Glu180Lys	C/T	1522501,1522502,1522503,1522504,43772	201,9	99	0,27	missense_variant	5 of 6 Predicted as Damaging
686Ad	17	7578392	TP53	p.Glu180Lys	C/T	1522501,1522502,1522503,1522504,43772	102,0	1515	0,05	missense_variant	5 of 6 Predicted as Damaging
101Ad	17	7578428	TP53	p.His168Tyr	G/A	43861	131,4	1082	0,07	missense_variant	4 of 6 Predicted as Damaging
168Ad	17	7578464	TP53	p.Arg156Cys	G/A	3403271,3403272,3403273,3403274,3403275,34032	710,9	482	0,23	missense_variant	2 of 6 Predicted as Damaging
169Ad	17	7578464	TP53	p.Arg156Cys	G/A	3403271,3403272,3403273,3403274,3403275,34032	5800,7	2066	0,35	missense_variant	2 of 6 Predicted as Damaging
101Ad	17	7579377	TP53	p.Gln104Ter	G/A	10886,2745029,308171,308172,3727867	37,7	415	0,06	stop_gained	2 of 6 Predicted as Damaging
101Ad	17	7579400	TP53	p.Ser96Phe	G/A	44447	55,5	413	0,07	missense_variant	1 of 6 Predicted as Damaging
151Ad	17	7579419	TP53	p.Ser90Pro	A/G		39,3	248	0,08	missense_variant	2 of 6 Predicted as Damaging
689Ad	17	7579433	TP53	p.Pro85Leu	G/A	45837	73,5	73	0,18	missense_variant	3 of 6 Predicted as Damaging
252Ad	17	7579472	TP53	p.Val73fs	-/C		119,9	133	0,34	frameshift_variant	
151Ad	17	7579476	TP53	p.Pro71Ser	G/A		3108,9	248	0,15	missense_variant	1 of 6 Predicted as Damaging
151Ad	17	7579864	TP53	p.Glu17Lys	C/T		233,0	508	0,12	missense_variant	6 of 6 Predicted as Damaging
689Ad	17	7579879	TP53	p.Pro12Ser	G/A		292,2	433	0,15	missense_variant	3 of 6 Predicted as Damaging
151Ad	17	7579887	TP53	p.Ser9Asn	C/T		78,2	510	0,07	missense_variant	2 of 6 Predicted as Damaging
261Ad	17	7579896	TP53	p.Ser6Leu	G/A		138,9	140	0,18	missense_variant	2 of 6 Predicted as Damaging
689Ad	17	37880216	ERBB2	p.Val754Met	G/A		101,0	225	0,12	missense_variant	4 of 6 Predicted as Damaging
101Ad	17	37880223	ERBB2	p.Arg756Lys	G/A		303,3	865	0,11	missense_variant	4 of 6 Predicted as Damaging
265Ad	17	37881332	ERBB2	p.Val842Ile	G/A	14065	1175,2	544	0,29	missense_variant	5 of 6 Predicted as Damaging
266Ad	17	37881332	ERBB2	p.Val842Ile	G/A	14065	3120,3	1184	0,33	missense_variant	5 of 6 Predicted as Damaging
249Ad	17	37881347	ERBB2	p.Ala847Thr	G/A		33,8	469	0,05	missense_variant	5 of 6 Predicted as Damaging
261Ad	17	37881408	ERBB2	p.Ala867Val	C/T		86,3	81	0,19	missense_variant	4 of 6 Predicted as Damaging
151Ad	17	37881439	ERBB2	p.Tyr871Ter	C/G		49,0	762	0,05	stop_gained	2 of 6 Predicted as Damaging
689Ad	17	37881444	ERBB2	p.Ala879Val	C/T		72,8	376	0,08	missense_variant	5 of 6 Predicted as Damaging
247Ad	17	37881446	ERBB2	p.Asp880Asn	G/A		32,2	151	0,07	missense_variant	4 of 6 Predicted as Damaging
101Ad	17	37881450	ERBB2	p.Gly881Glu	G/A		156,1	924	0,05	missense_variant	5 of 6 Predicted as Damaging
689Ad	17	37881452	ERBB2	p.Gly882Ser	G/A		62,3	454	0,07	missense_variant	4 of 6 Predicted as Damaging
689Ad	17	37881453	ERBB2	p.Gly882Asp	G/A		113,5	456	0,09	missense_variant	4 of 6 Predicted as Damaging
261Ad	18	48575103	SMAD4	p.Trp99Ter	G/A		34,8	600	0,05	stop_gained	2 of 6 Predicted as Damaging
151Ad	18	48575111	SMAD4	p.Pro102Leu	C/T	14088	99,5	1170	0,06	missense_variant	5 of 6 Predicted as Damaging
264Ad	18	48575111	SMAD4	p.Pro102Leu	C/T	14088	78,9	78	0,18	missense_variant	5 of 6 Predicted as Damaging
261Ad	18	48575159	SMAD4	p.Ala118Val	C/T	14215	41,0	605	0,05	missense_variant	5 of 6 Predicted as Damaging
689Ad	18	48575180	SMAD4	p.Ser125Asn	G/A		130,4	618	0,08	missense_variant	2 of 6 Predicted as Damaging
689Ad	18	48575194	SMAD4	p.Pro130Ser	C/T	33139	66,4	618	0,06	missense_variant	6 of 6 Predicted as Damaging
260Ad	18	48581217	SMAD4	p.Thr174Ile	C/T		57,6	1338	0,05	missense_variant	3 of 6 Predicted as Damaging
260Ad	18	48581223	SMAD4	p.Gly176Glu	G/A		65,8	1342	0,05	missense_variant	3 of 6 Predicted as Damaging
260Ad	18	48581271	SMAD4	p.Thr192Ile	C/T		100,2	1344	0,06	missense_variant	3 of 6 Predicted as Damaging
260Ad	18	48581288	SMAD4	p.Pro198Thr	C/A		3014,2	1339	0,30	missense_variant	3 of 6 Predicted as Damaging
263Ad	18	48581288	SMAD4	p.Pro198Thr	C/A		3310,2	1088	0,36	missense_variant	3 of 6 Predicted as Damaging
101Ad	18	48581301	SMAD4	p.Ala202Val	C/T		83,5	1304	0,05	missense_variant	3 of 6 Predicted as Damaging
272Ad	18	48584558	SMAD4	p.Pro244His	C/A		2625,9	950	0,34	missense_variant	3 of 6 Predicted as Damaging
151Ad	18	48584577	SMAD4	p.Gln250His	G/C		107,4	669	0,07	missense_variant	2 of 6 Predicted as Damaging
101Ad	18	48584588	SMAD4	p.Thr254Ile	C/T		42,5	759	0,05	missense_variant	2 of 6 Predicted as Damaging
261Ad	18	48584597	SMAD4	p.Pro257Leu	C/T		239,6	164	0,23	missense_variant	3 of 6 Predicted as Damaging
260Ad	18	48586259	SMAD4	p.Phe310Leu	T/C	1324558	112,4	852	0,07	missense_variant	3 of 6 Predicted as Damaging
689Ad	18	48586269	SMAD4	p.Pro313Leu	C/T		84,8	459	0,08	missense_variant	4 of 6 Predicted as Damaging
689Ad	18	48591858	SMAD4	p.Val341Ile	G/A		204,8	530	0,11	missense_variant	5 of 6 Predicted as Damaging
264Ad	18	48591862	SMAD4	p.Pro342Leu	C/T		38,5	69	0,12	missense_variant	5 of 6 Predicted as Damaging
689Ad	18	48591892	SMAD4	p.Gly352Glu	G/A		214,6	532	0,11	missense_variant	6 of 6 Predicted as Damaging

169Ad	18	48591919	SMAD4	p.Arg361His	G/A	14122	5667,7	3134	0,35	missense_variant	6 of 6 Predicted as Damaging
689Ad	18	48591919	SMAD4	p.Arg361His	G/A	14122	273,7	529	0,13	missense_variant	6 of 6 Predicted as Damaging
689Ad	18	48593421	SMAD4	p.Cys391Tyr	G/A		32,4	269	0,06	missense_variant	4 of 6 Predicted as Damaging
685Ad	18	48593465	SMAD4	p.Ala406Thr	G/A	14103	3440,8	1140	0,36	missense_variant	6 of 6 Predicted as Damaging
689Ad	18	48593502	SMAD4	p.Ala418Val	C/T		50,9	271	0,07	missense_variant	5 of 6 Predicted as Damaging
261Ad	18	48593505	SMAD4	p.Gly419Glu	G/A		83,4	88	0,17	missense_variant	6 of 6 Predicted as Damaging
261Ad	18	48603057	SMAD4	p.Thr453Ile	C/T		39,5	944	0,05	missense_variant	5 of 6 Predicted as Damaging
247Ad	18	48604659	SMAD4	p.Asp494Gly	A/G	84443	58,1	143	0,10	missense_variant	6 of 6 Predicted as Damaging
684Ad	18	48604659	SMAD4	p.Asp494Gly	A/G	84443	31,6	130	0,08	missense_variant	6 of 6 Predicted as Damaging
260Ad	18	48604665	SMAD4	p.Arg496His	G/A	14193	125,6	573	0,08	missense_variant	6 of 6 Predicted as Damaging
101Ad	18	48604667	SMAD4	p.Arg497Cys	C/T		39,7	753	0,05	missense_variant	6 of 6 Predicted as Damaging
101Ad	18	48604668	SMAD4	p.Arg497His	G/A	14113	33,6	755	0,05	missense_variant	5 of 6 Predicted as Damaging
260Ad	18	48604683	SMAD4	p.Arg502Lys	G/A	1389093	88,8	573	0,07	missense_variant	5 of 6 Predicted as Damaging
260Ad	18	48604689	SMAD4	p.Ser504Asn	G/A		34,7	571	0,05	missense_variant	5 of 6 Predicted as Damaging
249Ad	18	48604718	SMAD4	p.Pro514Ser	C/T	1711346	36,4	699	0,05	missense_variant	4 of 6 Predicted as Damaging
260Ad	18	48604750	SMAD4	p.Trp524Ter	G/A		35,1	569	0,05	stop_gained	2 of 6 Predicted as Damaging
261Ad	18	48604754	SMAD4	p.Glu526Lys	G/A	1151656	282,7	76	0,42	missense_variant	6 of 6 Predicted as Damaging
260Ad	19	1207009	STK11	p.Glu33Lys	G/A		131,5	594	0,08	missense_variant	4 of 6 Predicted as Damaging
689Ad	19	1207069	STK11	p.Asp53Asn	G/A		104,2	1015	0,06	missense_variant	5 of 6 Predicted as Damaging
689Ad	19	1207079	STK11	p.Gly56Glu	G/A		61,0	1014	0,05	missense_variant	6 of 6 Predicted as Damaging
101Ad	19	1220496	STK11	p.Val197Met	G/A		311,6	1119	0,10	missense_variant	4 of 6 Predicted as Damaging
260Ad	19	1220589	STK11	p.Pro203Ser	C/T		87,8	341	0,09	missense_variant	3 of 6 Predicted as Damaging
260Ad	19	1220595	STK11	p.Ala205Thr	G/A	20953	139,3	340	0,11	missense_variant	3 of 6 Predicted as Damaging
165Ad	19	1221246	STK11	p.Gly257Arg	G/A		32,9	118	0,08	missense_variant	6 of 6 Predicted as Damaging
260Ad	19	1223025	STK11	p.Pro321Leu	C/T		65,9	523	0,07	missense_variant	6 of 6 Predicted as Damaging
260Ad	19	1223039	STK11	p.Pro326Ser	C/T		109,6	529	0,08	missense_variant	2 of 6 Predicted as Damaging
101Ad	19	1223040	STK11	p.Pro326Leu	C/T		45,2	933	0,05	missense_variant	3 of 6 Predicted as Damaging
101Ad	19	1223046	STK11	p.Thr328Ile	C/T		122,9	938	0,07	missense_variant	2 of 6 Predicted as Damaging
260Ad	19	1223046	STK11	p.Thr328Ile	C/T		98,8	529	0,08	missense_variant	2 of 6 Predicted as Damaging
689Ad	19	1223051	STK11	p.Asp330Asn	G/A		97,7	387	0,09	missense_variant	4 of 6 Predicted as Damaging
689Ad	19	1223058	STK11	p.Trp332Ter	G/A		197,9	388	0,13	stop_gained	2 of 6 Predicted as Damaging
687Ad	19	1223061	STK11	p.Arg333His	G/A		850,6	1308	0,15	missense_variant	3 of 6 Predicted as Damaging
689Ad	19	1223061	STK11	p.Arg333His	G/A		596,5	388	0,24	missense_variant	3 of 6 Predicted as Damaging
249Ad	19	1223096	STK11	p.His345Tyr	C/T		30,2	526	0,05	missense_variant	2 of 6 Predicted as Damaging
101Ad	19	1223108	STK11	p.Glu349Lys	G/A		73,3	982	0,05	missense_variant	1 of 6 Predicted as Damaging
101Ad	19	1223111	STK11	p.Asp350Asn	G/A	1390434	52,0	985	0,05	missense_variant	2 of 6 Predicted as Damaging
101Ad	19	1223117	STK11	p.Asp352Asn	G/A		41,6	997	0,05	missense_variant	3 of 6 Predicted as Damaging
689Ad	19	1223117	STK11	p.Asp352Asn	G/A		105,0	405	0,09	missense_variant	3 of 6 Predicted as Damaging
101Ad	19	1223126	STK11	p.Asp355Asn	G/A		160,3	1125	0,07	missense_variant	2 of 6 Predicted as Damaging
689Ad	19	1223135	STK11	p.Asp358Asn	G/A		96,2	414	0,08	missense_variant	3 of 6 Predicted as Damaging

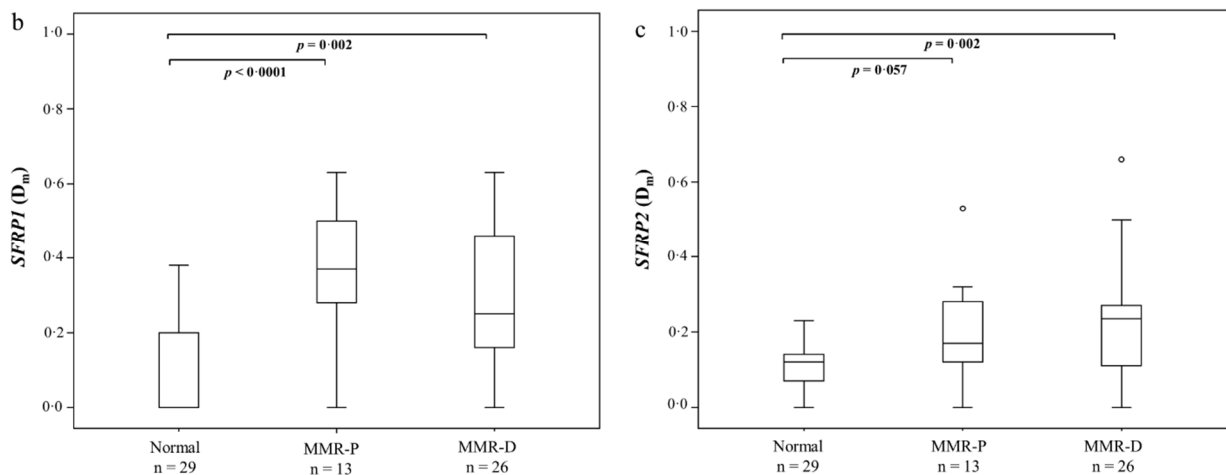
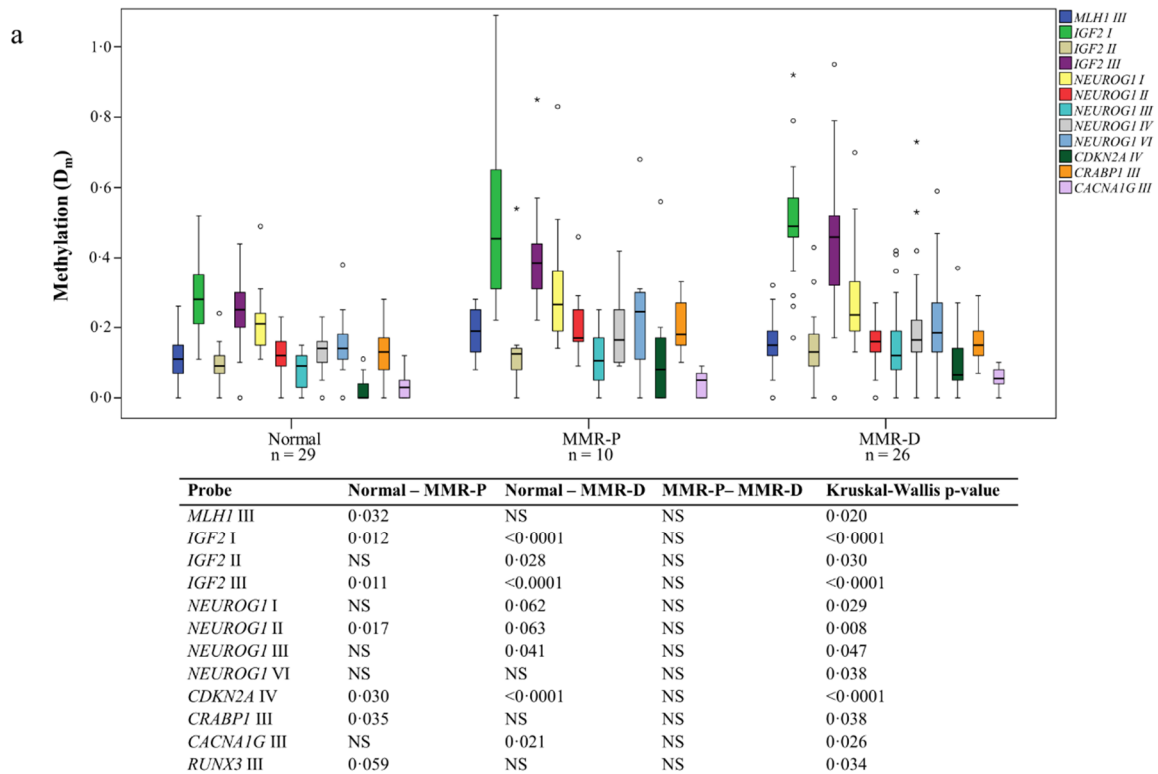
¹ *In silico* predictions were produced by SIFT, PolyPhen2 HVAR, MutationTaster, FATHMM, FATHMM MKL Coding. Stop-gained mutations produced predictions only by MutationTaster and FATHMM MKL Coding. Note: Stop_gained mutations produced predictions only by MutationTaster and FATHMM MKL Coding, and framehift mutations by none.

Abbreviations: Alt, altered nucleotide; Chr, chromosome; COSMIC, the Catalogue of Somatic Mutations in Cancer; HGVS, Human Genome Variation Society; Ref, reference nucleotide; VAF, variant allele frequency.

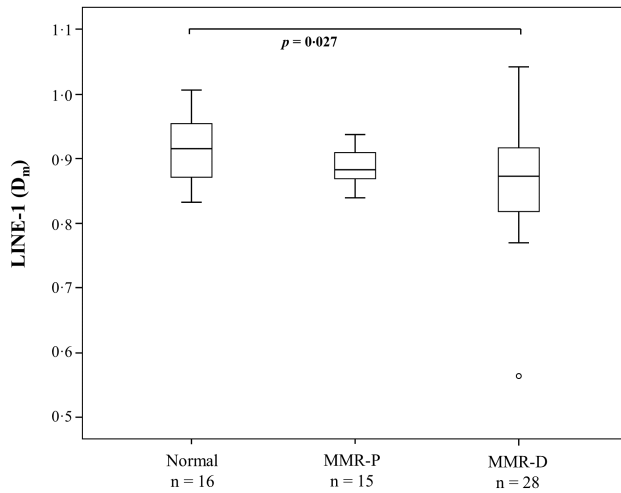
Methylation changes examined solely in adenomas with low-grade dysplasia



Supplementary Figure S1. Frequencies of methylated genes in normal colon, and MMR-P and MMR-D adenomas with low-grade dysplasia. a. Hypermethylation frequencies of CIMP marker genes and CIMP positive phenotype. b. Hypermethylation frequencies of candidate tumor suppressor genes. Bonferroni corrected two-sided *p* values are presented for pairwise comparisons. Abbreviations: MMR-D, MMR deficient; MMR-P, MMR proficient; NS, non-significant.



Supplementary Figure S2. Comparison of average degrees of methylation between normal colon, and MMR-P and MMR-D adenomas with low-grade dysplasia. **a.** The CIMP probes showing statistical significance ($p < 0.05$) with Kruskal-Wallis test. **b.** Average degree of methylation of *SFRP1*. **c.** Average degree of methylation of *SFRP2*. Bonferroni corrected two-sided p values less than 0.10 are presented for the pairwise comparisons. The upper and lower edges of the boxes are the 75th and 25th percentiles, the horizontal line inside the box denotes the median, the whiskers indicate the highest and lowest values, and the asterisks and open circles stand for outliers. Abbreviations: D_m , methylation dosage; MMR-D, MMR deficient; MMR-P, MMR proficient.



Supplementary Figure S3. Average degree of methylation of LINE-1 in normal colon, and MMR-D and MMR-P adenomas with low-grade dysplasia. Bonferroni corrected two-sided p values less than 0.10 are presented in the figure. The upper and lower edges of the boxes are the 75th and 25th percentiles, the horizontal line inside the box denotes the median, the whiskers indicate the highest and lowest values, and the asterisks and open circles stand for outliers. Abbreviations: D_m, methylation dosage; MMR-D, MMR deficient; MMR-P, MMR proficient.