

## Supplementary Tables

Horpaapan et al.

Exome sequencing characterizes the somatic mutation spectrum of early serrated lesions in a patient with serrated polyposis syndrome (SPS)

**Supplementary Table S1** Established causative or candidate genes for (hereditary) colorectal tumours and published genes related to serrated polyps (n = 74)

No.	Gene	Chr	Disease / pathway / susceptibility	Ref.
1	ACVR2	2q22-23	Target gene in MMR-deficient CRC	[1]
2	AHBD1	2	Found LoF mutation in serrated polyposis families	[2]
3	AIM2	1q22	Target gene in MMR-deficient CRC	[1]
4	APC	5q22.2	Familial adenomatous polyposis (FAP)	[3]
5	APC2	19p13.3	Wnt signalling pathway, depletion of intracellular beta-catenin, specifically expressed in brain	[4]
6	AXIN1	16p13.3	Regulation of Wnt-beta-catenin signaling	[1]
7	AXIN2	17q24	Regulation of Wnt-beta-catenin signaling	[4, 5]
8	BAX	19q13.3	Target gene in MMR-deficient CRC	[1]
9	BLM	15q26.1	Target gene in MMR-deficient CRC	[1]
10	BMPR1A	10q22.3	Juvenile polyposis syndrome (JPS)	[4]
11	BRAF	7q34	Oncogene, somatic mutations in CRC	[6]
12	BUB1B	15q15	Gastrointestinal adenomas and carcinomas	[7]
13	CA9	9p13.3	Found LoF mutation in serrated polyposis families	[2]
14	Caspase-5	11q22.2	target gene in MMR-deficient CRC	[1]
15	CASQ1	1p3.2	Found LoF mutation in serrated polyposis families	[2]
16	CDH1	16q22.1	Hereditary diffuse gastric cancer (HDGC)	[8]
17	CDX2	13q12.3	target gene in MMR-deficient CRC	[1]
18	CHEK2	22q12.1	Susceptibility for CRC	[9, 10]
19	CHK1	11q22	Target gene in MMR-deficient CRC	[1]
20	CNPY4	7q22.1	Found LoF mutation in serrated polyposis families	[2]
21	COL15A1	9q22.3	Found LoF mutation in serrated polyposis families	[2]
22	COL20A1	20q13	Found LoF mutation in serrated polyposis families	[2]
23	CREB3L3	19p13	Found LoF mutation in serrated polyposis families	[2]
24	CRYBA2	2q35	Frequently overexpressed in BRF-mutant colon cancer	[11]
25	CTNNB1	3p21	canonical Wnt signaling pathway	[12]
26	DDX31	9q34	Found LoF mutation in serrated polyposis families	[2]
27	E2F-4	16q21	Target gene in MMR-deficient CRC	[1]
28	EGFR	7p12	Oncogene, somatic mutations in lung cancer	[13, 14]
29	EMR2	19p13	Found LoF mutation in serrated polyposis families	[2]
30	ENDOG	9q34.1	Found LoF mutation in serrated polyposis families	[2]
31	EPCAM	2p21	Lynch syndrome / HNPCC	[15]
32	FAM123B	Xq11.2	canonical Wnt signaling pathway	[16, 17]
33	FBXW7	4q31.3	Cyclin E degradation, frequently mutated in CRC	[4]
34	FLI1	11q24.3	Candidate serrated polyposis gene	[18]
35	FSCN1	7p22.1	Frequently overexpressed in BRF-mutant colon cancer	[11]
36	FSIP2	2q32.1	Found LoF mutation in serrated polyposis families	[2]

37	GCA	2q24.2	Found LoF mutation in serrated polyposis families	[2]
38	GCSAM	3q13.2	Found LoF mutation in serrated polyposis families	[2]
39	GEM	8q22	Found LoF mutation in serrated polyposis families	[2]
40	GJA3	13q12.11	Candidate serrated polyposis gene	[18]
41	GPT	8q24.3	Found LoF mutation in serrated polyposis families	[2]
42	GREM1	15q13.3	Heredity mixed polyposis syndrome 1	[8]
43	GRWD1	19q13	Found LoF mutation in serrated polyposis families	[2]
44	GSK3B	3q13.3	Canonical Wnt signaling pathway	[5]
45	H3F3B	17q25	Found LoF mutation in serrated polyposis families	[2]
46	HDAC2	6q21	Candidate serrated polyposis gene	[19]
47	HDHD3	9q32	Candidate serrated polyposis gene	[18]
48	hRAD50	5q31	Target gene in MMR-deficient CRC	[1]
49	IDO2	8p11.21	Found LoF mutation in serrated polyposis families	[2]
50	IGF2	11p15.5	Candidate serrated polyposis gene	[19]
51	IGFBP7	4q12	Candidate serrated polyposis gene	[20]
52	IGFIIR	6q26-27	Target gene in MMR-deficient CRC	[1]
53	IGSF6	16p12.2	Found LoF mutation in serrated polyposis families	[2]
54	IMPACT	18q11	Found LoF mutation in serrated polyposis families	[2]
55	KRAS	12p12.1	Oncogene, frequently mutated in CRC	[6]
56	MAP2K4	17p12	MAPK pathway, mutated in CRC	[21, 22]
57	MBD4	3q21-q22	target gene in MMR-deficient CRC	[1]
58	MGAT5B	17q25	Found LoF mutation in serrated polyposis families	[2]
59	MGMT	10q26.3	Candidate serrated polyposis gene	[23]
60	MLH1	3p22.2	Candidate serrated polyposis gene	[20]
61	MLH3	14q24.3	Candidate serrated polyposis gene	[23]
62	MSH2	2p21	Candidate serrated polyposis gene	[23]
63	MSH3	5q11-q12	Target gene in MMR-deficient CRC	[1]
64	MSH6	2p16.3	Candidate serrated polyposis gene	[23]
65	MUC6	11p15	Frequently overexpressed in BRF-mutant colon cancer	[11]
66	MUTYH	1p32-34	MUTYH-associated polyposis (MAP)	[24]
67	MYH15	3q13.1	Found LoF mutation in serrated polyposis families	[2]
68	NCAN	19p13	Found LoF mutation in serrated polyposis families	[2]
69	NRAS	1p13.2	Noonan syndrome, rarely mutated in CRC	[25]
70	OR4L1	14q11	Found LoF mutation in serrated polyposis families	[2]
71	PDGFRA	4q12	Upregulated in CRC	[26]
72	PECR	2q35	Found LoF mutation in serrated polyposis families	[2]
73	PIK3CA	3q26.3	Cowden syndrome, frequently mutated in CRC	[4, 27]
74	PMS2	7p22.1	Candidate serrated polyposis gene	[23]
75	POLD1	19q13.3	Heredity multiple adenomas / CRC	[28]
76	POLD2	7p13	Candidate for hereditary multiple adenomas / CRC	[28]
77	POLD3	11q14	Candidate for hereditary multiple adenomas / CRC	[28]
78	POLD4	11q13	Candidate for hereditary multiple adenomas / CRC	[28]
79	POLE	12q24.3	Heredity multiple adenomas / CRC	[28]
80	POLE2	14q21	Candidate for hereditary multiple adenomas / CRC	[28]
81	POLE3	9q33	Candidate for hereditary multiple adenomas / CRC	[28]
82	POLE4	2p12	Candidate for hereditary multiple adenomas / CRC	[28]
83	PPP2R1B	11q23	MAPK pathway, candidate TSG, frequently mutated in CRC	[5]
84	PQLC1	18q23	Candidate serrated polyposis gene	[18]
85	PTEN	10q23.3	Target gene in MMR-deficient CRC	[1]
86	PTPN13	4q21	Found LoF mutation in serrated polyposis families	[2]
87	PTPRJ	11p11.2	Frequently mutated in colorectal adenomas / CRC	[8]

88	<i>PWP2</i>	21q22	Found LoF mutation in serrated polyposis families	[2]
89	<i>RASL10B</i>	17q12	Candidate serrated polyposis gene	[18]
90	<i>RGS19</i>	20q13	Found LoF mutation in serrated polyposis families	[2]
91	<i>RIZ</i>	1p36	Target gene in MMR-deficient CRC	[1]
92	<i>RNF43</i>	17q22	Play a role in serrated neoplasia pathway	[2]
93	<i>SEC16B</i>	1q25.2	Found LoF mutation in serrated polyposis families	[2]
94	<i>SCEL</i>	13q22.3	Found LoF mutation in serrated polyposis families	[2]
95	<i>SEC63</i>	6q21	Target gene in MMR-deficient CRC	[1]
96	<i>SEMG1</i>	20q13	Frequently overexpressed in <i>BRF</i> -mutant colon cancer	[11]
97	<i>SFRP1</i>	8p11.21	Candidate serrated polyposis gene	[19, 29]
98	<i>SLC22A2</i>	6q25.3	Found LoF mutation in serrated polyposis families	[2]
99	<i>SLC26A2</i>	5q32	Candidate serrated polyposis gene	[18]
100	<i>SLC27A6</i>	5q23.3	Found LoF mutation in serrated polyposis families	[2]
101	<i>SLC30A7</i>	1p21.2	Found LoF mutation in serrated polyposis families	[2]
102	<i>SLIT2</i>	4p15.31	Marker for CIMP	[23]
103	<i>SMAD2</i>	18q21.1	TGF-beta signaling pathway, frequently mutated in CRC	[4]
104	<i>SMAD4</i>	18q21.1	Juvenile polyposis syndrome (JPS)	[4]
105	<i>SSNA1</i>	9q34.3	Found LoF mutation in serrated polyposis families	[2]
106	<i>ST6GALNA C</i>	9q34.11	Found LoF mutation in serrated polyposis families	[2]
107	<i>STK11</i>	19p13.3	Target gene in MMR-deficient CRC	[1]
108	<i>SYTL1</i>	1p36.11	Found LoF mutation in serrated polyposis families	[2]
109	<i>TAS2R3</i>	7q34	Found LoF mutation in serrated polyposis families	[2]
110	<i>TBP</i>	6q27	Target gene in MMR-deficient CRC	[1]
111	<i>TCF4</i>	10q25.3	Target gene in MMR-deficient CRC	[1]
112	<i>TGFBTR2</i>	3p22	Target gene in MMR-deficient CRC	[1]
113	<i>TP53</i>	17p13.1	Li-Fraumeni syndrome	[1]
114	<i>TRNP1</i>	1p36	Frequently overexpressed in <i>BRF</i> -mutant colon cancer	[11]
115	<i>USP45</i>	6q16.2	Found LoF mutation in serrated polyposis families	[2]
116	<i>WIF1</i>	12q14.3	Inhibitor of Wnt signaling pathway	[29]
117	<i>WRN</i>	8p12	Candidate serrated polyposis gene	[19]
118	<i>ZIC2</i>	13q32	Frequently overexpressed in <i>BRF</i> -mutant colon cancer	[11]
119	<i>ZIC5</i>	13q32	Frequently overexpressed in <i>BRF</i> -mutant colon cancer	[11]
120	<i>ZNF491</i>	19p13.2	Found LoF mutation in serrated polyposis families	[2]
121	<i>ZNF568</i>	19q13.12	Found LoF mutation in serrated polyposis families	[2]
122	<i>ZNF614</i>	19q13.41	Found LoF mutation in serrated polyposis families	[2]
123	<i>ZNF860</i>	3p23	Found LoF mutation in serrated polyposis families	[2]

CRC, colorectal cancer; HNPCC, hereditary nonpolyposis colorectal cancer; LoF, loss of function; MMR, mismatch repair

**Supplementary Table S2** Primers used for validating 25 variants by Sanger sequencing

No.	Gene	Chr	Position	Ref	Allele	Mut cDNA	Protein	Tu-ID	Forward primer (5'-3')	Reverse primer (5'-3')	size
1	ABI3BP <sup>#</sup>	3	100499047	T	A	c.2036A>T	p.K679M	71	GTTTCAGAGCTGAGCTGTCA	CTGGCAACTCTACCAAGTTTC	196
2	CALD1 <sup>#</sup>	7	134617870	G	A	c.332G>A	p.R111Q	69	AGTGGAAGGGATGATGAGG	GAGCGACAGACTTGCATCTGT	136
3	CATSPERB <sup>#</sup>	14	92084032	G	T	c.2309C>A	p.P770H	71	TACATAACTGTCAGTATCATCAA	CCTTCAGAATAGATTCAAGTTG	213
4	CCBP2 <sup>#</sup>	3	42906178	A	T	c.184A>T	p.S62C	72	GGTGTCTTGGCAAAGTCT	GGCAGTGTACCAGAACAG	177
5	CENPQ	6	49459907	G	T	c.726G>T	p.L242F	79	GCGATTCGTTGACAATTATTG	GGTTGACATGCTTTCATCTG	224
6	CNTN5	11	99942566	G	T	c.1429G>T	p.A477S	70	GCTGGAATGTATCAGTGTGG	AATTAGAGCATGAAAAGAACAG	135
7	COL8A1 <sup>#</sup>	3	99513118	G	A	c.373G>A	p.E125K	71	CATACCCCTCTCTCTCTCT	CCTTAATTCCAGGTATCCCAT	144
8	CPZ	4	8621320	G	T	c.1935G>T	p.R645S	69, 71	CCACATTGTCATTGCCAA	CTTGTGGATGTCTGTGGC	415
9	CSPG4	15	75968509	G	T	c.6351C>A	p.D2117E	69	CCACAGCTCCAGAGTGAGAC	CTAGATGCTGGCAGCTGG	240
10	DNAI1 <sup>#</sup>	9	34506717	G	A	c.1156G>A	p.V386I	71	AAGAACCCAGCTCCCTGA	TTGGCTGAGCTGCAGAAGGA	170
11	FBLN5	14	92349339	G	T	c.821C>A	p.P274H	69	ACAGCCTTACCTGGCAGCTT	TCTCTGAGTTCTCTGCCAACAA	115
12	KIAA1033	12	105558425	G	T	c.3361G>T	p.E1121*	79	TTGGTATTTGCCATAATAAGTA	TTAAACCACACTGACCTTC	177
13	KLHDC1	14	50201340	G	T	c.857G>T	p.C286F	78	ATTGTATCCCAGAGACCTAATCT	GAAAGATATCCTCTCAATGGC	242
14	NEURL1B	5	172096909	G	T	c.153G>T	p.R51R	80	AGGAGTTCGGGAGGAGGCCTAAC	ATCGTGCAGGGTAAGCCGAA	330
15	NOL11	17	65716083	G	T	c.312+5G>T	SS	80	GTTGTACACGATAATAAGGTGAG	GAATGAAAACCTGATTAGGACCT	324
16	PPP3CB	10	75230956	G	T	c.681C>A	p.F227L	71	TCGGACCATAACAAGTCACAC	TTGGTATCGTTTCCTATGCAC	138
17	PROB1	5	138728291	G	T	c.2480C>A	p.P827H	78	CGCTCCCTGGGAGGGCTTT	TAGGGCCAGCAGGGTCCGAT	239
18	PRR23A	3	138725070	G	T	c.41C>A	p.P14H	73	TGGCGGGAGCTCCAGCACCA	CGCTCCCTACGTCCCTTGCTA	296
19	RAPH1	2	204305718	G	T	c.2195C>A	p.P732Q	71	GCTGAACTTGATGGATCTTCAG	CAATGGAGTTGTTCCACAC	146
20	RGS13	1	192613504	G	T	c.40G>T	p.D14Y	73	CCCAGTGAAGTATTCCATTAAC	CATATGACTGCTTCTGATGAA	365
21	RIF1	2	152321774	G	T	c.5740G>T	p.A1914S	78, 79	CCCCAAAAATGGAAGT	GGTTCTCTTGTCCATGAAAG	140
22	SLC27A3	1	153748613	G	T	c.781G>T	p.G261C	79	GTTTCTGTGGCTCTGGTCG	GTTCGGAGCTCCAGCCTTA	151
23	TRIM13	13	50587208	G	T	c.1132G>T	p.G378W	69	TGGTCCTACCATGTTCTAG	ACCAAATCTGAATTACCACTCT	308
24	UBE2CBP	6	83732195	G	T	c.823C>A	p.Q275K	80	GAGACCTGGATTCCCTAGGCT	CAGGTCTGGTTGTCCAGAG	162

25	VGLL2#	6	117589395	C	A	c.132C>A	p.S44R	70	ATCAGTCTGAACCGAATTGCG	TTATACTGGCTGGGGTTGG	176
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# mutations were validated

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