

Supplementary Table 1. Polymerase chain reaction (PCR) conditions and primer sequences used for this study*

Gene Name	GenBank accession number (position of amplicon)	Primer (5' to 3')	Temperature, °C (No. of cycles)	Product size (Restriction enzyme)	Fluorescent marker
Primers for <i>ClpP</i>	NC_000913 (nt 456368 to 456487)	F; TTTTGAAAGTTAAAGGGTGTATGA R; ATTCCACCACTTCAAAAACAA	55 (45)	120	
Primers for COBRA and Hi-SA					
RASSF2 Region 1	NC_000020 (nt 4707755 to 4707914)	F; TGAAGAGYGAGAGAAAAGAGAGGA R; TCCAACCAAACCTAAACAAACRATAA IM; CCAACCAAACCTAAACAAACGATAACCG IU; CCAACCAAACCTAAACAAACAATAACCA	59 (3), 57 (7), 55 (35)	160 (<i>HhaI</i>)	FAM
Region 2	NC_000020 (nt 4707073 to 4707203)	F; TTGGGGAGGGTTTGATAGTTT R; CRCACCCTACRCCCCTCTAAAA IM; CACCCTACGCCCTCTAAAACG	59 (3), 57 (7), 55 (35)	131 (<i>HhaI</i>)	VIC
SFRP2 Region 1	NC_000004 (nt154929516 to 154929654)	F; GTYGGAGTTTTTYGGAGTTG R; AACCCRCTCTCTTCRCTAAATAC IM; CGGAGTTTTTCGGAGTTGC	58 (3), 56 (7), 54 (15), 52 (20)	139 (<i>HhaI</i>)	NED
Region 2	NC_000004 (nt154929069 to 154929221)	F; GGTTGTTAGTTTTTYGGGGTTT R; CAACIAACCAAACCCCTACAACAT IM; GAACCAAACCCCTACAACATCG	59 (3), 57 (7), 55 (35)	153 (<i>HhaI</i>)	PET
Primers for bisulfite cloning and sequencing					
RASSF2 Region 1	NC_000020 (nt4707747 to 4707932)	F; AAGGGGTGGAGAGTGATATGA R; AACTCAAATCCAACCAAACCTAAA	59 (3), 57 (7), 55 (35)	186	
Region 2	NC_000020 (nt4707000 to 4707203)	F; TTGGGGAGGGTTTGATAGTTT R; ACCTCAAACACCAACTCC	59 (3), 57 (7), 55 (35)	204	
SFRP2	NC_000004 (nt154929074 to 154929361)	F; GGTTAAGAAAATTTTTGTTGTGTTTT R; AACCAAACCCCTACAACATC	59 (3), 57 (7), 55 (35)	288	

*The following primers and reaction conditions are shown: 1) primers for *E.coli ClpP*, a positive control for DNA recovery and bisulfite

modification, 2) primers for Combined Bisulfite Restriction Analysis (COBRA) and High-Sensitivity Assay for Bisulfite DNA (Hi-SA) of two

regions each from the human *RASF2* and *SFRP2* promoters, and primer sequences for cloning bisulfite-modified DNA from the human genes: F, forward primer; R, reverse primer; IM, internal primer specific for methylated alleles; IU, internal primer specific for unmethylated alleles. GenBank accession numbers for each of the gene sequences and nucleotides (nt) corresponding to the amplified fragments. Step-down PCR was applied for COBRA, Hi-SA, and cloning sequence. The F and R primer pairs were used for the amplification of *E.coli ClpP*, COBRA, and cloning sequences for bisulfite-modified DNA. Hi-SA was performed with F and R primers plus overlapping IM or IU primers to increase sensitivity for the methylated or unmethylated allele, respectively (see Supplementary Figure 2, available online). I's, Y's, and R's in the primer sequence denote inosinic acid, C + T, and A + G, respectively. PCR product size, and fluorescent primer tag and restriction enzyme used to detect methylated allele are also listed. FAM, VIC, NED, and PET are not abbreviations, but trademarks of Applied Biosystems Corporation or its subsidiaries in the US and certain other countries.

Supplementary Table 2. Performance characteristics of Recovery, Methylation, and Combination score with respect to the sensitivity for fecal samples with advanced lesions (colorectal cancer, colorectal advanced adenomas, and gastric cancer) and the specificity for those without advanced lesions (colorectal non-advanced adenomas, colorectal hyperplastic polyps and subjects without neoplastic or active diseases)

Type of Score	Score	1-Specificity %	Sensitivity %	True positive <i>n</i>	True negative <i>n</i>	False-positive <i>n</i>	False-negative <i>n</i>
Recovery score	4	7.1	49.2	65	143	11	67
	3	22.1	62.9	89	114	40	43
	2	40.9	81.1	107	91	63	25
	1	66.2	90.9	120	52	102	12
	0	100	100	132	0	154	0
Methylation score	4	0	6.8	9	154	0	132
	3	0	19.7	26	154	0	106
	2	3.3	36.4	48	149	5	84
	1	14.9	65.9	87	131	23	45
	0	100	100	132	0	154	0
Combination score	6.04	0	6.8	9	154	0	123
	4.88	0	18.2	24	154	0	108
	4.53	0	19.7	26	154	0	106
	3.72	0.7	31.1	41	153	1	91
	3.37	3.3	34.9	46	149	5	86
	3.02	3.3	36.4	48	149	5	84
	2.56	5.8	51.5	68	145	9	64
	2.21	9.7	58.3	77	139	15	55
	1.86	13	63.6	84	134	20	48
	1.51	14.9	65.9	87	131	23	45
	1.4	18.8	70.5	93	125	29	39
	1.05	27.3	72	95	112	42	37
	0.7	42.9	83.3	110	88	66	22
0.35	66.2	90.9	120	52	102	12	
0	100	100	132	0	154	0	

Supplementary Table 3. Performance characteristic of the cross validation data which was identical to the one for the combination score using the original coefficients from the logistic regression for the full data.

Type of score	Score	1-Specificity %	Sensitivity %	True positive <i>n</i>	True negative <i>n</i>	False-positive <i>n</i>	False-negative <i>n</i>
Cross validation	6.04	0	6.8	9	154	0	123
	4.88	0	18.2	24	154	0	108
	4.53	0	19.7	26	154	0	106
	3.72	0.7	31.1	41	153	1	91
	3.37	3.3	34.9	46	149	5	86
	3.02	3.3	36.4	48	149	5	84
	2.56	5.8	51.5	68	145	9	64
	2.21	9.7	58.3	77	139	15	55
	1.86	13	63.6	84	134	20	48
	1.51	14.9	65.9	87	131	23	45
	1.4	18.8	70.5	93	125	29	39
	1.05	27.3	72	95	112	42	37
	0.7	42.9	83.3	110	88	66	22
	0.35	66.2	90.9	120	52	102	12
	0	100	100	132	0	154	0