Table S1. The pater number of custom TaqMan copy number assays.

FBXW7 assay	ID#hs02920964_cn
MDM2 assay	ID#hs03082319_cn
SKP2 assay	ID#hs06086556_cn
β-TRCP assay	ID#hs03734483_cn
NEDD4-1 assay	ID#hs02225249_cn

Table S2. Distribution of demographic and environmental information of CRC patients and controls in each PS stratification.

Characteristics	Propensity score stratification (CRC, n = 435 and control, n = 443)[b]														
	1st			2nd			3rd			4th			5th		
	CRC (28)(%)	Controls (247)(%)	*P* value[a]	CRC (36)(%)	Controls (77)(%)	*P* value[a]	CRC (44)(%)	Controls (52)(%)	*P* value[a]	CRC (91)(%)	Controls (36)(%)	*P* value[a]	CRC (236)(%)	Controls (31)(%)	*P* value[a]
Age, years			0.343			0.882			0.425			0.936			0.767
Mean ± SD	59.1±11.9	59.5±10.5		59.6±12.0	60.4±11.2		59.4±11.6	59.2±10.5		60.5±11.4	60.6±10.6		60.7±11.1	59.4±10.5	
≤50	8(28.6%)	47(19.0%)		9(25.0%)	15(19.5%)		10(22.7%)	10(19.2%)		18(19.8%)	7(19.4%)		41(17.3%)	6(19.4%)	
50-60	5(17.9%)	84(34.0%)		11(30.6%)	25(32.5%)		15(34.1%)	19(36.5%)		28(30.8%)	10(27.8%)		74(31.4%)	12(38.7%)	
60-70	9(32.1%)	76(30.8%)		7(19.4%)	19(24.6%)		8(18.2%)	15(28.9%)		24(26.4%)	11(30.6%)		74(31.4%)	7(22.6%)	
>70	6(21.4%)	40(16.2%)		9(25.0%)	18(23.4%)		11(25.0%)	8(15.4%)		21(23.0%)	8(22.2%)		47(19.9%)	6(19.3%)	
Gender			0.748			0.753			0.795			0.391			0.117
Male	12(42.9%)	113(45.8%)		17(47.2%)	38(49.4%)		25(56.8%)	28(53.8%)		45(49.5%)	21(58.0%)		141(59.7%)	14(45.2%)	
Female	16(57.1%)	134(54.2%)		19(52.8%)	39(50.6%)		19(43.2%)	24(46.2%)		46(50.5%)	15(42.0%)		95(40.3%)	17(54.8%)	
BMI			0.081			0.064			0.562			0.056			0.485
Mean ± SD	23.0±4.1	24.0±4.1		23.9±3.7	23.0±4.5		23.8±3.9	24.2±4.2		23.5±3.6	25.2±4.8		24.0±3.9	23.3±3.7	
≤24	15(53.5%)	125(50.6%)		18(50.0%)	51(66.2%)		20(45.4%)	25(48.1%)		50(54.9%)	15(42.0%)		121(51.3%)	19(61.3%)	
24-28	5(17.9%)	84(34.0%)		14(38.9%)	15(19.5%)		19(43.2%)	18(34.6%)		31(34.1%)	11(29.4%)		77(32.6%)	8(25.8%)	
>28	8(28.6%)	38(15.4%)		4(11.1%)	11(14.3%)		5(11.4%)	9(17.3%)		10(11.0%)	10(28.6%)		38(16.1%)	4(12.9%)	
Education			0.519			0.958			0.800			0.823			0.825
Primary school and below	8(28.6%)	44(17.8%)		10(27.8%)	20(25.9%)		13(29.6%)	13(25.0%)		25(27.5%)	11(31.5%)		58(24.6%)	9(29.0%)	
Junior middle school	6(21.4%)	66(26.7%)		13(36.1%)	26(33.8%)		13(29.6%)	20(38.5%)		27(29.7%)	12(32.2%)		79(33.5%)	10(32.3%)	
Senior middle school	8(28.6%)	69(27.9%)		5(13.9%)	14(18.2%)		8(18.2%)	6(11.5%)		22(24.1%)	6(16.8%)		51(21.6%)	7(22.6%)	
University and above	6(21.4%)	68(27.6%)		8(22.2%)	17(22.1%)		10(22.8%)	13(25.0%)		17(18.7%)	7(19.5%)		48(20.3%)	5(16.1%)	
Occupation			0.014			0.670			0.723			0.787			0.568
White collar	3(10.7%)	34(13.8%)		6(16.7%)	10(13.0%)		8(18.2%)	6(11.5%)		14(15.3%)	4(10.5%)		46(19.5%)	4(12.9%)	

Blue collar	13(46.4%)	169(68.4%)		17(47.2%)	43(55.8%)		21(47.7%)	28(53.9%)		46(50.6%)	19(52.4%)		123(52.1%)	16(51.6%)	
Both	12(42.9%)	44(17.8%)		13(36.1%)	24(31.2%)		15(34.1%)	18(34.6%)		31(34.1%)	13(37.1%)		67(28.4%)	11(35.5%)	
Marriage			0.088			0.443			0.301			0.672			0.734
Married	28(100%)	219(88.7%)		35(97.2%)	72(93.5%)		42(95.5%)	48(92.3%)		88(96.7%)	34(95.1%)		225(95.3%)	30(96.8%)	
Others	0(0%)	28(11.3%)		1(2.8%)	5(6.5%)		2(4.5%)	4(7.7%)		3(3.3%)	2(4.9%)		11(4.7%)	1(3.2%)	
Nationality			0.851			0.871			0.458			0.608			0.281
The Han nationality	26(92.9%)	231(93.5%)		34(94.4%)	74(96.1%)		41(93.2%)	51(98.1%)		89(97.8%)	34(95.8%)		233(98.7%)	30(96.8%)	
Others	2(7.1%)	16(6.5%)		2(5.6%)	3(3.9%)		3(6.8%)	1(1.9%)		2(2.2%)	2(4.2%)		3(1.3%)	1(3.2%)	
Family history of colorectal cancer			0.092			0.852			0.999			0.240			0.016
No	16(57.1%)	101(40.9%)		16(44.4%)	33(42.9%)		16(36.3%)	19(36.5%)		16(17.6%)	10(27.3%)		18(7.6%)	7(22.6%)	
Yes	12(42.9%)	146(59.1%)		20(55.6%)	44(57.1%)		28(63.7%)	33(63.5%)		75(82.4%)	26(72.7%)		218(92.4%)	24(77.4%)	
Appendicitis			0.490			0.960			0.977			0.728			0.617
No	5(17.9%)	49(19.8%)		5(13.9%)	11(14.3%)		8(18.2%)	9(17.3%)		19(20.9%)	7(18.2%)		41(17.4%)	4(12.9%)	
Yes	23(82.1%)	198(80.2%)		31(86.1%)	66(85.7%)		36(81.8%)	43(82.7%)		72(79.1%)	29(81.8%)		195(82.6%)	27(87.1%)	
Refined grains, g/day			0.017			0.118			0.892			0.068			0.473
≤ 250	18(64.3%)	202(81.8%)		21(58.3%)	56(72.8%)		24(54.5%)	29(55.8%)		58(63.7%)	17(46.2%)		125(53.0%)	14(45.2%)	
> 250	10(35.7%)	45(18.2%)		15(41.7%)	21(27.2%)		20(45.5%)	23(44.2%)		33(36.3%)	19(53.8%)		111(47.0%)	17(54.8%)	
Roughage, g/week			0.426			0.527			0.350			0.557			0.926
< 50	10(35.7%)	106(42.9%)		14(38.9%)	35(45.5%)		17(38.6%)	16(30.8%)		41(45.1%)	14(39.2%)		114(48.3%)	15(48.4%)	
≥ 50	18(64.3%)	141(57.1%)		22(61.1%)	42(54.5%)		27(61.4%)	36(69.2%)		50(54.9%)	22(60.8%)		122(51.7%)	16(51.6%)	
Vegetable, times/week			0.294			0.750			0.708			0.590			0.674
≤ 2	15(53.6%)	108(43.7%)		20(55.6%)	45(58.4%)		24(54.5%)	30(57.7%)		57(62.6%)	21(57.3%)		147(62.3%)	20(64.5%)	
> 2	13(46.4%)	139(56.3%)		16(44.4%)	32(41.6%)		20(45.5%)	22(42.3%)		34(37.4%)	15(42.7%)		89(37.7%)	11(35.5%)	
Fruit, times/week			0.623			0.586			0.780			0.801			0.241
≤ 2	10(35.7%)	103(41.7%)		17(47.2%)	39(50.7%)		20(45.5%)	25(48.1%)		44(48.4%)	16(45.5%)		108(45.8%)	11(35.5%)	
> 2	18(64.3%)	144(58.3%)		19(52.8%)	38(49.3%)		24(54.5%)	27(51.9%)		47(51.6%)	20(54.5%)		128(54.2%)	20(64.5%)	
Fat meat			0.437			0.090			0.625			0.409			0.358
No	16(57.1%)	156(63.2%)		25(69.4%)	40(52.0%)		27(61.4%)	29(55.8%)		49(53.9%)	22(61.5%)		111(47.0%)	17(54.8%)	
Yes	12(42.9%)	91(36.8%)		11(30.6%)	37(48.0%)		17(38.6%)	23(44.2%)		42(46.1%)	14(38.5%)		125(53.0%)	14(45.2%)	
Fish, times/week			0.043			0.798			0.810			0.338			0.521

≤ 1	19(67.9%)	117(47.3%)		24(66.7%)	53(68.8%)		33(75.0%)	39(75.0%)		66(72.5%)	29(80.4%)		190(80.5%)	26(83.9%)	
> 1	9(32.1%)	130(52.7%)		12(33.3%)	24(31.2%)		11(25.0%)	13(25.0%)		25(27.5%)	7(19.6%)		46(19.5%)	5(16.1%)	
Seafood, times/week			0.129			0.798			0.940			0.764			0.219
≤ 1	19(67.9%)	134(54.3%)		24(66.7%)	53(68.8%)		32(72.7%)	39(75.0%)		67(73.6%)	25(70.6%)		153(64.8%)	23(74.2%)	
> 1	9(32.1%)	113(45.7%)		12(33.3%)	24(31.2%)		12(27.3%)	13(25.0%)		24(26.4%)	11(29.4%)		83(35.2%)	8(25.8%)	
Braised fish, times/week			0.700			0.860			0.684			0.571			0.813
≤ 1	21(75.0%)	176(71.3%)		26(72.2%)	54(70.1%)		31(70.5%)	38(73.1%)		58(63.7%)	25(69.2%)		148(62.7%)	19(61.3%)	
> 1	7(25.0%)	71(28.7%)		10(27.8%)	23(29.9%)		13(29.5%)	14(26.9%)		33(36.3%)	11(30.8%)		88(37.3%)	12(38.7%)	
Egg, /week			0.944			0.288			0.533			0.472			0.397
≤ 3	13(46.4%)	113(45.8%)		15(41.6%)	40(51.9%)		16(36.4%)	22(42.3%)		40(44.0%)	13(37.1%)		87(36.9%)	9(29.0%)	
> 3	15(53.6%)	134(54.2%)		21(58.4%)	37(48.1%)		28(63.6%)	30(57.7%)		51(56.0%)	23(62.9%)		149(63.1%)	22(71.0%)	
Tea			0.700			0.340			0.956			0.215			0.795
yes	7(25.0%)	55(22.3%)		8(22.2%)	23(29.9%)		11(25.0%)	13(25.0%)		26(28.6%)	6(17.5%)		63(26.7%)	9(29.0%)	
no	21(75.0%)	192(77.7%)		28(77.8%)	54(70.1%)		33(75.0%)	39(75.0%)		65(71.4%)	30(82.5%)		173(73.3%)	22(71.0%)	
Sausage, times/month			0.529			0.810			0.590			0.896			0.196
≤ 1	26(92.9%)	217(87.9%)		30(83.3%)	63(81.8%)		38(86.4%)	43(82.7%)		71(78.0%)	28(79.0%)		162(68.6%)	25(80.6%)	
> 1	2(7.1%)	30(12.1%)		6(16.7%)	14(18.2%)		6(13.6%)	9(17.3%)		20(22.0%)	8(21.0%)		74(31.4%)	6(19.4%)	
Spicy food, times/week			0.117			0.638			0.424			0.198			0.132
≤ 3	12(42.9%)	147(59.5%)		19(52.8%)	44(57.1%)		23(52.3%)	31(59.6%)		52(57.1%)	16(44.1%)		135(57.2%)	13(41.9%)	
> 3	16(57.1%)	100(40.5%)		17(47.2%)	33(42.9%)		21(47.7%)	21(40.4%)		39(42.9%)	20(55.9%)		101(42.8%)	18(58.1%)	
Garlic, times/week			0.636			0.827			0.915			0.921			0.891
≤ 3	15(53.6%)	145(58.7%)		22(61.1%)	46(59.7%)		27(61.4%)	31(59.6%)		50(55.0%)	19(53.8%)		134(56.8%)	17(54.8%)	
> 3	13(46.4%)	102(41.3%)		14(38.9%)	31(40.3%)		17(38.6%)	21(40.4%)		41(45.0%)	17(46.2%)		102(43.2%)	14(45.2%)	
Chinese pickled sour cabbage, times/month			0.550			0.439			0.276			0.934			0.731
≤ 2	19(67.9%)	152(61.5%)		18(50.0%)	45(58.4%)		23(52.3%)	33(63.5%)		52(57.1%)	20(55.9%)		89(37.7%)	11(35.5%)	
> 2	9(32.1%)	95(38.5%)		18(50.0%)	32(41.6%)		21(47.7%)	19(36.5%)		39(42.9%)	16(44.1%)		147(62.3%)	20(64.5%)	
Canned fruit, times/week			0.388			0.855			0.789			0.641			0.874
≤ 3	26(92.9%)	215(87.0%)		32(88.9%)	69(89.6%)		38(86.4%)	47(90.4%)		84(92.3%)	34(94.4%)		211(89.4%)	28(90.3%)	
> 3	2(7.1%)	32(13.0%)		4(11.1%)	8(10.4%)		6(13.6%)	5(9.6%)		7(7.7%)	2(5.6%)		25(10.6%)	3(9.7%)	
Canned meat, times/week			0.824			0.477			0.409			0.831			0.159
≤ 3	2(7.1%)	16(6.5%)		1(2.8%)	3(3.9%)		1(2.3%)	2(3.8%)		4(4.4%)	2(5.6%)		14(5.9%)	0(0%)	

> 3	26(92.9%)	231(93.5%)		35(97.2%)	74(96.1%)		43(97.7%)	50(96.2%)		87(95.6%)	34(94.4%)		222(94.1%)	31(100.00%)	
Tap-water			0.013			0.536			0.344			0.855			0.558
Yes	7(25.0%)	22(8.9%)		16(44.4%)	30(39.0%)		26(59.1%)	36(69.3%)		29(32.0%)	71(78.2%)		217(91.9%)	27(87.1%)	
No	21(75.0%)	225(91.1%)		20(55.6%)	47(61.0%)		18(40.9%)	16(30.7%)		7(8.0%)	20(21.8%)		19(8.1%)	4(12.9%)	
Leftovers, times/week			0.237			0.380			0.439			0.316			0.916
≤ 3	18(64.3%)	182(73.7%)		21(58.3%)	52(67.5%)		29(65.9%)	31(59.6%)		58(63.7%)	20(73.6%)		140(59.3%)	19(61.3%)	
> 3	10(35.7%)	65(26.3%)		15(41.7%)	25(32.5%)		15(34.1%)	21(40.4%)		33(36.3%)	16(26.4%)		96(40.7%)	12(38.7%)	
Physical exercise			0.161			0.918			0.650			0.897			0.933
Yes	19(67.9%)	137(55.5%)		23(63.9%)	49(63.6%)		33(75.0%)	41(78.9%)		81(89.0%)	32(89.5%)		218(92.4%)	28(90.3%)	
No	9(32.1%)	110(44.5%)		13(36.1%)	28(36.4%)		11(25.0%)	11(21.1%)		10(11.0%)	4(10.5%)		18(7.6%)	3(9.7%)	
Smoking			0.254			0.040			0.868			0.456			0.029
No	20(71.4%)	148(59.9%)		27(75.0%)	42(54.5%)		24(54.5%)	30(57.7%)		58(63.7%)	25(70.6%)		132(55.9%)	24(77.4%)	
Yes	8(28.6%)	99(40.1%)		9(25.0%)	35(45.5%)		20(45.5%)	22(42.3%)		33(36.3%)	11(29.4%)		104(44.1%)	7(22.6%)	
Drinking			**<0.001**			0.029			0.956			0.043			**0.007**
No	15(53.6%)	215(87.0%)		14(38.9%)	47(61.0%)		21(47.7%)	25(48.1%)		46(50.5%)	11(30.8%)		99(41.9%)	5(16.1%)	
Yes	13(46.4%)	32(13.0%)		22(61.1%)	30(39.0%)		23(52.3%)	27(51.9%)		45(49.5%)	25(69.2%)		137(58.1%)	26(83.9%)	

CRC, Colorectal Cancer; s.d., standard deviation; BMI, Body Mass Index.

[a] *P* value calculated using Student's t-test for continuous variables or Pearson's chi-squared test for categorical variables. *P* values < 0.01 were considered statistically significant.

[b] Individuals with extreme propensity scores were excluded (CRC cases [n = 83] and controls [n = 75]).

Table S3. The reclassification table and the analysis for categorical net reclassification improvement and integrated discrimination improvement in subgroups based on tumor location.

BI-model	Colon												Rectum											
	BI+Del-model				BI+Amp-model				BI+Var-model				BI+Del-model				BI+Amp-model				BI+Var-model			
	[0, 0.3)	[0.3, 0.6)	[0.6, 1]	RC %	[0, 0.3)	[0.3, 0.6)	[0.6, 1]	RC %	[0, 0.3)	[0.3, 0.6)	[0.6, 1]	RC %	[0, 0.3)	[0.3, 0.6)	[0.6, 1]	RC %	[0, 0.3)	[0.3, 0.6)	[0.6, 1]	RC %	[0, 0.3)	[0.3, 0.6)	[0.6, 1]	RC %
CRC cases																								
[0, 0.3)	59	7	0	11	60	6	0	9	50	16	0	24	44	0	0	0	44	0	0	0	44	0	0	0
[0.3, 0.6)	1	118	3	3	0	101	21	17	6	90	26	26	1	68	11	15	0	76	4	5	1	72	7	10
[0.6, 1]	0	3	138	2	0	0	141	0	0	1	140	1	0	4	61	6	0	7	58	11	0	7	58	11
Controls																								
[0, 0.3)	339	6	0	2	329	16	0	5	314	31	0	9	376	2	0	1	377	1	0	0	375	3	0	1
[0.3, 0.6)	6	133	0	4	7	123	9	12	17	115	7	17	11	112	6	13	0	124	5	4	9	115	5	11
[0.6, 1]	0	2	32	6	1	0	33	3	0	2	32	6	0	0	11	0	0	3	8	27	0	1	10	9
Total																								
[0, 0.3)	398	13	0	3	389	22	0	5	364	47	0	11	420	2	0	0	421	1	0	0	419	3	0	1
[0.3, 0.6)	7	251	3	4	7	224	30	14	23	205	33	21	12	180	17	14	0	200	9	4	10	187	12	11
[0.6, 1]	0	5	170	3	1	0	174	1	0	3	172	2	0	4	72	5	0	10	66	13	0	8	68	11
NRI (95% CI)[a]	0.022(-0.004-0.048), *P*=0.100				**0.049(0.013-0.086), *P*=0.008**				**0.070(0.021-0.119), *P*=0.005**				0.038(-0.007-0.082), *P*=0.098				-0.022(-0.058-0.015), *P*=0.240				-0.001(-0.045-0.042), *P*=0.948			
IDI (95% CI)[a]	**0.007(0.002-0.013), *P*=0.014**				**0.016(0.009-0.024), *P*<0.001**				**0.018(0.009-0.026), *P*<0.001**				**0.010(0.002-0.019), *P*=0.015**				0.003(-0.003-0.008), *P*=0.343				**0.011(0.002-0.021), *P*=0.018**			
Delta-AUC (95% CI)[a]	0.004(-0.003-0.011), *P*=0.291				**0.013(0.007-0.022), *P*<0.001**				**0.013(0.004-0.021), *P*=0.005**				**0.007(0.001-0.013), *P*=0.032**				0.001(-0.003-0.006), *P*=0.547				**0.008(0.001-0.015), *P*=0.034**			

CRC, colorectal cancer; RC, reclassification percent; CI, confidence interval; NRI, net reclassification improvement; IDI, integrated discrimination improvement; AUC, area under the curve

[a] *P* values < 0.025 were considered statistically significant.

Table S4. The reclassification table and the analysis for categorical net reclassification improvement and integrated discrimination improvement in subgroups based on tumor Duke's Stage.

BI-model	Duke's Stage A+B												Duke's Stage C+D											
	BI+Del-model				BI+Amp-model				BI+Var-model				BI+Del-model				BI+Amp-model				BI+Var-model			
	[0, 0.3)	[0.3, 0.6)	[0.6, 1]	RC %	[0, 0.3)	[0.3, 0.6)	[0.6, 1]	RC %	[0, 0.3)	[0.3, 0.6)	[0.6, 1]	RC %	[0, 0.3)	[0.3, 0.6)	[0.6, 1]	RC %	[0, 0.3)	[0.3, 0.6)	[0.6, 1]	RC %	[0, 0.3)	[0.3, 0.6)	[0.6, 1]	RC %
CRC cases																								
[0, 0.3)	61	2	0	3	61	2	0	3	55	8	0	13	43	0	0	0	43	0	0	0	43	0	0	0
[0.3, 0.6)	2	106	8	9	1	99	16	15	5	88	23	24	2	77	3	6	1	77	4	6	3	74	5	10
[0.6, 1]	0	4	136	3	0	3	137	2	0	5	135	4	0	2	72	3	0	3	71	4	0	3	71	4
Controls																								
[0, 0.3)	339	12	0	3	345	6	0	2	331	20	0	6	377	2	0	1	376	3	0	1	378	1	0	0
[0.3, 0.6)	8	121	3	8	9	115	8	13	16	109	7	17	11	106	4	12	3	116	2	4	11	106	4	12
[0.6, 1]	0	3	32	9	0	2	33	6	0	1	34	3	0	0	18	0	0	1	17	6	0	0	18	0
Total																								
[0, 0.3)	400	14	0	3	406	8	0	2	386	28	0	7	420	2	0	0	419	3	0	1	421	1	0	0
[0.3, 0.6)	10	227	11	8	10	214	4	14	21	197	30	21	13	183	7	10	4	193	6	5	14	180	9	11
[0.6, 1]	0	7	168	4	0	5	170	3	0	6	169	3	0	2	90	2	0	4	88	4	0	3	89	3
NRI (95% CI)[a]	0.005(-0.026-0.036), *P*=0.762				**0.038(0.004-0.072), *P*=0.029**				0.047(0.001-0.093), *P*=0.048				0.005(-0.026-0.035), *P*=0.765				-0.002(-0.032-0.028), *P*=0.900				0.007(-0.029-0.043), *P*=0.721			
IDI (95% CI)[a]	**0.008(0.002-0.014), *P*=0.007**				**0.011(0.004-0.019), *P*=0.003**				**0.016(0.007-0.025), *P*<0.001**				**0.012(0.004-0.020), *P*=0.003**				0.006(-0.001-0.013), *P*=0.060				**0.014(0.005-0.023), *P*=0.002**			
Delta-AUC (95% CI)[a]	0.005(-0.001-0.011), *P*=0.080				**0.010(0.002-0.018), *P*=0.015**				**0.012(0.003-0.021), *P*=0.011**				0.005(-0.003-0.014), *P*=0.215				0.004(-0.001-0.008), *P*=0.115				**0.008(0.001-0.015), *P*=0.025**			

CRC, colorectal cancer; RC, reclassification percent; CI, confidence interval; NRI, net reclassification improvement; IDI, integrated discrimination improvement; AUC, area under the curve.

[a] *P* values < 0.025 were considered statistically significant.

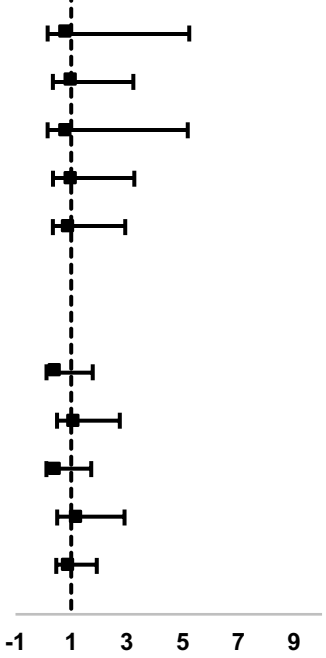
Figure S1. PS stratification analysis for the associations between gene CNVs and CRC risk. The forest plot showed the estimated ORs of the five genes associated with CRC risk and the bold squares indicated statistically significant.

Gene	Cases(535)/ Controls(442)	PS stratification adjusted[b] OR (95% CI)	*P* value[a]	1st Cases(28)/ Controls(247)	1st OR (95% CI)	2nd Cases(36)/ Controls(77)	2nd OR (95% CI)	3rd Cases(44)/ Controls(52)	3rd OR (95% CI)	4th Cases(91)/ Controls(36)	4th OR (95% CI)	5th Cases(263)/ Controls(31)	5th OR (95% CI)
MDM2													
Wt	417/436	1.000		26/243	1.000	33/75	1.000	43/51	1.000	88/36	1.000	227/31	1.000
Del	8/6	1.833 (0.437-7.687)	0.407	1/3	3.115 (0.313-31.043)	1/2	1.136 (0.100-12.974)	0/1	-	1/0	-	5/0	-
Amp	10/1	**34.449 (1.290-919.862)**	**0.035**	1/1	9.346 (0.568-153.872)	2/0	-	1/0	-	2/0	-	4/0	-
Del v.s. wt+amp		1.767 (0.423-7.387)	0.435		3.012 (0.303-29.980)		1.071 (0.094-12.216)		-		-		-
Amp *v.s.* del+wt		**33.496 (1.289-870.750)**	**0.035**		9.111 (0.554-149.851)		-		-		-		-
Del+amp *v.s.* wt		**3.996 (1.223-13.056)**	**0.022**		4.673 (0.816-26.755)		3.409 (0.544-21.368)		-		-		-
SKP2													
Wt	410/400	1.000		27/225	1.000	34/71	1.000	43/46	1.000	85/31	1.000	221/27	1.00
Del	16/28	**0.374 (0.162-0.864)**	**0.021**	1/13	0.641 (0.081-5.094)	1/4	0.515 (0.055-4.783)	0/5	-	4/3	0.486 (0.103, 2.297)	10/3	0.407 (0.106, 1.572)
Amp	9/15	0.512 (0.167-1.571)	0.242	0/9	-	1/2	1.029 (0.090-11.754)	1/1	1.093 (0.066-18.019)	2/2	0.365 (0.049-2.702)	5/1	0.611 (0.069-5.425)
Del v.s. wt+amp		**0.381 (0.165-0.880)**	**0.024**		0.664 (0.084-5.274)		0.514 (0.055-4.774)		**0.522 (0.429-0.636)**		-		0.413 (0.107-1.591)
Amp *v.s.* del+wt		0.538 (0.176-1.640)	0.276		-		1.057 (0.093-12.055)		1.186 (0.072-19.531)		0.382 (0.052-2.821)		0.649 (0.073-5.747)
Del+amp *v.s.* wt		**0.420 (0.212-0.831)**	**0.013**		0.379 (0.049-2.923)		0.588 (0.116-2.984)		0.219 (0.025-1.946)		0.438 (0.125-1.537)		0.458 (0.142-1.481)
FBXW7													
Wt	360/359	1.000		20/204	1.000	28/63	1.000	38/41	1.000	78/28	1.000	196/23	1.00
Del	40/41	1.065 (0.596-1.904)	0.831	5/23	2.217 (0.760-6.469)	5/5	2.286 (0.613-8.529)	3/6	0.539 (0.126-2.310)	4/3	0.496 (0.105-2.351)	23/4	0.675 (0.214-2.123)
Amp	35/43	0.709 (0.385-1.304)	0.268	3/20	1.020 (0.222-4.684)	3/9	0.762 (0.192-3.029)	3/5	0.809 (0.170-3.853)	9/5	0.669 (0.207-2.164)	17/4	0.499 (0.155-1.610)
Del v.s. wt+amp		1.086 (0.611-1.932)	0.778		2.117 (0.735-6.099)		2.323 (0.627-8.601)		0.561 (0.132-2.388)		0.506 (0.107-2.382)		0.729 (0.234-2.267)
Amp *v.s.* del+wt		0.694 (0.380-1.267)	0.234		0.869 (0.192-3.931)		0.687 (0.174-2.706)		0.860 (0.182-4.069)		0.680 (0.211-2.190)		0.524 (0.164-1.672)
Del+amp *v.s.* wt		0.922 (0.593-1.433)	0.717		1.898 (0.784-4.591)		1.231 (0.444-3.415)		0.647 (0.215-1.953)		0.690 (0.251-1.901)		0.587 (0.245-1.405)
β-TRCP													
Wt	401/414	1.000		26/232	1.000	32/72	1.000	42/49	1.000	82/35	1.000	219/26	1.00
Del	8/9	0.687 (0.227-2.081)	0.507	1/4	2.231 (0.240-20.714)	1/1	2.250 (0.136-37.108)	0/1	-	2/0	-	4/3	**0.164 (0.035-0.774)**
Amp	26/20	1.315 (0.597-2.899)	0.497	1/11	0.811 (0.101-6.538)	3/4	1.688 (0.357-7.981)	2/2	1.167 (0.157-8.645)	7/1	2.988 (0.354-25.201)	13/2	0.801 (0.172-3.743)
Del v.s. wt+amp		0.676 (0.223-2.053)	0.490		2.250 (0.243-20.864)		2.171 (0.132-35.729)				-		**0.161 (0.034-0.756)**
Amp *v.s.* del+wt		1.315 (0.598-2.893)	0.496		0.791 (0.098-6.368)		1.659 (0.351-7.835)		1.190 (0.161-8.818)		2.917 (0.346-24.594)		0.845 (0.182-3.936)
Del+amp *v.s.* wt		1.101 (0.573-2.117)	0.773		1.190 (0.258-5.495)		2.250 (0.529-9.564)		0.778 (0.124-4.878)		3.841 (0.469-31.481)		0.419 (0.143-1.227)
NEDD4-1													
Wt	380/398	1.000		22/228	1.000	31/68	1.000	39/45	1.000	78/31	1.000	210/26	1.00
Del	14/15	0.518 (0.183-1.471)	0.217	0/7	-	2/3	0.731 (0.073-7.313)	1/2	-	4/1	1.590 (0.171-14.791)	7/2	0.433 (0.085-2.197)
Amp	41/30	1.339 (0.747-2.400)	0.326	6/12	**5.182 (1.772-15.156)**	3/6	1.097 (0.257-4.673)	4/5	0.923 (0.232-3.680)	9/4	0.894 (0.256-3.119)	19/3	0.784 (0.217-2.832)
Del v.s. wt+amp		0.512 (0.182-1.440)	0.204		-		0.725 (0.073-7.231)		-		1.609 (0.174-14.908)		0.443 (0.088-2.236)
Amp *v.s.* del+wt		1.369 (0.765-2.451)	0.291		**5.341 (1.826-15.618)**		1.109 (0.261-4.717)		0.964 (0.242-3.838)		0.878 (0.252-3.054)		0.846 (0.236-3.038)
Del+amp *v.s.* wt		1.159 (0.697-1.926)	0.570		**3.273 (1.184-9.047)**		1.219 (0.377-3.938)		0.824 (0.242-2.806)		1.033 (0.340-3.142)		0.644 (0.228-1.822)

CI, confidence interval; OR, odds ratio; PS, propensity score.[a] *P* values< 0.05 were considered statistically significant.[b] individuals with extreme propensity scores were excluded (CRC cases [n = 83] and controls [n = 75]).

Figure S2. PS matching analysis for the associations between gene CNVs and CRC risk. The forest plot showed the estimated ORs of the five genes associated with CRC risk and the bold squares indicated statistically significant.

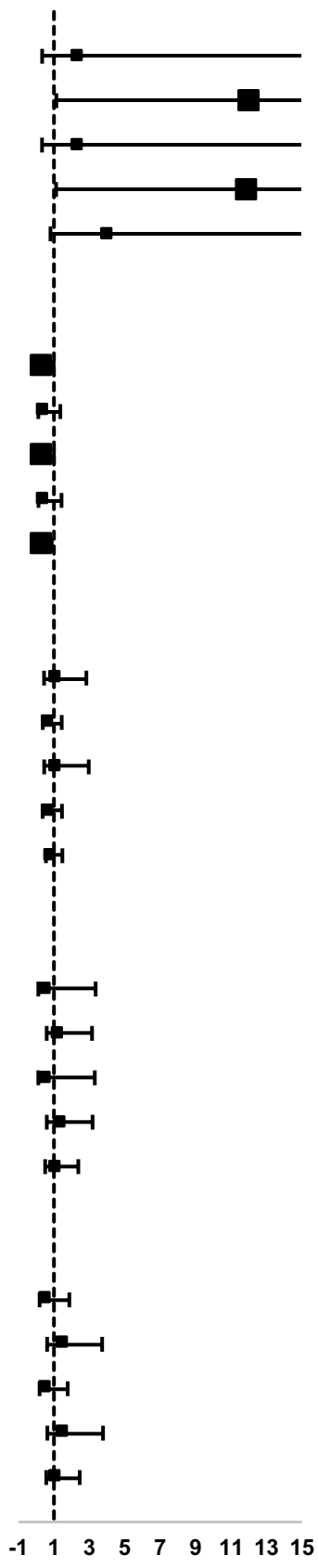
Gene	Cases(185)/ Controls(185)	PS matching		
		OR	95% CI	*P* value[a]
MDM2				
Wt	178/183	1.000		
Del	4/2	2.590	0.246-27.252	0.420
Amp	3/0	-	-	0.946
Del *v.s.* wt+amp		2.590	0.246-27.252	0.420
Amp *v.s.* del+wt		32.482	-	0.415
Del+amp *v.s*. wt		4.281	0.577-31.753	0.151
SKP2				
Wt	174/165	1.000		
Del	7/14	0.386	0.030-4.970	0.397
Amp	4/6	0.514	0.112-2.367	0.392
Del *v.s.* wt+amp		0.395	0.029-5.334	0.414
Amp *v.s.* del+wt		0.537	0.115-2.518	0.429
Del+amp *v.s*. wt		0.441	0.067-2.895	0.333
FBXW7				
Wt	154/149	1.000		
Del	18/17	1.028	0.395-2.678	0.953
Amp	13/19	0.682	0.302-1.539	0.352
Del *v.s.* wt+amp		1.051	0.400-2.760	0.916
Amp *v.s.* del+wt		0.681	0.299-1.553	0.356
Del+amp *v.s*. wt		0.840	0.491-1.439	0.525
β-TRCP				
Wt	172/172	1.000		
Del	4/5	0.899	0.154-5.235	0.903
Amp	9/8	1.051	0.342-3.229	0.930
Del *v.s.* wt+amp		0.889	0.153-5.181	0.893
Amp *v.s.* del+wt		1.063	0.346-3.264	0.914
Del+amp *v.s*. wt		1.003	0.342-2.938	0.995
NEDD4-1				
Wt	162/161	1.000		
Del	4/8	0.448	0.113-1.772	0.252
Amp	19/16	1.161	0.491-2.743	0.728
Del *v.s.* wt+amp		0.434	0.110-1.718	0.234
Amp *v.s.* del+wt		1.201	0.496-2.913	0.675
Del+amp *v.s*. wt		0.942	0.463-1.917	0.867



CI, confidence interval; OR, odds ratio; PS, propensity score. [a] *P* values calculated using conditional Logistic regression analysis. *P* values < 0.05 were considered statistically significant.

Figure S3. Sensitivity analysis for the associations between gene CNVs and CRC risk. The forest plot showed the estimated ORs of the five genes associated with CRC risk and the bold squares indicated statistically significant.

Gene	Cases(435)/ Controls(443)	PS adjusted[b] OR	95% CI	*P* value[a]
MDM2				
Wt	497/436	1.000		
Del	12/6	2.434	0.334- 17.737	0.362
Amp	9/1	**12.081**	**1.136- 128.477**	**0.039**
Del *v.s.* wt+amp		2.375	0.328- 17.177	0.373
Amp *v.s.* del+wt		**11.881**	**1.121- 125.954**	**0.040**
Del+amp *v.s*. wt		4.032	0.804- 20.228	0.087
SKP2				
Wt	490/400	1.000		
Del	19/28	**0.334**	**0.113- 0.985**	**0.047**
Amp	9/15	0.401	0.119- 1.359	0.142
Del *v.s.* wt+amp		**0.343**	**0.118- 0.999**	**0.050**
Amp *v.s.* del+wt		0.428	0.128- 1.427	0.167
Del+amp *v.s*. wt		**0.355**	**0.145- 0.873**	**0.026**
FBXW7				
Wt	360/359	1.000		
Del	40/41	1.120	0.443- 2.829	0.798
Amp	35/43	0.729	0.369- 1.438	0.359
Del *v.s.* wt+amp		1.153	0.449- 2.964	0.750
Amp *v.s.* del+wt		0.722	0.359- 1.452	0.357
Del+amp *v.s*. wt		0.899	0.548- 1.475	0.672
β-TRCP				
Wt	401/414	1.000		
Del	8/9	0.630	0.118- 3.353	0.576
Amp	26/20	1.364	0.591- 3.149	0.467
Del *v.s.* wt+amp		0.621	0.117- 3.304	0.563
Amp *v.s.* del+wt		1.377	0.596- 3.177	0.454
Del+amp *v.s*. wt		1.094	0.504- 2.374	0.818
NEDD4-1				
Wt	380/398	1.000		
Del	14/15	0.598	0.191- 1.868	0.374
Amp	41/30	1.512	0.615- 3.719	0.347
Del *v.s.* wt+amp		0.577	0.188- 1.774	0.335
Amp *v.s.* del+wt		1.538	0.628- 3.769	0.327
Del+amp *v.s*. wt		1.177	0.565-2.452	0.650



CI, confidence interval; OR, odds ratio; PS, propensity score. [a] *P* values calculated using unconditional Logistic regression analysis, *P* values < 0.05 were considered statistically significant. [b] individuals with extreme propensity scores were excluded (CRC [n=83] and control [n=75]).