

Supplementary Table 1

Prevalence of one-carbon metabolism genotypes according to neoplasia status of participants in the Norwegian Colorectal cancer Prevention (NORCCAP) screening study

Gene and SNP *	Genotype	No neoplasia	Low-risk colorectal adenoma	High-risk colorectal adenoma	P-value †
<i>MTHFR 677C>T</i>	CC	4463 (51.1%)	747 (54.1%)	200 (47.8%)	0.14
	CT	3563 (40.8%)	531 (38.5%)	183 (43.8%)	
	TT	708 (8.1%)	100 (7.3%)	35 (8.4%)	
<i>MTHFR 1298A>C</i>	AA	3706 (44.4%)	584 (44.3%)	182 (45.9%)	0.58
	AC	3587 (43.0%)	549 (41.7%)	169 (42.7%)	
	CC	1056 (12.6%)	184 (14.0%)	45 (11.4%)	
<i>MTR 2756A>G</i>	AA	5525 (66.1%)	863 (65.4%)	265 (67.3%)	0.85
	AG	2523 (30.2%)	403 (30.6%)	112 (28.4%)	
	GG	307 (3.7%)	53 (4.0%)	17 (4.3%)	
<i>MTRR 66A>G</i>	AA	1539 (18.9%)	257 (20.2%)	71 (18.4%)	0.51
	AG	3464 (42.6%)	548 (43.1%)	175 (45.4%)	
	GG	3136 (38.5%)	466 (36.7%)	139 (36.1%)	
<i>MTHFD1 1958G>A</i>	GG	2485 (29.8%)	436 (33.2%)	120 (30.5%)	0.12
	GA	4132 (49.5%)	633 (48.2%)	191 (48.6%)	
	AA	1724 (20.7%)	244 (18.6%)	82 (20.9%)	
<i>SLC19A1 80G>A</i>	GG	3040 (40.7%)	482 (41.0%)	148 (42.3%)	0.97
	GA	2623 (35.1%)	410 (34.8%)	122 (34.8%)	
	AA	1810 (24.2%)	285 (24.2%)	80 (22.9%)	
<i>TCN2 67A>G</i>	AA	6480 (78.1%)	1036 (79.0%)	317 (81.1%)	0.60
	AG	1661 (20.0%)	256 (19.5%)	67 (17.1%)	
	GG	152 (1.8%)	20 (1.5%)	7 (1.8%)	
<i>TCN2 776C>G</i>	CC	2696 (32.4%)	428 (32.7%)	136 (34.8%)	0.47
	CG	3955 (47.6%)	604 (46.2%)	188 (48.1%)	
	GG	1659 (20.0%)	276 (21.1%)	67 (17.1%)	
<i>BHMT 742G>A</i>	GG	4295 (51.6%)	706 (53.9%)	201 (51.0%)	0.61
	GA	3303 (39.7%)	493 (37.7%)	160 (40.6%)	
	AA	724 (8.7%)	110 (8.4%)	33 (8.4%)	
<i>CBS 699C>T</i>	CC	3753 (46.2%)	631 (49.5%)	174 (44.8%)	0.07
	CT	3281 (40.4%)	472 (37.1%)	150 (38.7%)	
	TT	1089 (13.4%)	171 (13.4%)	64 (16.5%)	
<i>CBS 844ins68</i>	Wild type	7377 (83.9%)	1139 (82.1%)	368 (87.4%)	0.03
	Heterozygote	1278 (14.5%)	231 (16.6%)	45 (10.7%)	
	Variant	137 (1.6%)	18 (1.3%)	8 (1.9%)	
<i>PON1 163T>A</i>	TT	3850 (46.9%)	584 (45.6%)	177 (45.5%)	0.83
	TA	3290 (40.1%)	533 (41.6%)	163 (41.9%)	
	AA	1063 (13.0%)	163 (12.7%)	49 (12.6%)	
<i>PON1 575A>G</i>	AA	4402 (52.9%)	710 (54.2%)	209 (52.8%)	0.29
	AG	3232 (38.8%)	491 (37.4%)	143 (36.1%)	
	GG	695 (8.3%)	110 (8.4%)	44 (11.1%)	

* Single Nucleotide Polymorphism (SNP)

† P-value (Chi-square test) for the difference in genotype frequencies between participants without neoplasia, low-risk colorectal adenoma, or high-risk colorectal adenoma

Supplementary Table 2

Associations between one-carbon metabolism genotypes and colorectal neoplasia of participants in the Norwegian Colorectal cancer Prevention (NORCCAP) screening study

Gene and SNP *	Genotype	Odds Ratio †	
		Low-risk colorectal adenoma (n=1378)	High-risk colorectal adenoma (n=418)
<i>MTHFR 677C>T</i>	CC	1.00	1.00
	CT	0.89 (0.79-1.00)	1.15 (0.93-1.41)
	TT	0.85 (0.68-1.06)	1.11 (0.77-1.61)
<i>MTHFR 1298A>C</i>	AA	1.00	1.00
	AC	0.97 (0.85-1.10)	0.95 (0.77-1.18)
	CC	1.08 (0.90-1.29)	0.84 (0.60-1.18)
<i>MTR 2756A>G</i>	AA	1.00	1.00
	AG	1.04 (0.91-1.18)	0.94 (0.75-1.18)
	GG	1.12 (0.83-1.52)	1.18 (0.71-1.96)
<i>MTRR 66A>G</i>	AA	1.00	1.00
	AG	0.97 (0.83-1.14)	1.14 (0.86-1.51)
	GG	0.89 (0.76-1.05)	0.97 (0.73-1.30)
<i>MTHFD1 1958G>A</i>	GG	1.00	1.00
	GA	0.87 (0.76-0.99)	0.96 (0.76-1.22)
	AA	0.81 (0.68-0.96)	0.99 (0.74-1.32)
<i>SLC19A1 80G>A</i>	GG	1.00	1.00
	GA	1.00 (0.86-1.15)	0.98 (0.77-1.26)
	AA	0.99 (0.85-1.16)	0.89 (0.68-1.18)
<i>TCN2 67A>G</i>	AA	1.00	1.00
	AG	0.98 (0.84-1.13)	0.83 (0.63-1.09)
	GG	0.79 (0.49-1.26)	0.90 (0.42-1.95)
<i>TCN2 776C>G</i>	CC	1.00	1.00
	CG	0.97 (0.85-1.11)	0.95 (0.75-1.19)
	GG	1.03 (0.87-1.21)	0.79 (0.58-1.06)
<i>BHMT 742G>A</i>	GG	1.00	1.00
	GA	0.92 (0.81-1.04)	1.06 (0.86-1.32)
	AA	0.91 (0.74-1.14)	0.97 (0.67-1.42)
<i>CBS 699C>T</i>	CC	1.00	1.00
	CT	0.86 (0.76-0.98)	1.00 (0.80-1.25)
	TT	0.93 (0.77-1.11)	1.26 (0.94-1.69)
<i>CBS 844ins68</i>	Wild type	1.00	1.00
	Heterozygote	1.20 (1.03-1.41)	0.73 (0.53-1.00)
	Variant	0.85 (0.51-1.39)	1.16 (0.56-2.39)
<i>PON1 163T>A</i>	TT	1.00	1.00
	TA	1.08 (0.95-1.23)	1.09 (0.88-1.36)
	AA	0.99 (0.82-1.19)	0.98 (0.71-1.36)
<i>PON1 575A>G</i>	AA	1.00	1.00
	AG	0.94 (0.83-1.07)	0.92 (0.74-1.15)
	GG	0.98 (0.79-1.22)	1.35 (0.96-1.89)

* Single Nucleotide Polymorphism (SNP)

† Adjusted for age, sex, and study centre