

Supplementary Table 1. Primer sequences used for PCR amplifications, sequencing reactions and promoter cloning. Underlined nucleotide sequences represent restriction site for cloning. Primers labeled with "seq" represent internal sequencing primers.

Gene	PCR reaction	forward	reverse	sequence covered
SHMT1	1	AGG GAC CTG CAG AAC TGA C	AGT ACA GAG GCA AGA TCA TTG	5' flanking
SHMT1	2	AAG TGT TCA GTG GAG AGC TAC	GTA GTC TTC CTG GAA ATC TTG	exon 1
SHMT1	3	CCT GTG AAC TGT CAG GAA AG	TTT AAT TCT GGA AGC TAC ACA TG	exon 2
SHMT1	4	CTT CAG TGT TAT CAC ATG CTG	TAC TAA AAC CTT TGA GGA GGA	exon 3
SHMT1	5	CAA GGA AAT AAA AGC TAG GAG	TGA GTG GAT CTA AGT CTC CTG	exons 4 & 5
SHMT1	5-seqF	GAG ATG GAG TTT CGC TCT T		exons 4 & 5
SHMT1	5-seqR		ATA AAA GAT AAG TCA CGC ATC	exons 4 & 5
SHMT1	6	CTC CCT CAA CTG AAT CTG AAC	TAG GAC ATC ATT CCT CTT GTC	exons 6 & 7
SHMT1	7	CCT ACT CTG TGT TAG CAT CTC	GTT ACA AAT CAG TTC TCC ATG	exon 8
SHMT1	8	CTG TTC TGA GGA CAA GCA GTC	TGA CAT TGA AAA GCA AGG AAG	exon 9
SHMT1	9	TGC AGA TGG GAG AGG AGT G	CCA AAG TAA ATT GAA CTG CTG	exon 10
SHMT1	9-seqR		GAG CCT TTA CCA TCA ATG T	exon 10
SHMT1	10	AGG CAC AAA TGT CAG AAT GTC	GCA TTT CTC TGT GGG TTG TTA	exon 11
SHMT1	11	TAC TGG GTG CAT CTT GTT TAC	AGT AAT TGA GGT AAG CAT GGA	exon 12
SHMT1	12	ATT GTC TGC CAC TAA ATA GCT	TTC TGC TGT AAA TCA GAA GTG	exon 12 and 3' flanking
SHMT1	13	ATA GTG GGC AGT CTC CTT TAC	GGT GGC ATT TAT CTC AAT CTG	3' flanking
SHMT1	Promoter reporter assay	AGG ACA <u>ACG CGT</u> CTC TGC CTC CCA GGC TCA AG	AGG ACA <u>CTC GAG</u> CCC CCG GAG GCG CCC AAT C	5' flanking
SHMT1	rs669340 reporter assay	AGG ACA <u>GGT ACC</u> TCA CAC TTT CTC CTT TGT CTG	AGG ACA <u>ACG CGT</u> AAG AGA ACA AGA CCC TGT CTC	intron 1
SHMT1	rs7207306 reporter assay	AGG ACA <u>GGT ACC</u> TAT TTG GAA AGA GTG ACC ACC	AGG ACA <u>ACG CGT</u> CAT AAC CAG CAG AGC ATA GAG	intron 5
SHMT2	1	ACA TAC CAC CAT GCC TAG GT	CTC AAA CTT GTG CTT CTA GG	5' flanking, exon1, and exon 2
SHMT2	1seqF	CTTGGCTTATCAGAATCACTG		5' flanking, exon1, and exon 2
SHMT2	1seqR1		TAGGGTGCCTACTGAATATC	5' flanking, exon1, and exon 2
SHMT2	1seqF1	CACAAGCTAATGCACTAGTC		5' flanking, exon1, and exon 2
SHMT2	1seqR2		AAAGGCTCAGCTTGTGAGAC	5' flanking, exon1, and exon 2
SHMT2	1seqF2	CCATTTACGTGGCATTAG		5' flanking, exon1, and exon 2
SHMT2	1seqR3		CACATCTCAGGATCACTGTC	5' flanking, exon1, and exon 2
SHMT2	1seqF3	GATTTGTCTGGACTGTTGTG		5' flanking, exon1, and exon 2
SHMT2	2	TTC CTT TCT TAT CTC CCT CAA	CTT GTT GGC AGT GAT GGA TAC	exons 3-10
SHMT2	2seqR1		GTGAGAGGAAGTAAGAAGGC	exons 3-10
SHMT2	2seqF1	ACTGTGGACCATACAGATGG		exons 3-10
SHMT2	2seqR2		CTTGGTACACTGGATTCCAG	exons 3-10
SHMT2	2seqF2	GACCTGAGAGGAATTCATTC		exons 3-10
SHMT2	3	GGC TAC TCA CTG GTA TCA GGT	CTT GGG ATC TGT GTC TGA TTC	exons 10-12 and 3' flanking
SHMT2	3seqR1		TAAGTGAGAGGTCTTCCCTC	exons 10-12 and 3' flanking
SHMT2	3seqF1	CTCAAAGTTACTCTCCTTCC		exons 10-12 and 3' flanking
SHMT2	3seqR2		ATCCACTTCTTCCACTCCTC	exons 10-12 and 3' flanking
SHMT2	3seqF2	CTTCTGTTGGCTCACGTAG		exons 10-12 and 3' flanking

Supplementary Table 2. *SHMT1* and *SHMT2* polymorphisms. The table lists variant sequence locations, DNA sequence alterations, amino acid sequence alterations, rs numbers (when available) and MAF values for both the "Human Variation Panel" and "1000 Genomes" data.

Gene	Chr	Location (build36)	Location	Nucleotide	RefSNP ID	Sequence Change	Amino Acid	MAF			1000 Genomes MAF		
								AA	EA	HCA	AA	EA	HCA
SHMT1	17	18208440	5'FR	-1049		A→G		0.000	0.000	0.005	NA	NA	NA
SHMT1	17	18208394	5'FR	-1003	rs57739150	C→G		0.021	0.000	0.000	0.037	NA	NA
SHMT1	17	18208380	5'FR	-989		C→G		0.016	0.000	0.000	0.011	NA	NA
SHMT1	17	18208289	5'FR	-898	rs60510653	A→G		0.135	0.005	0.000	0.190	0.004	0.003
SHMT1	17	18208216	5'FR	-825	rs62072547	T→C		0.031	0.141	0.000	0.006	0.092	NA
SHMT1	17	18208109	5'FR	-718	rs9303145	C→G		0.120	0.000	0.000	0.132	NA	NA
SHMT1	17	18208106	5'FR	-715		C→T		0.010	0.000	0.198	NA	0.004	0.129
SHMT1	17	18208095	5'FR	-704		C→T		0.000	0.005	0.000	NA	NA	NA
SHMT1	17	18208046	5'FR	-655		C→T		0.005	0.000	0.000	NA	NA	NA
SHMT1	17	18208030	5'FR	-639		G→A		0.005	0.000	0.000	NA	NA	NA
SHMT1	17	18207934	5'FR	-543	rs7213472	A→G		0.135	0.005	0.000	0.190	NA	NA
SHMT1	17	18207887	5'FR	-496		A→G		0.000	0.005	0.000	NA	NA	NA
SHMT1	17	18207764	5'FR	-373	rs643333	C→A		0.089	0.242	0.036	0.011	0.277	0.090
SHMT1	17	18207738	5'FR	-347	rs9907337	C→T		0.083	0.000	0.000	0.083	0.005	NA
SHMT1	17	18207700	5'FR	-309	rs638416	C→G		0.260	0.404	0.448	0.253	0.385	0.454
SHMT1	17	18207655	5'FR	-264		G→A		0.036	0.000	0.000	0.052	NA	NA
SHMT1	17	18207634	5'FR	-243		A→G		0.000	0.011	0.000	NA	NA	NA
SHMT1	17	18207619	5'FR	-228		C→T		0.000	0.000	0.005	NA	NA	NA
SHMT1	17	18207573	5'UTR	-182		C→T		0.016	0.011	0.000	NA	0.018	NA
SHMT1	17	18207549	5'UTR	-158		G→C/A		0.016/0	0.005/0	0/0.005	NA	NA	NA
SHMT1	17	18207511	5'UTR	-120		C→T		0.047	0.000	0.000	0.040	0.002	NA
SHMT1	17	18207468	5'UTR	-77		G→A		0.000	0.000	0.005	NA	NA	NA
SHMT1	17	18207341	intron 1	70	rs35311598	G(6)→G(7)		0.208	0.250	0.036	NA	NA	NA
SHMT1	17	18207315	intron 1	76		C→T		0.022	0.000	0.000	NA	NA	NA
SHMT1	17	18207292	intron 1	119	rs672356	C→T		0.187	0.255	0.036	0.155	0.284	0.077
SHMT1	17	18207257	intron 1	154	rs9900382	G→A		0.110	0.005	0.000	0.135	0.004	NA
SHMT1	17	18207220	intron 1	191		G(4)→G(3)		0.089	0.000	0.000	NA	NA	NA
SHMT1	17	18207184	intron 1	227		G→A		0.000	0.005	0.000	NA	NA	NA
SHMT1	17	18199816	intron 2	109		G→A		0.047	0.000	0.000	0.049	0.002	NA
SHMT1	17	18197704	intron 3	7	rs2273026	G→A		0.104	0.125	0.182	0.072	0.092	0.201
SHMT1	17	18197701	intron 3	10		T→C		0.094	0.005	0.000	0.103	NA	NA
SHMT1	17	18192106	intron 4	258		C→T		0.000	0.000	0.005	NA	NA	NA
SHMT1	17	18192034	intron 4	330		T→C		0.000	0.000	0.016	NA	NA	NA
SHMT1	17	18191987	intron 4	377		C→T		0.000	0.000	0.020	NA	NA	NA
SHMT1	17	18191961	intron 4	403	rs12451807	A→C		0.109	0.240	0.333	NA	NA	NA
SHMT1	17	18191957	intron 4	407	rs4924850	A→C		0.130	0.000	0.000	NA	NA	NA

SHMT1	17	18191819	intron 4	-124	rs28479066	G→A		0.130	0.005	0.000	0.152	NA	NA
SHMT1	17	18191694	exon 5	360		C→T	Gly(120)Gly	0.000	0.005	0.000	NA	NA	NA
SHMT1	17	18184858	intron 5	-6		C→G		0.010	0.000	0.000	NA	NA	NA
SHMT1	17	18184598	intron 6	173	rs62072544	G→A		0.109	0.234	0.333	0.170	0.198	0.214
SHMT1	17	18184597	intron 6	174	rs62072543	C→T		0.109	0.234	0.333	0.170	0.198	0.214
SHMT1	17	18184523	intron 6	248		G→A		0.000	0.000	0.005	NA	NA	NA
SHMT1	17	18184522	intron 6	349		C→T		0.000	0.000	0.005	NA	NA	NA
SHMT1	17	18184363	intron 6	-69	rs9897954	C→T		0.109	0.000	0.000	0.089	0.011	NA
SHMT1	17	18184249	exon 7	647		A→G	Lys(216)Arg	0.031	0.000	0.000	0.009	0.004	NA
SHMT1	17	18184178	exon 7	718		G→A	Val(240)Met	0.005	0.000	0.000	NA	NA	NA
SHMT1	17	18179737	intron 7	-23	rs2273028	C→T		0.500	0.260	0.036	0.494	0.313	0.093
SHMT1	17	18179717	intron7	-3		C→T		0.016	0.000	0.000	0.011	0.002	NA
SHMT1	17	18177381	intron 8	-54		C→G		0.005	0.000	0.000	NA	NA	NA
SHMT1	17	18177241	exon 9	1018	rs7215148	G→C	Glu(340)Gln	0.016	0.000	0.000	NA	NA	NA
SHMT1	17	18177199	intron 9	6		G→A		0.010	0.000	0.000	0.006	NA	NA
SHMT1	17	18177104	intron 9	101		C→T		0.000	0.000	0.005	NA	NA	NA
SHMT1	17	18177064	intron 9	141	rs2273029	C→T		0.115	0.234	0.333	0.172	0.249	0.260
SHMT1	17	18177063	intron 9	142		G→A		0.000	0.005	0.000	NA	NA	NA
SHMT1	17	18174896	intron 9	-186		C→T		0.000	0.005	0.000	NA	NA	NA
SHMT1	17	18174873	intron 9	-163		C→T		0.036	0.000	0.000	0.049	NA	NA
SHMT1	17	18174753	intron 9	-43	rs8080285	A→C		0.260	0.005	0.000	0.259	0.018	NA
SHMT1	17	18174745	intron 9	-35		C→T		0.000	0.005	0.000	NA	NA	NA
SHMT1	17	18173683	intron 10	-26	rs2125154	A→C		0.193	0.000	0.000	0.172	0.016	NA
SHMT1	17	18173453	intron 10	-256		G→A		0.000	0.005	0.000	NA	NA	NA
SHMT1	17	18173296	intron 11	21	rs6502648	G→T		0.188	0.000	0.000	0.167	0.016	NA
SHMT1	17	18173243	intron 11	74	rs17806333	A→G		0.000	0.005	0.000	NA	NA	NA
SHMT1	17	18173113	intron 11	-155		G→A		0.000	0.005	0.000	NA	NA	NA
SHMT1	17	18172861	exon 12	1380		C→T	Ala(460)Ala	0.037	0.000	0.000	0.049	NA	NA
SHMT1	17	18172828	exon 12	1413		C→T	Phe(471)Phe	0.005	0.000	0.000	NA	NA	NA
SHMT1	17	18172821	exon 12	1420	rs1979277	C→T	Leu(474)Phe	0.337	0.266	0.036	0.356	0.299	0.095
SHMT1	17	18172742	3'UTR	1499	rs1979276	C→G		0.200	0.260	0.036	0.155	0.302	0.090
SHMT1	17	18172737	3'UTR	1504		C→T		0.011	0.026	0.000	0.009	0.021	0.005
SHMT1	17	18172723	3'UTR	1518		C→T		0.379	0.729	0.964	0.376	0.318	0.093
SHMT1	17	18172522	3'UTR	1719	rs12952556	A→G		0.347	0.266	0.036	0.362	0.304	0.093

SHMT2	12	55911274	intron2	224		deletion of TCCT		0.396	0.313	0.411	NA	NA	NA
SHMT2	12	55911343	intron2	293		G→A		0.000	0.000	0.036	NA	NA	0.026
SHMT2	12	55911812	exon4	361		C→T	Arg(121)Cys	0.000	0.000	0.005	NA	NA	NA
SHMT2	12	55912217	intron4	244		G→A		0.057	0.000	0.083	0.078	NA	0.124
SHMT2	12	55912285	exon5	537	rs11557166	C→T	Asp(179)Asp	0.026	0.000	0.083	0.037	NA	0.124
SHMT2	12	55912632	intron6	7		deletion of G		0.000	0.000	0.005	NA	NA	NA
SHMT2	12	55912711	intron6	89		C→T		0.021	0.000	0.000	0.046	0.002	0.003
SHMT2	12	55912834	exon7	798	rs2229715	G→A	Ser(266)Ser	0.005	0.000	0.000	NA	NA	NA
SHMT2	12	55912849	exon7	812	rs2229716	G→A	Ala(271)Ala	0.000	0.026	0.000	0.003	0.037	0.003
SHMT2	12	55913109	intron7	216		deletion of T		0.005	0.000	0.000	NA	NA	NA
SHMT2	12	55913128	intron7	235		G→A		0.026	0.000	0.000	0.029	NA	NA
SHMT2	12	55913277	exon8	905		A→C	Lys(302)Thr	0.005	0.000	0.000	NA	NA	NA
SHMT2	12	55913341	exon8	969	rs2229717	G→T	Leu(323)Leu	0.026	0.042	0.193	0.026	0.046	0.124
SHMT2	12	55913423	intron8	28		G→T		0.005	0.000	0.005	NA	NA	NA
SHMT2	12	55913454	intron8	59		G→A		0.005	0.000	0.000	NA	NA	NA
SHMT2	12	55913472	intron8	77		C→A		0.005	0.000	0.000	NA	NA	NA
SHMT2	12	55913792	intron9	80		A→G		0.011	0.021	0.000	NA	0.018	NA
SHMT2	12	55913858	exon10	1183		C→T	Arg(395)Trp	0.000	0.005	0.000	NA	NA	NA
SHMT2	12	55913984	intron10	30	rs34095989	G→A		0.203	0.432	0.224	0.138	0.431	0.387
SHMT2	12	55914055	exon11	1282		G→A	Ala(428)Thr	0.010	0.000	0.000	0.014	0.002	NA
SHMT2	12	55914083	exon11	1310		G→A	Arg(437)His	0.000	0.000	0.031	NA	NA	NA
SHMT2	12	55914129	exon11	1356	rs2229718	C→T	Val(452)Val	0.005	0.000	0.000	NA	NA	NA
SHMT2	12	55914504	3'UTR	1608		C→T		0.000	0.000	0.005	NA	NA	NA
SHMT2	12	55914680	3'UTR	1784		deletion of TCTT		0.000	0.026	0.000	NA	NA	NA
SHMT2	12	55914854	3'UTR	1958		deletion of GCTCCCA		0.016	0.000	0.000	NA	NA	NA
SHMT2	12	55914866	3'UTR	1970		G→A		0.005	0.000	0.000	NA	NA	NA
SHMT2	12	55915071	3'FR	2175		G→T		0.005	0.000	0.000	NA	NA	NA
SHMT2	12	55915080	3'FR	2184		G→T		0.000	0.000	0.057	NA	NA	0.031
SHMT2	12	55915118	3'FR	2222		G→A		0.016	0.000	0.000	NA	NA	NA
SHMT2	12	55915184	3'FR	2288		G→A		0.005	0.005	0.000	NA	NA	NA
SHMT2	12	55915234	3'FR	2338		G→A		0.000	0.005	0.000	NA	NA	NA

SHMT2	12	55915285	3'FR	2389		C→G		0.000	0.005	0.000	NA	NA	NA
SHMT2	12	55915536	3'FR	2640		G→C		0.000	0.005	0.000	NA	NA	NA
SHMT2	12	55915550	3'FR	2654		insertion of GAGTGGGAAG		0.005	0.000	0.000	NA	NA	NA
SHMT2	12	55915582	3'FR	2686		G→A		0.000	0.005	0.000	NA	NA	NA
SHMT2	12	55915773	3'FR	2877		G→A		0.000	0.000	0.005	NA	NA	NA
SHMT2	12	55915793	3'FR	2897	rs58212469	A→C		0.016	0.000	0.000	0.049	NA	NA
SHMT2	12	55915875	3'FR	2979		G→A		0.010	0.047	0.005	NA	0.039	NA
SHMT2	12	55916005	3'FR	3109		A→G		0.010	0.000	0.000	0.003	NA	NA
SHMT2	12	55916048	3'FR	3152		A→G		0.010	0.000	0.000	0.014	NA	NA

SHMT1

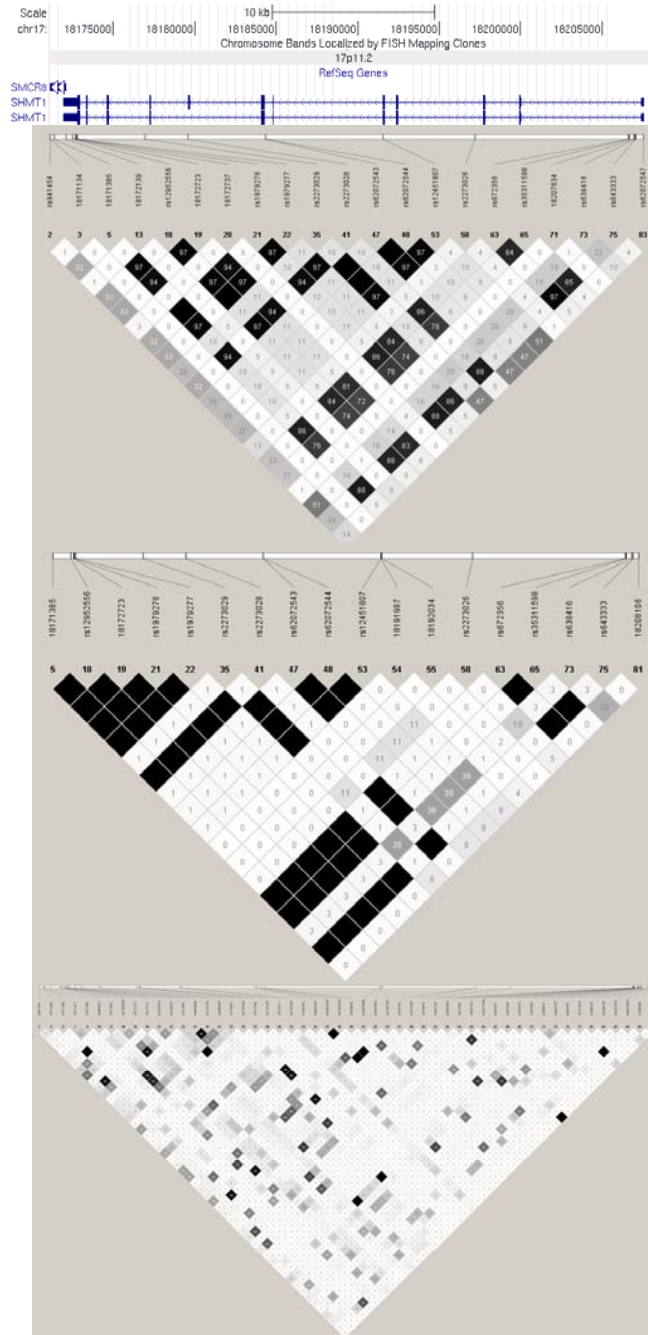
SHMT2

Supplementary Figure 1: LD plots (r^2), based on the gene resequencing, generated with Haploview. The variants graphed represent polymorphisms with ethnic specific MAFs $\geq 1\%$ (EA, HCA, or AA) in *SHMT1* (left) and *SHMT2* (right). The figures at the top represent the genetic structures of *SHMT1* and *SHMT2*, as defined by the UCSC Genome Browser.

EA

HCA

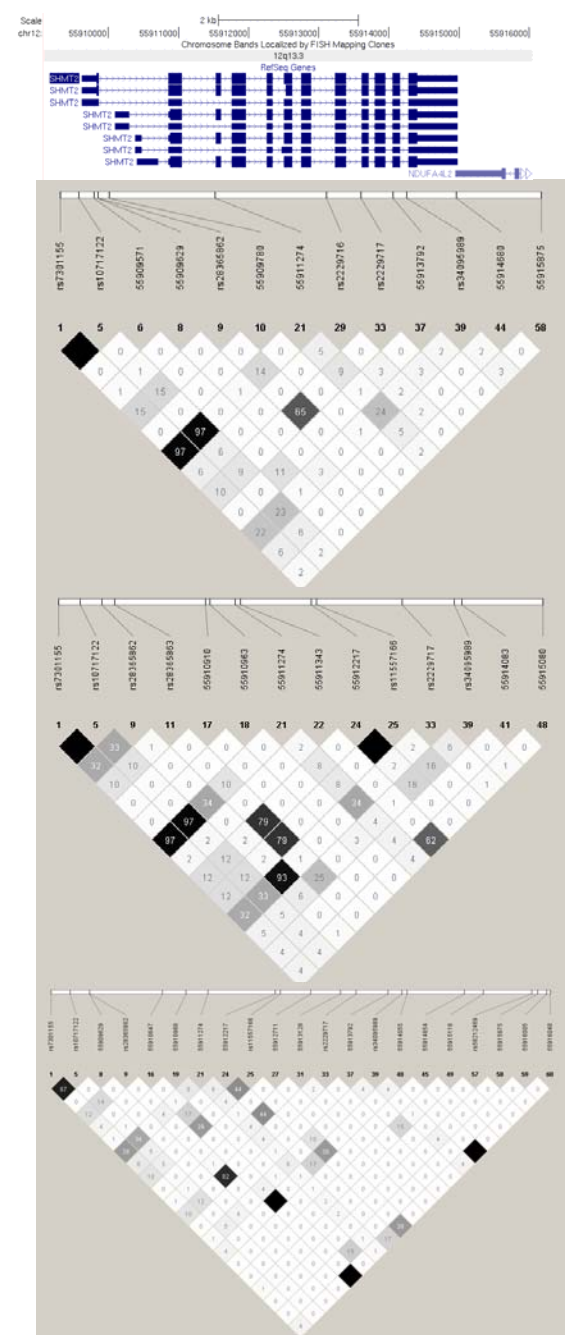
AA

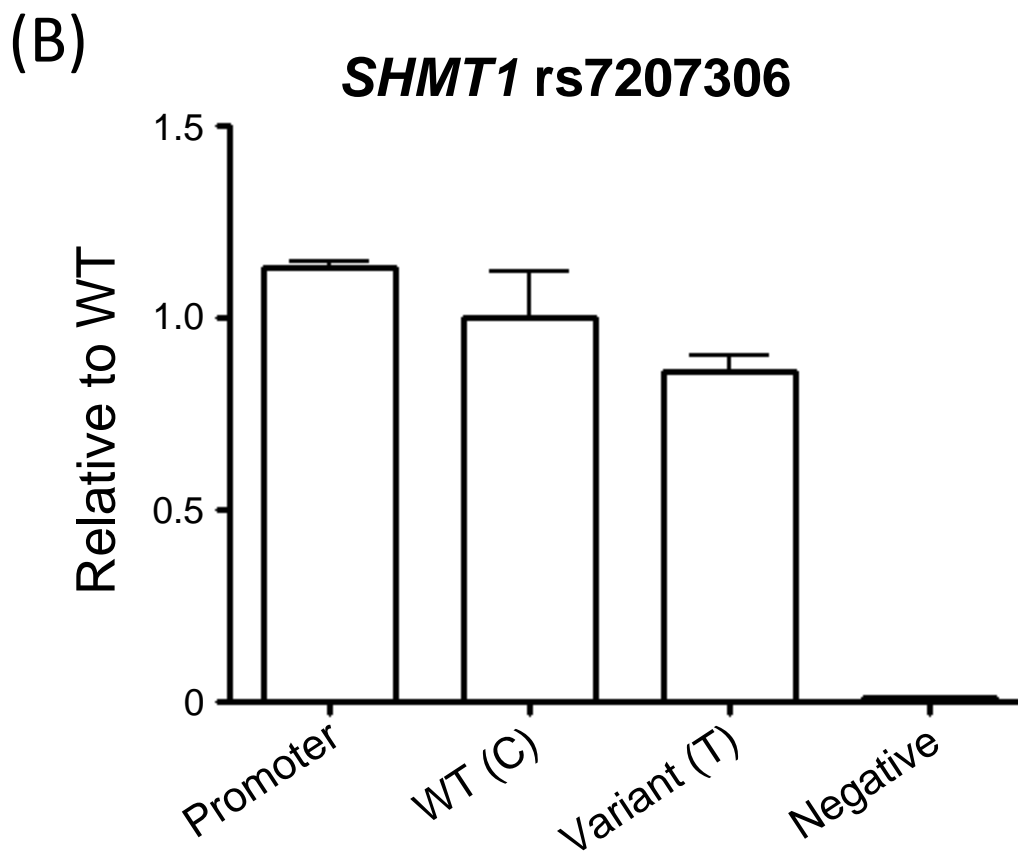
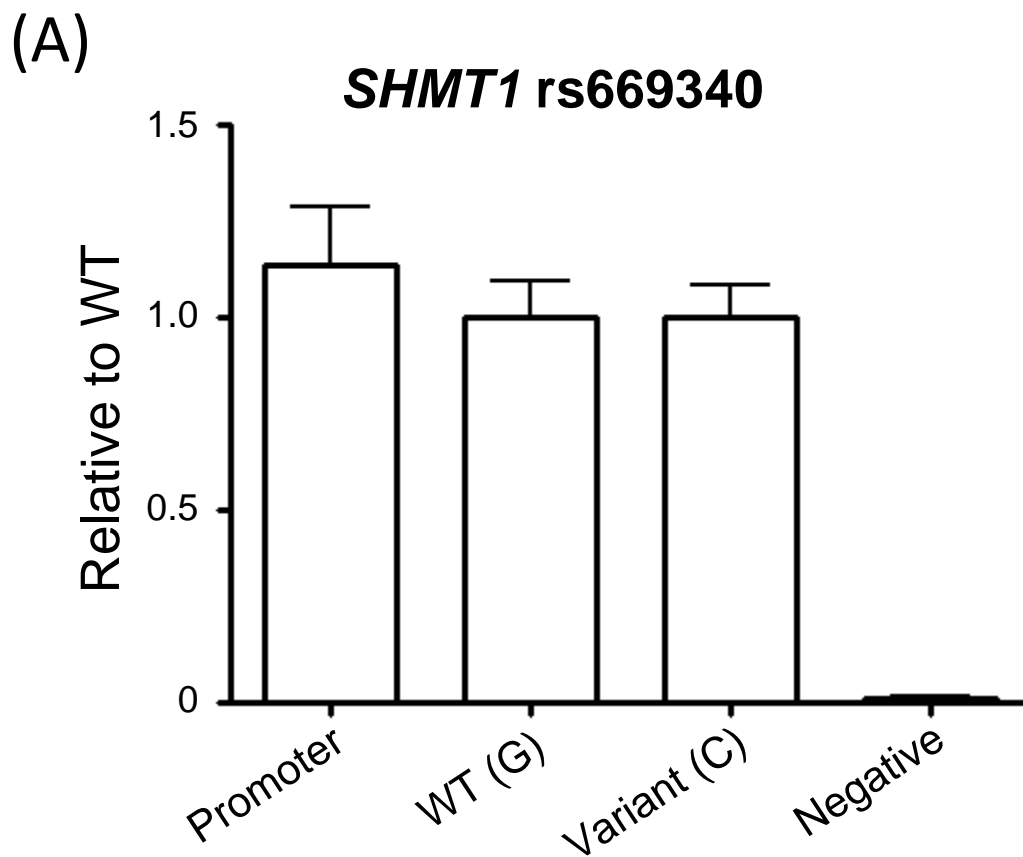


EA

HCA

AA





Supplemental Figure 2. Dual reporter assays for (A) rs669340 and (B) rs7207306. Error bars indicate SEM.