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Supplemental Data

Genome-wide Association Study of Vitamin B6, Vitamin B12, Folate, and Homocysteine Blood Concentrations

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Figure S1. **Quantile-quantile plots for the genome-wide association of vitamin-B6, -B12, folate and homocysteine.** The blue dotted line indicates the 95% confidence band and the QQ-plots for (A) vitamin-B6, (B) vitamin-B12 (C) folate and (D) homocysteine analyses.

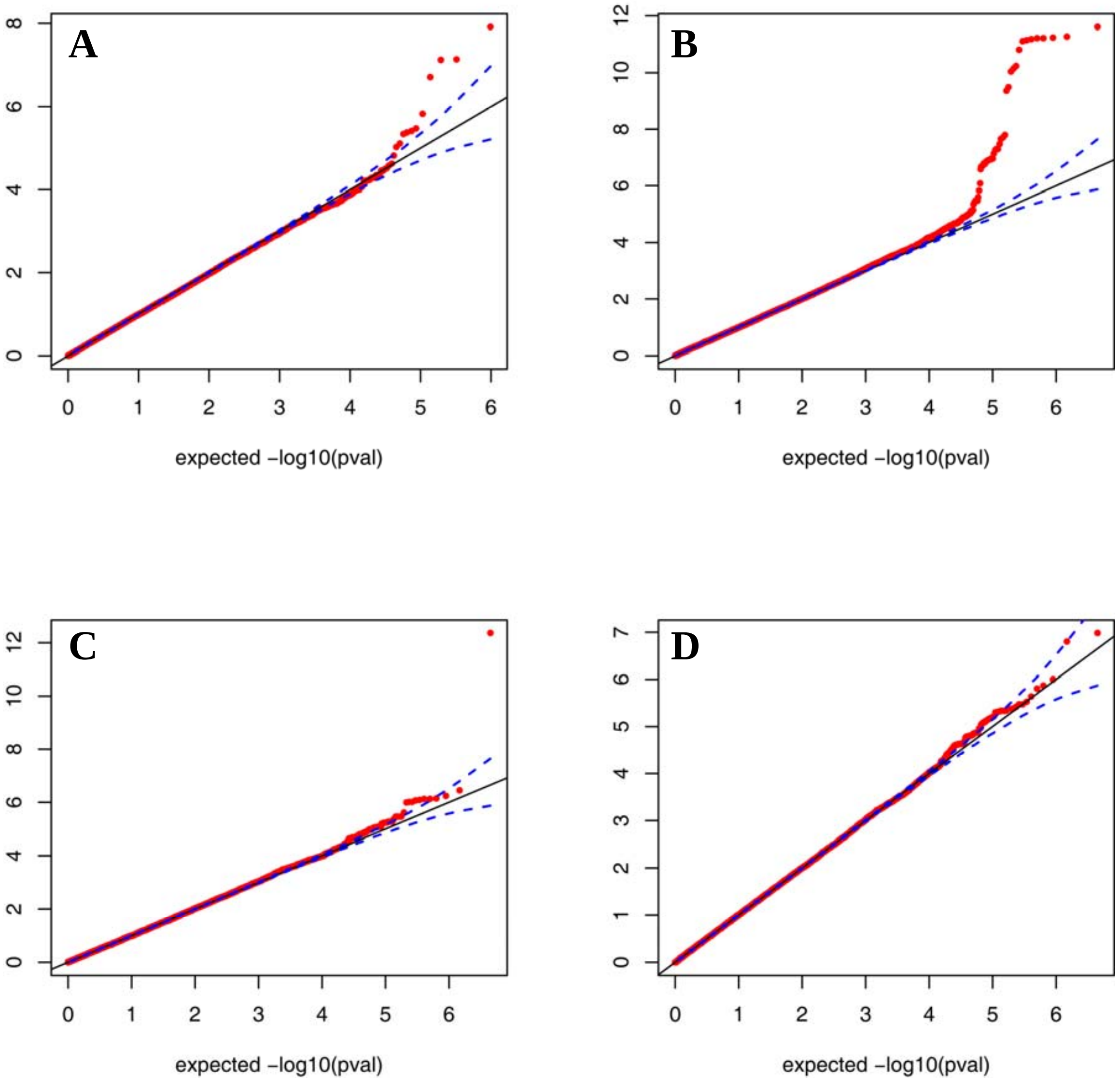

Figure S2. Associations of SNPs within 250kb of *ALPL* with plasma vitamin-B6. The figures display –log10 p-values for plasma vitamin-B6 with *ALPL* (top panel). The SNP (rs4654748, P-1.21 x 10^{-8}) with the strongest evidence of association is indicated (red diamond). The degree of linkage disequilibrium (r^2) is displayed as r2 ≥ 0.8 (red circles), ≥ 0.6 (orange), ≥0.4 (green), and ≥0.2 (light blue). The location of genes that mapped +/- 250kb of the most significant SNP is displayed in the bottom panel.

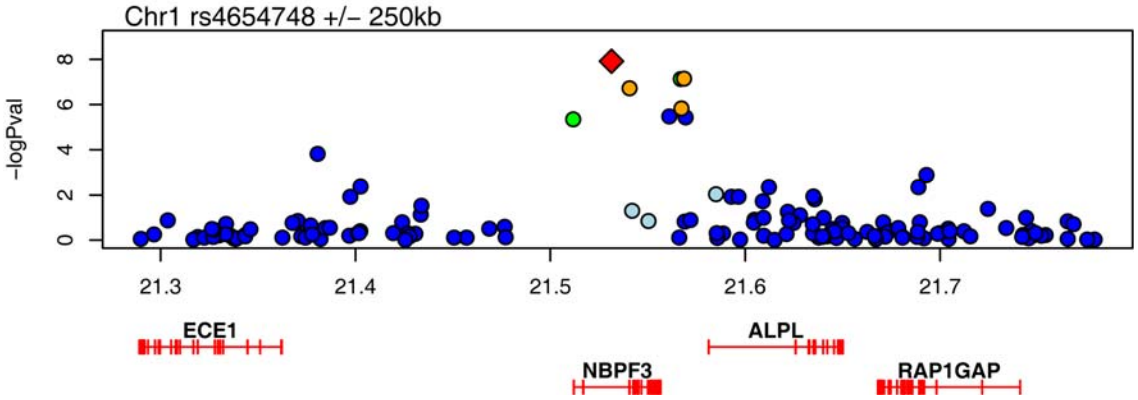

Figure S3. Associations of SNPs in the loci for plasma vitamin-B12. The panel displays the –log10 p-values for plasma vitamin-B12 with (A) *FUT2*, (B), *CUBN*, and (C) *TCN1*. The SNP with the strongest evidence of association is indicated (red diamond). The degree of linkage disequilibrium (r^2) is displayed as r2 $\geq$ 0.8 (red circles), $\geq$ 0.6 (orange), $\geq$0.4 (green), and $\geq$0.2 (light blue). The location of genes that mapped 150~250kb of the most significant SNP is displayed in the bottom panels.

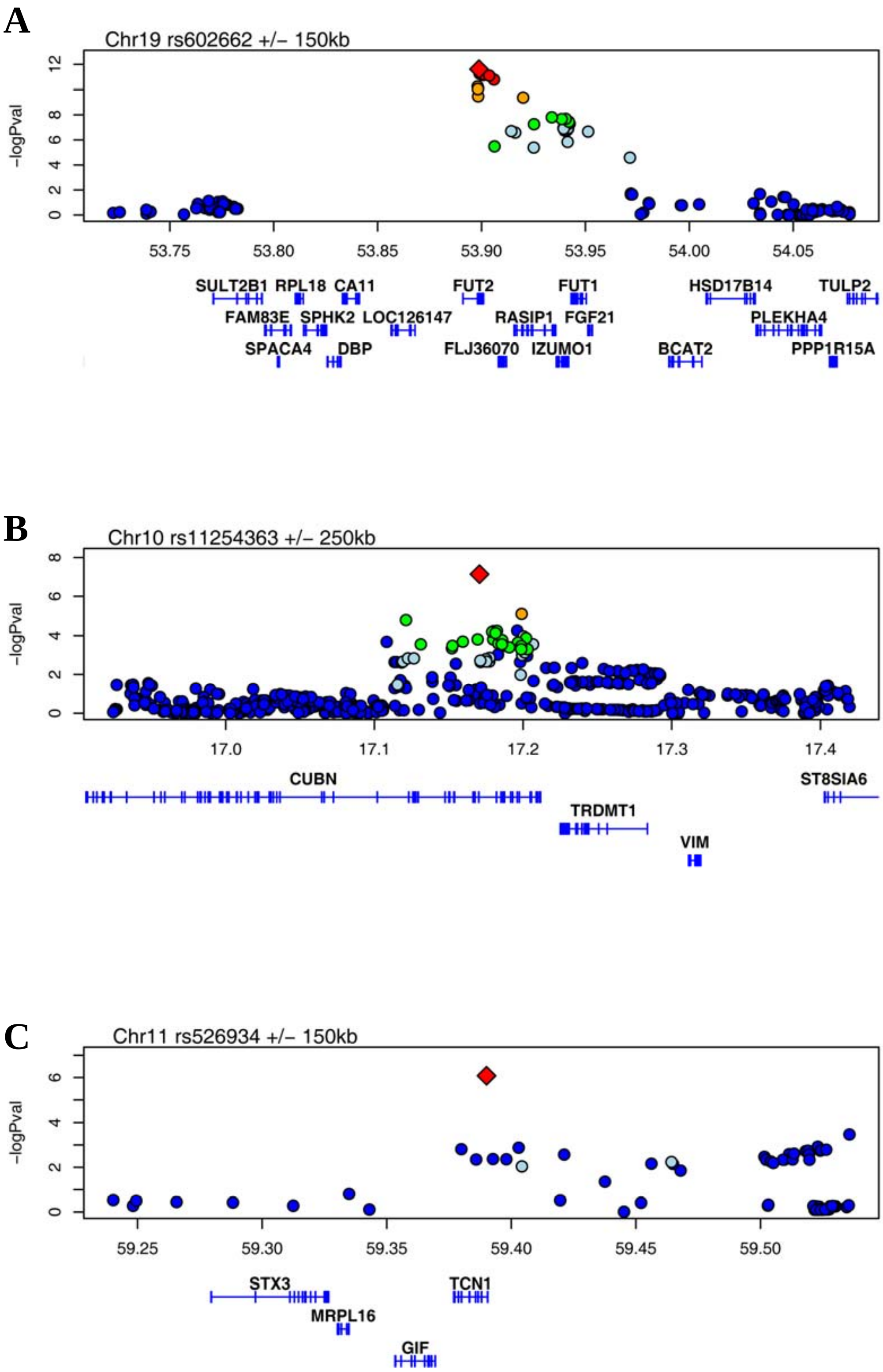

Figure S4. Associations of SNPs in the loci for plasma homocysteine. The panel displays the –log10 p-values for plasma vitamin-B12 with (A) *MTHFR*, and (B), *SYT9*. The SNP with the strongest evidence of association is indicated (red diamond). The degree of linkage disequilibrium (r^2) is displayed as r2 ≥ 0.8 (red circles), ≥ 0.6 (orange), ≥0.4 (green), and ≥0.2 (light blue). The location of genes that mapped 250kb of the most significant SNP is displayed in the bottom panels.

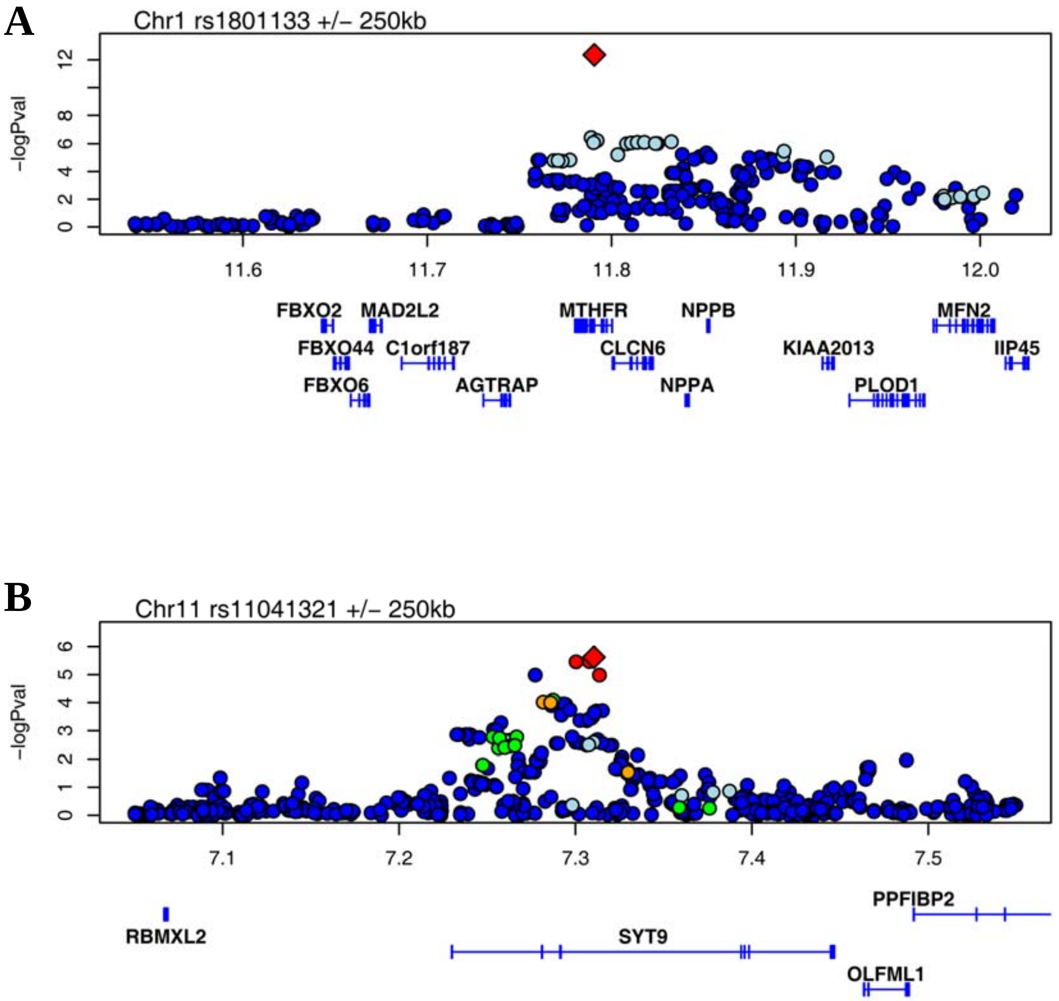

Figure S5. Associations of SNPs in the loci for plasma folate. The panel displays the –log10 p-values for plasma vitamin-B12 with (A) *MTHFR*, and (B), *PRICKLE2*. The SNP with the strongest evidence of association is indicated (red diamond). The degree of linkage disequilibrium (r^2) is displayed as r2 $\geq$ 0.8 (red circles), $\geq$ 0.6 (orange), $\geq$0.4 (green), and $\geq$0.2 (light blue). The location of genes that mapped 250kb of the most significant SNP is displayed in the bottom panels.

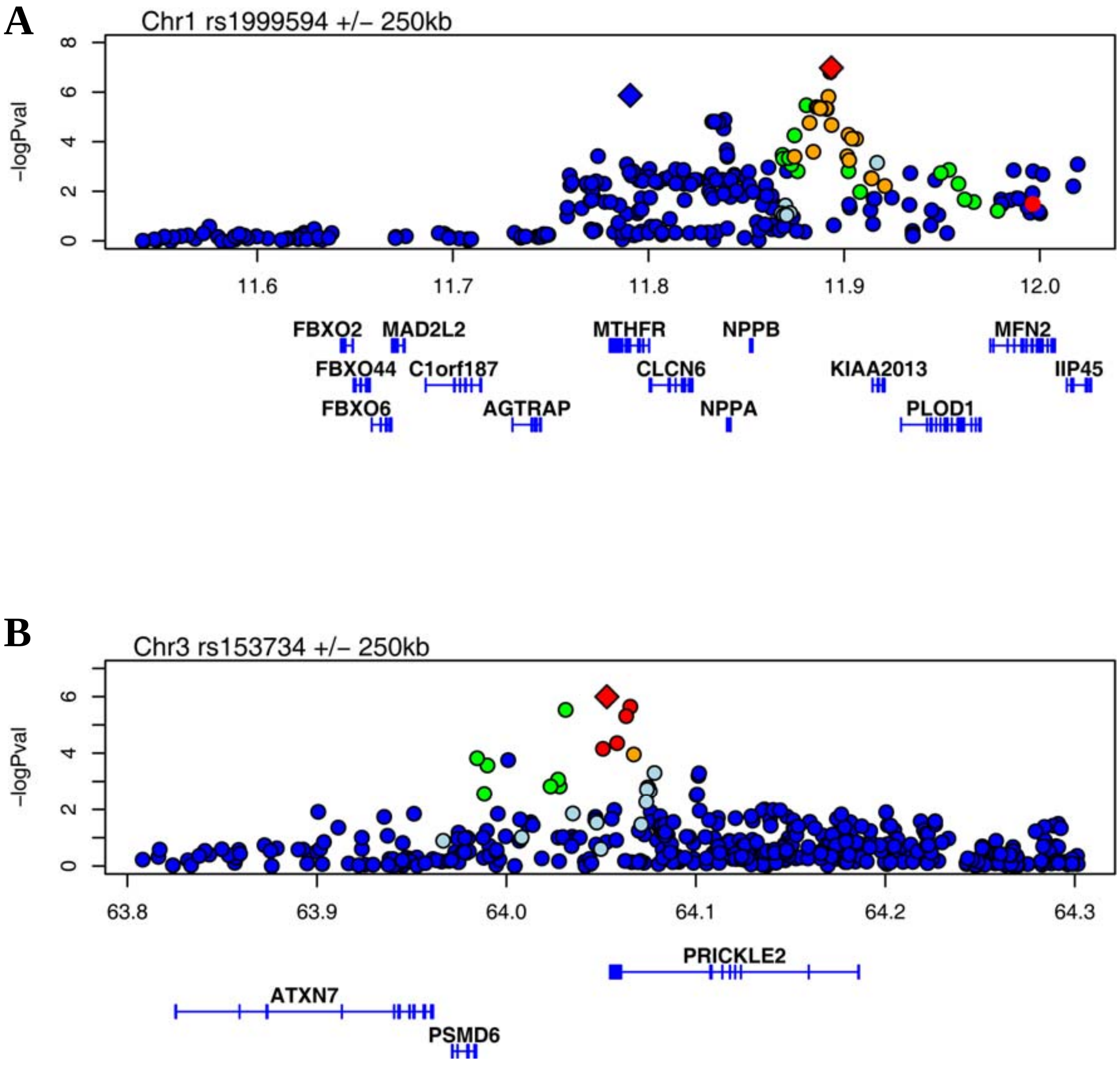

Table S1. Association of Candidate Gene polymorphisms with blood B-vitamins and Homocysteine.

Trait	Chr	Position (bp)	Gene	Total # SNPs	Top SNP	Alleles (+/-)	Frequency (+)^{1}	Effect (SE)^{2}	P value
Vitamin-B6	1	11,785,193	MTHFR	29	rs2274976	G/A	0.98	-0.28(0.14)	0.0449
(N=1178)	1	233,384,869	MTR	124	rs10737812	C/T	0.53	0.05(0.04)	0.2009
	5	7,938,959	MTRR	37	rs162036	A/G	0.87	0.11(0.06)	0.0435
	5	78,452,172	BHMT	16	rs567754	C/T	0.65	-0.05(0.04)	0.1623
	5	79,980,896	DHFR	26	rs10072026	T/C	0.90	0.08(0.06)	0.2273
	7	94,582,097	PON1	36	rs662	A/G	0.71	0.05(0.04)	0.2426
	11	49,151,666	FOLH1	35	rs202718	C/T	0.88	0.07(0.06)	0.2020
	14	63,940,963	MTHFD1	33	rs8011839	C/T	0.83	0.06(0.05)	0.2782
	21	43,360,522	CBS	22	rs234712	G/A	0.91	-0.12(0.07)	0.0702
	22	29,328,115	TCN2	31	rs16988828	A/G	0.88	-0.09(0.06)	0.1098
Vitamin-B12	1	11,796,429	MTHFR	29	rs17037397	A/C	0.02	0.11(0.13)	0.0185
(N=2927)	1	233,338,585	MTR	124	rs7541539	A/C	0.03	-0.10(0.11)	0.0832
	5	7,952,909	MTRR	37	rs10520874	C/G	0.09	-0.08(0.05)	0.0680
	5	78,444,816	BHMT	16	rs651852	T/C	0.45	0.06(0.03)	0.0388
	5	79,974,578	DHFR	26	rs12189317	T/C	0.12	0.04(0.05)	0.1930
	7	94,593,277	PON1	36	rs2272365	A/C	0.77	0.06(0.04)	0.1374
	11	49,127,350	FOLH1	35	rs16906158	T/C	0.92	-0.10(0.06)	0.4222
	14	63,976,018	MTHFD1	33	rs17101854	A/G	0.03	-0.10(0.09)	0.1005
	21	43,361,464	CBS	22	rs234715	T/G	0.20	0.03(0.04)	0.2817
	22	29,335,623	TCN2	31	rs757874	T/G	0.24	-0.07(0.04)	0.0403
Folate	1	11,790,644	MTHFR	29	rs1801133	A/G	0.02	-0.14(0.03)	$1.36\text{x}10^{-6}$
(N=2932)	1	233,310,590	MTR	124	rs10925240	T/C	0.03	0.04(0.03)	0.1590
	5	7,940,456	MTRR	37	rs162039	T/C	0.09	-0.07(0.04)	0.1114
	5	78,444,816	BHMT	16	rs651852	T/C	0.45	0.08(0.03)	0.0030
	5	79,980,896	DHFR	26	rs10072026	T/C	0.12	-0.05(0.04)	0.2368
	7	94,597,343	PON1	36	rs854570	A/C	0.77	-0.06(0.03)	0.0312
	11	49,173,275	FOLH1	35	rs202700	T/C	0.92	0.11(0.03)	0.0008
	14	63,953,859	MTHFD1	33	rs17751556	T/C	0.03	0.10(0.06)	0.0691
	21	43,348,783	CBS	22	rs2124459	T/C	0.20	0.08(0.03)	0.0034
	22	29,335,110	TCN2	31	rs5997703	C/G	0.24	0.03(0.03)	0.2348
Homocysteine	1	11,790,644	MTHFR	29	rs1801133	A/G	0.02	0.24(0.03)	$4.36\text{x}10^{-13}$
(N=2965)	1	233,314,404	MTR	124	rs12060264	A/G	0.03	0.10(0.03)	0.0005
	5	7,932,950	MTRR	37	rs7703033	A/G	0.09	0.09(0.03)	0.0048
	5	78,455,565	BHMT	16	rs6860725	T/C	0.45	0.03(0.03)	0.1358
	5	79,975,227	DHFR	26	rs11951910	T/C	0.12	0.03(0.04)	0.0809
	7	94,572,359	PON1	36	rs3917577	T/C	0.77	0.11(0.04)	0.0266
	11	49,148,927	FOLH1	35	rs202720	C/G	0.92	0.05(0.04)	0.0827
	14	63,953,859	MTHFD1	33	rs17751556	T/C	0.03	-0.13(0.06)	0.0377
	21	43,351,566	CBS	22	rs6586282	T/C	0.20	-0.16(0.04)	0.0002
	22	29,331,414	TCN2	31	rs9606756	A/G	0.24	-0.07(0.05)	0.2210

[1] Allele frequencies are the average from the three GWAS studies for vitamin-B12, folate and homocysteine analyses and from the InCHIANTI study for vitamin-B6

[2] Units of effect size are in standard deviation of the transformed phenotype