

SUPPLEMENTAL MATERIAL

Genome-wide association study of homocysteine levels in Filipinos provides evidence for *CPS1* in women and a stronger *MTHFR* effect in young adults

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Supplemental Table 1: Descriptive characteristics of n=1,786 CLHNS mothers

	Mean (range) or %	Standard deviation or N
Homocysteine (mmol/L)	11.4 (5 – 36)	3.0
Age (years)	48.5 (35 – 69)	6.1
Number of previous pregnancies		
1 – 4	27.9%	499
5 – 10	60.9%	1,087
11+	11.2%	200
Post-menopausal	38%	685
Body mass index (kg/m ²)	24.3 (12 – 42)	4.4
Affected with diabetes	5%	89
Folate intake (µg/day)	312.6 (4.2 – 1,405.7)	165.0
Vitamin B ₆ intake (mg/day)	0.99 (0.07 – 4.77)	0.53
Vitamin B ₁₂ intake (µg/day)	4.44 (0.03 – 42.78)	0.11

Supplemental Table 2: Descriptive characteristics of n=1,679 offspring

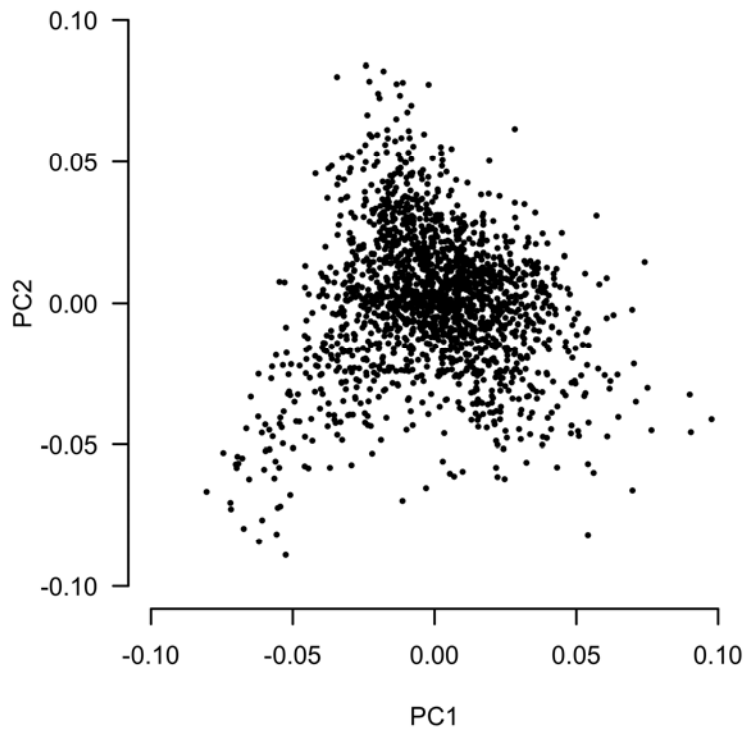
	Mean (range) or %	Standard deviation or N
Age	21.5 (20.8 – 22.3)	0.3
Males	54.8%	920
Homocysteine	14.4 (6 – 66)	5.6
Body mass index	21.1 (14 – 40)	3.1
Folate intake (µg/day)	577.8 (11.6 – 1845.9)	285.8
Vitamin B ₆ intake (mg/day)	1.95 (0.16 – 9.83)	1.00
Vitamin B ₁₂ intake (µg/day)	8.40 (0.05 – 107.44)	7.38
Females	44.2%	759
Homocysteine	10.7 (6 – 48)	3.0
Body mass index	20.4 (14 – 41)	3.3
Folate intake (µg/day)	362.5 (5.8 – 2178.1)	206.3
Vitamin B ₆ intake (mg/day)	1.52 (0.06 – 6.38)	0.84
Vitamin B ₁₂ intake (µg/day)	6.16 (0.19 – 55.61)	5.54

Supplemental Table 3: Association results for CPS1 SNP rs7422339 with cardiovascular disease risk factors

	Mean (SD)			<i>P</i>
	CC	CA	AA	
Total cholesterol	184.9 (40.6)	189.0 (36.5)	190.8 (43.5)	0.0094
High-density lipoprotein cholesterol	41.1 (10.4)	40.8 (10.4)	39.6 (11.0)	0.56
Low-density lipoprotein cholesterol	117.5 (34.3)	122.1 (32.6)	125.1 (35.9)	0.0010
Triglycerides	132.1 (97.2)	129.8 (67.6)	126.0 (57.1)	0.48
C-reactive protein	2.7 (6.1)	2.4 (5.1)	2.7 (8.2)	0.29
Fasting glucose	116.7 (34.8)	119.1 (40.5)	112.6 (20.5)	0.89
Body mass index	24.3 (4.4)	24.3 (4.4)	24.3 (4.3)	0.84

Supplemental Table 4: Association of log-Hcy and covariates considered, including 10 principal components from EIGENSOFT analysis of population structure

Covariate	<i>P</i>
Age	3.7×10^{-18}
Number of previous pregnancies	0.0059
Menopause status	1.0×10^{-21}
Principal components	
1	0.89
2	0.0007
3	0.0055
4	0.96
5	0.21
6	0.98
7	0.45
8	0.058
9	0.86
10	0.23



Supplemental Figure 1: Limited extent of genetic heterogeneity in CLHNS mothers.

Plot of first two principal components measuring extent of genetic heterogeneity. Principle components are based on 1,571 CHLNS subjects with estimated cumulative pair-wise identity-by-descent < 0.1 using 13,972 independent SNPs (estimated $r^2 < 0.005$ between all pairs of SNPs within 1 Mb) with observed MAF > 0.05 .