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SUPPLEMENTAL METHODS

Genotyping Quality Control and Data Preparation for the Genome-Wide Association Study (GWAS)

In a preliminary analysis for sample-level quality control, 10 subjects were excluded, based on gender discrepancy between self-report and genotypes (n = 7) and abnormal sex chromosomes (n = 3; one XYY male and two XX/XO mosaic females). Sixteen subjects with incomplete anthropometric data were removed. Siblings from 77 families reported entry into the study. These included two siblings from 74 families and three siblings from three families. Pair-wise tests for relatedness and population stratification within all the genotyped samples were performed using PLINK v2 (1) and a set of 25718 single nucleotide polymorphisms (SNPs). All selected SNPs had pair-wise intermarker linkage disequilibrium (LD) $r^2 < 0.04$ for both short and long-range blocks of SNPs, minor allele frequency > 0.1 and genotype call rates > 0.99. These analyses identified additional pairs of individuals that appeared closely related to the level of first cousins. In order to reduce effects of relatedness, only one individual from each family was retained. In total, 175 individuals were removed due to relatedness. Finally, principal components analysis was performed using the EIGENSOFT v3.0 software (2) and this same low-LD subset of 25718 SNPs. Based on these analyses, two samples were detected as ethnic outliers (six standard deviations away from the mean) and were dropped. The full data preparation process resulted in a final dataset of 2232 study samples in the GWAS association analysis.

Quality control assessment was performed on 1008829 SNPs. SNPs were excluded in two stages:

In stage one, SNPs were dropped that had less than 95% call rates and then samples with less than 97% call rates (n = 57) or that showed cryptic relatedness were dropped.

In stage two, SNPs were dropped that had (a) less than 98% call rates; (b) greater than one Mendelian error using HapMap trios (n = 583); (c) greater than one discordant genotype using both HapMap controls (n = 880), and (d) discordant genotypes from two or more pairs among the 14 study duplicates (n = 1765) allowing for one error. SNPs with extreme deviation from Hardy-Weinberg equilibrium ($P < 1 \times 10^{-4}$) were flagged for future reference and remained in the analysis (*n* = 3512). We also measured LD in our dataset and examined LD plots using the HaploView program (3). The data were checked for batch effects using several methods and no significant batch effects were detected. These methods included a) descriptive statistics per batch (average minor allele frequency, average genotyping call rate across all SNPs for each plate) and b) association test results comparing each batch to the others (average *P* value, number of significant results at a particular threshold). The final dataset contained 757337 genotyped SNPs (3512 of these SNPs had $P < 1 \times 10^{-4}$ for a test of Hardy-Weinberg equilibrium) for 2232 samples after quality control testing and after excluding monomorphic and low minor allele frequency SNPs (minor allele frequency < 0.01). Genotype and phenotype data will be deposited in dbGAP.

GWAS Statistical Analysis

Results for plasma pyridoxal 5'-phosphate (PLP), pyridoxal (PL), and 4-pyridoxic acid (PA) were available for 2158 of the 2232 subjects who had vitamin B-6 intake from fortified foods/supplements < 11 mg/day in the last week and who also had DNA samples that passed the genotype quality control, so the discovery analysis for plasma PLP, PL, and PA relates to these 2158 individuals and 757337 SNPs. The distribution of the plasma PLP, PL, and PA concentrations in the study participants deviated significantly from a normal distribution and a $\log_{10}$ transformation was used to approximately normalize the PLP, PL, and PA values for the linear regression analyses. Standard descriptive statistics were performed on the observed plasma PLP, PL, and PA concentrations both before and after $\log_{10}$ transformation. For the GWAS analysis, genotyped and imputed autosomal SNPs that passed quality control were tested for association with both untransformed and $\log_{10}$ transformed plasma PLP, PL, and PA concentrations, adjusted for age and sex. Sixty-six subjects whose vitamin B-6 intake from fortified foods/supplements was > 11 mg/day in the last week had been removed from the GWAS analysis, and the amount of vitamin B-6 intake from fortified foods/supplements in the last week for the remaining 2158 subjects was also included as a covariate in the analyses of PLP, PL and PA. The genomic control lambda was calculated for the untransformed and $\log_{10}$ transformed versions of plasma PLP, PL and PA concentrations (**Supplemental Table 4**). In the simple linear regression model, the association test for each marker was performed assuming an additive genetic model (i.e., number of minor alleles, 0, 1, and 2) using PLINK v2. SNPs reaching genome-wide statistical significance ($P < 5.0 \times 10^{-8}$) are presented in **Table 3** of the paper for the analysis of $\log_{10}$ transformed PLP. No SNP reached genome-wide statistical significance for the analysis of $\log_{10}$ transformed PL or PA. Manhattan plots and quantile-quantile (Q-Q) plots for PLP (**Supplemental Figures 4-7**) and for PL and PA (**Supplemental Figures 9 and 10**) were generated using R scripts. To further evaluate the distribution of *P* values obtained in the analysis of plasma PLP, Q-Q plots without chromosome 1 (this chromosome had the most statistically significant SNPs for plasma PLP) were also generated to remove the effect on the plots of these extremely significant SNPs (Supplemental Figures 4-7).

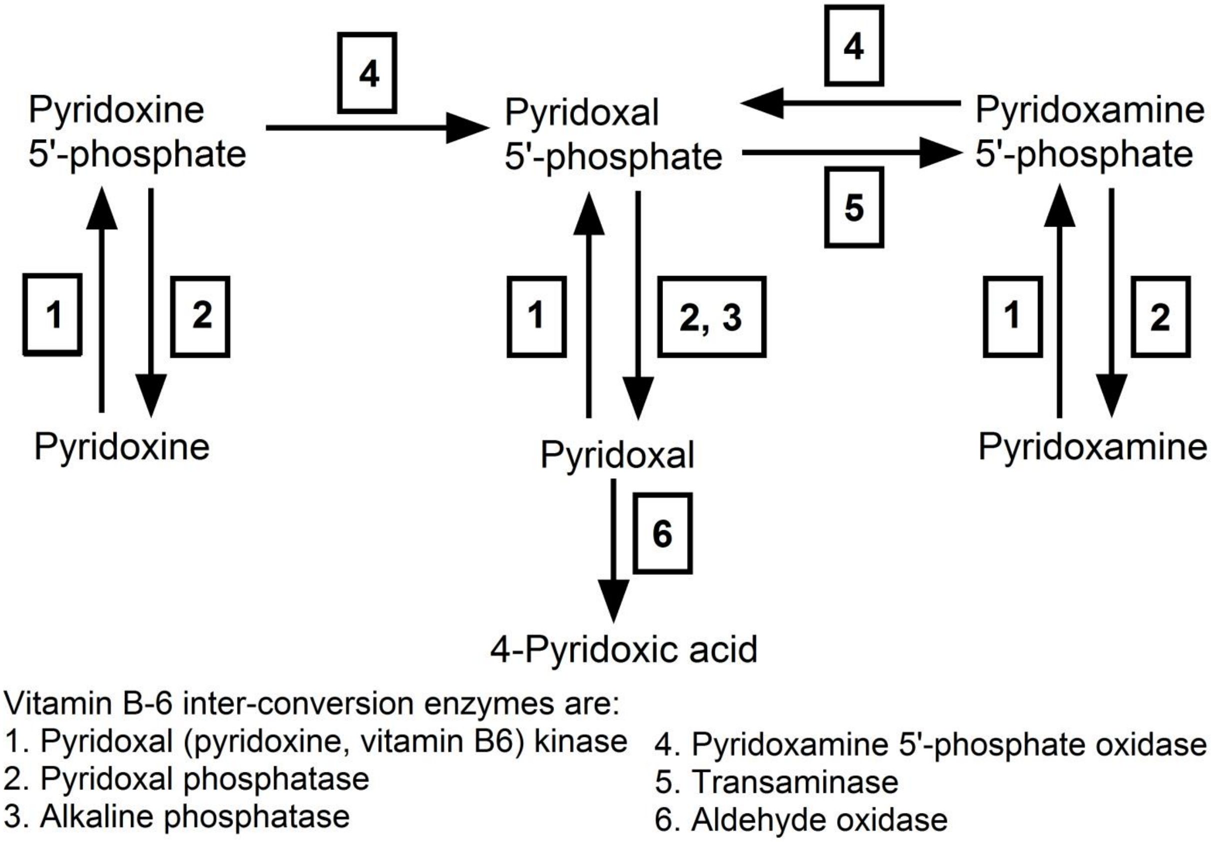
References

1. Purcell S, Neale B, Todd-Brown K, Thomas L, Ferreira MA, Bender D, Maller J, Sklar P, de Bakker PI, Daly MJ, et al. PLINK: a tool set for whole-genome association and population-based linkage analyses. Am J Hum Genet 2007;81:559-75.

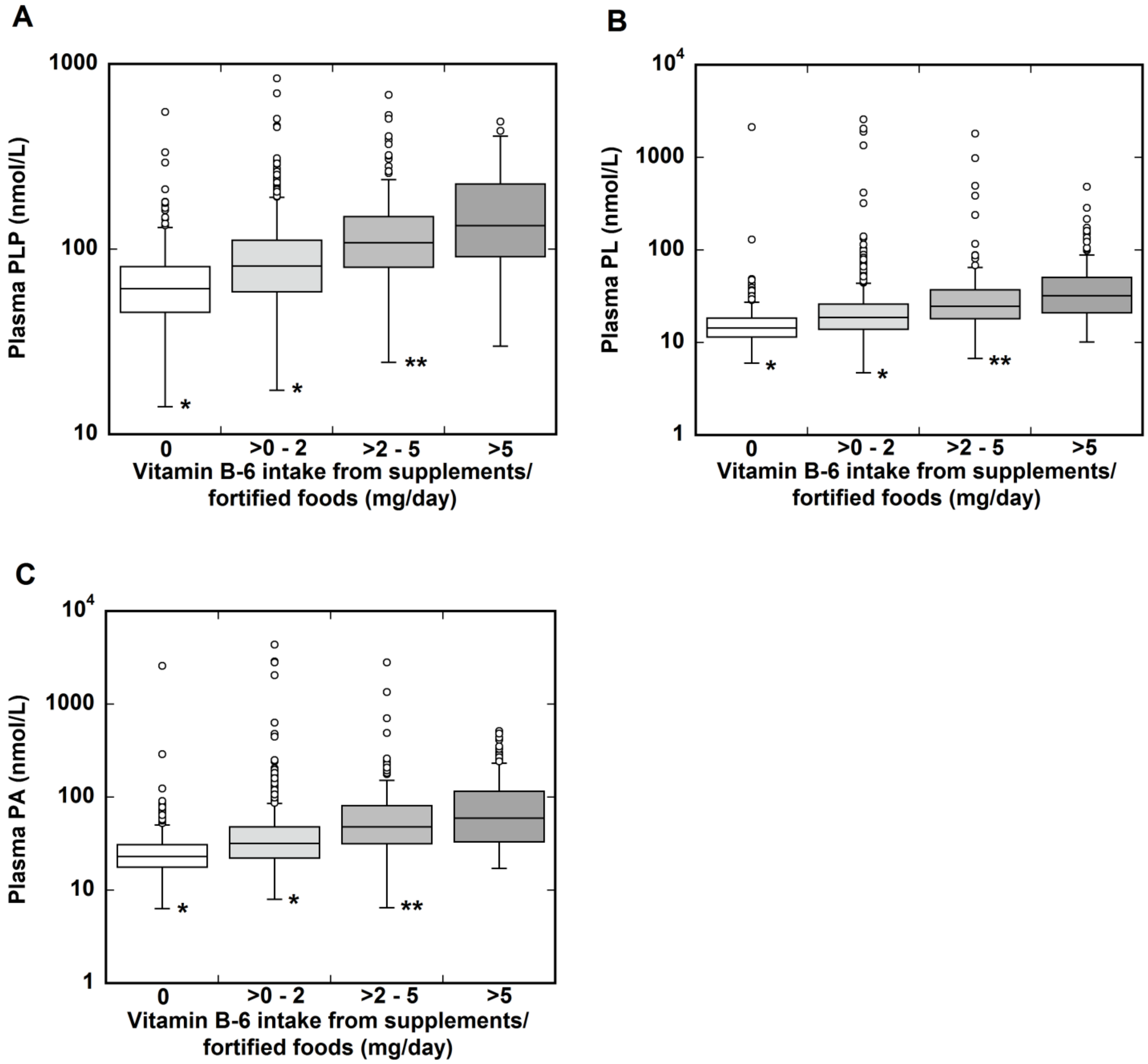
2. Kang HM, Sul JH, Service SK, Zaitlen NA, Kong SY, Friemer NB, Sabatti C, Eskin E. Variance component model to account for sample structure in genome-wide association studies. Nat Genet 2010;42:348-54.

3. Barrett JC, Fry B, Maller J, Daly MJ. Haploview: analysis and visualization of LD and haplotype maps. Bioinformatics 2005;21:263-5.

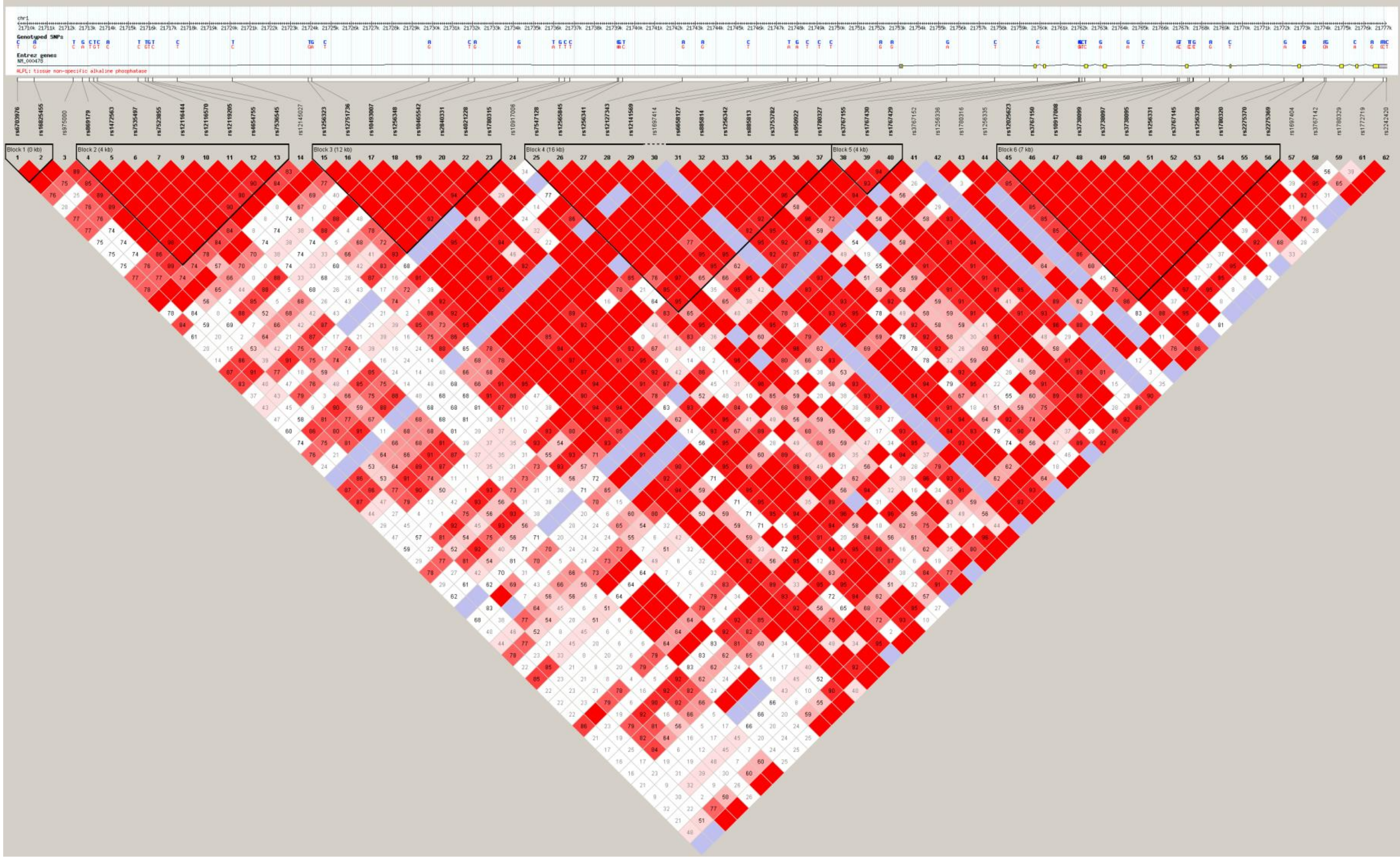
ONLINE SUPPORTING MATERIAL



SUPPLEMENTAL FIGURE 1 Vitamin B-6 metabolism.



SUPPLEMENTAL FIGURE 2 Plasma B-6 vitamer concentrations in healthy Irish adults according to category of vitamin B-6 intake from fortified foods/ supplements. Concentrations of (A) PLP, (B) PL, and (C) PA in plasma are presented for all subjects (*n* = 2345) according to four categories of the amount of vitamin B-6 intake from fortified foods/supplements. The number of subjects in the 0, >0 – 2, >2 – 5, and >5 mg/day categories of intake were 337, 1667, 224, and 117, respectively. Wilcoxon rank sum test was used to compare plasma B-6 vitamer concentrations between pairs of vitamin B-6 intake categories. *$P < 0.0001$ for all comparisons between the indicated category and each higher vitamin B-6 intake category. **$P < 0.05$ for all comparisons between the indicated category and each higher vitamin B-6 intake category. PLP, pyridoxal 5’-phosphate; PL, pyridoxal; PA, 4-pyridoxic acid.



SUPPLEMENTAL FIGURE 3 Low-resolution diagram of linkage disequilibrium (*D'*) across the *ALPL* gene – based on data for the HapMap CEU population. *ALPL*, tissue non-specific alkaline phosphatase; CEU, sample of Utah residents with Northern and Western European ancestry in the HapMap project.

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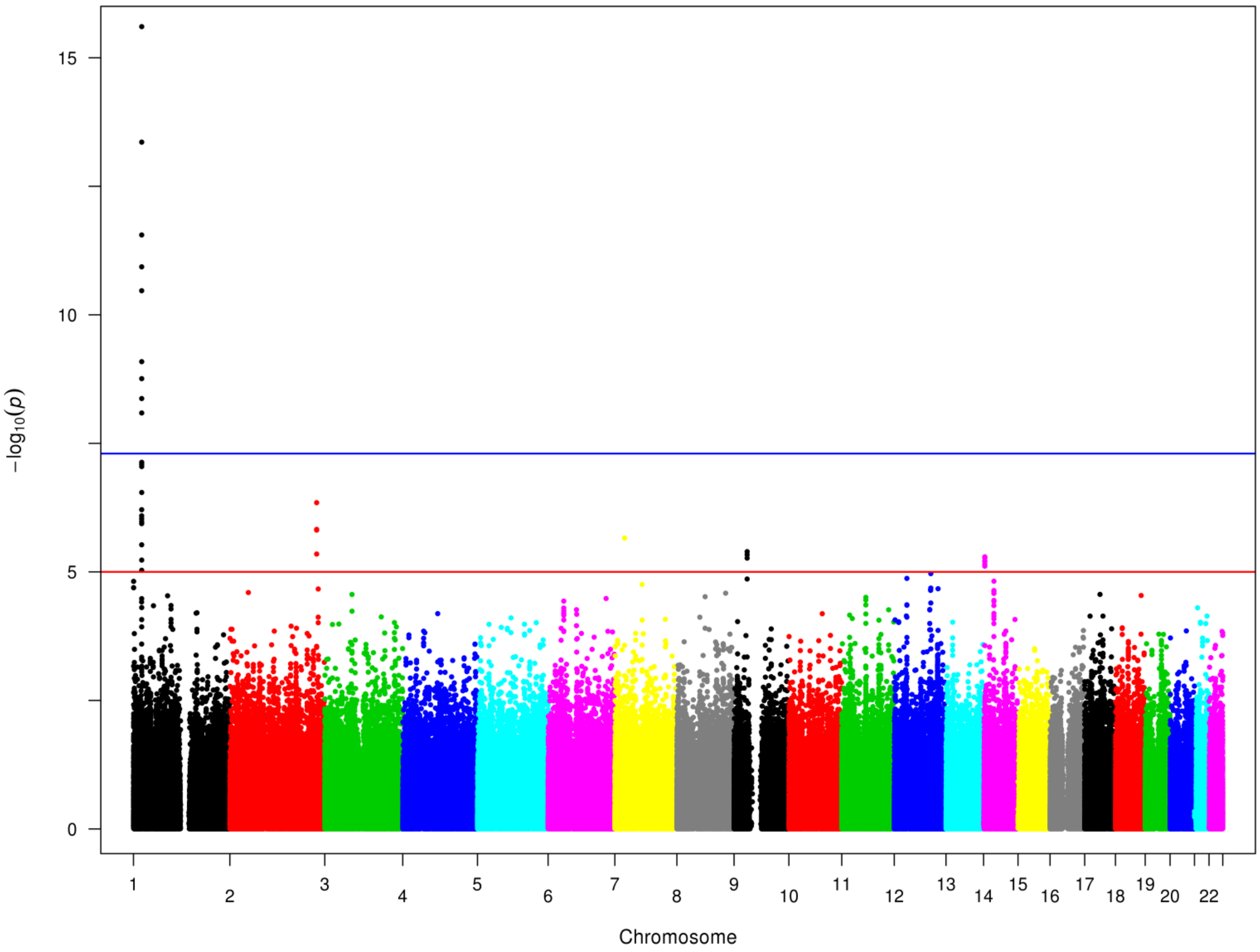

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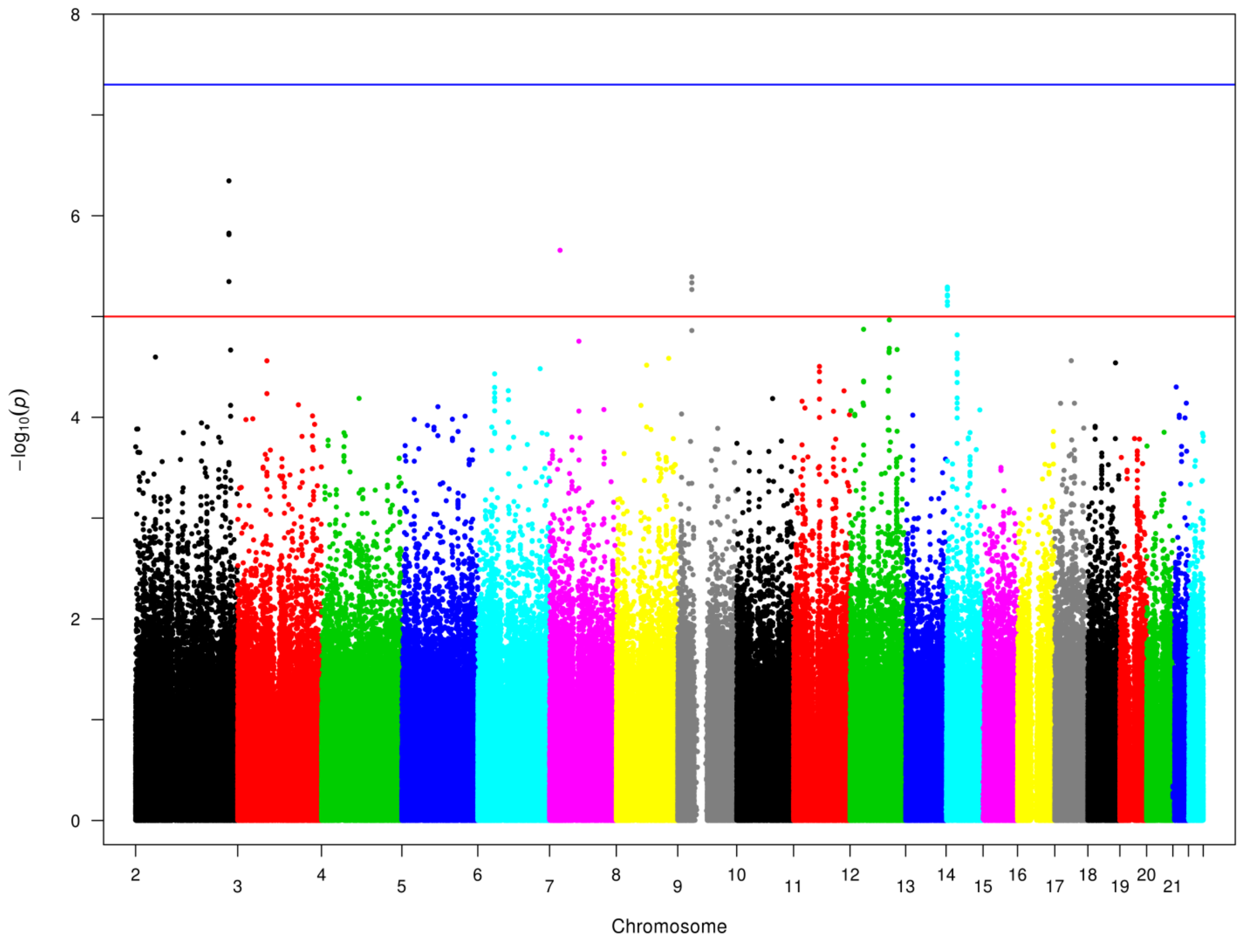

SUPPLEMENTAL FIGURE 4 (A) Manhattan plot of association results of $\log_{10}$ transformed plasma pyridoxal 5'-phosphate concentration adjustment for age, sex and vitamin B-6 intake from fortified foods/supplements, using genotype data on 757337 polymorphisms in healthy Irish adults. (B) Same plot excluding chromosome 1. The two horizontal lines in the plots represent thresholds for suggestive significance ($P = 1 \times 10^{-5}$; red line) and genome-wide significance ($P = 5 \times 10^{-8}$; blue line).

ONLINE SUPPORTING MATERIAL

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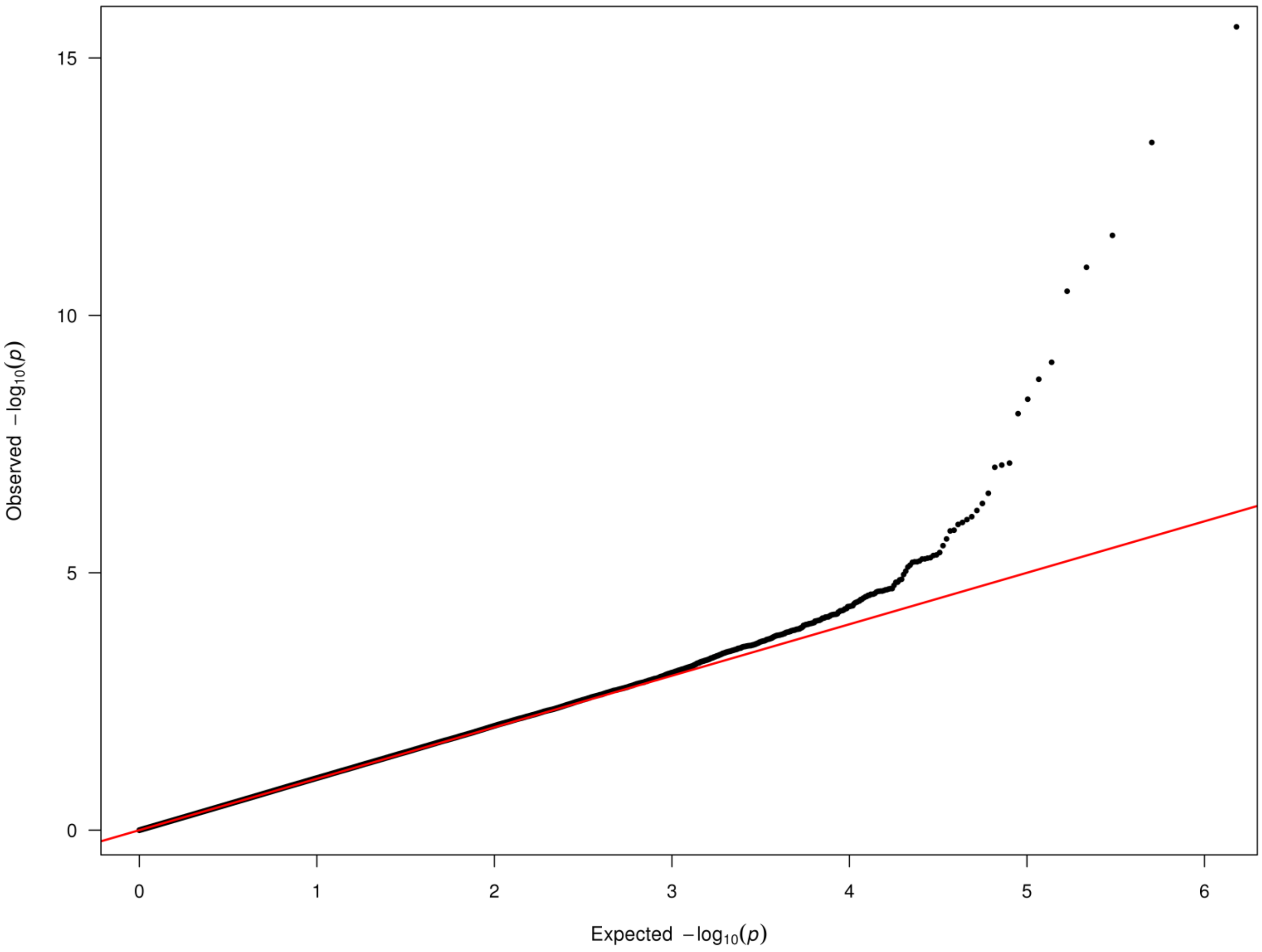

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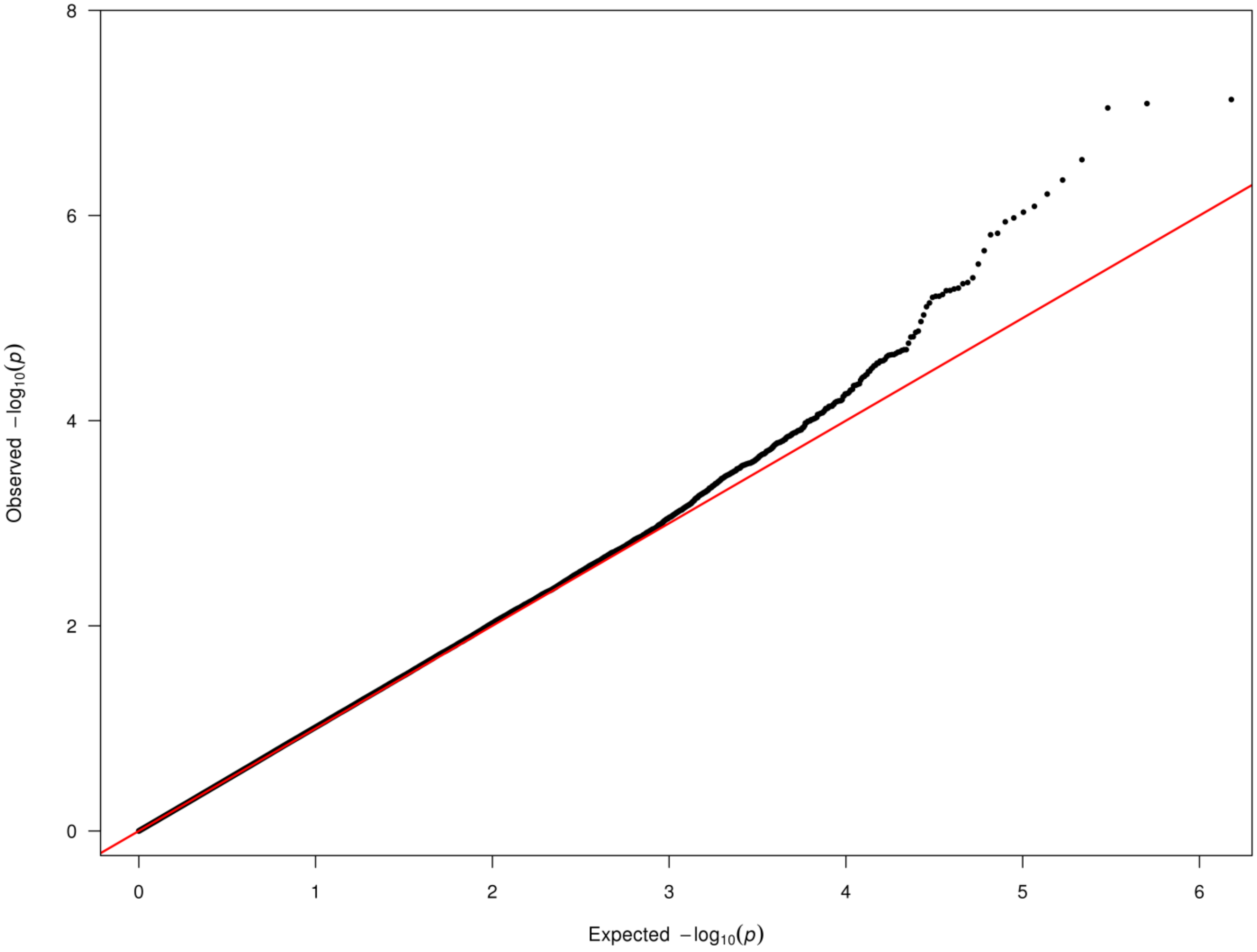

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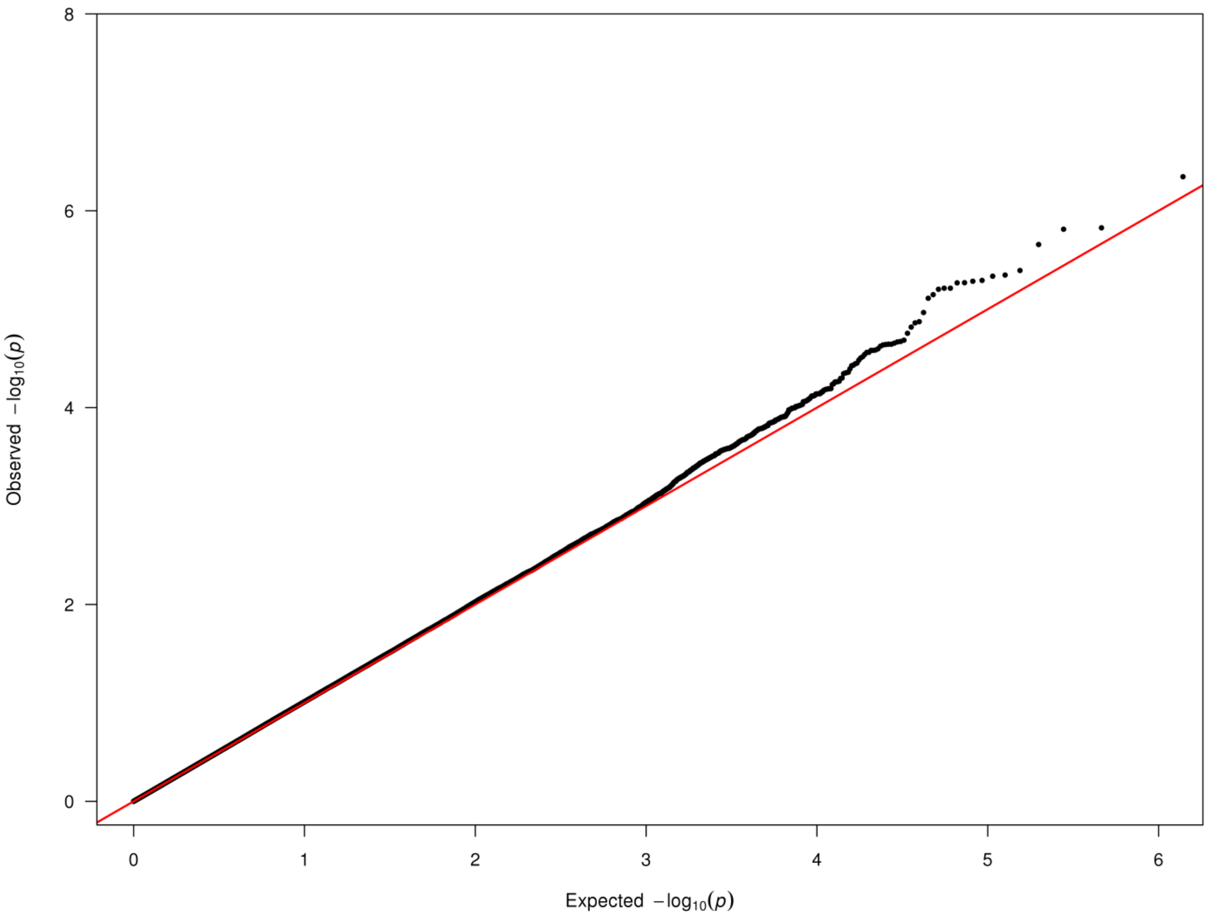

SUPPLEMENTAL FIGURE 5 Quantile-quantile plots of $\log_{10}$ transformed plasma pyridoxal 5’-phosphate concentration with adjustment for age, sex and vitamin B-6 intake from fortified foods/supplements, using genotype data on 757337 polymorphisms in healthy Irish adults (A) after quality control testing and (B) truncated at $-\log_{10}(P) = 8$. (C) Same plot as in A but excluding chromosome 1.

ONLINE SUPPORTING MATERIAL

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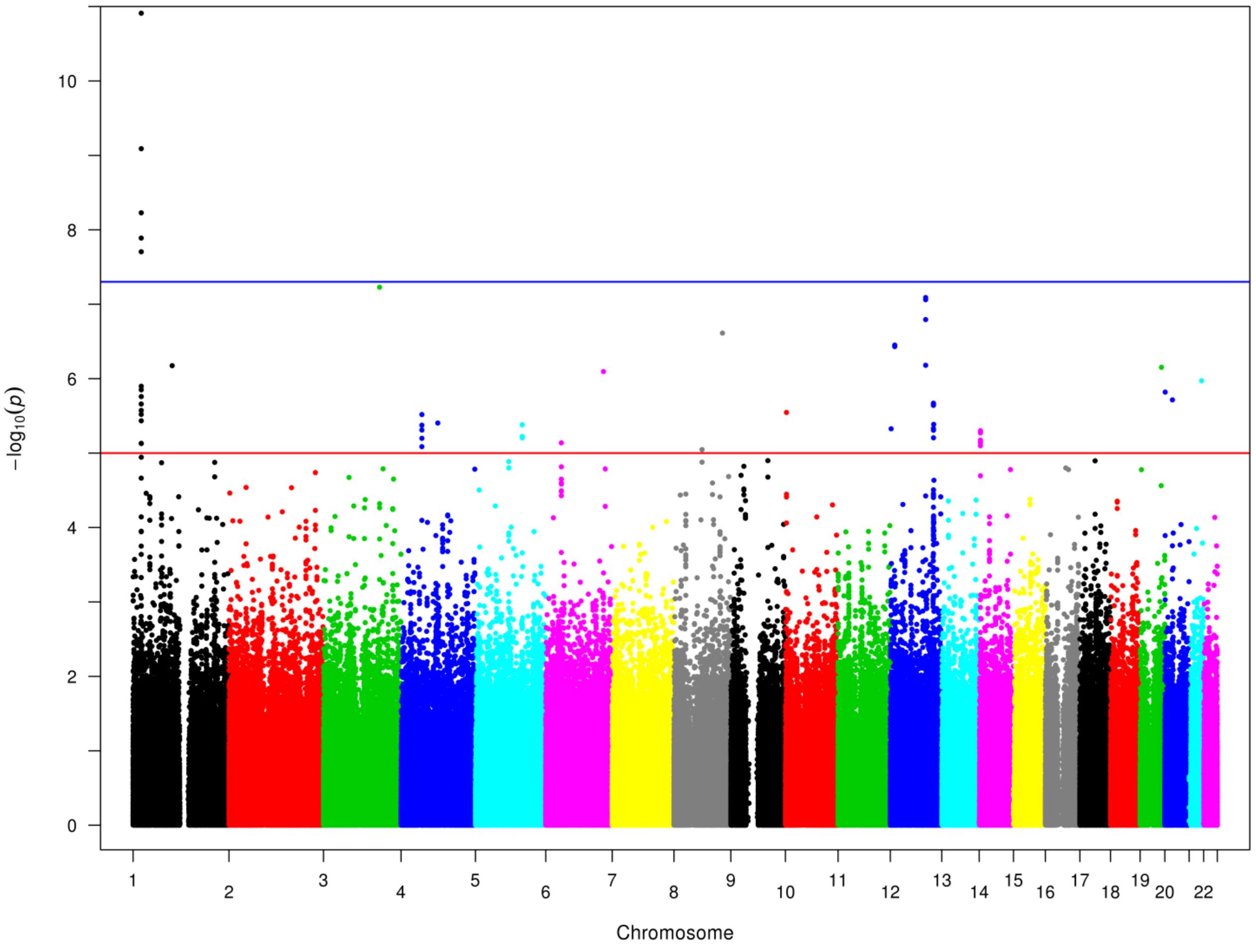

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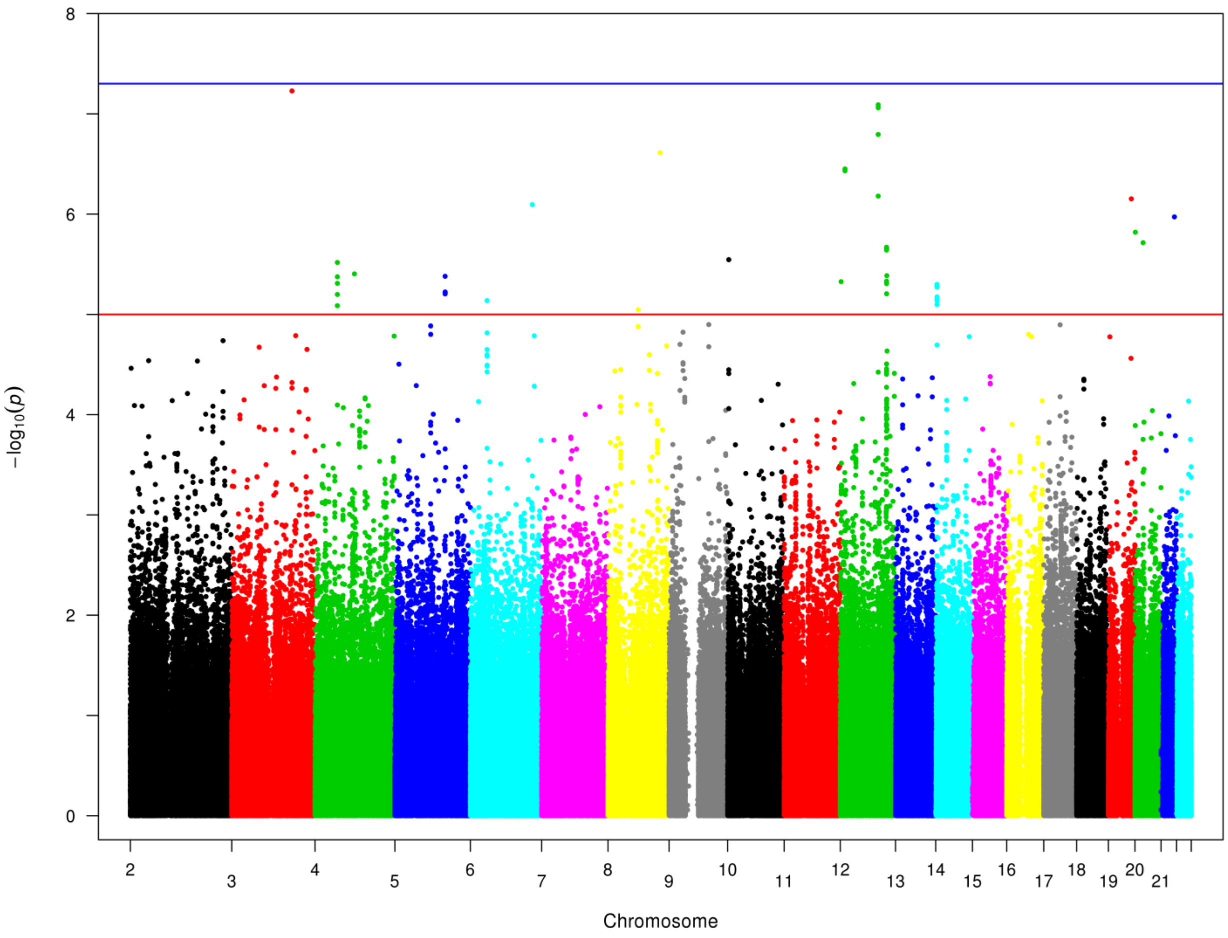

SUPPLEMENTAL FIGURE 6 (A) Manhattan plot of association results of untransformed plasma pyridoxal 5’-phosphate concentration with adjustment for age, sex and vitamin B-6 intake from fortified foods/supplements, using genotype data on 757337 polymorphisms in healthy Irish adults. (B) Same plot excluding chromosome 1. The two horizontal lines in the plots represent thresholds for suggestive significance ($P = 1 \times 10^{-5}$; red line) and genome-wide significance ($P = 5 \times 10^{-8}$; blue line).

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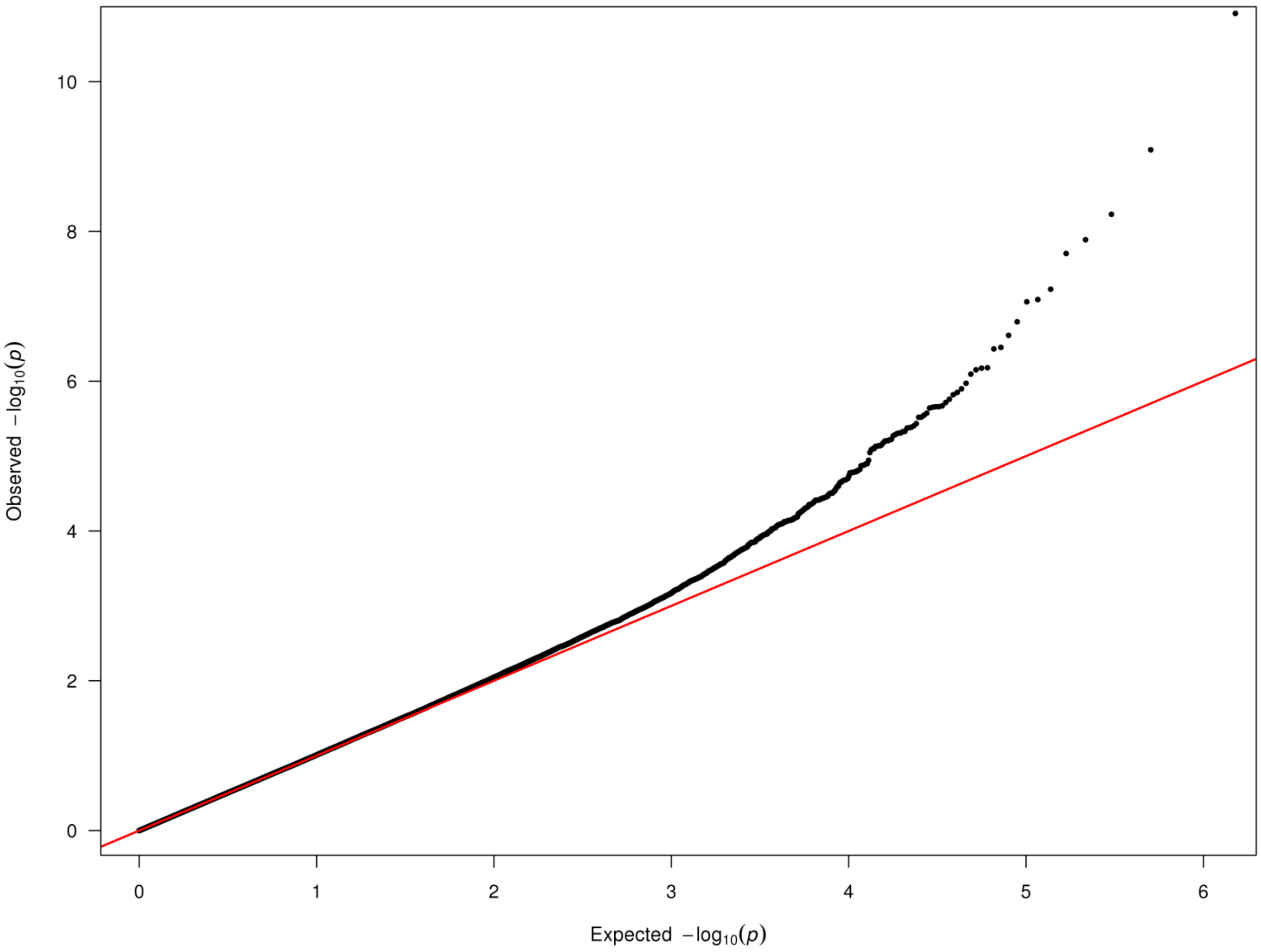
A



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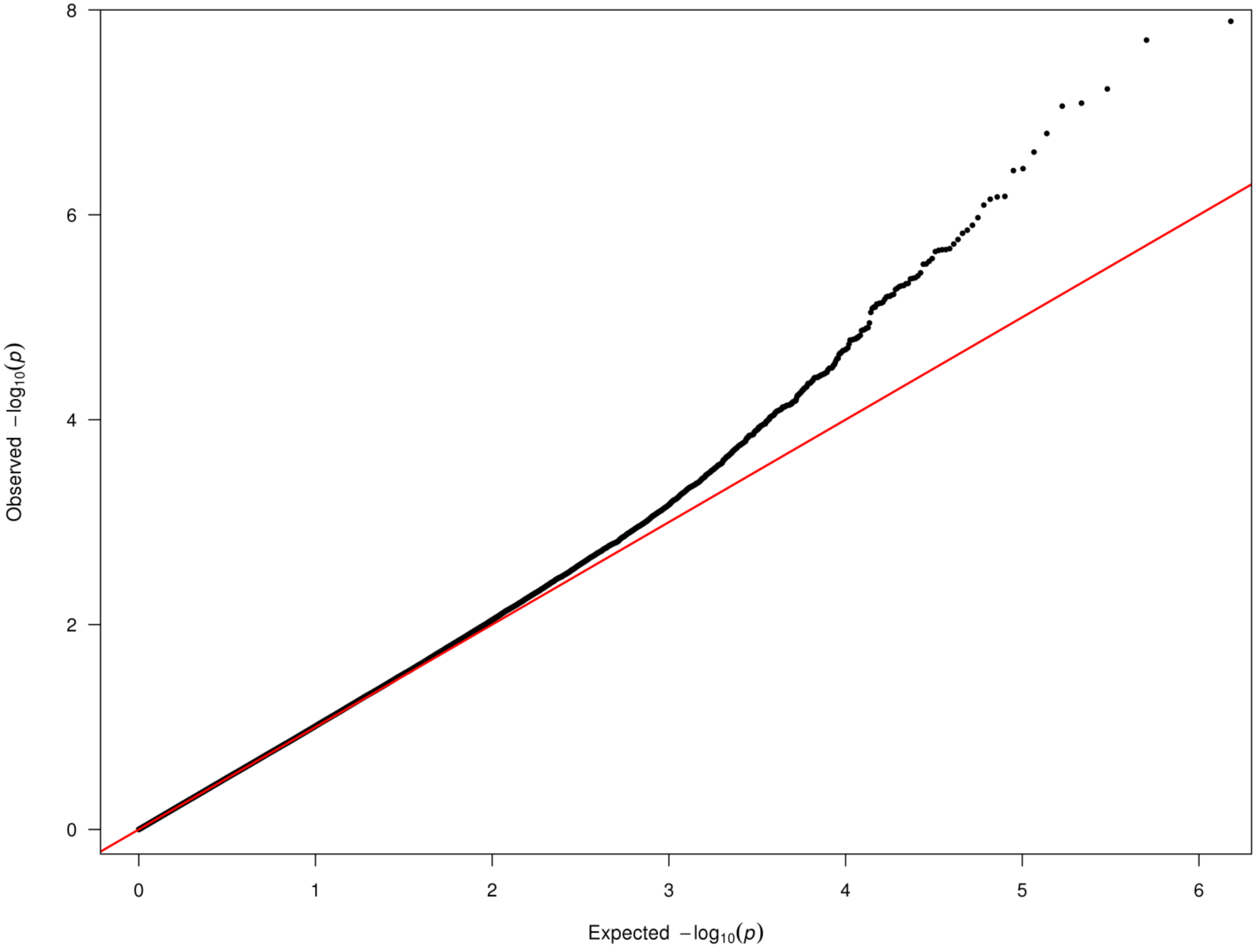

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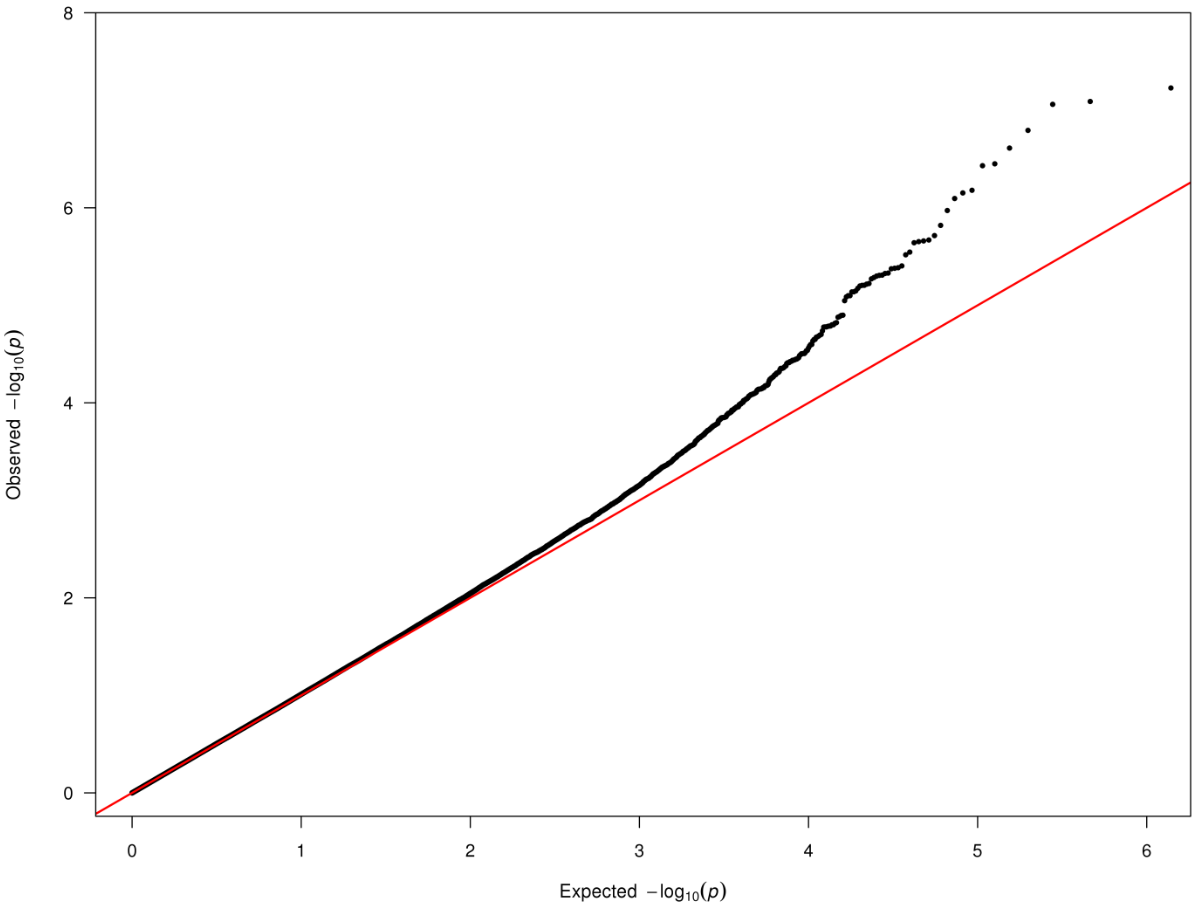
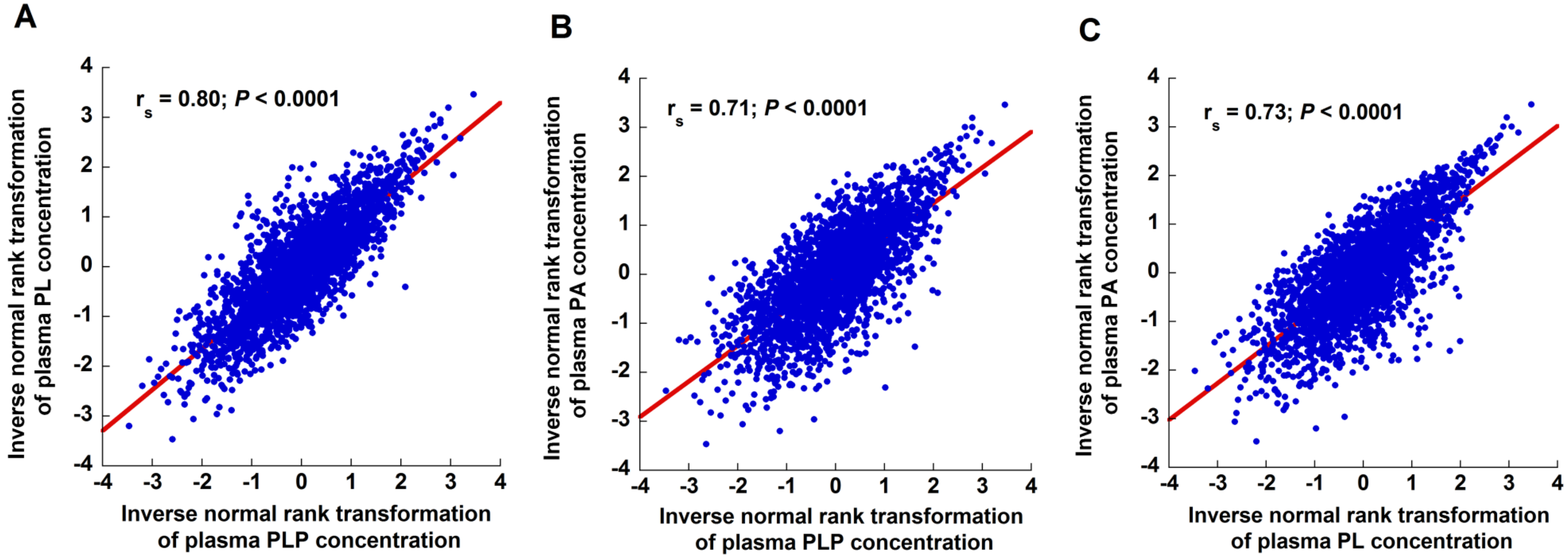


SUPPLEMENTAL FIGURE 7 Quantile-quantile plots of untransformed plasma pyridoxal 5'-phosphate concentration with adjustment for age, sex and vitamin B-6 intake from fortified foods/supplements, using genotype data on 757337 polymorphisms in healthy Irish adults (A) after quality control testing and (B) truncated at $-\log_{10}(P) = 8$. (C) Same plot as in A but excluding chromosome 1.



SUPPLEMENTAL FIGURE 8 Correlations between plasma PLP, PL, and PA concentrations in healthy Irish adults, represented by scatter plots with a linear regression line. Spearman rank correlation coefficients (r_s) were calculated for the associations between (A) plasma PLP and PL concentrations, (B) plasma PLP and PA concentrations, and (C) plasma PL and PA concentrations. Before testing for correlation, an inverse normal rank transformation of plasma PLP, PL, and PA concentrations was performed to generate normally distributed data. PLP, pyridoxal 5’-phosphate; PL, pyridoxal; PA, 4-pyridoxic acid.

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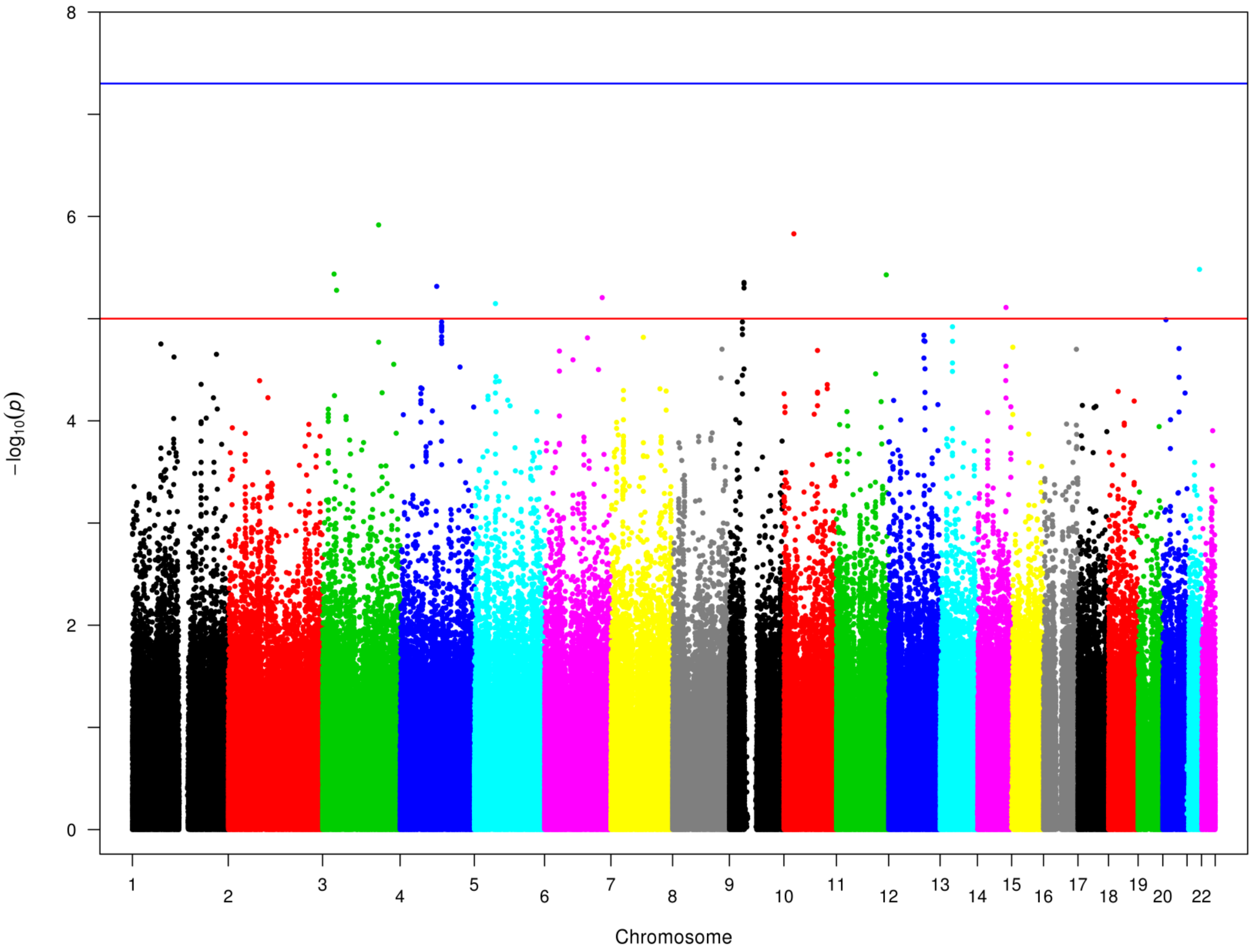

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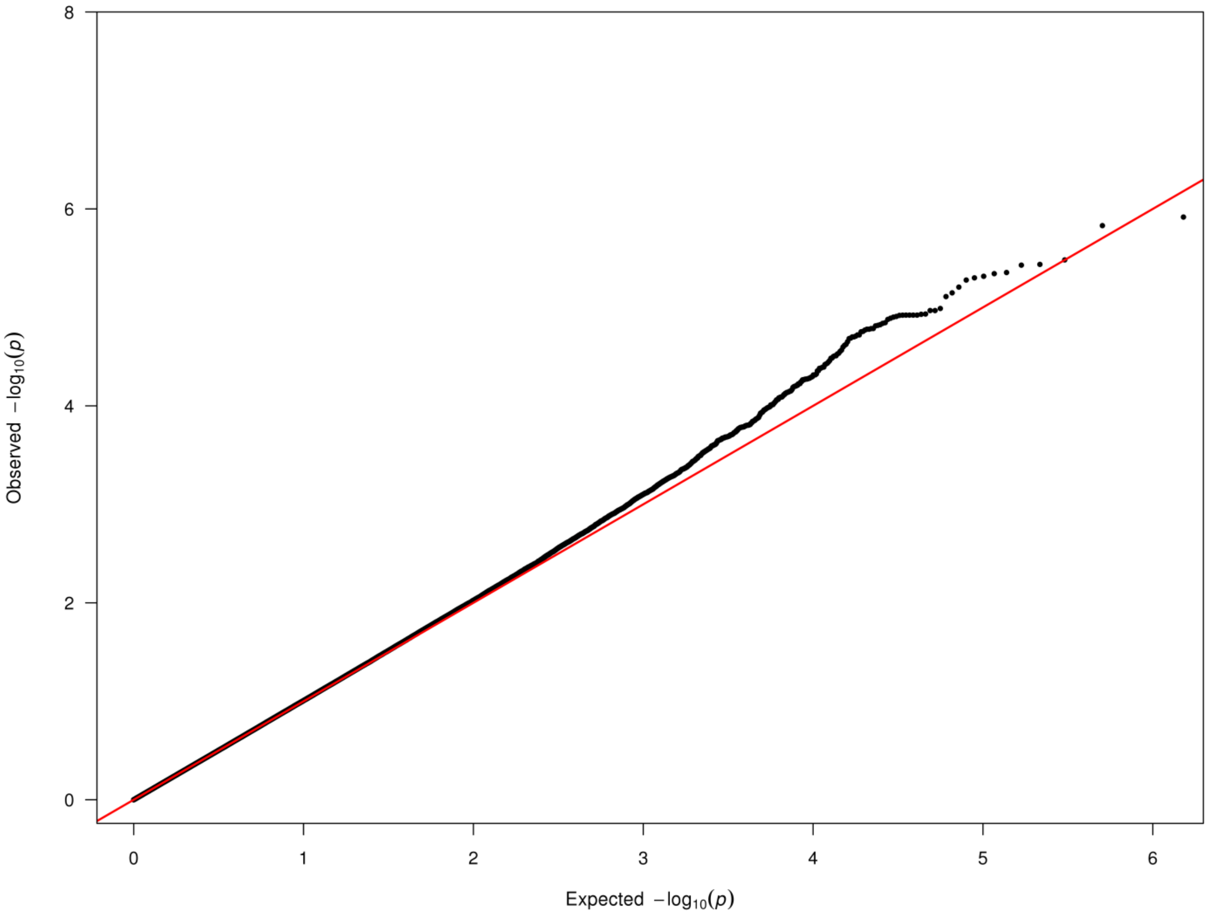

SUPPLEMENTAL FIGURE 9 (A) Manhattan plot and (B) quantile-quantile plot of $\log_{10}$ transformed plasma pyridoxal concentration with adjustment for age, sex and vitamin B-6 intake from fortified foods/supplements, using genotype data on 757337 polymorphisms in healthy Irish adults. In the Manhattan plot, the two horizontal lines represent thresholds for suggestive significance ($P = 1 \times 10^{-5}$; red line) and genome-wide significance ($P = 5 \times 10^{-8}$; blue line).

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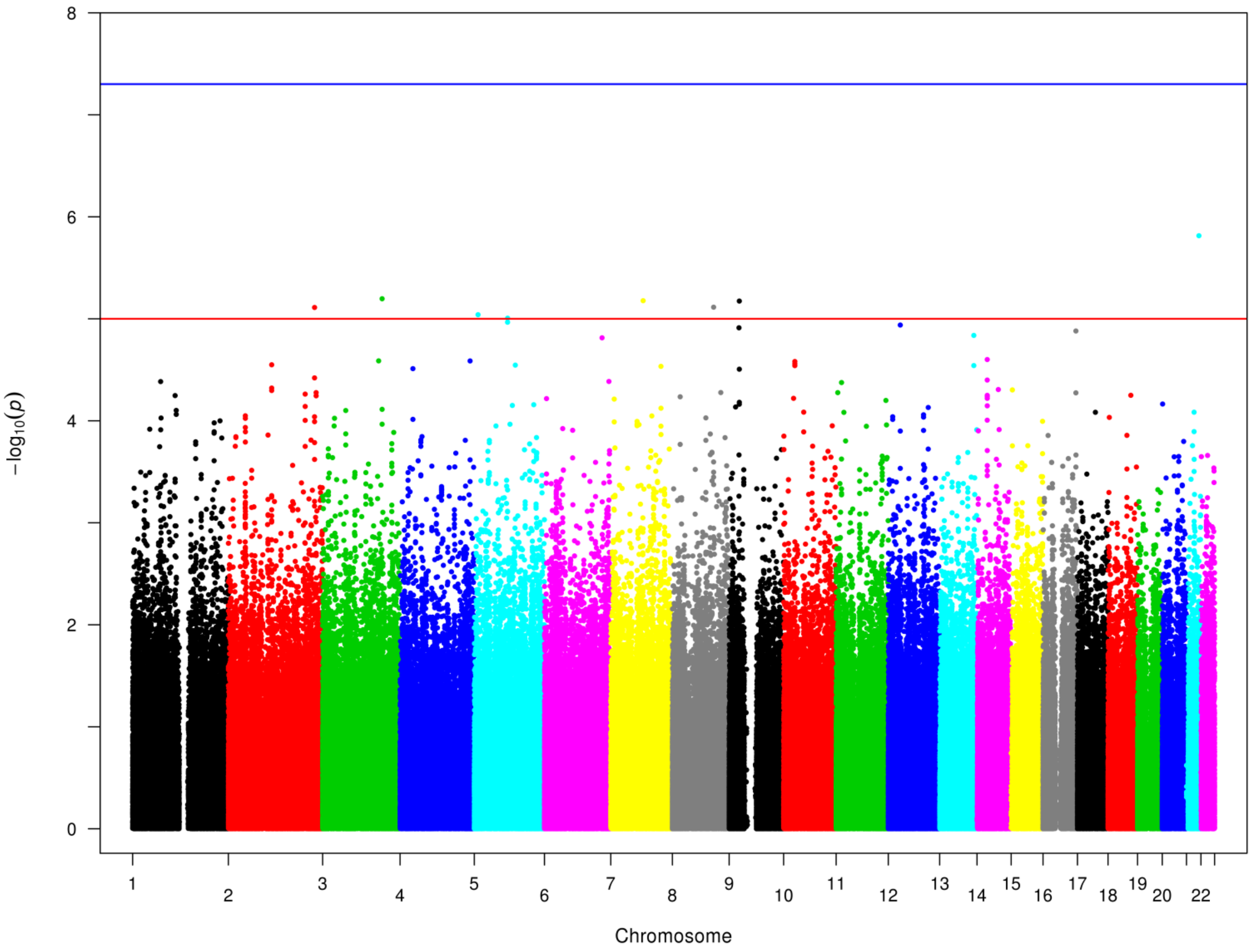
A



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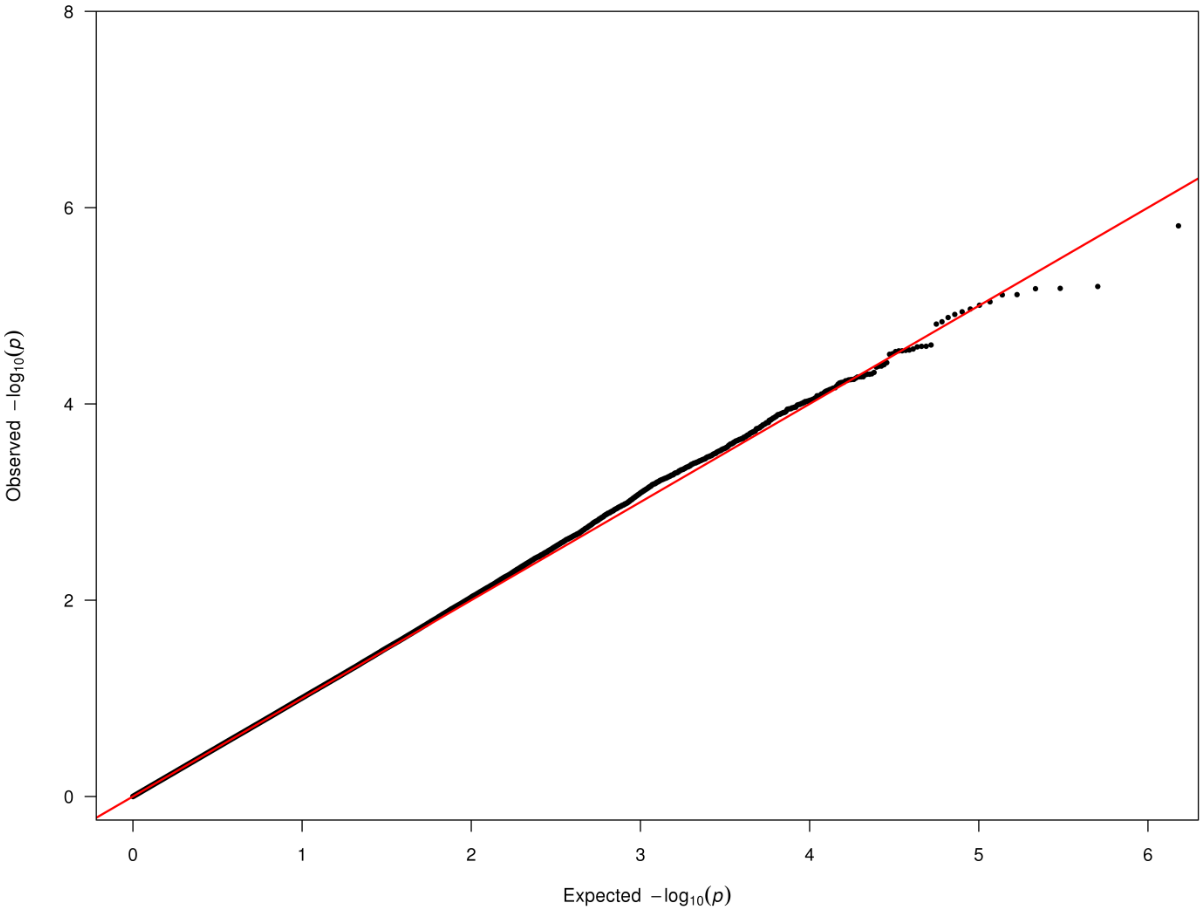
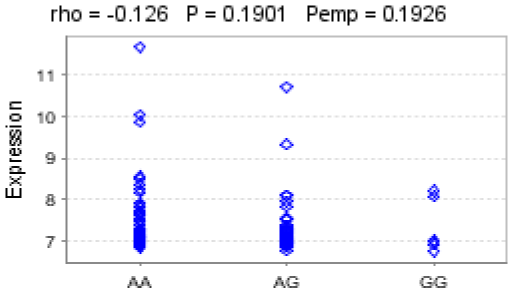
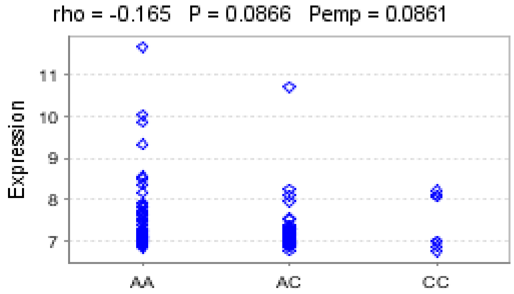


SUPPLEMENTAL FIGURE 10 (A) Manhattan plot and (B) quantile-quantile plot of $\log_{10}$ transformed plasma 4-pyridoxic acid concentration with adjustment for age, sex and vitamin B-6 intake from fortified foods/supplements, using genotype data on 757337 polymorphisms in healthy Irish adults. In the Manhattan plot, the two horizontal lines represent thresholds for suggestive significance ($P = 1 \times 10^{-5}$; red line) and genome-wide significance ($P = 5 \times 10^{-8}$; blue line).

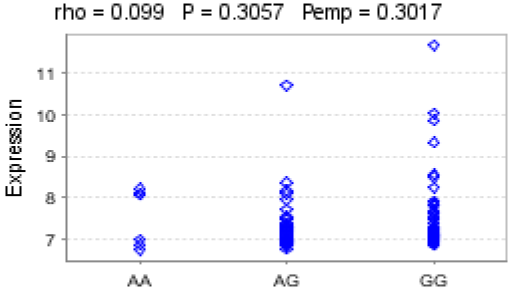
A ***ALPL* rs1256335**



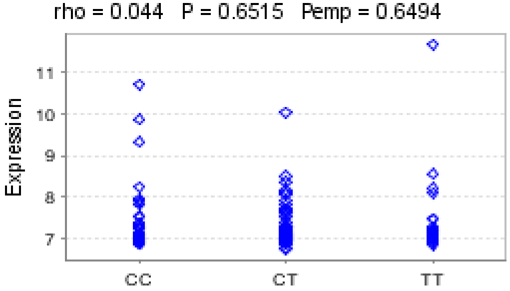
B ***ALPL* rs1772719**



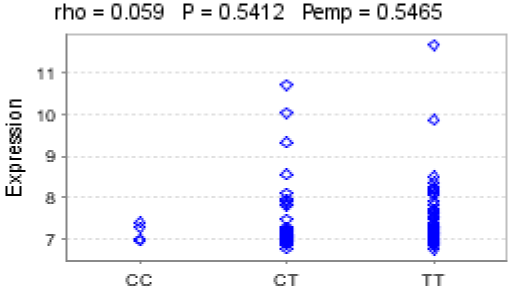
C ***ALPL* rs2275370**



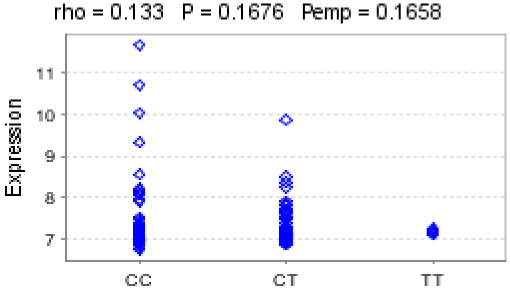
D ***NBPF3* rs4654748**



E ***ALPL* rs12145027**



F ***ALPL* rs1256331**



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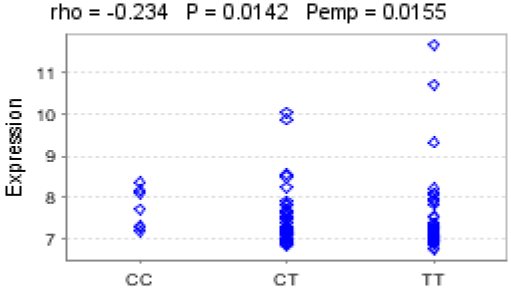
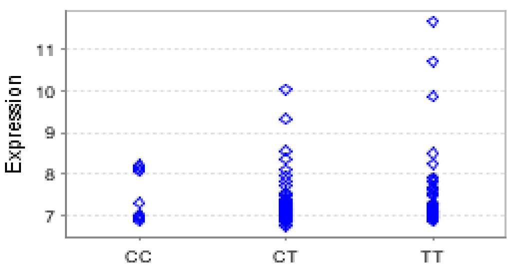


H ***ALPL* rs1780315**



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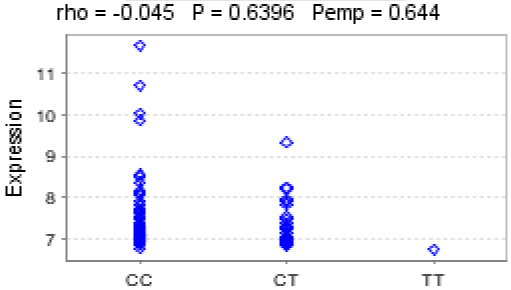

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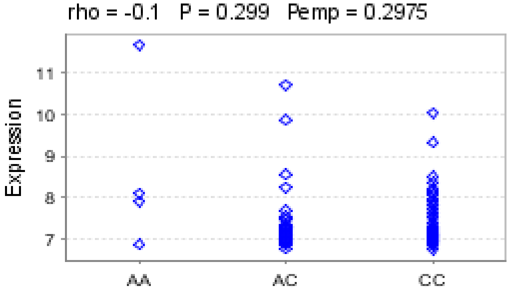
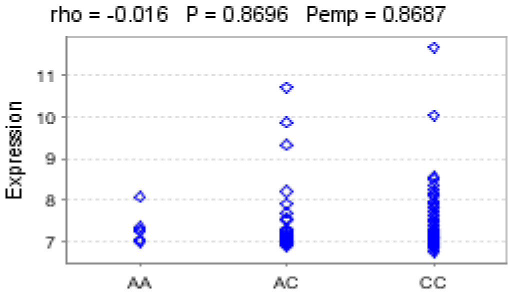
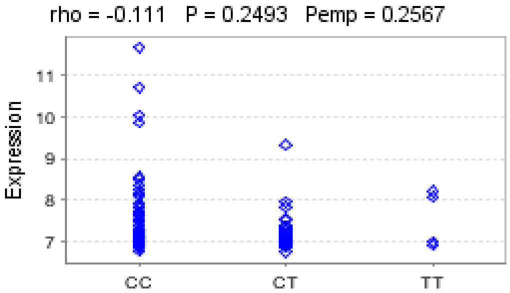


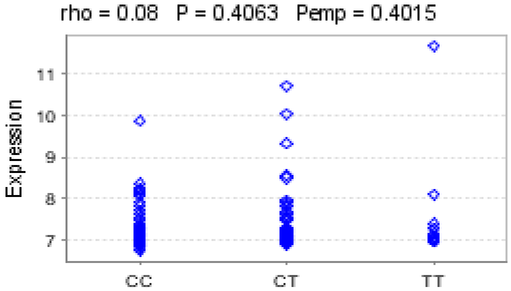
K *ALPL* **rs6664097**



L *ALPL* **rs1256342**



M *ALPL* **rs7536545**



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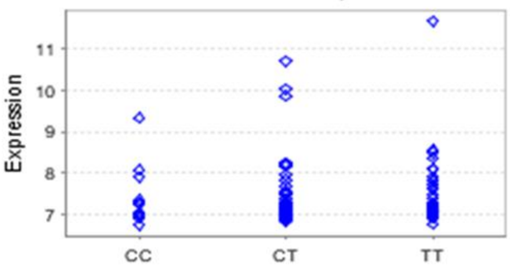

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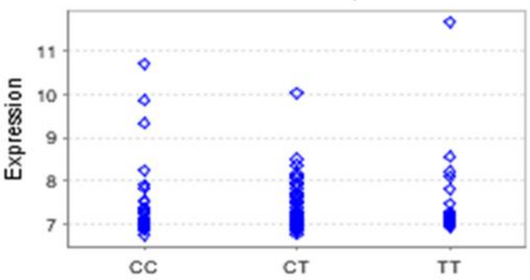

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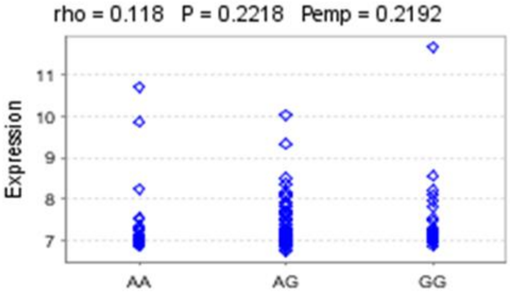
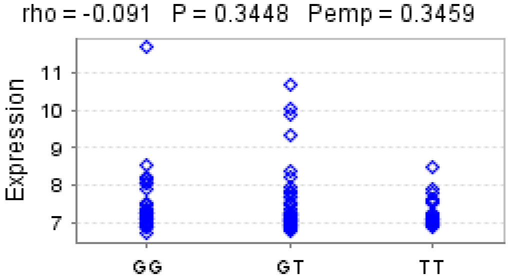


Q ***ALPL* rs4021228**



SUPPLEMENTAL FIGURE 11 Association between *ALPL* gene expression and *ALPL* SNP genotypes in lymphoblastoid cell lines from the HapMap CEU population. Permutation (*n* = 10000) was used to generate adjusted *P* values (Pemp). *ALPL*, tissue non-specific alkaline phosphatase; CEU, sample of Utah residents with Northern and Western European ancestry in the HapMap project; SNP, single nucleotide polymorphism.

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SUPPLEMENTAL TABLE 1 Characteristics of the study sample of healthy Irish adults (*n* = 2345)

Characteristic	**Vitamin B-6 intake from fortified foods/supplements**		**P**[1]
	Yes (*n* = 2008)	**No (*n* = 337)**	
Male, *n* (%)	850 (42.3)	127 (37.7)	0.12
Age,[2,3] years	22 (21 – 23)	23 (21 – 24)	0.03
Body mass index,[2,3] kg/m^2	22.6 (21.1 – 24.5)	22.4 (20.9 – 24.0)	0.04
Alcohol intake,[2,3] g/day	19.4 (10.0 – 34.1)	17.6 (10.0 – 31.5)	0.30
Serum cotinine,[2,3] nmol/L	5.0 (1.5 – 18.7)	5.2 (1.6 – 34.2)	0.40
Plasma creatinine,[2] µmol/L	64.8 (56.5 – 74.6)	63.4 (55.9 – 74.1)	0.43

[1] Comparison between subjects who consumed vitamin B-6 from fortified foods/supplements and subjects who did not consume vitamin B-6 from fortified foods/supplements; Fisher's exact test used to compare the proportion of males; Wilcoxon rank sum test used to compare other characteristics.

[2] Values are median (inter-quartile range).

[3] 16 subjects had missing data for age, 30 subjects had missing data for body mass index, 2 subjects had missing data for alcohol intake, and 63 subjects had missing data for serum cotinine.

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SUPPLEMENTAL TABLE 2 Tests for associations between SNPs in vitamin B-6 metabolism genes and plasma PLP concentration in healthy Irish adults[1]

SNP	Chr	Base pair position[2]	Gene	Gene region	Major, minor alleles	Minor allele frequency	β[3]	Standard error	*P*
rs4654748	1	21786068	*ALPL*	5' near gene (*NBPF3* intron)	C, T	0.48	0.15	0.03	4.61×10^{-8}
rs6664097	1	21834693	*ALPL*	5' near gene	C, A	0.22	-0.15	0.03	6.47×10^{-6}
rs6703976	1	21836934	*ALPL*	intron	C, T	0.10	-0.21	0.05	2.23×10^{-6}
rs869180	1	21839730	*ALPL*	intron	G, A	0.32	0.13	0.03	1.54×10^{-5}
rs1472563	1	21840498	*ALPL*	intron	C, T	0.43	-0.07	0.03	1.13×10^{-2}
rs12116570	1	21843256	*ALPL*	intron	T, G	0.14	0.03	0.04	0.50
rs7536545	1	21844822	*ALPL*	intron	C, T	0.38	0.11	0.03	1.77×10^{-4}
rs12145027	1	21847548	*ALPL*	intron	T, C	0.24	0.18	0.03	4.67×10^{-8}
rs9628653	1	21848962	*ALPL*	intron	T, A	0.23	0.15	0.03	8.84×10^{-6}
rs1890431	1	21852078	*ALPL*	intron	C, T	0.45	0.07	0.03	1.11×10^{-2}
rs1256348	1	21859210	*ALPL*	intron	C, T	0.10	-0.14	0.05	3.54×10^{-3}
rs1780315	1	21863956	*ALPL*	intron	T, C	0.29	-0.14	0.03	1.63×10^{-6}
rs10917006	1	21864206	*ALPL*	intron	C, T	0.09	-0.14	0.05	4.89×10^{-3}
rs1256341	1	21866829	*ALPL*	intron	T, C	0.27	0.16	0.03	1.09×10^{-6}
rs12566520	1	21874187	*ALPL*	intron	G, A	0.15	0.02	0.04	0.67
rs6658127	1	21875390	*ALPL*	intron	G, A	0.32	0.07	0.03	2.01×10^{-2}
rs1256342	1	21876492	*ALPL*	intron	C, T	0.15	-0.17	0.04	1.89×10^{-5}
rs4654757	1	21884318	*ALPL*	intron	A, G	0.22	-0.02	0.03	0.46
rs1780326	1	21885121	*ALPL*	intron	G, T	0.35	0.02	0.03	0.45
rs2071424	1	21886819	*ALPL*	intron	C, T	0.37	0.07	0.03	1.07×10^{-2}
rs3767154	1	21889016	*ALPL*	intron	T, C	0.16	0.03	0.04	0.37
rs3767153	1	21889215	*ALPL*	intron	C, A	0.36	0.07	0.03	1.37×10^{-2}
rs1767429	1	21889340	*ALPL*	intron	A, G	0.44	0.00	0.03	0.96

rs3767152	1	21889381	*ALPL*	intron	G, A	0.04	0.05	0.07	0.54
rs1256336	1	21889506	*ALPL*	intron	C, T	0.22	0.04	0.03	0.30
rs1256335	1	21890386	*ALPL*	intron	A, G	0.22	-0.24	0.03	7.39×10^{-13}
rs3767151	1	21894104	*ALPL*	intron	C, T	0.13	-0.08	0.04	0.06
rs1256331	1	21895008	*ALPL*	intron	C, T	0.23	0.16	0.03	3.47×10^{-7}
rs1780318	1	21895625	*ALPL*	intron	T, A	0.06	-0.29	0.06	2.22×10^{-7}
rs1256328	1	21896767	*ALPL*	intron	C, T	0.15	-0.12	0.04	3.04×10^{-3}
rs1780320	1	21899491	*ALPL*	intron	G, A	0.28	0.11	0.03	3.79×10^{-4}
rs2275370	1	21900420	*ALPL*	intron	G, A	0.21	-0.21	0.03	1.17×10^{-9}
rs1536934	1	21901277	*ALPL*	intron	G, A	0.11	-0.06	0.04	0.16
rs3767142	1	21901558	*ALPL*	intron	G, A	0.28	0.07	0.03	1.85×10^{-2}
rs1780329	1	21902950	*ALPL*	intron	C, A	0.19	-0.16	0.03	2.89×10^{-6}
rs1772719	1	21904374	*ALPL*	3' UTR	A, C	0.23	-0.22	0.03	4.70×10^{-12}
rs2242421	1	21904574	*ALPL*	3' UTR	A, G	0.08	-0.01	0.05	0.91
rs1772720	1	21905007	*ALPL*	3' near gene	G, A	0.07	-0.29	0.05	2.66×10^{-8}
rs3121206	1	21907604	*ALPL*	3' near gene	A, G	0.18	0.06	0.04	0.08
rs2325751	17	46017801	*PNPO*	5' near gene	T, G	0.42	-0.03	0.03	0.25
rs16949651	17	46019601	*PNPO*	intron	A, G	0.12	-0.04	0.04	0.34
rs11079804	17	46020698	*PNPO*	exon2	C, T	0.18	0.00	0.04	0.99
rs2325750	17	46022330	*PNPO*	intron	A, G	0.32	0.01	0.03	0.77
rs2002136	17	46022889	*PNPO*	intron	C, T	0.35	-0.01	0.03	0.80
rs16949676	17	46024500	*PNPO*	3' UTR	G, C	0.07	-0.03	0.06	0.57
rs1986694	17	46026031	*PNPO*	3' UTR	G, C	0.11	-0.06	0.05	0.21
rs1986693	17	46026156	*PNPO*	3' UTR	G, A	0.22	0.03	0.03	0.46
rs4794318	17	46028071	*PNPO*	3' near gene	G, A	0.15	0.00	0.04	0.91
rs11651753	17	46029089	*PNPO*	3' near gene	C, T	0.44	-0.01	0.03	0.87
rs3096	17	46029432	*PNPO*	3' near gene (3’ UTR of *PRR15L*)	T, G	0.33	-0.01	0.03	0.74
rs2838356	21	45147282	*PDXK*	intron	A, G	0.09	-0.03	0.05	0.52
rs6518318	21	45149133	*PDXK*	intron	C, T	0.38	-0.02	0.03	0.57
rs2838357	21	45149518	*PDXK*	intron	A, G	0.12	0.01	0.04	0.83

rs766242	21	45151472	*PDXK*	intron	C, T	0.14	-0.01	0.04	0.77
rs9974754	21	45151874	*PDXK*	intron	G, A	0.31	-0.05	0.03	0.12
rs13050307	21	45153751	*PDXK*	intron	A, G	0.17	0.12	0.04	1.86×10^{-3}
rs1106797	21	45170285	*PDXK*	intron	G, A	0.31	0.02	0.03	0.57
rs2006288	21	45172860	*PDXK*	intron	G, T	0.15	0.01	0.04	0.74
rs7527	21	45175958	*PDXK*	3' UTR	T, C	0.45	0.01	0.03	0.73
rs2070535	21	45176304	*PDXK*	3' UTR	C, T	0.40	0.00	0.03	0.99
rs3746954	21	45177255	*PDXK*	3' UTR	C, A	0.19	0.03	0.04	0.48
rs3204323	21	45180708	*PDXK*	3' UTR	G, A	0.08	0.00	0.05	0.99
rs762407	21	45181446	*PDXK*	3' UTR	G, A	0.30	0.02	0.03	0.55
rs3211247	21	45181492	*PDXK*	3' UTR	T, C	0.26	-0.06	0.03	0.08
rs1299	21	45182064	*PDXK*	3' UTR	C, T	0.23	0.05	0.03	0.13
rs6000855	22	38061450	*PDXP*	intron	G, C	0.43	0.01	0.03	0.87

[1] *ALPL*, tissue non-specific alkaline phosphatase; Chr, chromosome number; *NBPF3*, neuroblastoma breakpoint family, member 3; *PDXK*, pyridoxal kinase; *PDXP*, pyridoxal phosphatase; PLP, pyridoxal 5’-phosphate; *PNPO*, pyridoxamine 5’-phosphate oxidase; *PRR15L*, proline rich 15-like; SNP, single nucleotide polymorphism; UTR, untranslated region.

[2] Based on National Center for Biotechnology Information – Genome Reference Consortium Human genome build 37/human genome 19 assembly.

[3] Linear regression model adjusted for amount of vitamin B-6 intake from fortified foods/supplements, sex, body mass index, serum cotinine, and alcohol intake; outcome variable was inverse normal rank transformation of plasma PLP concentration.

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SUPPLEMENTAL TABLE 3 Tests for associations between SNPs in vitamin B-6 metabolism genes and plasma PL and PA concentrations in healthy Irish adults[1]

SNP	Gene	PL			PA		
		β[2]	Standard error	*P*	β[2]	Standard error	*P*
rs4654748	*ALPL*	0.01	0.03	0.67	0.00	0.03	0.96
rs6664097	*ALPL*	-0.02	0.03	0.56	-0.05	0.03	0.12
rs6703976	*ALPL*	-0.10	0.05	2.87×10^{-2}	-0.08	0.05	0.09
rs869180	*ALPL*	0.02	0.03	0.51	0.02	0.03	0.46
rs1472563	*ALPL*	-0.05	0.03	0.06	-0.05	0.03	0.08
rs12116570	*ALPL*	0.04	0.04	0.32	0.06	0.04	0.14
rs7536545	*ALPL*	0.06	0.03	0.05	0.04	0.03	0.19
rs12145027	*ALPL*	0.08	0.03	1.17×10^{-2}	0.07	0.03	0.05
rs9628653	*ALPL*	0.07	0.03	2.76×10^{-2}	0.05	0.03	0.11
rs1890431	*ALPL*	0.04	0.03	0.21	0.05	0.03	0.08
rs1256348	*ALPL*	-0.03	0.05	0.52	-0.01	0.05	0.87
rs1780315	*ALPL*	-0.04	0.03	0.22	-0.03	0.03	0.27
rs10917006	*ALPL*	-0.02	0.05	0.64	-0.13	0.05	1.00×10^{-2}
rs1256341	*ALPL*	0.06	0.03	0.08	0.01	0.03	0.69
rs12566520	*ALPL*	-0.03	0.04	0.44	0.01	0.04	0.85
rs6658127	*ALPL*	0.04	0.03	0.19	0.03	0.03	0.28
rs1256342	*ALPL*	-0.07	0.04	0.10	-0.07	0.04	0.08
rs4654757	*ALPL*	-0.05	0.03	0.18	-0.02	0.03	0.64
rs1780326	*ALPL*	0.01	0.03	0.68	-0.01	0.03	0.66
rs2071424	*ALPL*	0.02	0.03	0.54	0.03	0.03	0.30
rs3767154	*ALPL*	-0.01	0.04	0.89	0.03	0.04	0.48
rs3767153	*ALPL*	0.02	0.03	0.61	0.02	0.03	0.50
rs1767429	*ALPL*	0.01	0.03	0.66	0.03	0.03	0.33
rs3767152	*ALPL*	0.10	0.08	0.17	0.11	0.08	0.15
rs1256336	*ALPL*	0.03	0.04	0.41	0.02	0.04	0.64
rs1256335	*ALPL*	-0.07	0.03	4.25×10^{-2}	-0.07	0.03	0.05
rs3767151	*ALPL*	-0.08	0.04	0.06	-0.08	0.04	0.05
rs1256331	*ALPL*	0.06	0.03	0.05	0.06	0.03	0.09
rs1780318	*ALPL*	-0.02	0.06	0.74	0.05	0.06	0.43
rs1256328	*ALPL*	-0.02	0.04	0.58	-0.02	0.04	0.60
rs1780320	*ALPL*	0.03	0.03	0.29	0.02	0.03	0.59
rs2275370	*ALPL*	-0.03	0.03	0.38	-0.01	0.03	0.83
rs1536934	*ALPL*	-0.09	0.04	0.05	-0.08	0.05	0.09
rs3767142	*ALPL*	0.00	0.03	0.91	0.00	0.03	0.99
rs1780329	*ALPL*	-0.07	0.04	3.70×10^{-2}	-0.04	0.04	0.21
rs1772719	*ALPL*	-0.06	0.03	0.08	-0.03	0.03	0.41

rs2242421	*ALPL*	-0.07	0.05	0.18	-0.07	0.05	0.20
rs1772720	*ALPL*	-0.06	0.05	0.28	-0.02	0.05	0.73
rs3121206	*ALPL*	0.06	0.04	0.12	0.03	0.04	0.35
rs2325751	*PNPO*	-0.05	0.03	0.11	-0.01	0.03	0.72
rs16949651	*PNPO*	-0.07	0.04	0.10	-0.06	0.04	0.14
rs11079804	*PNPO*	-0.01	0.04	0.81	-0.04	0.04	0.35
rs2325750	*PNPO*	0.02	0.03	0.55	0.01	0.03	0.86
rs2002136	*PNPO*	-0.01	0.03	0.80	0.01	0.03	0.72
rs16949676	*PNPO*	-0.06	0.06	0.25	-0.05	0.06	0.41
rs1986694	*PNPO*	-0.08	0.05	0.07	-0.05	0.05	0.25
rs1986693	*PNPO*	0.05	0.03	0.11	0.03	0.03	0.31
rs4794318	*PNPO*	0.01	0.04	0.86	0.02	0.04	0.58
rs11651753	*PNPO*	-0.03	0.03	0.24	-0.03	0.03	0.25
rs3096	*PNPO*	-0.02	0.03	0.44	-0.02	0.03	0.44
rs2838356	*PDXK*	-0.03	0.05	0.60	-0.04	0.05	0.43
rs6518318	*PDXK*	-0.03	0.03	0.24	-0.02	0.03	0.57
rs2838357	*PDXK*	0.01	0.04	0.90	-0.01	0.04	0.91
rs766242	*PDXK*	0.00	0.04	0.95	-0.01	0.04	0.88
rs9974754	*PDXK*	-0.01	0.03	0.88	-0.02	0.03	0.52
rs13050307	*PDXK*	0.07	0.04	0.07	0.07	0.04	0.08
rs1106797	*PDXK*	0.01	0.03	0.84	0.01	0.03	0.78
rs2006288	*PDXK*	0.00	0.04	0.95	-0.01	0.04	0.89
rs7527	*PDXK*	-0.01	0.03	0.73	-0.00	0.03	0.95
rs2070535	*PDXK*	0.00	0.03	0.91	0.01	0.03	0.83
rs3746954	*PDXK*	0.01	0.04	0.71	0.03	0.04	0.47
rs3204323	*PDXK*	0.04	0.05	0.48	-0.01	0.05	0.88
rs762407	*PDXK*	0.01	0.03	0.79	0.01	0.03	0.68
rs3211247	*PDXK*	-0.03	0.03	0.37	-0.04	0.03	0.22
rs1299	*PDXK*	0.03	0.03	0.41	0.05	0.03	0.15
rs6000855	*PDXP*	0.02	0.03	0.45	0.02	0.03	0.57

[1] *ALPL*, tissue non-specific alkaline phosphatase; PA, 4-pyridoxic acid; *PDXK*, pyridoxal kinase; *PDXP*, pyridoxal phosphatase; PL, pyridoxal; *PNPO*, pyridoxamine 5’-phosphate oxidase; SNP, single nucleotide polymorphism.

[2] Linear regression model adjusted for amount of vitamin B-6 intake from fortified foods/ supplements, sex, body mass index, serum cotinine, and alcohol intake; outcome variables were inverse normal rank transformation of plasma PL and PA concentrations.

SUPPLEMENTAL TABLE 4 Genomic control (lambda) results for plasma pyridoxal 5'-phosphate GWAS after adjustment for age, sex and vitamin B-6 intake from fortified foods/supplements in a study population of healthy Irish adults[1]

B-6 vitamer	**Transformation of plasma B-6 vitamer concentration**	**Lambda = Median(of T^2)/0.456**	**Number of markers with (-log*P*value) > 7**
pyridoxal 5'-phosphate	none	1.012	8
	$\log_{10}$ transformation	1.008	12
pyridoxal	none	1.055	67
	$\log_{10}$ transformation	1.004	0
4-pyridoxic acid	none	1.055	66
	$\log_{10}$ transformation	1.006	0

[1] Lambda is defined as the median of the observed chi-squared test statistic (T^2) divided by 0.456. The ideal range of lambda is from approximately 0.95 to 1.10. GWAS, genome-wide association study.

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SUPPLEMENTAL TABLE 5 GWAS results based on data from healthy Irish adults for 10 SNPs that had failed genotyping assays on the MALDI-TOF mass spectrometer[1]

SNP	**Chr**	**Base pair position[2]**	**Gene**	**Gene region**	**Major, minor alleles**	**Minor allele frequency**	**B-6 vitamer outcome variable[3]**	**β[4]**	**Standard error**	***P***
rs4021228	1	21863691	*ALPL*	intron	G, T	0.47	PLP	0.04	0.01	4.25×10^{-9}
							PL	0.02	0.01	0.04
							PA	0.01	0.01	0.17
rs1256342[5]	1	21876492	*ALPL*	intron	G, A	0.14	PLP	-0.04	0.01	2.66×10^{-5}
							PL	-0.03	0.01	0.04
							PA	-0.02	0.01	0.14
rs885813[6]	1	21877074	*ALPL*	intron	C, T	0.39	PLP	0.01	0.01	0.41
							PL	-0.01	0.01	0.58
							PA	-0.01	0.01	0.56
rs1256336[7]	1	21889506	*ALPL*	intron	C, T	0.23	PLP	0.00	0.01	0.78
							PL	0.00	0.01	0.96
							PA	0.00	0.01	0.70
rs1697406	1	21904267	*ALPL*	3' UTR	G, A	0.09	PLP	0.02	0.01	0.11
							PL	0.00	0.02	0.77
							PA	0.00	0.02	0.93
rs1107204	21	45138118	*PDXK*	5' near gene	C, A	0.43	PLP	-0.01	0.01	0.34
							PL	-0.01	0.01	0.49
							PA	0.00	0.01	0.78

rs2838358[8]	21	45151046	*PDXK*	intron	T, C	0.35	PLP	0.00	0.01	0.76
							PL	0.00	0.01	0.71
							PA	0.00	0.01	0.87
rs749326	22	38051019	*PDXP*	5' near gene	C, T	0.11	PLP	0.01	0.01	0.49
							PL	0.01	0.01	0.31
							PA	0.03	0.02	0.04
rs9622677	22	38054262	*PDXP*	5' near gene	A, C	0.42	PLP	0.00	0.01	0.73
							PL	-0.01	0.01	0.54
							PA	0.00	0.01	0.87
rs713835	22	38064650	*PDXP*	3' near gene	C, T	0.33	PLP	-0.01	0.01	0.49
							PL	-0.01	0.01	0.37
							PA	-0.01	0.01	0.26

[1] *n* = 2158 subjects. *ALPL*, tissue non-specific alkaline phosphatase; Chr, chromosome number; GWAS, genome-wide association study; MALDI-TOF, Matrix-Assisted Laser Desorption/Ionization – Time-of-Flight; PA, 4-pyridoxic acid; *PDXK*, pyridoxal (pyridoxine, vitamin B-6) kinase; *PDXP*, pyridoxal (pyridoxine, vitamin B-6) phosphatase; PL, pyridoxal; PLP, pyridoxal 5'-phosphate; SNP, single nucleotide polymorphism; UTR, untranslated region.

[2] Based on National Center for Biotechnology Information – Genome Reference Consortium Human genome build 37/human genome 19 assembly.

[3] Outcome variable in linear regression model was $\log_{10}$ transformation of plasma PLP, PL, or PA concentration, as indicated.

[4] Linear regression model was adjusted for age and sex.

[5] Nearby rs4385672 (base pair position 21872404 on chromosome 1) that failed genotyping on the MALDI-TOF mass spectrometer; r^2 = 0.52 for linkage disequilibrium between rs4385672 and rs1256342.

[6] Nearby rs12141569 (base pair position 21873002 on chromosome 1) that failed genotyping on the MALDI-TOF mass spectrometer; r^2 = 0.82 for linkage disequilibrium between rs12141569 and rs885813.

[7] Nearby rs1256323 (base pair position 21851312 on chromosome 1) that failed genotyping on the MALDI-TOF mass spectrometer; r^2 = 0.62 for linkage disequilibrium between rs1256323 and rs1256336.

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[8] Nearby rs2838355 (base pair position 45144013 on chromosome 21) that failed genotyping on the MALDI-TOF mass spectrometer; $r^2 = 0.93$ for linkage disequilibrium between rs2838355 and rs2838358.

SUPPLEMENTAL TABLE 6 Gene-based analysis of association between plasma B-6 vitamer concentrations and SNPs in vitamin B-6 inter-conversion enzyme genes in healthy Irish adults[1,2]

B-6 vitamer	Method used to estimate genetic variant function[3]	Genes tested for association with plasma B-6 vitamer concentrations		
		ALPL[4]	***PDXK***[5]	***PNPO***[6]
PLP	β-spline	4.04×10^{-15}	0.23	0.99
	Fourier spline	5.87×10^{-15}	0.35	0.94
PL	β-spline	0.03	0.77	0.52
	Fourier spline	0.27	0.63	0.26
PA	β-spline	0.34	0.92	0.96
	Fourier spline	0.67	0.98	0.88

[1] *ALPL*, tissue non-specific alkaline phosphatase; PA, 4-pyridoxic acid; *PDXK*, pyridoxal (pyridoxine, vitamin B-6) kinase; PL, pyridoxal; PLP, pyridoxal 5’-phosphate; *PNPO*, pyridoxamine 5’-phosphate oxidase; SNP, single nucleotide polymorphism.

[2] $n = 2345$ subjects.

[3] In gene-based analyses, we treated a person’s genetic data as a stochastic function and used the observed genotype data and functional data analysis techniques in the form of β-spline or Fourier spline basis functions to estimate a genetic variant function. We used the estimated genetic variant function in functional linear model regression analyses to test for association between the genetic variants and the inverse normal rank transformation of B-6 vitamer concentrations. We applied F-distributed test statistics to the functional linear models to determine statistical significance of the association tests.

[4] 39 SNPs in or near the *ALPL* gene were used in gene-based analyses. Values are P values from applying F-distributed test statistics to functional linear model regression analysis.

[5] 15 SNPs in or near the *PDXK* gene were used in gene-based analysis. Values are P values from applying F-distributed test statistics to functional linear model regression analysis.

[6] 11 SNPs in or near the *PNPO* gene were used in gene-based analysis. Values are P values from applying F-distributed test statistics to functional linear model regression analysis.

SUPPLEMENTAL TABLE 7 Potential regulatory regions in or near the *ALPL* gene that overlap the base pair positions of *ALPL* SNPs associated with plasma pyridoxal 5'-phosphate concentration in healthy Irish adults[1]

SNP	Open chromatin	Region of histone modification by methylation or acetylation	Transcription factor binding sites	Regions of RNA polymerase II-bound chromatin interactions	Binding site for RNA-binding protein
rs4654748					√
rs6664097	√	√	√		
rs6703976					√
rs869180					√
rs7536545					√
rs12145027					√
rs9628653				√	√
rs1780315					√
rs1256341					√
rs1256342	√	√	√	√	√
rs1256335					√
rs1256331	√	√	√		√
rs1780318	√	√	√		√
rs2275370	√	√	√	√	√
rs1780329					√
rs1772719	√	√		√	√
rs1772720				√	
rs1780324					
rs1697421					
rs1780321					
rs4021228					√
rs1780316					

[1] *ALPL*, tissue non-specific alkaline phosphatase; SNP, single nucleotide polymorphism.

SUPPLEMENTAL TABLE 8 Regions of open chromatin that coincide with base pair positions of SNPs associated with plasma pyridoxal 5'-phosphate concentration in healthy Irish adults[1]

SNP	**Open chromatin location[2]**	**Cell line**	**Cell type**	**Data source**
rs1772719	chr1:21904340-21904686	Cerebrum_frontal_OC	cerebrum:	wgEncodeOpenChromDnase
rs1772719	chr1:21902824-21904681	Chorion	fetal membrane:chorion cells	wgEncodeOpenChromDnase
rs1772719	chr1:21904058-21904503	Frontal_cortex_OC	frontal cortex:	wgEncodeOpenChromDnase
rs1772719	chr1:21903766-21904457	GM12891	blood:lymphoblastoid cell; B-cell	wgEncodeOpenChromDnase
rs1772719	chr1:21903667-21904507	GM12892	blood:lymphoblastoid cell; B-cell	wgEncodeOpenChromDnase
rs1772719	chr1:21904317-21904438	GM13977	blood:lymphoblastoid cell	wgEncodeOpenChromDnase
rs1772719	chr1:21903698-21904793	H7-hESC	embryonic stem cell:embryonic stem cell	wgEncodeOpenChromDnase
rs1772719	chr1:21904194-21904407	HSMM	muscle:Myoblast	wgEncodeOpenChromDnase
rs1772719	chr1:21904271-21904417	Huh-7	liver:	wgEncodeOpenChromDnase
rs1772719	chr1:21903768-21904759	iPS	induced pluripotent stem cell:Stem cell	wgEncodeOpenChromDnase
rs1772719	chr1:21903749-21904775	Monocytes-CD14+	blood:Mononuclear Cell	wgEncodeOpenChromDnase
rs1772719	chr1:21904301-21904615	PanIslets	pancreas:	wgEncodeOpenChromDnase
rs2275370	chr1:21900417-21901350	8988T	pancreatic gland:Adenocarcinoma	wgEncodeOpenChromDnase
rs2275370	chr1:21900336-21900955	CD20+_RO01794	blood:B-lymphocyte	wgEncodeOpenChromDnase
rs2275370	chr1:21900398-21901734	Cerebellum_OC	cerebrum:	wgEncodeOpenChromDnase
rs2275370	chr1:21900373-21901787	Cerebrum_frontal_OC	cerebrum:	wgEncodeOpenChromDnase
rs2275370	chr1:21900414-21902574	Chorion	fetal membrane:chorion cells	wgEncodeOpenChromDnase
rs2275370	chr1:21900050-21902599	GM12891	blood:lymphoblastoid cell; B-cell	wgEncodeOpenChromDnase
rs2275370	chr1:21900059-21900926	GM12892	blood:lymphoblastoid cell; B-cell	wgEncodeOpenChromDnase
rs2275370	chr1:21900347-21900950	GM13977	blood:lymphoblastoid cell	wgEncodeOpenChromDnase
rs2275370	chr1:21900140-21900878	GM19239	blood:lymphoblastoid cell	wgEncodeOpenChromDnase
rs2275370	chr1:21900059-21902035	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeOpenChromDnase
rs2275370	chr1:21900092-21902232	H7-hESC	embryonic stem cell:embryonic stem cell	wgEncodeOpenChromDnase
rs2275370	chr1:21900223-21901695	H9ES	embryonic stem cell:embryonic stem cell	wgEncodeOpenChromDnase
rs2275370	chr1:21900033-21902286	Heart_OC	heart:	wgEncodeOpenChromDnase
rs2275370	chr1:21900401-21901012	HEK293T	kidney: (embryo)	wgEncodeOpenChromDnase

rs2275370	chr1:21900370-21901270	Hela-S3	cervix:carcinoma	wgEncodeOpenChromDnase
rs2275370	chr1:21900273-21900959	Hela-S3	cervix:carcinoma	wgEncodeOpenChromDnase
rs2275370	chr1:21900044-21901003	Hepatocyte	liver:Hepatocyte	wgEncodeOpenChromDnase
rs2275370	chr1:21900297-21901597	HSMM_emb	muscle:Myoblast (embryo)	wgEncodeOpenChromDnase
rs2275370	chr1:21900391-21900949	Huh-7.5	liver:	wgEncodeOpenChromDnase
rs2275370	chr1:21900381-21901014	Huh-7	liver:	wgEncodeOpenChromDnase
rs2275370	chr1:21900298-21902050	HUVEC	blood vessel:Endothelial Cell	wgEncodeOpenChromDnase
rs2275370	chr1:21900338-21901650	IMR90	lung:Fibroblast (fetal)	wgEncodeOpenChromDnase
rs2275370	chr1:21900150-21901755	iPS	induced pluripotent stem cell:Stem cell	wgEncodeOpenChromDnase
rs2275370	chr1:21900386-21900938	iPS_CWRU1	induced pluripotent stem cell:Stem cell	wgEncodeOpenChromDnase
rs2275370	chr1:21900137-21901180	LNCaP	prostate:adenocarcinoma	wgEncodeOpenChromDnase
rs2275370	chr1:21900263-21901186	LNCaP	prostate:adenocarcinoma	wgEncodeOpenChromDnase
rs2275370	chr1:21900121-21901673	MCF-7	breast:adenocarcinoma	wgEncodeOpenChromDnase
rs2275370	chr1:21900373-21901114	MCF-7	breast:adenocarcinoma	wgEncodeOpenChromDnase
rs2275370	chr1:21900329-21902080	Medullo_D341	brain:medulloblastoma	wgEncodeOpenChromDnase
rs2275370	chr1:21900049-21900636	Monocytes-CD14+	blood:Mononuclear Cell	wgEncodeOpenChromDnase
rs2275370	chr1:21900200-21901505	SK-N-SH	brain:Neuroblastoma	wgEncodeOpenChromDnase
rs2275370	chr1:21900366-21901402	Stellate	liver:Stellate cell	wgEncodeOpenChromDnase
rs2275370	chr1:21900117-21900983	T-47D	breast:Epithelial Cell	wgEncodeOpenChromDnase
rs2275370	chr1:21900134-21900420	Hela-S3	cervix:carcinoma	wgEncodeOpenChromFaire
rs2275370	chr1:21900239-21900999	Hela-S3	cervix:carcinoma	wgEncodeOpenChromFaire
rs1780318	chr1:21894983-21895843	CD20+_RO01794	blood:B-lymphocyte	wgEncodeOpenChromDnase
rs1780318	chr1:21895478-21895998	Chorion	fetal membrane:chorion cells	wgEncodeOpenChromDnase
rs1780318	chr1:21895416-21895640	Fibrobl_GM03348	skin:Fibroblast	wgEncodeOpenChromDnase
rs1780318	chr1:21894886-21895690	Fibrobl_GM03348	skin:Fibroblast	wgEncodeOpenChromDnase
rs1780318	chr1:21894681-21896655	GM12891	blood:lymphoblastoid cell; B-cell	wgEncodeOpenChromDnase
rs1780318	chr1:21894656-21895952	GM12892	blood:lymphoblastoid cell; B-cell	wgEncodeOpenChromDnase
rs1780318	chr1:21895371-21895761	GM18507	blood:lymphoblastoid cell	wgEncodeOpenChromDnase
rs1780318	chr1:21895104-21895942	GM19238	blood:lymphoblastoid cell	wgEncodeOpenChromDnase

rs1780318	chr1:21894529-21895880	GM19239	blood:lymphoblastoid cell	wgEncodeOpenChromDnase
rs1780318	chr1:21894771-21895855	H7-hESC	embryonic stem cell:embryonic stem cell	wgEncodeOpenChromDnase
rs1780318	chr1:21895361-21895921	Hepatocyte	liver:Hepatocyte	wgEncodeOpenChromDnase
rs1780318	chr1:21893533-21895786	HSMM	muscle:Myoblast	wgEncodeOpenChromDnase
rs1780318	chr1:21894765-21895785	HSMM_emb	muscle:Myoblast (embryo)	wgEncodeOpenChromDnase
rs1780318	chr1:21895244-21895791	HSMM_FSHD	muscle:Myoblast	wgEncodeOpenChromDnase
rs1780318	chr1:21895320-21895742	HSMMtube	muscle:Myotube	wgEncodeOpenChromDnase
rs1780318	chr1:21894631-21895631	HTR8svn	blastula:Trophoblast	wgEncodeOpenChromDnase
rs1780318	chr1:21895472-21895640	IMR90	lung:Fibroblast (fetal)	wgEncodeOpenChromDnase
rs1780318	chr1:21894749-21895666	iPS	induced pluripotent stem cell:Stem cell	wgEncodeOpenChromDnase
rs1780318	chr1:21895460-21895693	K562	blood:Leukemia cell	wgEncodeOpenChromDnase
rs1780318	chr1:21894877-21895735	K562	blood:Leukemia cell	wgEncodeOpenChromDnase
rs1780318	chr1:21894364-21896457	K562	blood:Leukemia cell	wgEncodeOpenChromDnase
rs1780318	chr1:21894651-21895669	K562	blood:Leukemia cell	wgEncodeOpenChromDnase
rs1780318	chr1:21894347-21896629	K562	blood:Leukemia cell	wgEncodeOpenChromDnase
rs1780318	chr1:21894418-21896035	K562	blood:Leukemia cell	wgEncodeOpenChromDnase
rs1780318	chr1:21894553-21895826	Monocytes-CD14+	blood:Mononuclear Cell	wgEncodeOpenChromDnase
rs1780318	chr1:21893907-21895640	Myometr	myometrium:myometrial cell	wgEncodeOpenChromDnase
rs1780318	chr1:21893640-21895673	Osteobl	bone:Osteoblast	wgEncodeOpenChromDnase
rs1780318	chr1:21894716-21895683	PanIslets	pancreas:	wgEncodeOpenChromDnase
rs1780318	chr1:21895474-21895711	Psoas_muscle_OC	psoas muscle:	wgEncodeOpenChromDnase
rs1780318	chr1:21893965-21895749	Stellate	liver:Stellate cell	wgEncodeOpenChromDnase
rs1780318	chr1:21894653-21895628	Urothelia	urothelium:Ureter cell	wgEncodeOpenChromDnase
rs1780318	chr1:21893954-21895711	Urothelia	urothelium:Ureter cell	wgEncodeOpenChromDnase
rs1780318	chr1:21895440-21895730	HBVP	blood vessel:Pericyte	wgEncodeUwDnase
rs1256331	chr1:21894664-21895480	8988T	pancreatic gland:Adenocarcinoma	wgEncodeOpenChromDnase
rs1256331	chr1:21894983-21895843	CD20+_RO01794	blood:B-lymphocyte	wgEncodeOpenChromDnase
rs1256331	chr1:21894685-21895386	Cerebellum_OC	cerebrum:	wgEncodeOpenChromDnase
rs1256331	chr1:21894782-21895325	Cerebrum_frontal_OC	cerebrum:	wgEncodeOpenChromDnase

rs1256331	chr1:21894104-21895395	Chorion	fetal membrane:chorion cells	wgEncodeOpenChromDnase
rs1256331	chr1:21894886-21895690	Fibrobl_GM03348	skin:Fibroblast	wgEncodeOpenChromDnase
rs1256331	chr1:21894822-21895105	Fibrobl_GM03348	skin:Fibroblast	wgEncodeOpenChromDnase
rs1256331	chr1:21894927-21895158	FibroP	skin:Fibroblast	wgEncodeOpenChromDnase
rs1256331	chr1:21894773-21895170	FibroP_AG08396	skin:Fibroblast	wgEncodeOpenChromDnase
rs1256331	chr1:21894836-21895214	Gliobla	brain:Glioblastoma	wgEncodeOpenChromDnase
rs1256331	chr1:21894681-21896655	GM12891	blood:lymphoblastoid cell; B-cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894656-21895952	GM12892	blood:lymphoblastoid cell; B-cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894477-21895416	GM13976	blood:lymphoblastoid cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894741-21895476	GM13977	blood:lymphoblastoid cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894529-21895880	GM19239	blood:lymphoblastoid cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894967-21895585	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894771-21895855	H7-hESC	embryonic stem cell:embryonic stem cell	wgEncodeOpenChromDnase
rs1256331	chr1:21895007-21895218	H9ES	embryonic stem cell:embryonic stem cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894739-21895021	Hepatocyte	liver:Hepatocyte	wgEncodeOpenChromDnase
rs1256331	chr1:21894722-21895326	HMEC	breast:Epithelial Cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894757-21895185	HPDE6-E6E7	pancreatic duct:	wgEncodeOpenChromDnase
rs1256331	chr1:21893533-21895786	HSMM	muscle:Myoblast	wgEncodeOpenChromDnase
rs1256331	chr1:21894765-21895785	HSMM_emb	muscle:Myoblast (embryo)	wgEncodeOpenChromDnase
rs1256331	chr1:21893568-21895213	HSMM_FSHD	muscle:Myoblast	wgEncodeOpenChromDnase
rs1256331	chr1:21894631-21895631	HTR8svn	blastula:Trophoblast	wgEncodeOpenChromDnase
rs1256331	chr1:21894825-21895198	HUVEC	blood vessel:Endothelial Cell	wgEncodeOpenChromDnase
rs1256331	chr1:21893555-21895267	IMR90	lung:Fibroblast (fetal)	wgEncodeOpenChromDnase
rs1256331	chr1:21894749-21895666	iPS	induced pluripotent stem cell:Stem cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894973-21895280	iPS_CWRU1	induced pluripotent stem cell:Stem cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894833-21895489	iPS_NIHi7	induced pluripotent stem cell:Stem cell	wgEncodeOpenChromDnase
rs1256331	chr1:21895003-21895229	K562	blood:Leukemia cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894877-21895735	K562	blood:Leukemia cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894364-21896457	K562	blood:Leukemia cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894961-21895568	K562	blood:Leukemia cell	wgEncodeOpenChromDnase

rs1256331	chr1:21894651-21895669	K562	blood:Leukemia cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894347-21896629	K562	blood:Leukemia cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894418-21896035	K562	blood:Leukemia cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894851-21895238	MCF-7	breast:adenocarcinoma	wgEncodeOpenChromDnase
rs1256331	chr1:21894721-21895082	MCF-7	breast:adenocarcinoma	wgEncodeOpenChromDnase
rs1256331	chr1:21894818-21895300	MCF-7	breast:adenocarcinoma	wgEncodeOpenChromDnase
rs1256331	chr1:21894982-21895258	Melano	skin:Melanocyte	wgEncodeOpenChromDnase
rs1256331	chr1:21894553-21895826	Monocytes-CD14+	blood:Mononuclear Cell	wgEncodeOpenChromDnase
rs1256331	chr1:21893907-21895640	Myometr	myometrium:myometrial cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894924-21895137	NHEK	skin:keratinocyte	wgEncodeOpenChromDnase
rs1256331	chr1:21893640-21895673	Osteobl	bone:Osteoblast	wgEncodeOpenChromDnase
rs1256331	chr1:21894016-21895208	PanIsletD	pancreas:	wgEncodeOpenChromDnase
rs1256331	chr1:21894716-21895683	PanIslets	pancreas:	wgEncodeOpenChromDnase
rs1256331	chr1:21894703-21895363	pHTE	trachea:Epithelial Cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894801-21895104	ProgFib	skin:Fibroblast	wgEncodeOpenChromDnase
rs1256331	chr1:21894067-21895281	Psoas_muscle_OC	psoas muscle:	wgEncodeOpenChromDnase
rs1256331	chr1:21894788-21895162	RWPE1	prostate:Epithelial Cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894933-21895566	SK-N-SH	brain:Neuroblastoma	wgEncodeOpenChromDnase
rs1256331	chr1:21893965-21895749	Stellate	liver:Stellate cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894653-21895628	Urothelia	urothelium:Ureter cell	wgEncodeOpenChromDnase
rs1256331	chr1:21893890-21895557	Urothelia	urothelium:Ureter cell	wgEncodeOpenChromDnase
rs1256331	chr1:21893954-21895711	Urothelia	urothelium:Ureter cell	wgEncodeOpenChromDnase
rs1256331	chr1:21893869-21895609	Urothelia	urothelium:Ureter cell	wgEncodeOpenChromDnase
rs1256331	chr1:21894822-21895159	HTR8svn	blastula:Trophoblast	wgEncodeOpenChromFaire
rs1256331	chr1:21894853-21895170	Urothelia	urothelium:Ureter cell	wgEncodeOpenChromFaire
rs1256331	chr1:21894857-21895221	Urothelia	urothelium:Ureter cell	wgEncodeOpenChromFaire
rs1256331	chr1:21894980-21895130	H7-hESC	embryonic stem cell:embryonic stem cell	wgEncodeUwDgf
rs1256331	chr1:21894920-21895070	HA-h	brain; hippocampus:	wgEncodeUwDgf
rs1256331	chr1:21894920-21895070	HA-sp	spinal cord:astrocyte	wgEncodeUwDgf
rs1256331	chr1:21894880-21895030	HCFaa	heart:Fibroblast	wgEncodeUwDgf

rs1256331	chr1:21894920-21895070	HEEpiC	esophagus:Epithelial Cell	wgEncodeUwDgf
rs1256331	chr1:21894860-21895010	HIPEpiC	eye:Epithelial Cell	wgEncodeUwDgf
rs1256331	chr1:21894880-21895030	HMVEC-LLy	blood vessel:Endothelial Cell	wgEncodeUwDgf
rs1256331	chr1:21894920-21895070	HMVEC-dBl-Neo	blood vessel:Endothelial Cell	wgEncodeUwDgf
rs1256331	chr1:21894900-21895050	HMVEC-dBl-Ad	blood vessel:Endothelial Cell	wgEncodeUwDgf
rs1256331	chr1:21894920-21895070	HMVEC-dLy-Neo	blood vessel:Endothelial Cell	wgEncodeUwDgf
rs1256331	chr1:21894920-21895070	HMVEC-LBl	blood vessel:Endothelial Cell	wgEncodeUwDgf
rs1256331	chr1:21894920-21895070	HUVEC	blood vessel:Endothelial Cell	wgEncodeUwDgf
rs1256331	chr1:21894880-21895030	M059J	brain:Glioblastoma	wgEncodeUwDgf
rs1256331	chr1:21894900-21895050	NH-A	brain:astrocyte	wgEncodeUwDgf
rs1256331	chr1:21894880-21895030	NHLF	lung:Fibroblast	wgEncodeUwDgf
rs1256331	chr1:21894940-21895090	RPMI-7951	skin:Melanoma	wgEncodeUwDgf
rs1256331	chr1:21894880-21895030	SAEC	small airway:Epithelial Cell	wgEncodeUwDgf
rs1256331	chr1:21894980-21895070	HBVSMC	blood vessel:Smooth muscle cell	wgEncodeUwDnase
rs1256331	chr1:21894940-21895090	HEEpiC	esophagus:Epithelial Cell	wgEncodeUwDnase
rs1256331	chr1:21894940-21895050	HMVEC-dBl-Ad	blood vessel:Endothelial Cell	wgEncodeUwDnase
rs1256331	chr1:21894900-21895050	HMVEC-dLy-Neo	blood vessel:Endothelial Cell	wgEncodeUwDnase
rs1256331	chr1:21894920-21895050	HMVEC-LBl	blood vessel:Endothelial Cell	wgEncodeUwDnase
rs1256331	chr1:21894860-21895010	HNPCEpiC	eye:Endothelial Cell	wgEncodeUwDnase
rs1256331	chr1:21894920-21895050	HRE	kidney:Epithelial Cell	wgEncodeUwDnase
rs1256331	chr1:21894880-21895030	M059J	brain:Glioblastoma	wgEncodeUwDnase
rs1256331	chr1:21894860-21895010	bone_marrow_MSC	bone marrow:fibroblastoid cell	wgEncodeUwDnase
rs1256331	chr1:21894900-21895050	NH-A	brain:astrocyte	wgEncodeUwDnase
rs1256331	chr1:21894920-21895070	NHBE_RA	bronchial:Epithelial Cell	wgEncodeUwDnase
rs1256331	chr1:21894900-21895050	NHLF	lung:Fibroblast	wgEncodeUwDnase
rs1256331	chr1:21894900-21895030	PrEC	prostate:Epithelial Cell	wgEncodeUwDnase
rs1256331	chr1:21894960-21895070	RPMI-7951	skin:Melanoma	wgEncodeUwDnase
rs1256331	chr1:21894900-21895050	SAEC	small airway:Epithelial Cell	wgEncodeUwDnase
rs6664097	chr1:21834656-21837062	Frontal_cortex_OC	frontal cortex:	wgEncodeOpenChromDnase

rs6664097	chr1:21834677-21837318	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeOpenChromDnase
rs6664097	chr1:21834693-21836492	Hepatocyte	liver:Hepatocyte	wgEncodeOpenChromDnase
rs1256342	chr1:21876416-21876772	Hepatocyte	liver:Hepatocyte	wgEncodeOpenChromDnase
rs1256342	chr1:21876431-21876923	K562	blood:Leukemia cell	wgEncodeOpenChromDnase
rs1256342	chr1:21876455-21876586	Melano	skin:Melanocyte	wgEncodeOpenChromDnase

[1] SNP, single nucleotide polymorphism.

[2] Based on National Center for Biotechnology Information – Genome Reference Consortium Human genome build 37/human genome 19 assembly.

ONLINE SUPPORTING MATERIAL

SUPPLEMENTAL TABLE 9 Regions of histone modification by methylation or acetylation that coincide with base pair positions of SNPs associated with plasma pyridoxal 5'-phosphate concentration in healthy Irish adults[1]

SNP	Histone marker	Location[2]	Cell line	Cell type	Data source
rs1772719	H3K4me1	chr1:21896306-21930307	A549	lung:Epithelial Cell	wgEncodeBroadHistone
rs1772719	H3K4me2	chr1:21903411-21923201	A549	lung:Epithelial Cell	wgEncodeBroadHistone
rs1772719	H4K20me1	chr1:21889255-21956984	A549	lung:Epithelial Cell	wgEncodeBroadHistone
rs1772719	H4K20me1	chr1:21852998-22050404	Dnd41	blood:T-lymphocyte; Leukemia	wgEncodeBroadHistone
rs1772719	H3K36me3	chr1:21877875-21906791	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs1772719	H3K9ac	chr1:21894277-21906732	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs1772719	H4K20me1	chr1:21828171-22115109	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs1772719	H4K20me1	chr1:21836544-23901982	Hela-S3	cervix:carcinoma	wgEncodeBroadHistone
rs1772719	H4K20me1	chr1:21881787-22003486	HepG2	liver:carcinoma	wgEncodeBroadHistone
rs1772719	H3K4me1	chr1:21891033-21924025	HMEC	breast:Epithelial Cell	wgEncodeBroadHistone
rs1772719	H4K20me1	chr1:21892330-21906656	HMEC	breast:Epithelial Cell	wgEncodeBroadHistone
rs1772719	H3K36me3	chr1:21828979-21915960	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1772719	H3K9ac	chr1:21887245-21906254	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1772719	H3K36me3	chr1:21880031-21907378	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1772719	H3K4me1	chr1:21826693-21927461	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1772719	H4K20me1	chr1:17184307-25646596	K562	blood:Leukemia cell	wgEncodeBroadHistone
rs1772719	H3K9ac	chr1:21904370-21904943	CD14+_RO01746	blood:Mononuclear Cell	wgEncodeBroadHistone
rs1772719	H3K9ac	chr1:21903870-21904880	CD14+_RO01746	blood:Mononuclear Cell	wgEncodeBroadHistone
rs1772719	H3K9ac	chr1:21870065-21905328	NH-A	brain:astrocyte	wgEncodeBroadHistone
rs1772719	H4K20me1	chr1:21896110-21904797	NHDF-Ad	bronchial:Fibroblast	wgEncodeBroadHistone
rs1772719	H4K20me1	chr1:21882192-22031744	NHEK	skin:keratinocyte	wgEncodeBroadHistone
rs1772719	H4K20me1	chr1:21893145-21906700	Osteobl	bone:Osteoblast	wgEncodeBroadHistone
rs2275370	H3K4me1	chr1:21900244-21900479	NT2-D1	testis:	wgEncodeSydhHistone
rs2275370	H3K9acB	chr1:21900402-21901854	NT2-D1	testis:	wgEncodeSydhHistone
rs2275370	H3K4me1	chr1:21896306-21930307	A549	lung:Epithelial Cell	wgEncodeBroadHistone
rs2275370	H4K20me1	chr1:21889255-21956984	A549	lung:Epithelial Cell	wgEncodeBroadHistone
rs2275370	H4K20me1	chr1:21852998-22050404	Dnd41	blood:T-lymphocyte; Leukemia	wgEncodeBroadHistone

rs2275370	H4K20me1	chr1:21890246-21904276	GM12878	blood:B-lymphocyte	wgEncodeBroadHistone
rs2275370	H3K27ac	chr1:21899990-21902326	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs2275370	H3K36me3	chr1:21877875-21906791	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs2275370	H3K4me1	chr1:21899964-21901759	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs2275370	H3K4me2	chr1:21900072-21902254	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs2275370	H3K9ac	chr1:21894277-21906732	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs2275370	H4K20me1	chr1:21828171-22115109	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs2275370	H4K20me1	chr1:21836544-23901982	Hela-S3	cervix:carcinoma	wgEncodeBroadHistone
rs2275370	H4K20me1	chr1:21900283-21900451	Hela-S3	cervix:carcinoma	wgEncodeBroadHistone
rs2275370	H4K20me1	chr1:21900319-21900551	Hela-S3	cervix:carcinoma	wgEncodeBroadHistone
rs2275370	H4K20me1	chr1:21881787-22003486	HepG2	liver:carcinoma	wgEncodeBroadHistone
rs2275370	H3K4me1	chr1:21891033-21924025	HMEC	breast:Epithelial Cell	wgEncodeBroadHistone
rs2275370	H3K4me1	chr1:21899691-21902606	HMEC	breast:Epithelial Cell	wgEncodeBroadHistone
rs2275370	H4K20me1	chr1:21892330-21906656	HMEC	breast:Epithelial Cell	wgEncodeBroadHistone
rs2275370	H3K27ac	chr1:21899152-21902681	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs2275370	H3K36me3	chr1:21828979-21915960	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs2275370	H3K4me1	chr1:21899268-21902877	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs2275370	H3K4me2	chr1:21899716-21902302	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs2275370	H3K9ac	chr1:21887245-21906254	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs2275370	H3K9ac	chr1:21899509-21902564	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs2275370	H3K36me3	chr1:21880031-21907378	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs2275370	H3K4me1	chr1:21826693-21927461	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs2275370	H3K4me1	chr1:21900142-21901971	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs2275370	H3K9ac	chr1:21899919-21902873	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs2275370	H3K27ac	chr1:21899376-21902740	HUVEC	blood vessel:Endothelial Cell	wgEncodeBroadHistone
rs2275370	H3K4me1	chr1:21899278-21903118	HUVEC	blood vessel:Endothelial Cell	wgEncodeBroadHistone
rs2275370	H3K4me2	chr1:21899533-21902567	HUVEC	blood vessel:Endothelial Cell	wgEncodeBroadHistone
rs2275370	H3K9ac	chr1:21900095-21902426	HUVEC	blood vessel:Endothelial Cell	wgEncodeBroadHistone
rs2275370	H4K20me1	chr1:21892564-21900631	HUVEC	blood vessel:Endothelial Cell	wgEncodeBroadHistone
rs2275370	H4K20me1	chr1:17184307-25646596	K562	blood:Leukemia cell	wgEncodeBroadHistone

rs2275370	H3K9ac	chr1:21870065-21905328	NH-A	brain:astrocyte	wgEncodeBroadHistone
rs2275370	H3K4me1	chr1:21900297-21902185	NH-A	brain:astrocyte	wgEncodeBroadHistone
rs2275370	H3K4me1	chr1:21900369-21901577	NHDF-Ad	bronchial:Fibroblast	wgEncodeBroadHistone
rs2275370	H4K20me1	chr1:21896110-21904797	NHDF-Ad	bronchial:Fibroblast	wgEncodeBroadHistone
rs2275370	H4K20me1	chr1:21882192-22031744	NHEK	skin:keratinocyte	wgEncodeBroadHistone
rs2275370	H4K20me1	chr1:21893145-21906700	Osteobl	bone:Osteoblast	wgEncodeBroadHistone
rs2275370	H3K36me3	chr1:21881080-21902435	Osteobl	bone:Osteoblast	wgEncodeBroadHistone
rs2275370	H3K4me1	chr1:21900227-21902018	Osteobl	bone:Osteoblast	wgEncodeBroadHistone
rs1780318	H4K20me1	chr1:21889255-21956984	A549	lung:Epithelial Cell	wgEncodeBroadHistone
rs1780318	H4K20me1	chr1:21852998-22050404	Dnd41	blood:T-lymphocyte; Leukemia	wgEncodeBroadHistone
rs1780318	H4K20me1	chr1:21890246-21904276	GM12878	blood:B-lymphocyte	wgEncodeBroadHistone
rs1780318	H3K36me3	chr1:21877875-21906791	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs1780318	H3K9ac	chr1:21894277-21906732	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs1780318	H4K20me1	chr1:21828171-22115109	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs1780318	H4K20me1	chr1:21836544-23901982	Hela-S3	cervix:carcinoma	wgEncodeBroadHistone
rs1780318	H4K20me1	chr1:21881787-22003486	HepG2	liver:carcinoma	wgEncodeBroadHistone
rs1780318	H3K4me1	chr1:21891033-21924025	HMEC	breast:Epithelial Cell	wgEncodeBroadHistone
rs1780318	H4K20me1	chr1:21892330-21906656	HMEC	breast:Epithelial Cell	wgEncodeBroadHistone
rs1780318	H3K27ac	chr1:21890234-21897015	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1780318	H3K36me3	chr1:21828979-21915960	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1780318	H3K4me1	chr1:21890032-21897342	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1780318	H3K4me3	chr1:21893070-21896375	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1780318	H3K9ac	chr1:21887245-21906254	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1780318	H3K9ac	chr1:21892933-21896094	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1780318	H3K27ac	chr1:21890758-21896874	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1780318	H3K27ac	chr1:21892734-21896390	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1780318	H3K36me3	chr1:21880031-21907378	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1780318	H3K4me1	chr1:21826693-21927461	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1780318	H3K4me1	chr1:21889674-21897482	HSMMtube	muscle:Myotube	wgEncodeBroadHistone

rs1780318	H3K4me2	chr1:21890662-21896706	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1780318	H3K4me2	chr1:21893216-21896214	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1780318	H3K4me3	chr1:21893182-21896644	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1780318	H3K9ac	chr1:21890216-21897448	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1780318	H4K20me1	chr1:21892564-21900631	HUVEC	blood vessel:Endothelial Cell	wgEncodeBroadHistone
rs1780318	H4K20me1	chr1:17184307-25646596	K562	blood:Leukemia cell	wgEncodeBroadHistone
rs1780318	H3K4me2	chr1:21893167-21896165	NH-A	brain:astrocyte	wgEncodeBroadHistone
rs1780318	H3K9ac	chr1:21870065-21905328	NH-A	brain:astrocyte	wgEncodeBroadHistone
rs1780318	H3K9ac	chr1:21892932-21896090	NH-A	brain:astrocyte	wgEncodeBroadHistone
rs1780318	H3K27ac	chr1:21892889-21896280	NH-A	brain:astrocyte	wgEncodeBroadHistone
rs1780318	H3K4me1	chr1:21892908-21896584	NH-A	brain:astrocyte	wgEncodeBroadHistone
rs1780318	H4K20me1	chr1:21882192-22031744	NHEK	skin:keratinocyte	wgEncodeBroadHistone
rs1780318	H4K20me1	chr1:21893145-21906700	Osteobl	bone:Osteoblast	wgEncodeBroadHistone
rs1780318	H3K36me3	chr1:21881080-21902435	Osteobl	bone:Osteoblast	wgEncodeBroadHistone
rs1780318	H3K4me1	chr1:21890276-21896926	Osteobl	bone:Osteoblast	wgEncodeBroadHistone
rs1780318	H3K4me2	chr1:21892998-21896321	Osteobl	bone:Osteoblast	wgEncodeBroadHistone
rs1256331	H4K20me1	chr1:21889255-21956984	A549	lung:Epithelial Cell	wgEncodeBroadHistone
rs1256331	H4K20me1	chr1:21852998-22050404	Dnd41	blood:T-lymphocyte; Leukemia	wgEncodeBroadHistone
rs1256331	H4K20me1	chr1:21890246-21904276	GM12878	blood:B-lymphocyte	wgEncodeBroadHistone
rs1256331	H3K36me3	chr1:21877875-21906791	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs1256331	H3K9ac	chr1:21894277-21906732	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs1256331	H4K20me1	chr1:21828171-22115109	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs1256331	H4K20me1	chr1:21836544-23901982	Hela-S3	cervix:carcinoma	wgEncodeBroadHistone
rs1256331	H4K20me1	chr1:21881787-22003486	HepG2	liver:carcinoma	wgEncodeBroadHistone
rs1256331	H3K4me1	chr1:21891033-21924025	HMEC	breast:Epithelial Cell	wgEncodeBroadHistone
rs1256331	H3K4me1	chr1:21894797-21895405	HMEC	breast:Epithelial Cell	wgEncodeBroadHistone
rs1256331	H4K20me1	chr1:21892330-21906656	HMEC	breast:Epithelial Cell	wgEncodeBroadHistone
rs1256331	H3K27ac	chr1:21890234-21897015	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1256331	H3K36me3	chr1:21828979-21915960	HSMM	muscle:Myoblast	wgEncodeBroadHistone

rs1256331	H3K4me1	chr1:21890032-21897342	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1256331	H3K4me2	chr1:21894182-21895499	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1256331	H3K4me3	chr1:21893070-21896375	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1256331	H3K79me2	chr1:21894635-21895322	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1256331	H3K9ac	chr1:21887245-21906254	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1256331	H3K9ac	chr1:21892933-21896094	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1256331	H3K27ac	chr1:21890758-21896874	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1256331	H3K27ac	chr1:21892734-21896390	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1256331	H3K36me3	chr1:21880031-21907378	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1256331	H3K4me1	chr1:21826693-21927461	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1256331	H3K4me1	chr1:21889674-21897482	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1256331	H3K4me2	chr1:21890662-21896706	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1256331	H3K4me2	chr1:21893216-21896214	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1256331	H3K4me3	chr1:21893182-21896644	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1256331	H3K9ac	chr1:21890216-21897448	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1256331	H3K4me1	chr1:21894971-21895076	HUVEC	blood vessel:Endothelial Cell	wgEncodeBroadHistone
rs1256331	H4K20me1	chr1:21892564-21900631	HUVEC	blood vessel:Endothelial Cell	wgEncodeBroadHistone
rs1256331	H4K20me1	chr1:17184307-25646596	K562	blood:Leukemia cell	wgEncodeBroadHistone
rs1256331	H3K4me2	chr1:21893167-21896165	NH-A	brain:astrocyte	wgEncodeBroadHistone
rs1256331	H3K9ac	chr1:21870065-21905328	NH-A	brain:astrocyte	wgEncodeBroadHistone
rs1256331	H3K9ac	chr1:21892932-21896090	NH-A	brain:astrocyte	wgEncodeBroadHistone
rs1256331	H3K27ac	chr1:21892889-21896280	NH-A	brain:astrocyte	wgEncodeBroadHistone
rs1256331	H3K4me1	chr1:21892908-21896584	NH-A	brain:astrocyte	wgEncodeBroadHistone
rs1256331	H3K4me1	chr1:21893386-21895511	NHDF-Ad	bronchial:Fibroblast	wgEncodeBroadHistone
rs1256331	H4K20me1	chr1:21882192-22031744	NHEK	skin:keratinocyte	wgEncodeBroadHistone
rs1256331	H3K4me3	chr1:21894408-21895295	Osteobl	bone:Osteoblast	wgEncodeBroadHistone
rs1256331	H4K20me1	chr1:21893145-21906700	Osteobl	bone:Osteoblast	wgEncodeBroadHistone
rs1256331	H3K36me3	chr1:21881080-21902435	Osteobl	bone:Osteoblast	wgEncodeBroadHistone
rs1256331	H3K4me1	chr1:21890276-21896926	Osteobl	bone:Osteoblast	wgEncodeBroadHistone
rs1256331	H3K4me2	chr1:21892998-21896321	Osteobl	bone:Osteoblast	wgEncodeBroadHistone

rs6664097	H4K20me1	chr1:21832439-21841269	A549	lung:Epithelial Cell	wgEncodeBroadHistone
rs6664097	H3K4me2	chr1:21834160-21837519	CD20+	blood:B-lymphocyte	wgEncodeBroadHistone
rs6664097	H4K20me1	chr1:21832714-21847825	Dnd41	blood:T-lymphocyte; Leukemia	wgEncodeBroadHistone
rs6664097	H4K20me1	chr1:21830164-21849234	GM12878	blood:B-lymphocyte	wgEncodeBroadHistone
rs6664097	H3K27ac	chr1:21831818-21853187	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs6664097	H3K36me3	chr1:21829361-21850163	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs6664097	H3K4me1	chr1:21834142-21841715	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs6664097	H3K4me2	chr1:21834641-21838214	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs6664097	H3K4me3	chr1:21834493-21838408	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs6664097	H3K79me2	chr1:21827741-21886513	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs6664097	H3K9ac	chr1:21834647-21838352	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs6664097	H4K20me1	chr1:21828171-22115109	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs6664097	H4K20me1	chr1:21834085-21843716	HMEC	breast:Epithelial Cell	wgEncodeBroadHistone
rs6664097	H3K36me3	chr1:21828979-21915960	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs6664097	H3K4me1	chr1:21834400-21841508	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs6664097	H3K4me2	chr1:21834454-21840900	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs6664097	H3K4me3	chr1:21834459-21839640	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs6664097	H3K9ac	chr1:21834446-21840122	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs6664097	H3K27ac	chr1:21828182-21849981	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs6664097	H3K36me3	chr1:21833004-21853210	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs6664097	H3K4me1	chr1:21826693-21927461	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs6664097	H3K4me1	chr1:21834382-21841023	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs6664097	H3K4me2	chr1:21834404-21839992	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs6664097	H3K4me3	chr1:21834672-21839480	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs6664097	H3K79me2	chr1:21834395-21837677	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs6664097	H3K9ac	chr1:21834457-21839878	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs6664097	H3K9me1	chr1:21832579-21848617	K562	blood:Leukemia cell	wgEncodeBroadHistone
rs6664097	H4K20me1	chr1:17184307-25646596	K562	blood:Leukemia cell	wgEncodeBroadHistone
rs6664097	H3K4me2	chr1:21834391-21837118	NH-A	brain:astrocyte	wgEncodeBroadHistone

rs6664097	H4K20me1	chr1:21832971-21840272	NHDF-Ad	bronchial:Fibroblast	wgEncodeBroadHistone
rs6664097	H4K20me1	chr1:21828381-21848949	NHEK	skin:keratinocyte	wgEncodeBroadHistone
rs6664097	H4K20me1	chr1:21834416-21841922	NHLF	lung:Fibroblast	wgEncodeBroadHistone
rs6664097	H4K20me1	chr1:21830429-21875378	Osteobl	bone:Osteoblast	wgEncodeBroadHistone
rs6664097	H3K4me2	chr1:21834416-21839594	Osteobl	bone:Osteoblast	wgEncodeBroadHistone
rs1256342	H4K20me1	chr1:21852998-22050404	Dnd41	blood:T-lymphocyte; Leukemia	wgEncodeBroadHistone
rs1256342	H3K27ac	chr1:21858946-21882075	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs1256342	H3K4me1	chr1:21855989-21885122	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs1256342	H3K79me2	chr1:21827741-21886513	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs1256342	H4K20me1	chr1:21828171-22115109	H1-hESC	embryonic stem cell:embryonic stem cell	wgEncodeBroadHistone
rs1256342	H4K20me1	chr1:21836544-23901982	Hela-S3	cervix:carcinoma	wgEncodeBroadHistone
rs1256342	H3K27ac	chr1:21859830-21885748	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1256342	H3K27ac	chr1:21876086-21881777	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1256342	H3K36me3	chr1:21828979-21915960	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1256342	H3K4me1	chr1:21856365-21885706	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1256342	H3K4me1	chr1:21876232-21878188	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1256342	H3K4me2	chr1:21876368-21877578	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1256342	H3K79me2	chr1:21834943-21878854	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1256342	H3K9ac	chr1:21862560-21885410	HSMM	muscle:Myoblast	wgEncodeBroadHistone
rs1256342	H3K4me1	chr1:21826693-21927461	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1256342	H3K79me2	chr1:21869174-21878689	HSMMtube	muscle:Myotube	wgEncodeBroadHistone
rs1256342	H3K4me1	chr1:21876380-21878200	K562	blood:Leukemia cell	wgEncodeBroadHistone
rs1256342	H4K20me1	chr1:17184307-25646596	K562	blood:Leukemia cell	wgEncodeBroadHistone
rs1256342	H3K4me1	chr1:21876427-21877330	CD14+_RO01746	blood:Mononuclear Cell	wgEncodeBroadHistone
rs1256342	H3K9ac	chr1:21870065-21905328	NH-A	brain:astrocyte	wgEncodeBroadHistone
rs1256342	H3K4me1	chr1:21875753-21881643	Osteobl	bone:Osteoblast	wgEncodeBroadHistone

[1] SNP, single nucleotide polymorphism.

[2] Based on National Center for Biotechnology Information – Genome Reference Consortium Human genome build 37/human genome 19 assembly.

ONLINE SUPPORTING MATERIAL

SUPPLEMENTAL TABLE 10 Transcription factor binding sites that coincide with base pair positions of SNPs associated with plasma pyridoxal 5'-phosphate concentration in healthy Irish adults[1]

SNP	Transcrition factor	Location[2]	Cell line	Cell type	Data source
rs2275370	Rad21	chr1:21900378-21901669	HCT-116	colon:colorectal carcinoma	wgEncodeHaibTfbs
rs2275370	CTCF	chr1:21900364-21901087	A549	lung:Epithelial Cell	wgEncodeSydhTfbs
rs2275370	Max	chr1:21900405-21900437	HepG2	liver:carcinoma	wgEncodeSydhTfbs
rs2275370	CHD1	chr1:21900282-21901159	IMR90	lung:Fibroblast (fetal)	wgEncodeSydhTfbs
rs2275370	COREST	chr1:21900339-21900878	K562	blood:Leukemia cell	wgEncodeSydhTfbs
rs2275370	Znf143	chr1:21900349-21900853	K562	blood:Leukemia cell	wgEncodeSydhTfbs
rs2275370	CTCF	chr1:21899985-21901136	SK-N-SH	brain:Neuroblastoma	wgEncodeSydhTfbs
rs2275370	Rad21	chr1:21900103-21901304	SK-N-SH	brain:Neuroblastoma	wgEncodeSydhTfbs
rs2275370	SMC3	chr1:21900244-21901196	SK-N-SH	brain:Neuroblastoma	wgEncodeSydhTfbs
rs2275370	eGFP-JunD	chr1:21900332-21901174	K562	blood:Leukemia cell	wgEncodeUchicagoTfbs
rs1780318	Pol2	chr1:21895439-21895729	H1-hESC	embryonic stem cell	wgEncodeOpenChromChip
rs1256331	Pol2	chr1:21894952-21895122	H1-hESC	embryonic stem cell	wgEncodeOpenChromChip
rs1256331	Pol2	chr1:21895002-21895026	MCF-7	breast:adenocarcinoma	wgEncodeOpenChromChip
rs1256331	ZNF263	chr1:21894970-21895362	HEK293-T-REx	kidney: (embryo)	wgEncodeSydhTfbs
rs1256331	c-Fos	chr1:21894712-21895209	HUVEC	blood vessel:Endothelial Cell	wgEncodeSydhTfbs
rs1256331	COREST	chr1:21893570-21895197	IMR90	lung:Fibroblast (fetal)	wgEncodeSydhTfbs
rs1256331	c-Fos	chr1:21894875-21895084	MCF10A-Er-Src	breast:Epithelial Cell	wgEncodeSydhTfbs
rs1256331	c-Fos	chr1:21894812-21895097	MCF10A-Er-Src	breast:Epithelial Cell	wgEncodeSydhTfbs
rs1256331	c-Fos	chr1:21894808-21895115	MCF10A-Er-Src	breast:Epithelial Cell	wgEncodeSydhTfbs
rs1256331	c-Fos	chr1:21894884-21895013	MCF10A-Er-Src	breast:Epithelial Cell	wgEncodeSydhTfbs
rs1256331	c-Myc	chr1:21894858-21895043	MCF10A-Er-Src	breast:Epithelial Cell	wgEncodeSydhTfbs
rs6664097	USF-1	chr1:21834460-21834722	H1-hESC	embryonic stem cell	wgEncodeHaibTfbs
rs6664097	USF-1	chr1:21834469-21834753	K562	blood:Leukemia cell	wgEncodeHaibTfbs

rs6664097	USF2	chr1:21834496-21834703	Hela-S3	cervix:carcinoma	wgEncodeSydhTfbs
rs1256342	CEBPB	chr1:21876492-21876774	K562	blood:Leukemia cell	wgEncodeSydhTfbs
rs1256342	Pol2	chr1:21873788-21877632	K562	blood:Leukemia cell	wgEncodeSydhTfbs
rs1256342	RFX5	chr1:21876446-21876631	K562	blood:Leukemia cell	wgEncodeSydhTfbs

[1] SNP, single nucleotide polymorphism.

[2] Based on National Center for Biotechnology Information – Genome Reference Consortium Human genome build 37/human genome 19 assembly.

SUPPLEMENTAL TABLE 11 Regions of RNA polymerase II-chromatin interaction that coincide with base pair positions of SNPs associated with plasma pyridoxal 5’-phosphate concentration in healthy Irish adults[1]

SNP	RNA polymerase II - Chromatin interaction regions[2]	Cell line	Cell type	Data source
rs1772719	chr1:21895568..21902242 - chr1:21903321..21907610	K562	blood:Leukemia cell	wgEncodeGisChiaPet
rs2275370	chr1:21835335..21836204 - chr1:21900257..21901466	K562	blood:Leukemia cell	wgEncodeGisChiaPet
rs1772720	chr1:21895568..21902242 - chr1:21903321..21907610	K562	blood:Leukemia cell	wgEncodeGisChiaPet
rs9628653	chr1:21834816..21836716 - chr1:21848420..21850010	K562	blood:Leukemia cell	wgEncodeGisChiaPet
rs1256342	chr1:21875110..21878053 - chr1:21879038..21881539	K562	blood:Leukemia cell	wgEncodeGisChiaPet

[1] SNP, single nucleotide polymorphism.

[2] Based on National Center for Biotechnology Information – Genome Reference Consortium Human genome build 37/human genome 19 assembly.

SUPPLEMENTAL TABLE 12 SNPs associated with plasma pyridoxal 5'-phosphate concentration in healthy Irish adults and that are located in a binding site for an RNA binding protein encoded by the *PABPC1* gene[1]

SNP	Location[2]	Cell line	Cell type	Data source
rs1256335	chr1:21835858-21904905	GM12878	Blood:B-lymphocyte	wgEncodeSunyAlbanyGeneSt
rs1772719	chr1:21835858-21904905	GM12878	Blood:B-lymphocyte	wgEncodeSunyAlbanyGeneSt
rs2275370	chr1:21835858-21904905	GM12878	Blood:B-lymphocyte	wgEncodeSunyAlbanyGeneSt
rs4654748	chr1:21835858-21904905	GM12878	Blood:B-lymphocyte	wgEncodeSunyAlbanyGeneSt
rs12145027	chr1:21835858-21904905	GM12878	Blood:B-lymphocyte	wgEncodeSunyAlbanyGeneSt
rs1780318	chr1:21835858-21904905	GM12878	Blood:B-lymphocyte	wgEncodeSunyAlbanyGeneSt
rs1256331	chr1:21835858-21904905	GM12878	Blood:B-lymphocyte	wgEncodeSunyAlbanyGeneSt
rs1256341	chr1:21835858-21904905	GM12878	Blood:B-lymphocyte	wgEncodeSunyAlbanyGeneSt
rs1780315	chr1:21835858-21904905	GM12878	Blood:B-lymphocyte	wgEncodeSunyAlbanyGeneSt
rs6703976	chr1:21835858-21904905	GM12878	Blood:B-lymphocyte	wgEncodeSunyAlbanyGeneSt
rs1780329	chr1:21835858-21904905	GM12878	Blood:B-lymphocyte	wgEncodeSunyAlbanyGeneSt
rs9628653	chr1:21835858-21904905	GM12878	Blood:B-lymphocyte	wgEncodeSunyAlbanyGeneSt
rs869180	chr1:21835858-21904905	GM12878	Blood:B-lymphocyte	wgEncodeSunyAlbanyGeneSt
rs1256342	chr1:21835858-21904905	GM12878	Blood:B-lymphocyte	wgEncodeSunyAlbanyGeneSt
rs7536545	chr1:21835858-21904905	GM12878	Blood:B-lymphocyte	wgEncodeSunyAlbanyGeneSt
rs4021228	chr1:21835858-21904905	GM12878	Blood:B-lymphocyte	wgEncodeSunyAlbanyGeneSt

[1] SNP, single nucleotide polymorphism; *PABPC1*, poly(A) binding protein, cytoplasmic 1.

[2] Based on National Center for Biotechnology Information – Genome Reference Consortium Human genome build 37/human genome 19 assembly.