

Elevated homocysteine, glutathione and cysteinylglycine concentrations in patients homozygous for the Chuvash polycythemia VHL mutation

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Supplemental Tables 1-2

Table 1. Clinical characteristics of participants according to VHL 598C>T status.*

	VHL wildtype (N=37)	VHL 598C>T heterozygotes (N=4)	VHL 598C>T homozygotes (N=3)	P** Overall	P** Homozygote vs. wildtype
Clinical evaluation					
Age (years)	33 (3)	9 (9)	29 (3)	0.026	0.7
Female sex (no. and %)	21 (57%)	2 (50%)	20 (59%)	0.9	0.9
Phlebotomy therapy (no. and %)	0 (0%)	0 (0%)	14 (41%)	<0.001	<0.001
Mean blood pressure (mm Hg) ¹	90 (2)	84 (5)	79 (2)	0.014	0.005
Body mass index (kg/m ²) ²	20.4 (0.5)	19.5 (1.4)	19.6 (0.5)	0.5	0.3
Hemoglobin (g/dL)	13.6 (0.4)	14.5 (1.2)	18.5 (0.4)	<0.001	<0.001
Folate (ng/ml)	6.7 (0.5) ^a	3.8 (1.5)	4.2 (0.5)	0.002	0.003
Vitamin B12 (pg/mL)	408 (21)	414 (64)	369 (22)	0.4	0.6
GGT (U/L) ³	15 (14-17)	16 (13-20)	23 (21-25)	0.003	0.001
Plasma thiol concentrations					
Homocysteine (uM) ⁴	16.6 (0.9)	18.6 (2.7)	23.2 (0.9)	<0.001	<0.001
Cysteine (uM) ⁵	189 (5)	179 (13)	161 (5)	0.008	0.002
Glutathione (uM) ²	13.3 (1.2)	7.9 (3.8)	20.1 (1.3)	<0.001	<0.001
Cysteinylglycine (uM) ⁶	63.2 (3.1)	73.4 (8.9)	85.9 (3.3)	<0.001	<0.001

*Values are mean (SE) unless otherwise indicated. **Two-sided P values; ANOVA for continuous variables and Pearson chi square for categorical variables.

¹Geometric mean and SE range. ¹ANOVA with adjustment for age, hemoglobin, homocysteine and glutathione levels ²ANOVA with adjustment for age ³ANOVA with adjustment for age, sex, alcohol consumption and glutathione level ⁴ANOVA with adjustment for vitamin B12 level ⁵ANOVA with adjustment for homocysteine and cysteinylglycine levels; ⁶ANOVA with adjustment for glutathione and gamma glutamyl transpeptidase levels.

Table 2. Multivariate linear regression analysis of mean blood pressure.

Independent covariate	Estimated change in mean blood pressure (mm Hg)	95% confidence interval	P
VHL598C>T (homozygote vs. normal)	-8.8	-2.4 - -15.2	0.008
Homocysteine (increase of 6.6 uM)*	+2.5	+0.1 - +4.9	0.039
Glutathione (increase of 6.8 uM)*	-2.5	-0.5 - -4.6	0.015
Age (decrease of 4 years)*	-1.2	-0.6 - -1.8	<0.001
Hemoglobin (increase of 4.9 g/dL)*	+5.9	+1.3 - +10.2	0.013

*Average change between participants with normal alleles and VHL598C>T homozygotes in the present study.

Figure 1

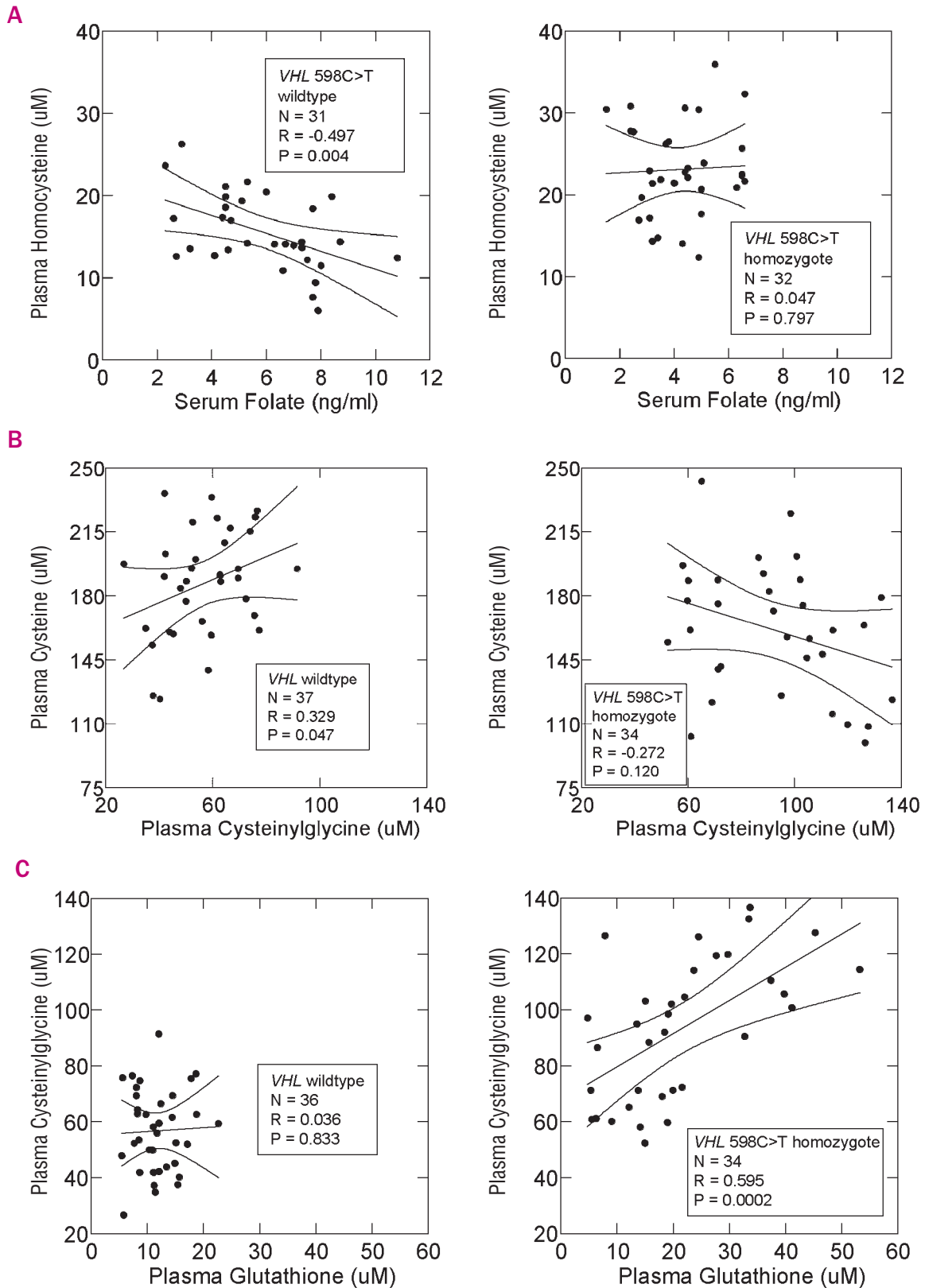


Figure 1. (A) Relationship between plasma homocysteine and serum folate levels in participants with serum vitamin B12 concentration >200 pg/ml. Plasma homocysteine concentrations have the expected inverse correlation with serum folate levels in participants with normal *VHL* alleles but not *VHL* 598C>T homozygotes, in whom they tend to be elevated with the entire spectrum of serum folate concentrations. (B) Plasma cysteine concentrations correlate positively with plasma cysteinylglycine in participants with *VHL* wildtype alleles and negatively in *VHL* 598C>T homozygotes. (C) Plasma cysteinylglycine concentrations have a significant positive correlation with plasma glutathione levels in *VHL* 598C>T homozygotes but not participants with normal *VHL* alleles. c. Positive linear correlation of plasma concentrations of homocysteine and cysteinylglycine in participants with normal *VHL* alleles and *VHL* 598C>T homozygotes.