

**Folate/homocysteine metabolism and lung cancer risk among smokers**

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**Supporting information, S2 Table****S2 Table. Median (interquartile ranges), N, of serum folate, RBC folate, corrected RBC folate and homocysteine defined by genotypes in C1 metabolism genes.**

Two outlying extreme values were deleted from the analyses: serum folate = 800.5; 565.4 nmol/l.

Variable		Lung cancer cases*	Controls*	P <sub>wilcoxon</sub>
<b>MTHFR c.665C&gt;T</b>				
Serum folates nmol/L	CC	18.8 ( 14.3-24.7), 65	17.7 (13.4-23.4), 157	0.383
	CT	20.4 ( 13.6-24.0), 55	17.6 (12.9-22.7), 198	0.227
	TT	16.75 ( 10.3-20.6), 12	16.1 (11.1-22.0), 39	0.885
	P <sub>Kruskal-Wallis</sub>		0.505	0.591
RBC folates nmol/L	CC	533.3 ( 436.1-721.9), 47	508.35 (363.3-697.9), 110	0.538
	CT	563.3 ( 378.75-674.8), 36	496.4 (382.7-638.1), 147	0.463
	TT	627.35 ( 349.6-972.1), 10	607.1 (482.6-852.2), 22	0.889
	P <sub>Kruskal-Wallis</sub>		0.714	0.108
RBC folates corrected nmol/L	CC	512.6 (401.4-688.0), 47	473.05 (345.6-680.0), 110	0.582
	CT	527.9 (358.5-634.8), 36	470.95 (362.3-602.0), 146	0.454
	TT	609.55 (335.2-942.0), 10	594.95 (457.7-827.7), 22	0.889
	P <sub>Kruskal-Wallis</sub>		0.624	0.082
Homocysteine μmol/L	CC	15.2 (11.4-18.6), 63	14.4 (11.6-18.5), 157	0.954
	CT	15.55 (11.4-18.3), 54	14.8 (12.2-18.7), 199	0.488
	TT	16.75 (14.85-20.5), 12	15.3 (12.3-18.9), 39	0.297
	P <sub>Kruskal-Wallis</sub>		0.365	0.838
<b>MTHFR c.1268A&gt;C</b>				
Serum folates nmol/L	AA	19.7 (14.3-23.8), 69	17.7 (13.25-23.9), 192	0.606
	AC	18.1 (14.3-25.4), 49	16.5 (12.7-22.4), 169	0.174
	CC	19.15 (14.1-28.8), 14	19.9 (12.5-23.4), 33	0.816
	P <sub>Kruskal-Wallis</sub>		0.935	0.475
RBC folates nmol/L	AA	539.5 (372.3-756.7), 51	516.75 (388.4-670.4), 138	0.487
	AC	560.4 (411.6-661.4), 31	481.1 (358.5-642.2), 115	0.345
	CC	566.4 (442-791.3), 11	672.2 (468.9-831.1), 26	0.332
	P <sub>Kruskal-Wallis</sub>		0.746	0.006
RBC folates corrected nmol/L	AA	515.2 (343.5-729.2), 51	477.6 (367.7-633.3), 137	0.480
	AC	531.1 (378.6-622.8), 31	446.6 (345.5-601.8), 115	0.373
	CC	541.8 (407.6-764.1), 11	642.3 (451.8-794.8), 26	0.349
	P <sub>Kruskal-Wallis</sub>		0.762	0.005
Homocysteine μmol/L	AA	15.88 (11.7-19.6), 67	15.0 (12.0-18.8), 193	0.602
	AC	15.4 (11.2-17.25), 48	14.6 (12.1-18.75), 168	0.328
	CC	14.85 (11.3-18.6), 14	14.05 (11.3-16.0), 34	0.602
	P <sub>Kruskal-Wallis</sub>		0.443	0.187
<b>CBS c.844_845ins68</b>				
Serum folates nmol/L	DD	19.15 (14.3-24.3), 110	17.5 (12.9-23.1), 341	0.248
	I allele	19.85 (13.8-25.6), 22	17.0 (14.5-22.4), 53	0.503
	P <sub>Kruskal-Wallis</sub>		0.710	0.904
RBC folates nmol/L	DD	554.0 (395.7-711.25), 80	506.5 (383.3-677.4), 249	0.512
	I allele	560.4 (457.6-773.1), 13	508.7 (398.9-660.4), 30	0.488
	P <sub>Kruskal-Wallis</sub>		0.603	0.979

RBC folates corrected nmol/L	DD	520.55 (370.2-677.1), 80	474.6 (364.65-645.8), 248	0.544
	I allele	534.7 (441.5-731.7), 13	478.5 (376.3-633.3), 30	0.456
	$P_{\text{Kruskal-Wallis}}$		0.580	0.977
Homocysteine $\mu\text{mol/L}$	DD	16.0 (11.8-18.7), 107	14.8 (12.1-18.7), 342	0.971
	I allele	14.5 (10.2-18.3), 22	12.8 (11.7-17.7), 53	0.991
	$P_{\text{Kruskal-Wallis}}$		0.338	0.057
<b>SHMT1 c.1420C&gt;T</b>				
Serum folates nmol/L	CC	20.4 (13.6-24.3), 53	17.2 (12.2-22.4), 164	0.203
	CT	18.6 (14.3-24.5), 61	17.7 (13.8-23.1), 185	0.649
	TT	20.05 (15.6-21.5), 18	15.6 (12.2-24.3), 45	0.589
	$P_{\text{Kruskal-Wallis}}$		0.966	0.499
RBC folates nmol/L	CC	566.2 (372.3-733.7), 37	483.3 (383.5-643.3), 119	0.217
	CT	560.4 (401.5-675.2), 49	532.2 (387.25-741.55), 124	0.721
	TT	533.3 (443.4-790.9), 7	511.95 (356.05-669.6), 36	0.551
	$P_{\text{Kruskal-Wallis}}$		0.859	0.349
RBC folates corrected nmol/L	CC	524.7 (343.5-705.9), 37	458.4 (367.7-624.6), 119	0.261
	CT	531.1 (378.4-653.6), 49	507.9 (370.5-699.6), 123	0.727
	TT	512.6 (415.1-752.0), 7	473.8 (336.4-635.05), 36	0.529
	$P_{\text{Kruskal-Wallis}}$		0.827	0.403
Homocysteine $\mu\text{mol/L}$	CC	14.2 (10.3-17.8), 53	14.7 (11.8-18.65), 164	0.263
	CT	16.6 (13.6-18.7), 58	14.7 (12.2-18.3), 185	0.188
	TT	14.95 (11.2-19.6), 18	14.65 (12.4-18.9), 46	0.565
	$P_{\text{Kruskal-Wallis}}$	14.2 (10.3-17.8), 53		0.902
<b>MTHFD1 c.1958G&gt;A</b>				
Serum folates nmol/L	GG	19.6 (14.5-24.3), 30	18.9 (13.1-23.8), 82	0.679
	GA	18.4 (13.6-24.7), 63	17.5 (12.9-22.9), 182	0.657
	AA	20.4 (14.3-24.7), 39	16.65 (12.0-22.4), 130	0.195
	$P_{\text{Kruskal-Wallis}}$		0.790	0.439
RBC folates nmol/L	GG	582.3 (507.05-808.0), 24	524.4 (391.2-741.4), 59	0.136
	GA	522.35 (362.85-712.65), 44	508.35 (382.65-636.65), 124	0.533
	AA	523.6 (371.8-656.0), 25	497.6 (383.0-728.35), 96	0.638
	$P_{\text{Kruskal-Wallis}}$		0.205	0.624
RBC folates corrected nmol/L	GG	556.75 (475.3-776.75), 24	486.1 (370.5-701.2), 59	0.141
	GA	502.5 (340.95-677.1), 44	476.05 (364.3-599.55), 124	0.560
	AA	501.6 (328.5-616.3), 25	470.9 (362.3-707.6), 95	0.610
	$P_{\text{Kruskal-Wallis}}$		0.204	0.648
Homocysteine $\mu\text{mol/L}$	GG	16.6 (11.2-18.7), 29	14.7 (12.5-19.6), 83	0.974
	GA	15.8 (11.7-18.6), 61	14.9 (12.0-18.7), 181	0.881
	AA	14.8 (11.4-18.1), 39	14.4 (11.6-18.0), 131	0.979
	$P_{\text{Kruskal-Wallis}}$		0.746	0.504
<b>MTRR c.66A&gt;G</b>				
Serum folates nmol/L	GG	20.4 (15.9-24.3), 50	18.1 (12.7-23.1), 119	0.154
	GA	18.8 (13.6-22.9), 58	17.6 (13.1-23.4), 190	0.792
	AA	19.6 (13.6-26.55), 24	16.3 (12.5-22.0), 85	0.226
	$P_{\text{Kruskal-Wallis}}$		0.337	0.593
RBC folates nmol/L	GG	533.3 (372.3-702.6), 35	462 (333.8-655.1), 81	0.314
	GA	579.5 (442.0-733.7), 39	513.6 (421-667.0), 134	0.383
	AA	527.5 (371.8-755.0), 19	559.4 (386.65-736.45), 64	0.884
	$P_{\text{Kruskal-Wallis}}$		0.707	0.205

RBC folates corrected nmol/L	GG	508.8 (343.5-676.9), 35	441.0 (319.4-621.9), 81	0.304
	GA	565.5 (405.7-692.7), 39	482.3 (389.0-636.6), 134	0.438
	AA	515.2 (324.7-722.2), 19	527.3 (362.3-699.1), 63	0.965
	P <sub>Kruskal-Wallis</sub>		0.694	0.194
Homocysteine μmol/L	GG	15.4 (11.9-19.65), 48	14.9 (11.8-18.7), 118	0.909
	GA	15.6 (11.4-18.3), 57	14.7 (12.2-18.7), 190	0.618
	AA	16.2 (10.55-18.75), 24	14.2 (12.0-17.7), 87	0.821
	P <sub>Kruskal-Wallis</sub>		0.870	0.822
MTR c.2756A>G				
Serum folates nmol/L	AA	19.0 (14.1-23.6), 91	18.1 (13.4-23.1), 243	0.765
	AG	19.85 (14.3-25.85), 36	16.5 (12.0-23.1), 133	0.154
	GG	24.0 (14.7-25.6), 5	14.95 (12.2-20.4), 18	0.526
	P <sub>Kruskal-Wallis</sub>		0.669	0.253
RBC folates nmol/L	AA	539.5 (389.9-675.2), 65	505.6 (388.4-672.2), 174	0.482
	AG	566.2 (428.5-719.9), 25	517.4 (375.4-725.9), 93	0.730
	GG	745.8 (354.9-755), 3	475.5 (374.5-588.2), 12	0.536
	P <sub>Kruskal-Wallis</sub>		0.811	0.822
RBC folates corrected nmol/L	AA	515.2 (362-653.6), 65	474.4 (370.8-633.5), 173	0.453
	AG	534.7 (389.3-684.4), 25	497.5 (359.8-699.6), 93	0.782
	GG	688.0 (314.5-722.2), 3	434.55 (360.6-566.65), 12	0.633
	P <sub>Kruskal-Wallis</sub>		0.891	0.754
Homocysteine μmol/L	AA	15.7 (11.2-18.3), 89	14.7 (12-18.6), 245	0.538
	AG	15.88 (12.5-19.2), 35	14.5 (11.85-18.5), 132	0.426
	GG	14.8 (13.7-19.8), 5	16.45 (12.5-18.7), 18	0.857
	P <sub>Kruskal-Wallis</sub>		0.769	0.655
TYMS 3'UTR ins/del				
Serum folates nmol/L	II	19.7 (13.6-24), 67	18.1 (13.8-23.4), 179	0.789
	ID	18.1 (14.3-24.3), 61	17.1 (12.9-23.1), 182	0.345
	DD	22.45 (17.55-25.2), 4	13.8 (11.1-17.7), 33	0.078
	P <sub>Kruskal-Wallis</sub>		0.744	0.032
RBC folates nmol/L	II	602.0 (444.2-756.7), 46	502.05 (372.3-727.5), 126	0.111
	ID	491.55 (372.05-632.5), 44	515.4 (391.6-670.0), 125	0.441
	DD	411.6 (259.8-1446.6), 3	454.2 (364.55-580.45), 28	0.875
	P <sub>Kruskal-Wallis</sub>		0.132	0.372
RBC folates corrected nmol/L	II	572.4 (405.7-729.2), 46	473.45 (352.3-680.0), 126	0.115
	ID	468.85 (340.95-605.5), 44	486.55 (372.15-634.5), 124	0.456
	DD	378.6 (242.2-1406.7), 3	425.8 (340.35-560.25), 28	0.875
	P <sub>Kruskal-Wallis</sub>		0.124	0.428
Homocysteine μmol/L	II	14.8 (11.4-17.5), 65	15.5 (12.7-19.2), 179	0.050
	ID	16.25 (11.95-19.5), 60	13.6 (11.6-18.3), 183	0.173
	DD	18.65 (17.55-20.05), 4	14.7 (12.0-17.7), 33	0.056
	P <sub>Kruskal-Wallis</sub>		0.060	0.042
TYMS 5'UTR 2R/3R				
Serum folates nmol/L	2R/2R	20.5 (15.15-25.15), 32	18.5 (14.4-22.65), 72	0.317
	2R/3R	18.6 (13.8-24.3), 66	17.0 (12.5-23.1), 205	0.504
	3R/3R	19.05 (14.5-24.0), 34	17.2 (12.7-22.9), 117	0.477
	P <sub>Kruskal-Wallis</sub>		0.522	0.400
RBC folates nmol/L	2R/2R	570.4 (395.5-748.75), 20	512.6 (385.3-684.2), 47	0.709
	2R/3R	567.0 (411.6-733.7), 45	541.5 (391.6-689.2), 146	0.526
	3R/3R	521.85 (351.55-671.7), 28	454.55 (358.5-619.7), 86	0.538
	P <sub>Kruskal-Wallis</sub>		0.412	0.069

RBC folates corrected nmol/L	2R/2R	535.8 (368.3-712.2), 20	477.0 (367.0-657.7), 47	0.737
	2R/3R	541.8 (382.4-688.0), 45	517.85 (371.5-658.7), 146	0.548
	3R/3R	494.65 (326.6-628.8), 28	430.1 (343.6-578.4), 85	0.552
	P <sub>Kruskal-Wallis</sub>		0.396	0.049
Homocysteine μmol/L	2R/2R	14.8 (11.2-18.1), 31	15.95 (12.15-20.2), 72	0.222
	2R/3R	15.55 (11.95-18.7), 64	14.3 (11.75-18.15), 204	0.415
	3R/3R	16.3 (11.4-19.4), 34	14.7 (12.1-18.8), 119	0.949
	P <sub>Kruskal-Wallis</sub>		0.705	0.103
DHFR c.86+60_78ins22				
Serum folates nmol/L	II	18.5 (13.95-22.9), 36	17.7 (13.1-23.6), 119	0.909
	ID	20.4 (14.4-25.6), 72	17.2 (12.6-22.9), 196	0.042
	DD	18.0 (12.1-23.45), 24	17.5 (12.7-22.7), 79	0.827
	P <sub>Kruskal-Wallis</sub>		0.222	0.747
RBC folates nmol/L	II	466.5 (353.2-656.0), 31	512.8 (429.3-670.0), 86	0.194
	ID	590.9 (457.25-766.15), 48	506.3 (354.9-688.85), 136	0.068
	DD	544.9 (372.3-682.0), 14	492.2 (382.7-616.7), 57	0.823
	P <sub>Kruskal-Wallis</sub>		0.055	0.661
RBC folates corrected nmol/L	II	441.5 (328.5-622.8), 31	486.55 (398.3-628.1), 86	0.171
	ID	563.5 (439.55-729.1), 48	469.1 (332.9-654.5), 135	0.065
	DD	513.15 (343.5-641.3), 14	464.0 (361.4-595.0), 57	0.868
	P <sub>Kruskal-Wallis</sub>		0.066	0.633
Homocysteine μmol/L	II	16.4 (11.9-17.8), 35	14.6 (12.0-18.5), 118	0.434
	ID	14.7 (11.2-18.3), 70	14.5 (12.4-18.7), 198	0.366
	DD	15.84 (12.3-19.9), 24	15.0 (11.7-18.6), 79	0.728
	P <sub>Kruskal-Wallis</sub>		0.503	0.907
TCN2 c.776C>G				
Serum folates nmol/L	CC	19.3 (13.8-23.8), 39	17.0 (12.7-23.1), 124	0.450
	CG	19.5 (14.75-24.7), 64	17.8 (12.9-23.4), 182	0.273
	GG	18.1 (13.6-24.0), 29	17.35 (13.4-22.1), 88	0.820
	P <sub>Kruskal-Wallis</sub>		0.638	0.829
RBC folates nmol/L	CC	623.35 (446.5-692.3), 24	513.7 (381.8-670.4), 89	0.188
	CG	548.3 (419.5-752.4), 45	494.5 (392.3-684.7), 129	0.470
	GG	491.55 (339.7-722.3), 24	510.2 (346.4-652.1), 61	0.643
	P <sub>Kruskal-Wallis</sub>		0.369	0.972
RBC folates corrected nmol/L	CC	596.15 (417.95-665.25), 24	478.5 (359.1-642.5), 89	0.192
	CG	516.4 (382.4-729.2), 45	460.2 (370.75-643.25), 128	0.510
	GG	468.85 (309.9-685.0), 24	472.5 (332.2-614.7), 61	0.588
	P <sub>Kruskal-Wallis</sub>		0.342	0.955
Homocysteine μmol/L	CC	13.75 (10.2-16.7), 38	14.2 (12.0-17.7), 125	0.093
	CG	16.5 (12-18.8), 62	14.7 (11.7-18.9), 182	0.516
	GG	16.4 (13.7-20.6), 29	15.45 (13.1-19.45), 88	0.611
	P <sub>Kruskal-Wallis</sub>		0.014	0.153
SLC19A1 c.80G>A				
Serum folates nmol/L	GG	18.1 (12.7-23.8), 35	16.4 (12.9-23.1), 114	0.941
	GA	19.15 (14.4-23.8), 68	17.7 (12.7-23.4), 190	0.483
	AA	22.4 (15.6-25.4), 29	17.7 (13.4-22.2), 90	0.035
	P <sub>Kruskal-Wallis</sub>		0.194	0.933
RBC folates nmol/L	GG	572.4 (434-733.25), 28	511.85 (388.2-755.45), 80	0.512
	GA	546.85 (396.25-692.3), 44	515.2 (387.05-688.45), 140	0.924
	AA	517.2 (371.8-756.7), 21	482.6 (372.3-639.7), 59	0.330
	P <sub>Kruskal-Wallis</sub>		0.726	0.331

RBC folates corrected nmol/L	GG	539.3 (409.95-708.85), 28	484.2 (371.5-705.6), 79	0.485
	GA	519.95 (370.3-659.1), 44	488.4 (367.35-656.6), 140	0.970
	AA	481.9 (332.9-726.5), 21	452.9 (347.5-621.5), 59	0.370
	$P_{\text{Kruskal-Wallis}}$		0.739	0.320
Homocysteine $\mu\text{mol/L}$	GG	15.25 (12.0-18.3), 34	14.45 (12.0-18.7), 114	0.897
	GA	16.3 (11.2-18.7), 67	14.7 (11.9-18.4), 191	0.925
	AA	15.45 (11.85-16.9), 28	15.55 (12.5-18.9), 90	0.688
	$P_{\text{Kruskal-Wallis}}$		0.957	0.857