

Supplemental material for “**Environmental arsenic exposure and DNA methylation of the tumor suppressor gene *p16* and the DNA repair gene *MLH1*; effect of arsenic metabolism and genotype**”

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Supplemental Table 1. Spearman's rank correlations for urinary arsenic concentration and different *p16* and *MLH1* methylation positions (N = 202)^a

	<i>p16</i>							<i>MLH1</i>			
	P1	P2	P3	P4	P5	P6	P7	P1	P2	P3	P4
Arsenic ^b	0.21**	0.19**	0.17*	0.16*	0.19**	0.20**	0.16*	0.22**	0.17*	0.13	0.21**
<i>p16</i> P1 (position 1)		0.82**	0.81**	0.83**	0.82**	0.79**	0.76**	0.44**	0.44**	0.62**	0.50**
<i>p16</i> P2			0.90**	0.90**	0.90**	0.86**	0.85**	0.55**	0.52**	0.73**	0.55**
<i>p16</i> P3				0.89**	0.85**	0.80**	0.79**	0.56**	0.53**	0.72**	0.58**
<i>p16</i> P4					0.84**	0.83**	0.84**	0.53**	0.55**	0.71**	0.59**
<i>p16</i> P5						0.85**	0.82**	0.60**	0.42**	0.74**	0.49**
<i>p16</i> P6							0.82**	0.54**	0.50**	0.73**	0.47**
<i>p16</i> P7								0.57**	0.42**	0.73**	0.47**
<i>MLH1</i> P1									0.32**	0.70**	0.33**
<i>MLH1</i> P2										0.43**	0.74**
<i>MLH1</i> P3											0.46**

^a**P* <0.05; ***P* <0.01

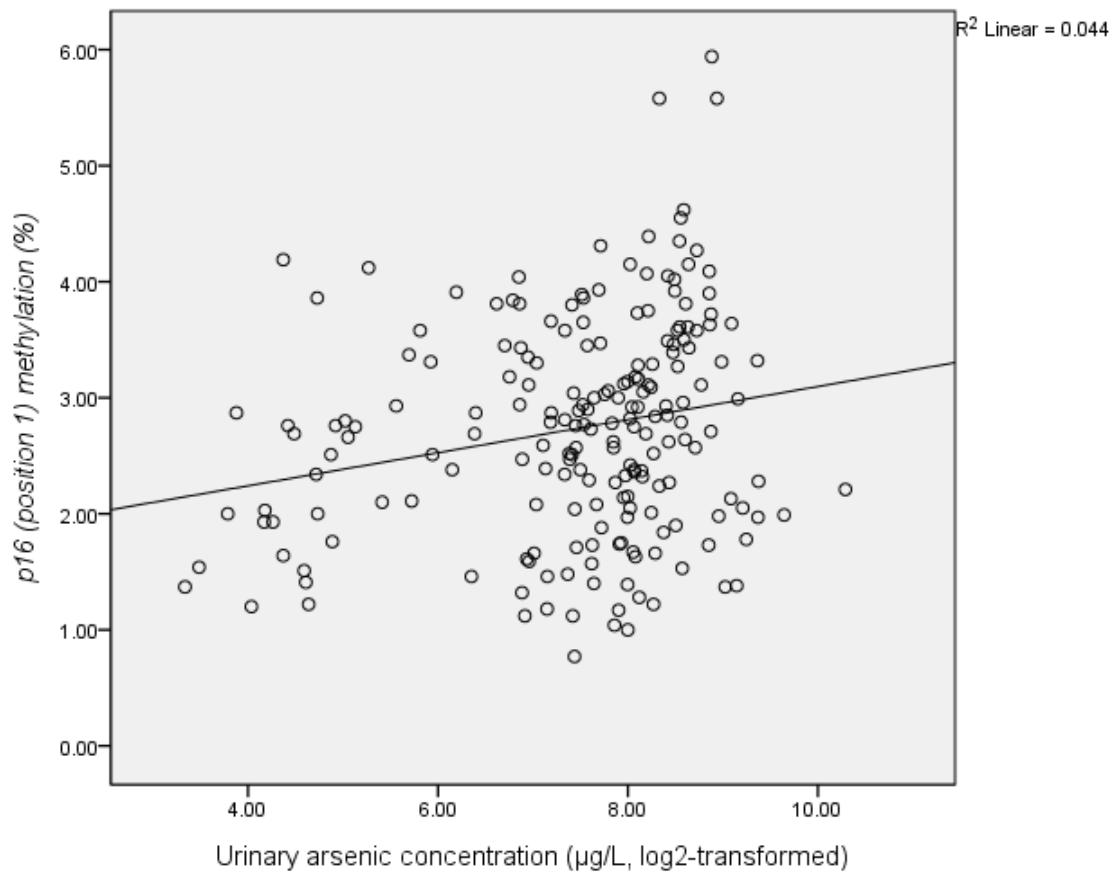
^bUrinary arsenic concentration adjusted to specific gravity (1.015 g/ml).

Supplemental Table 2: Associations between concentrations of urinary arsenic (\log_2 -transformed) and fractions (%) of urinary arsenic metabolites and degree of *LINE1* methylation.

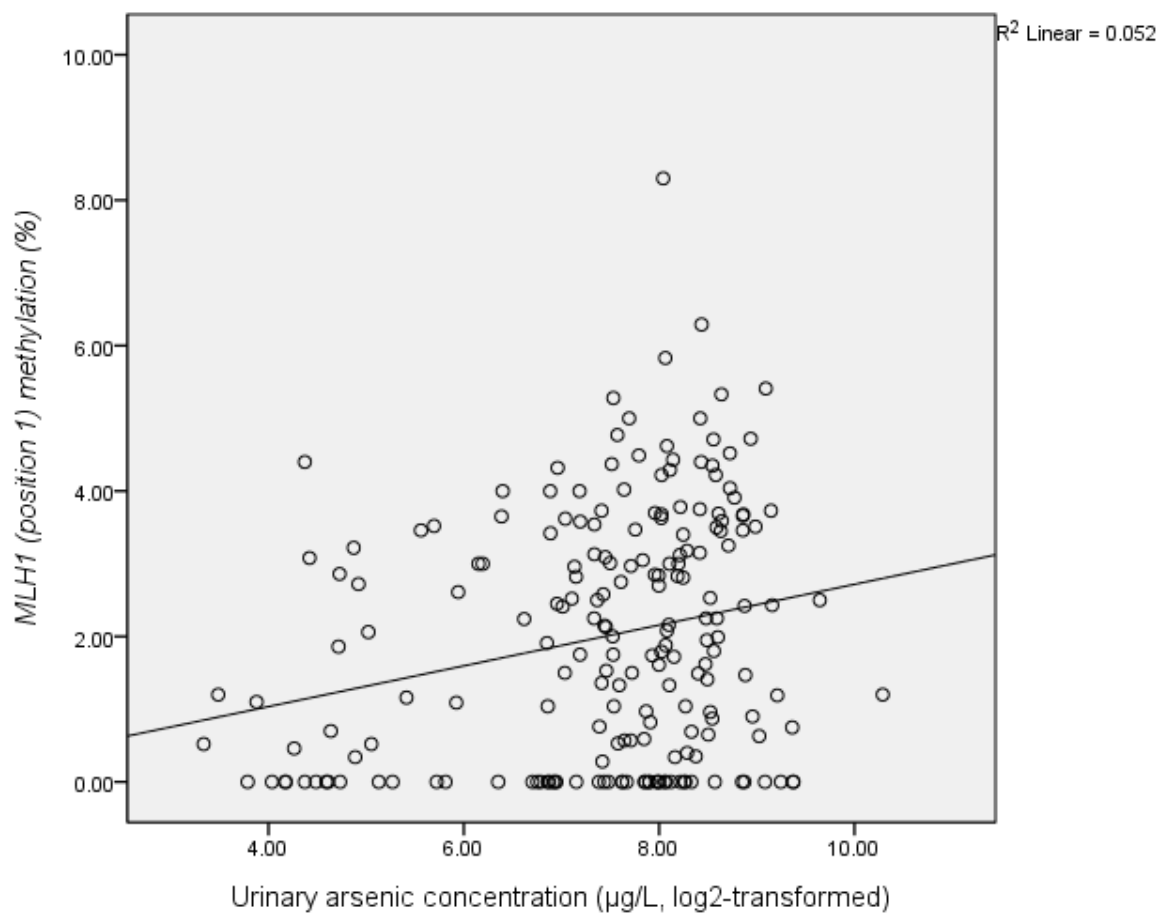
Predictor		β_1 (95% CI)	p-value
Urinary arsenic	Unadjusted ^a	0.094 (-0.082 to 0.27)	0.30
	Model 1	0.12 (-0.059 to 0.30)	0.19
	Model 2	0.14 (-0.039 to 0.33)	0.12
Inorganic arsenic (%)	Analysis 1 ^b	-0.0075 (-0.046 to 0.031)	0.70
	Analysis 2	-0.016 (-0.055 to 0.022)	0.41
MMA (%)	Analysis 1	0.023 (-0.053 to 0.099)	0.56
	Analysis 2	0.0088 (-0.068 to 0.086)	0.82
DMA (%)	Analysis 1	0.0012 (-0.031 to 0.033)	0.94
	Analysis 2	0.010 (-0.023 to 0.043)	0.54

^aUnadjusted model (N=202): Methylation (%) = $\alpha_1 + \beta_1$ arsenic concentrations (\log_2 -transformed); Model 1: model adjusted for age and coca chewing; Model 2: model with additional adjustments for cadmium in urine (\log_2 -transformed) and selenium and zinc in blood.

^bAnalysis 1 (N=202): Methylation (%) = $\alpha_1 + \beta_1$ fraction of arsenic metabolite + β_2 arsenic concentrations (\log_2 -transformed); Analysis 2: model adjusted for age and coca chewing.



Supplemental Figure 1: Scatter plot of the association between the degree of *p16* methylation (%) and urinary arsenic concentration (µg/L, log₂-transformed) ($\beta = 0.14$; $p = 0.0028$).



Supplemental Figure 2: Scatter plot of the association between the degree of *MLH1* methylation (%) and urinary arsenic concentration (µg/L, log₂-transformed) ($\beta = 0.28$; $p = 0.0011$).