DOI: 10.1289/EHP6263

Note to readers with disabilities: *EHP* strives to ensure that all journal content is accessible to all readers. However, some figures and Supplemental Material published in *EHP* articles may not conform to 508 standards due to the complexity of the information being presented. If you need assistance accessing journal content, please contact ehp508@niehs.nih.gov. Our staff will work with you to assess and meet your accessibility needs within 3 working days.

Supplemental Material

Locus-Specific Differential DNA Methylation and Urinary Arsenic: An Epigenome-Wide Association Study in Blood among Adults with Low-to-Moderate Arsenic Exposure

Anne K. Bozack, Arce Domingo-Relloso, Karin Haack, Mary V. Gamble, Maria Tellez-Plaza, Jason G. Umans, Lyle G. Best, Joseph Yracheta, Matthew O. Gribble, Andres Cardenas, Kevin A. Francesconi, Walter Goessler, Wan-Yee Tang, M. Daniele Fallin, Shelley A. Cole, and Ana Navas-Acien

Table of Contents

- **Table S1.** Studies identified reporting the association between As exposure and DNA methylation measured using the 450K and 850K microarrays and included in the lookup approach.
- **Table S2.** Descriptive characteristics for eligible participants and participants for DNA methylation analysis.
- **Table S3.** Linear models for the association between ln(total urinary arsenic levels) and imputed cell type proportions.
- **Table S4.** Differentially methylated CpG sites associated with ln(total urinary arsenic levels) at $P_{\text{FDR}} < 0.05$, and effects sizes and p-values stratified by sex.
- **Table S5.** Differentially methylated CpG sites associated with ln(total urinary arsenic concentration) at $P_{\text{FDR}} < 0.05$, and effects sizes and *p*-values stratified by smoking status.
- **Table S6.** Differentially methylated CpG sites associated with ln(total urinary arsenic concentration) at $P_{\text{FDR}} < 0.05$, and effects sizes and p-values stratified by study center.
- **Table S7.** Differentially methylated CpG sites associated with ln(total urinary arsenic levels) at $P_{\rm FDR} < 0.05$, and effects sizes and *p*-values stratified by diabetes status.

Table S8. Results of a linear model for the association between urinary As levels and M-values of cg14595618, annotated to HK1, including the interaction term ln(total urinary As) × diabetes status and adjusted age, sex, BMI, smoking status, education, study center (Arizona, Oklahoma, North and South Dakota), estimated glomerular filtration rate, and cell type proportion estimates.

Table S9. Differentially methylated CpG sites associated with ln(total urinary arsenic levels) at at $P_{\rm FDR} < 0.05$ in our primary analyses, and results from sensitivity analyses performed on probetype normalized data.

Table S10. Differentially methylated CpG sites associated with ln(total urinary arsenic levels) at at $P_{\rm FDR} < 0.05$ in our primary analyses, and results from sensitivity analyses using ReFACTor, a reference-free approach to adjusted for cell type proportions.

Figure S1. Flowchart of eligible participant and participants selected for DNA methylation analysis.

Figure S2. Q-Q plot from *limma* models of M-values of ln(total urinary arsenic levels) adjusted for age, sex, BMI, self-reported smoking status, education (< high school, high school graduate or GED, > high school), study center (Arizona, Oklahoma, North and South Dakota), estimated glomerular filtration rate, and cell type proportion estimates.

Figure S3. Sensitivity analyses for probe-type normalization. Q-Q plot from *limma* models of M-values normalized using single sample Noob and RCP normalization adjusted for age, sex, BMI, self-reported smoking status, education (< high school, high school graduate or GED, > high school), study center (Arizona, Oklahoma, North and South Dakota), estimated glomerular filtration rate, and cell type proportion estimates.

Figure S4. Sensitivity analyses for reference-free cell type proportion adjustment. Q-Q plot from *limma* models of M-values adjusted for age, sex, BMI, self-reported smoking status, education (< high school, high school graduate or GED, > high school), study center (Arizona, Oklahoma, South Dakota), estimated glomerular filtration rate, and six ReFACTor components.

References

Additional File- Excel Document