# ARSENIC EXPOSURE AND DNA METHYLATION WITHIN REPETITIVE ELEMENTS IN ELDERLY MEN

**Angeliki Lambrou**, *Departments of Environmental Health and Epidemiology, Harvard School of Public Health, Boston, MA, USA*
**Andrea Baccarelli,** *Department of Environmental Health, Harvard School of Public Health, Boston, MA, USA*
**Robert O. Wright,** *Department of Environmental Health, Harvard School of Public Health and Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA*
**Marc Weisskopf,** *Departments of Environmental Health and Epidemiology, Harvard School of Public Health, Boston, MA, USA*
**Letizia Tarantini,** *Center of Molecular and Genetic Epidemiology, Universitá degli Studi di Milano & IRCCS Ca', Granda Policlinico Maggiore Hospital Foundation, Milan, Italy*
**Chitra Amarasiriwardena,** *Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA*
**Pantel Vokonas,** *VA Normative Aging Study, Veterans Affairs Boston Healthcare System and Department of Medicine, Boston University School of Medicine, Boston, MA, USA*
**Joel Schwartz,** *Departments of Environmental Health and Epidemiology, Harvard School of Public Health, Boston, MA, USA*

**Background and Aims:** Arsenic (As) exposure has been linked to epigenetic modifications such as DNA methylation in *in vitro* and animal studies. This association has also being explored in highly exposed human populations, but studies among populations environmentally exposed to low As levels are lacking. We aimed to evaluate the association between As exposure and DNA methylation changes in repetitive elements in a population of community-dwelling elderly men. We also explored the possibility of effect modification by plasma folate, cobalamine (B12), and pyridoxine (B6).
**Methods:** We measured toenail As levels by inductively coupled plasma mass spectrometry and DNA methylation in Alu and Long Interspersed Nucleotide Element-1 (LINE-1) repetitive elements by quantitative polymerase chain reaction-pyrosequencing of blood leukocytes. The study population was 581 participants from the Normative Aging Study in Boston, USA, with 434, 140, and 7 of them having 1, 2 and 3 visits, respectively, between 1999-2002 and 2006-2007. We used mixed effects models and included interaction terms to assess potential effect modification by plasma folate, B12, and B6.
**Results:** There was a trend of increasing Alu and decreasing LINE-1 DNA methylation as arsenic exposure increased. In subjects with plasma folate below the median (less than 14.1 ng/ml), As was positively associated with Alu DNA methylation (b=0.08; 95%CI, 0.03 to 0.13 for one interquartile range [0.06 mcg/g] increase in As) while a negative association was observed in subjects with plasma folate above the median
(b=-0.08; 95%CI, -0.17 to 0.01).
**Conclusions:** In our study, the association between As exposure and DNA methylation in Alu repetitive elements varied by folate level, a factor that participates in one-carbon metabolism. This suggests a potential role for nutritional factors in As toxicity.