Association between particulate air pollution and methylation of transcript variants of mRNA in an elderly cohort: Veterans Administration Normative Aging Study

Marie-Abele Bind, Harvard School of Public Health, US
Andrea Baccarelli, Harvard School of Public Health, US
Letizia Tarantini, University of Milan, Italy
Helen Suh, Harvard School of Public Health, US
Pantel Vokonas, Boston University School of Medicine, US
Joel Schwartz, Harvard School of Public Health, US

Background and Aims: The mechanisms of particle effects are still being elucidated but may include epigenetic changes. We investigated the association between exposure to PM$_{2.5}$ and methylation of transcript variants of mRNA in the elderly, a suspected risk group.

Methods: We examined the relationship between PM$_{2.5}$ and methylation of transcript variants of mRNA in leukocytes in 141 men participating in the NAS study (1999-2007). We selected 1258 transcripts variants of mRNA (out of 24211) that displayed the largest variance across participants. We randomly split our data set in a test set (n=79) and a validation set (n=62). We investigated the intermediate- (24h mean, 2, 7, and 30 days moving average (MA$_{2day}$, MA$_{7day}$, MA$_{30day}$)), and long-term (1 year moving average (MA$_{1year}$)) effects of PM$_{2.5}$ adjusting for age, body mass index, smoking, temperature, season, and percentages of neutrophil and lymphocyte in differential blood count.

Results: We found a significant positive association between PM$_{2.5}$ (MA$_{7day}$) and methylation of ubiquitin-conjugating enzyme E2A ($p_{test}=0.017$, $p_{validation}=0.009$). This enzyme is required for post-replicative DNA damage repair and plays a role in blood pressure regulation. We observed a significant positive association between PM$_{2.5}$ (MA$_{7day}$) and methylation of ATP-binding cassette ($p_{test}=0.032$, $p_{validation}=0.007$).

PM$_{2.5}$ (MA$_{30day}$) was associated with methylation of dual specificity phosphatase 10 ($p_{test}=0.010$, $p_{validation}=0.015$).

We found a significant negative association between PM$_{2.5}$ (MA$_{1year}$) and methylation of microsomal triglyceride transfer protein (MTTP) ($p_{test}=0.035$, $p_{validation}=0.011$). MTTP is a common genetic variation in multiple metabolic pathways which influences susceptibility to low HDL-cholesterol and coronary heart disease. We observed a significant positive association between PM$_{2.5}$ (MA$_{1year}$) and methylation of immunoglobulin-like and fibronectin type III domain containing 1 ($p_{test}=0.0008$, $p_{validation}=0.0313$). We obtained a significant positive association between PM$_{2.5}$ (MA$_{1year}$) and methylation of cerebellin 1 precursor, a cerebellum-specific protein ($p_{test}=0.006$, $p_{validation}=0.019$).

Conclusions: Our results suggest an association between intermediate- and long-term exposures to particulate air pollution and methylation transcript variants of mRNA.