METAL-RICH PARTICULATE MATTER INFLUENCE EPSTEIN-BARR VIRUS METHYLATION IN PERIPHERAL BLOOD LEUKOCYTES.

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Background and Aims: Epstein-Barr virus (EBV), after primary infection, persists in most individuals as a lifelong asymptomatic infection of B-lymphocytes. The expression of latent viral oncogenes is under epigenetic control by DNA methylation. DNA methylation inhibits expression of viral latency proteins which are recognized by cytotoxic T cells. We aimed at evaluating effects of PM exposure on EBV DNA methylation in workers in an electric furnace steel plant with well-characterized exposure to metal-rich particulate matter.
Methods: We measured EBV DNA methylation content (in Wp promoter) through bisulfite PCR Pyrosequencing on EBV-positive, leukocytes DNA obtained from 48 workers on the first day of a work week (baseline, after 2 days off work) and after 3 days of work (post-exposure). We determined individual exposure to inhalable particles and metals for all subjects. Paired t-test was used to compare baseline and post-exposure samples. Linear mixed models were fitted to evaluate the association between metal-rich particle exposure and EBV DNA methylation.
Results: Our date showed a change between EBV methylation measured at the baseline and at the post-exposure (difference postexposure-baseline=-9.5%, p-value=0.009). Multivariable mixed models adjusted for age, body mass index and smoking, Nickel, Arsenic and Lead had a positive association with EBV methylation (Nickel: • =16.16, p-value<0.001; Arsenic: • =13.0, p-value=0.02; Lead: • =16.53, p-value<0.001).
Conclusions: The difference observed comparing baseline and post-exposure samples may be suggestive of a rapid change in EBV methylation induced by air particles, while correlation between EBV methylation and metal exposure may represent an adaptive mechanism. These results, however, should be further characterized in future investigations on the effects air particles.

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