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EFFECTS OF METAL-RICH AIR PARTICLES ON DNA METHYLATION AND ON COAGULATION FUNCTION AMONG FOUNDRY WORKERS IN ITALY

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Objectives To investigate the effects of PM and metal components on blood DNA methylation of inflammation/coagulation related genes, among a group of foundry workers with well-characterised exposure to fine particles.

Methods We recruited 63 male foundry workers (mean age=44y) in which we previously demonstrated a PM exposure-related pro-coagulant effect. Individual exposure to PM₁₀, PM₁, and metals was estimated based on area PM measurements and time spent by the study subjects in each area. Quantitative DNA methylation analysis of NOS3 and Et-1 genes was performed through bisulfite PCR-pyrosequencing on blood leucocyte DNA obtained on the first day of a work week and after 3 days of work. Linear mixed models were fitted to

evaluate the association between particles-metals exposure and methylation and between methylation and coagulation function (PT, aPTT, Endogenous Thrombin Potential (ETP)).

Results Workers resulted exposed to a wide range of particle levels (PM₁₀ from 73 to 1220 microg/m³) and of metal components (particularly Mn, Fe, Zn). We observed negative PM exposure-related correlations with NOS3 DNA methylation ($\beta=-0.86$, $p=0.01$ for PM₁₀ and $\beta=-1.12$, $p=0.02$ for PM₁). Zinc and Iron levels were negatively associated with NOS3 and Et-1 methylation. Finally, NOS3 and Et-1 methylation were negatively associated with ETP ($\beta=-45.02$, $p=0.001$ for NOS3 and $\beta=-16.40$, $p=0.03$ for Et-1).

Conclusions Our results linked for the first time a test for global coagulation function (ETP) and DNA hypo-methylation of two candidate inflammation-related genes, and in turn DNA methylation and metal-rich PM exposure, suggesting a possible common path for PM exposure, methylation and blood coagulation.



Effects of metal-rich air particles on DNA methylation and on coagulation function among foundry workers in Italy

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