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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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10.1136/oemed-2011-100382.169

**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 PM<sub>10</sub>, PM<sub>1</sub>, 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 (PM<sub>10</sub> from 73 to 1220 microg/m<sup>3</sup>) 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 PM<sub>10</sub> and  $\beta=-1.12$ ,  $p=0.02$  for PM<sub>1</sub>). 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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*Occup Environ Med* 2011 68: A52-A53  
doi: 10.1136/oemed-2011-100382.169

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