169 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 trough 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 (β=-0.86, p=0.01 for PM10 and β=-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 (β=-45.02, p=0.001 for NOS3 and β=-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.