DIFFERENTIAL EXPRESSION OF MICRORNAS IN SUBJECTS EXPOSED TO METAL RICH PARTICULATE MATTER

Laura Angelici, *Center of Molecular and Genetic Epidemiology, Department of Environmental and Occupational Health, Università degli Studi di Milano, Milan, Italy*
Valeria Motta, *Center of Molecular and Genetic Epidemiology, Department of Environmental and Occupational Health, Università degli Studi di Milano, Milan, Italy*
Francesco Nordio, *Center of Molecular and Genetic Epidemiology, Department of Environmental and Occupational Health, Università degli Studi di Milano, Milan, and Department of Clinical Medicine, Nephrology and Health Sciences, University of Parma Medical School, Parma, Italy*
Fabio Frascati, *Institute for biomedical technologies, National Research Council, Milan, Italy*
Valentina Tinaglia, *Scuola di Dottorato di Medicina Molecolare e Dipartimento Scienze e Tecnologie Biomediche, Università degli Studi di Milano, Milan, Italy*
Valentina Bollati, *Center of Molecular and Genetic Epidemiology, Department of Environmental and Occupational Health, Università degli Studi di Milano, Milan, Italy*
Pier Alberto Bertazzi, *Center of Molecular and Genetic Epidemiology, Department of Environmental and Occupational Health, Università degli Studi di Milano, and Fondazione Cà Granda, IRCCS Ospedale Maggiore Policlinico, Milan, Italy*
Cristina Battaglia, *Scuola di Dottorato di Medicina Molecolare e Dipartimento Scienze e Tecnologie Biomediche, Università degli Studi di Milano, Milan, Italy*
Andrea Baccarelli, *Exposure, Epidemiology and Risk Program, Department of Environmental Health, Harvard School of Public Health, Boston, Massachusetts, USA*

Background and Aims: Altered patterns of gene expression mediate the effects of particulate matter (PM) on human health, but mechanisms through which PM modifies gene expression are largely undetermined. MicroRNAs (miRNAs) are highly conserved, noncoding small RNAs that regulate the expression of broad gene networks at the posttranscriptional level. We evaluated the potential effects of exposure to PM and PM metal components on microRNAs expression in 10 workers at an electric-furnace steel plant in Brescia, Italy.
Methods: We measured expression in blood leukocyte RNA on the first day of a workweek (baseline, after two days off work) and after 3 days of work (postexposure). All subjects in the study were no smokers with a means age of 46y and a characterized exposure to metal rich PM (about 3 times greater than environmental levels in the same area). Gene expression was profiled at baseline (n=10) and postexposure (n=10) using an Affymetrix GeneChip miRNA Array. Differential expression of miRNAs was determined with Limma (R-based Bioconductor package), which employs an empirical Bayes approach to calculate a moderated t-statistic. miRNAs with $p < 0.05$ and the absolute value of FC >2 were considered as differential miRNAs (DEMs). Predicted miRNA targets were determined using the miRanda algorithm, DEMs were subjected to pathway exploration using the Ingenuity Pathway Analysis (IPA) software.
Results: Four miRNAs – hsa-miR-421, hsa-miR-29, hsa-miR-146, hsa-let-7g – were found to be up-regulated. Bioinformatics analysis on these selected miRNAs showed as top ranked network RNA Post-Transcriptional Modification and Cell Morphology whereas the main diseases and disorders involved were Genetic Disorder, Cardiovascular Disease and Neurological Disease.
Conclusions: Changes in miRNAs expression may represent a novel mechanism mediating responses to PM and its metal components.