

## EFFECTS OF METAL-RICH PARTICULATE MATTER EXPOSURE ON EXOSOME-ASSOCIATED MICRORNAS.

**Valentina Bollati**, Center of Molecular and Genetic Epidemiology, Department of Environmental and Occupational Health, University of Milan, Fondazione Cà Granda, IRCCS Ospedale Maggiore Policlinico, Milan, Italy.

**Giovanna Rizzo**, Center of Molecular and Genetic Epidemiology, Department of Environmental and Occupational Health, University of Milan, Fondazione Cà Granda, IRCCS Ospedale Maggiore Policlinico, Milan, Italy.

**Laura Angelici**, Center of Molecular and Genetic Epidemiology, Department of Environmental and Occupational Health, University of Milan, Fondazione Cà Granda, IRCCS Ospedale Maggiore Policlinico, Milan, Italy.

**Francesco Nordio**, Center of Molecular and Genetic Epidemiology, Department of Environmental and Occupational Health, University of Milan, Fondazione Cà Granda, IRCCS Ospedale Maggiore Policlinico, Milan, Italy.

**Laura Pergoli**, Center of Molecular and Genetic Epidemiology, Department of Environmental and Occupational Health, University of Milan, Fondazione Cà Granda, IRCCS Ospedale Maggiore Policlinico, Milan, Italy.

**Matteo Bonzini**, Department of Experimental Medicine, University of Insubria, Varese, Italy.

**Letizia Tarantini**, Center of Molecular and Genetic Epidemiology, Department of Environmental and Occupational Health, University of Milan, Fondazione Cà Granda, IRCCS Ospedale Maggiore Policlinico, Milan, Italy.

**Pietro Apostoli**, Occupational Medicine and Industrial Hygiene, University of Brescia, Department of Experimental and Applied Medicine, Brescia, Italy.

**Andrea Baccarelli**, Exposure, Epidemiology and Risk Program, Department of Environmental Health, Harvard School of Public Health, Boston, Massachusetts, USA.

**Pier Alberto Bertazzi**, Center of Molecular and Genetic Epidemiology, Department of Environmental and Occupational Health, University of Milan, Fondazione Cà Granda, IRCCS Ospedale Maggiore Policlinico, Milan, Italy.

**Background and Aims:** Epidemiological studies have reported an increased risk for cardiovascular disease (CVD) in relation to exposure to metal-rich particulate matter. Cell-derived membrane vesicles (exosomes) are released in plasma and transfer microRNAs. Exosomes might mediate the effects of air pollution, since potentially they could be produced by the respiratory system, reach the systemic circulation and lead to the development of CVD. The aim of the present study was to identify effects of exposure to metal-rich particulate matter on exosomes-associated microRNAs expression in workers of an electric furnace steel plant with well characterized exposure.

**Methods:** Plasma exosomes were isolated by ultracentrifuge from 55 steel workers on the first day of a workweek (baseline) and after three days of work (post-exposure). We measured the expression of the 88 most abundantly expressed and best characterized micro RNA sequences by SYBR green chemistry. The relative expression of miRNAs was measured by real-time PCR using SNORD48, SNORD47, SNORD44 and RNU6-2 as endogenous controls. Relative quantification of miRNA expression was calculated using the  $2^{-\Delta\Delta Ct}$  method. Paired t-tests were used to compare baseline and post-exposure samples.

**Results:** Expression profiling of 88 human miRNAs extracted from baseline and paired post-exposure blood samples identified 6 miRNAs which showed significant differential expression between the two samples. Among the most notable changes were miR-302c and miR-128 which were up-regulated by 13.9- and 5.6-fold respectively ( $p < 0.001$ ), and miR-28-3p and let-7g which were up-regulated by 3.6- and 2.26-fold ( $p = 0.01$ ), miR-125a-5p and miR-181a that were up-regulated 3- and 1.7-fold ( $p < 0.02$ ).

**Conclusion:** These results propose a new role for exosomes in mediating the effects of air pollution exposure on CVD risk. Our findings, if confirmed, could lead to the identification of potentially reversible alterations that might be also considered as potential target for new diagnostic and therapeutic interventions.

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