Abstract

Ozone (O3) is a criteria **air** pollutant that is associated with numerous adverse health effects, including altered respiratory immune responses. Despite its deleterious health effects, possible **epigenetic** mechanisms underlying O3-induced health effects remain understudied. MicroRNAs (miRNAs) are **epigenetic** regulators of genomic response to environmental insults and unstudied in relationship to O3 inhalation exposure. Our objective was to test whether O3 inhalation exposure significantly alters miRNA expression profiles within the human bronchial airways. Twenty healthy adult human volunteers were exposed to 0.4 ppm O3 for 2 h. Induced sputum samples were collected from each subject 48 h preexposure and 6 h postexposure for evaluation of miRNA expression and markers of inflammation in the airways. Genomewide miRNA expression profiles were evaluated by microarray analysis, and in silico predicted mRNA targets of the O3-responsive miRNAs were identified and validated against previously measured O3-induced changes in mRNA targets. Biological network analysis was performed on the O3-associated miRNAs and mRNA targets to reveal potential associated response signaling and functional enrichment. Expression analysis of the sputum samples revealed that O3 exposure significantly increased the expression levels of 10 miRNAs, namely miR-132, miR-143, miR-145, miR-199a*, miR-199b-5p, miR-222, miR-223, miR-25, miR-424, and miR-582-5p. The miRNAs and their predicted targets were associated with a diverse range of biological functions and disease signatures, noted among them inflammation and immune -related disease. The present study shows that O3 inhalation exposure disrupts select miRNA expression profiles that are associated with inflammatory and immune response signaling. These findings provide novel insight into **epigenetic** regulation of responses to O3 exposure.