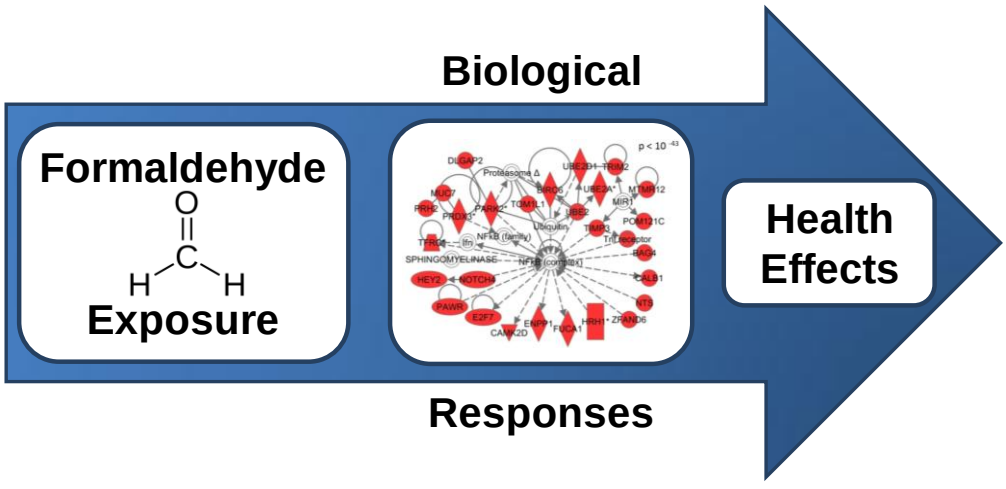

Formaldehyde: Big Effects from Small Molecules

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Abstract

Formaldehyde is an indoor and outdoor air pollutant known to cause cancer in the upper respiratory tract. Despite its adverse health effects, there is a lack of knowledge regarding formaldehyde's influence on gene expression, regulators of gene expression, and cellular signaling pathways. Recent research investigations have uncovered microRNAs (miRNAs) as small, single-stranded, noncoding RNA molecules approximately 22 nucleotides in length. These molecules are receiving widespread attention, as they act as critical regulators of gene expression that influence cellular disease state. While studies have compared miRNA levels between diseased and healthy tissue, this study is the first to examine perturbations in miRNA expression levels resulting from formaldehyde exposure. This study set out to investigate whether miRNA expression profiles are modified by formaldehyde exposure. The hypothesis was that formaldehyde inhalation exposure significantly alters miRNA expression profiles within airway cells, representing a novel mechanism through which formaldehyde may induce disease. This hypothesis was first tested *in vitro*, where human lung epithelial cells were grown at an air-liquid interface and exposed to gaseous formaldehyde at 1 parts per million (ppm) for four hours. Formaldehyde exposure was found to significantly decrease the expression of 89 miRNAs. The investigation was then expanded using an *in vivo* model, where nonhuman primates (Cynomolgus macaque) received 0, 2, or 6 ppm formaldehyde for six hours per day across two days. Within the nasal tissue, 3 and 13 miRNAs were identified as altered in response to 2 and 6 ppm formaldehyde, respectively. Formaldehyde-altered miRNAs were assessed further by predicting gene targets influenced by miRNAs. Analysis of the predicted targets revealed that formaldehyde exposure potentially alters signaling pathways associated with inflammation, cancer, and cell cycle via miRNA-mediated mechanisms. Altogether, this study reveals that formaldehyde alters miRNA patterns which regulate the expression of critical genes and their associated signaling pathways, potentially leading to disease.