Health Consequences of Wildfire Smoke: Unraveling its Potential Effect on our DNA

By Rohma Ramay

Climate change has resulted in an increased frequency of wildfires across the globe; there is an urgent need to address the health consequences of exposure to smoke from these wildfires. Wildfire smoke is comprised of a complex mixture of gases, vapor, and particles including carbon monoxide, nitrogen oxide, ozone, volatile organic compounds (VOCs), and fine particulate matter (PM2.5). Out of these components, PM2.5 is of particular importance because, due to its small size, it can penetrate deep within the lungs and enter the bloodstream, causing a wide range of health concerns.[1] The World Health Organization (WHO) designates PM2.5 as a substantial threat to public health and PM2.5 exposure has been known to cause both respiratory and cardiovascular effects.[2] Recent research into the mechanism of health effects caused by PM2.5 suggest a role of epigenetic modifications such as changes in gene expression. Here we review emerging evidence on how PM2.5 exposure from wildfire smoke influences gene expression through epigenetic mechanisms.

The Science of Epigenetics

Prior research illustrates that the mechanism of adverse health effects of PM2.5 may be anchored in epigenetics: the change in gene expression resulting from variations in DNA methylation, histone modification, and the function of non-coding RNA molecules. These changes can lead to either a significant increase or decrease gene suppression based on the specific chemical change initiated.[3]

For example, changes in DNA methylation and histone modifications after PM2.5 have been linked to the onset of certain diseases such as dementia, diabetes and hypertension.[4] Since metabolic intermediates are key factors in DNA methylation, disruptions in metabolic homeostasis can alter cell-specific methylation patterns and contribute to diseases like type 2 diabetes.[4] In hypertension, aberrant DNA methylation – particularly in gene regulatory regions – may influence key pathways related to disease pathology. Altered methylation patterns have also been associated with age-related diseases such as dementia.[4,5] This signifies the importance of environmental exposures in shaping the epigenome.[6]

How PM2.5 from Wildfire Smoke Modifies the Epigenome

Researchers conducted a study at the California National Primate Research Center (CNPRC) in which they collected nasal epithelium samples of primates to perform whole genome bisulfite sequencing from two groups of adult female rhesus macaques. One group was born before the 2008 California Wildfires, and exposed to wildfire smoke early in life, while the other group was born in 2009 with no exposure to wildfire smoke in early life.[7] The study identified 3370 differentially methylated regions (≥5% methylation change; $p < 0.05$) and one gene (FLOT2) with significantly altered expression (false discovery rate (FDR) < 0.05, fold-change ≥ 1.2). These alterations primarily affected genes related to

https://doi.org/10.29173/hsi489
Received 28 March 2025
Accepted 1 July 2025

immune processes. These findings suggest that early-life exposure to wildfire smoke may lead to long-term gene modifications.[7]

Another study by Schuller et al. used a genetically engineered mouse strain that lacks the apolipoprotein E (ApoE) gene. ApoE−/− is an established animal model used for environmental toxicology studies due to its increased sensitivity to oxidative stress and inflammation, permitting evaluation of the epigenetic changes produced by exposure to wildfire smoke.[8] Their results showed that after 40 days of exposure, these mouse models expressed sperm DNA methylation changes, which can impact alterations in gene expression.[8] Variation was observed in 3353 differentially methylated regions. Most of this change was hypermethylation which targets a variety of developmental processes.[8] Similarly, another study investigated the intergenerational effects of PM2.5 exposure, highlighting additional epigenetic mechanisms involved. Studies have shown that paternal exposure to PM2.5 may lead to epigenetic changes that predispose first and second-generation offspring to metabolic disorders. Small RNAs (sRNAs) play a critical role in mediating these effects.[9] It was found that piR033435 and piR006695 regulate first-generation sperm methylation by binding to the 3′-untranslated region of *Tet1* mRNA, leading to the hypermethylation of testosterone genes and ultimately, impairing the function of Leydig cells leading to hypogonadism.[9]

A recent study by Jiang et al. (2025) details how PM2.5 exposure disrupts the brain's epigenetic landscape through hyper- and hypomethylation of genes involved in synaptic signaling, inflammation, and neuronal integrity.[10] These alterations were linked to impaired memory, learning deficits, and transgenerational effects due to inherited epigenetic changes. The study highlights DNA methylation of synaptic genes such as SHANK3, histone acetylation linked to amyloid toxicity, and microRNA dysregulation as key mediators of PM2.5-induced cognitive impairment – underscoring the complex pathways through which air pollution can shape long-term brain health.[10]

A 15-year cohort study conducted in Isfahan, Iran, found that long-term exposure to PM2.5 through ambient air pollution was significantly associated with an increased incidence of cardiovascular disease including acute myocardial infarction and ischemic heart disease.[11] The results showed that the risk of non-fatal cardiovascular events rose with higher PM2.5 levels, among older adults, smokers, and individuals with hypertension or diabetes. Thus, higher concentrations of PM2.5 were associated with more pronounced adverse cardiovascular outcomes.[11]

Collectively, these studies highlight the detrimental impact of PM2.5, while many studies involve animal models, their conserved epigenetic response suggests relevance to human physiology and underscores the importance of understanding the effect of PM2.5 on the human epigenome through further studies. Translating animal studies to humans suggests that alterations in gene expression mediated by PM2.5 can also have a significant impact on the developing fetus and cause reproductive abnormalities leading to a variety of health outcomes ranging from neurological effects to changes in the immune response. Therefore, there is a growing need to conduct detailed studies that evaluate the underlying epigenetic mechanisms of PM2.5 exposure in humans.

Can these Epigenetic Changes be Reversed?

Although epigenetic changes from PM2.5 may present long-lasting effects, recent studies suggest that these changes may not be permanent. Since epigenetic changes are largely influenced by environmental factors and lifestyle changes, adjusting these external factors may help restore normal gene expression.[12] For example, PM2.5 can increase the production of reactive oxygen species (ROS) leading to the hypomethylation of the p16INK4a promoter- a regulatory region of the p16INK4a gene involved in senescence (the reversible halt of cellular replication), DNA damage, and tumorigenesis.[12] However, the antioxidant N-acetylcysteine (NAC) may reverse these ROS-mediated epigenetic modifications.[12] Although NAC is not naturally found in foods, dietary intake of cysteine – its precursor – may support antioxidant defenses. Cysteine is abundant in protein-rich foods such as chicken, turkey, yogurt, and eggs, as well as in sulfur-containing vegetables like garlic and onions. Increasing cysteine intake through diet may help reduce oxidative epigenetic damage induced by environmental exposures such as PM2.5.[13]

In contrast, a 2012 review by Ji and Khurana Hershey highlights growing evidence that PM2.5 exposure induces a range of epigenetic changes – such as DNA methylation alterations, histone modifications, and

dysregulated miRNA expression that may persist long after exposure. These changes could even be inherited across generations, emphasizing the importance of early-life exposures in shaping long-term health outcomes.[14] However, it is important to consider that individual susceptibility to PM2.5 may also be influenced by genetic predisposition and social determinants of health, which could act as confounding variables when evaluating the epigenetic and health outcomes of PM2.5 exposure. While further research is still required to understand the mechanism of potential reversal of epigenetic changes, supplementation with antioxidants and lifestyle changes in diet can potentially aid in reducing the downstream health risks associated with wildfire smoke.

With the growing body of research outlining the epigenetic effects of PM2.5, there is an urgent need for reform in both government and environmental policies to reduce unwanted exposure to these pollutants. Some of these changes would include air quality monitoring, stricter wildfire prevention laws, and public health surveillance initiatives.[15] Further research is required to delineate the mechanisms behind epigenetic alterations and to better understand the health effects that this exposure may cause. Current findings demonstrate adverse effects of PM2.5 on gene expression through histone modification, DNA methylation, and changes in non-coding RNA function. Given the increased frequency of wildfires due to climate change, there is a strong need to study the health effects of PM2.5 exposure and the long-term consequences of it, especially in areas that are more susceptible to wildfire events. Without adequate research and policy-driven action, the health consequences of PM2.5 exposure through wildfire smoke could not only affect current populations but potentially future generations as well.

Rohma Ramay is currently completing a Master's in Applied Clinical Pharmacology with a specialization in Biomedical Toxicology at the University of Toronto. Her research focuses on the incidence of radiation necrosis in breast cancer patients with brain metastases treated with antibody-drug conjugates and stereotactic radiosurgery, conducted at the Sunnybrook Odette Cancer Centre.

References

1. Long-Term PM2.5 Exposure and Risks of Ischemic Heart Disease and Stroke Events: Review and Meta-Analysis - PubMed. https://pubmed.ncbi.nlm.nih.gov/33381983/
2. Wildfires.https://www.who.int/health-topics/wildfires#tab=tab_1
3. Genetic and epigenetic influence on the response to environmental particulate matter - PubMed. https://pubmed.ncbi.nlm.nih.gov/22196522/
4. Han L, Liu Y, Duan S, Perry B, Li W, He Y. DNA methylation and hypertension: emerging evidence and challenges. Brief Funct Genomics. 2016 Nov;15(6):460–9. doi: 10.1093/bfgp/elw014.
5. Kim M. DNA methylation: a cause and consequence of type 2 diabetes. Genomics Inform. 2019 Dec;17(4):e38. doi:10.5808/GI.2019.17.4.e38. PMID: 31896238; PMCID: PMC6944052.
6. Air pollution and DNA methylation: effects of exposure in humans - PubMed. Accessed February 18, 2025. https://pubmed.ncbi.nlm.nih.gov/31481107/
7. Brown AP, Cai L, Laufer BI, Miller LA, LaSalle JM, Ji H. Long-term effects of wildfire smoke exposure during early life on the nasal epigenome in rhesus macaques. Environ Int. 2022;158:106993. doi:10.1016/j.envint.2021.106993
8. Simulated Wildfire Smoke Significantly Alters Sperm DNA Methylation Patterns in a Murine Model - PMC. Accessed February 12, 2025. https://pmc.ncbi.nlm.nih.gov/articles/PMC8473101/
9. Inter- and trans-generational impacts of real-world PM2.5 exposure on male-specific primary hypogonadism | Cell Discovery. Accessed February 18, 2025. https://www.nature.com/articles/s41421-024-00657-0
10. The Role of Epigenetic Mechanisms in the Development of PM2.5-Induced Cognitive Impairment. Accessed February 11, 2025. https://www.mdpi.com/2305-6304/13/2/119
11. Jalali S, Karbakhsh M, Momeni M, Taheri M, Amini S, Mansourian M, Sarrafzadegan N. Long-term exposure to PM2.5 and cardiovascular disease incidence and mortality in an Eastern Mediterranean country: findings based on a 15-year cohort study. Environ Health. 2021 Oct 28;20(1):112. doi:10.1186/s12940-021-00797-w. PMID: 34711250; PMCID: PMC8555193.
12. DNA hypomethylation, ambient particulate matter, and increased blood pressure: findings from controlled human exposure experiments - PubMed. Accessed February 13, 2025. https://pubmed.ncbi.nlm.nih.gov/23782920/
13. Sekhar RV, Patel SG, Guthikonda AP, Reid M, Balasubramanyam A, Taffet GE, Jahoor F. Deficient synthesis of glutathione underlies oxidative stress in aging and can be corrected by dietary cysteine and glycine supplementation. Am J Clin Nutr. 2011 Sep;94(3):847–53. doi:10.3945/ajcn.110.003483. PMID: 21795440; PMCID: PMC3155927.
14. Ji H, Khurana Hershey GK. Genetic and epigenetic influence on the response to environmental particulate matter. J Allergy Clin Immunol. 2012 Jan;129(1):33–41. doi:10.1016/j.jaci.2011.11.008. PMID: 22196522; PMCID: PMC3268704.
15. Government of Canada. Government of Canada actions to reduce air pollution [Internet]. Ottawa: Environment and Climate Change Canada; 2024 Oct 28 [cited 2025 May 20]. Available from: https://www.canada.ca/en/environment-climate-change/campaigns/canadian-environment-week/clean-air-day/action-air-pollution.html