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Inhaled Microplastics: Emerging Toxicological Mechanisms and Lung Cancer Risk

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Abstract: Global plastic pollution is rising, drawing attention to health risks from respiratory exposure to micro- and nanoplastics (MNPs); at the same time, lung cancer is also the leading cause of cancer-related deaths worldwide. In recent years, many research groups have studied the relationship between MNPs exposure and the development of lung cancer. Inhalation is the main way for MNPs to enter the respiratory system, and the primary response of cells to plastic particles is an increase in oxidative stress. The consequences of MNP exposure mainly include oxidative stress, DNA damage, inflammatory reaction, macrophage polarization and epithelial-mesenchymal transformation (EMT). These physiological processes eventually induce the malignant transformation of normal cells. In summary, this review systematically sorts out and improves the toxicological theory and mechanism of MNPs driving the malignant transformation of tissues, aiming to provide a scientific basis for environmental health risk assessment and lung cancer prevention and control.

Keywords: MPs; NPs; Lung cancer; Tumor microenvironment; Toxicity

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1. Introduction

Plastics possess structural stability and are widely used, resulting in their persistent accumulation in the environment.[1]. Plastics remaining in the environment are decomposed into smaller fragments through ultraviolet irradiation, mechanical wear, hydrolysis and biodegradation, forming tiny MPs particles with a particle size of less than 5 mm and NPs with a particle size range of less than 1 to 100 nm [2]. Due to the small size of microplastics and nanoparticles, they can enter different entities of the environment, including water, air and soil, and cause serious pollution. Under the action of natural media such as wind and water flow, micro-nanoplastics are widely migrated and diffused in the ecosystem [3]. Early research on micro-nanoplastics (MNPs) mainly focused on marine ecosystems, and found that wind direction and ocean currents were key drivers of their global distribution [4]. In recent years, atmospheric microplastic (MNP) pollution has

gradually attracted people's attention, and climate and seasonal changes are the main influences on its spatial and temporal distribution [5].

The equal composition of microns and nanoparticles and other pollutants (heavy metals and volatile organic compounds) is suspended particles (PM), and its particle size ranges from 2.5 μ m to 10 μ m or more [6]. Smaller particles have stronger penetration ability and higher toxicity. PM size is 2.5. It has been proven that it can directly damage DNA in lung tissue and induce pro-inflammatory factors, thus inducing or promoting cancer progression. Clinical and experimental studies have proved that the incidence of lung cancer among non-smokers and smokers has increased significantly in urban areas polluted by PM [7]. The current high incidence of NSCLC, coupled with the widespread presence of microplastics in inhaled air, naturally raises concerns about its potential role in the pathogenesis of cancer and its clinical significance.

2. Exposure and deposition of MNPs in the respiratory system

The atmosphere enables significant MNP dispersal. Urban monitoring in Guangzhou and Xi'an, China, has revealed MP and NP abundances reaching up to 1.8×10^5 items/m³ and 5×10^5 items/m³, respectively, exposing urban populations to chronic, high-concentration MNP inhalation. Indoor MNP concentrations often exceed outdoor levels, primarily driven by fiber shedding from ubiquitous synthetic textiles and everyday clothing [8]. An analysis of PM2.5 in Indian cities pointed out that the concentration of PET microplastics in the air can reach up to 158 ng/m^3, further highlighting the prevalence of respiratory exposure to MNPs [9]. After inhalation exposure, MNPs can be deposited in different areas of the respiratory tract. The sedimentation process is mainly mediated by mechanisms such as inertial impact, gravitational settlement, Brown diffusion and interception [10]. Specifically, large particles (> 10 μm) are mainly deposited in the upper respiratory tract by inertial impact; medium-sized particles are deposited in the bronchioles by gravity when the air flow slows down; while nanoplastics (NPs) are mainly deep and deposited in the alveolar region through Brown diffusion [11]. The respiratory system mainly relies on the mucus ciliation (MCC) mechanism to excrete exogenous micro-nanoplastics (MNPs). However, particles with a diameter of < 2.5 um can often escape this mechanism; when the accumulation of these particles in the lungs exceeds the body's clearance threshold, it may induce lung injury [12].

Pauly et al. (1998) [13] detected 87% of MNP in lung tissue samples of lung cancer patients for the first time [14], among which polypropylene (PP) and polyethylene (PET) are the main polymers in lung parenchyma and BALF [12,15]. Plastic industry workers and textile workers are exposed to high concentrations of particles for a long time, and their risk of pneumoconiosis, asthma, lymphocytic bronchitis, interstitial fibrosis, and even lung cancer is significantly increased [16].

3. Toxicological mechanisms of MP-induced lung cancer

3.1. Oxidative stress

Oxidative stress is the core trigger for lung toxicity induced by MNPs. Studies have confirmed that MNPs can significantly promote the production of reactive oxygen (ROS) in pulmonary epithelial cells. Take polystyrene microplastics (PS-MPs) as an example. This substance not only destroys the mitochondrial electron transfer chain and interferes with the purine metabolism, resulting in a large accumulation of mitochondrial active oxygen species (mROS) [17,18]. It can also deplete antioxidants such as GSH, SOD and

CAT. It weakens the antioxidant defense system of the lungs. In addition, MNPs will also interfere with the Keap1/Nrf2 signaling pathway and inhibit the transposition of Nrf2 to the nucleus [19]. This continuous oxidative stress state will further activate the MAPK/ERK and p38 signaling pathways, causing cell cycle disorder, apoptosis escape and abnormal proliferation [20]. More seriously, excessive ROS can induce lipid peroxidation and cause serious DNA damage (such as base modification and DNA fragmentation). If these genetic damages are not effectively repaired and continue to accumulate in cells, they will lead to the activation of proto-oncogenes and the inactivation of tumor suppressor genes, eventually promoting the malignant transformation of normal lung epithelial cells, and causing excessive proliferation and aggregation of abnormal cells in the lungs [16].

3.2. Inflammatory response

Inflammation is the body's key defense response to harmful stimuli. Studies show that MNPs can trigger an inflammatory cascade by activating the TLR/MyD88/NF-κB signaling pathway, inducing the release of inflammatory factors such as IL-1β, IL-6 and TNF-α [21], which leads to chronic lung injury. Animal experiments confirmed that long-term exposure to MNPs of PET, PP and other materials will induce the aggregation of macrophages in the lungs of mice, causing granulomatous inflammatory lesions [22,23]. This focal inflammation not only directly causes tissue damage, but also recruits medullary inhibitory cells (MDSCs), thus constructing an immune escape microenvironment for the occurrence of tumors. In addition, MNPs can also induce iron death in normal alveoli and bronchial epithelial cells through the HIF-1α/HO-1 pathway, eventually causing tissue fibrosis reshaping[24]. For existing tumor-causing cells (such as in vitro A549 lung cancer cell model), internalized polystyrene nanoplastics (PS-NPs) can further upregulate the expression of IL-8 and NF-κB, enhancing the potential of the tumor itself to promote inflammation and invasion [25].

3.3. Immune dysfunction

Alveolar macrophages (AMs) are the main defense force for immune surveillance and early removal of malignant cells in the body's lungs[26]. Granules with a diameter of 0.5 μm are easily internalized by pulmonary macrophages after inhalation. Continuous phagocytic accumulation will lead to lysosomal overload, increased lysosomal membrane permeability (LMP) and obstruction of autophagy function [27,28]. This process will directly activate NLRP3 inflammatory bodies and trigger cell death (Pyroptosis), releasing damage-related molecular patterns (DAMPs) and IL-1β and other pro-inflammatory factors. This kind of macrophage death and functional exhaustion caused by overload directly weakens the immune monitoring ability of the lungs, so that abnormal cells with early mutations can escape and be removed. Not only that, but MNPs can also deeply reshape the early cancer-promoting microenvironment and even the late tumor microenvironment (TME) by inducing the phenotypic polarization of living macrophages [29]. Specifically, early M1 phenotypic polarization dominates chronic inflammatory damage, and long-term exposure to MNPs such as polystyrene (PS) or polymethyl methacrylate (PMMA) will induce macrophages to transform into the M2 phenotype, making them similar to tumor-related macrophages (TAMs) characteristics [26]. These M2-like cells can continuously secrete IL-10 and TGF-β, thus inhibiting T cell activity and promoting local tissue fibrosis and angiogenesis.

3.4. Fibrosis and epithelial-mesenchymal transition (EMT)

Epithelial-interstitial transformation (EMT) is a highly dynamic biological process; in the process, epithelial cells gradually lose their original characteristics and obtain the phenotype of mesenchymal cells, thus playing a key role in the invasion and metastasis of lung cancer. From the molecular mechanism, the TGF-β/Smad2/3 signaling pathway is a classic pathway for MNPs to induce EMT in lung cells [30,31]. MNPs exposure can activate key transcription factors such as Snail1/2, Twist1 and ZEB1 downstream of the pathway, breaking the original balance of cells. This abnormal EMT driven by transcription factors is manifested by severe down-regulation of the expression of epithelial markers, such as E-calcium mucotin, and significant upregulation of interstitial markers such as waveform protein and α-SMA [32]. The transformation of phenotype gives cancer cells stronger movement and degradation ability, allowing them to break through the cell basal membrane and enter the blood circulation system, thus accelerating the early invasion and distant metastasis of the tumor [33].

3.5. Other mechanisms

Micro/nanoplastics (MNPs) can adsorb environmental carcinogens such as polycyclic aromatic hydrocarbons (PAHs), heavy metals and phthalates through π-π accumulation and electrostatic action [34]. In the A549 cell model, it was observed that MNPs induce oxidative stress and genetic toxicity after carrying the attached pollutants into the cell [35]. In addition, MNPs will also interfere with the microecology of the lungs. Changing the composition of respiratory symbiotic bacteria they will lead to a flora imbalance and aggravate chronic inflammatory reactions. This continuous microecological imbalance will abnormally activate the TLR signaling pathway and change the local tumor microenvironment (TME) [36].

4. Effects of plastics on signaling pathways in lung cancer cells

Existing studies suggest that combined exposure to micro/nanoplastics (MNPs) and ozone may reduce the response rate of patients with non-small cell lung cancer (NSCLC) to immunotherapy and shorten their recurrence-free survival. Studies show that polystyrene nanoplastics (PS-NPs) are internalized by A549 lung cancer cells, significantly upregulating inflammatory mediators such as IL-8, NF-κB and TNF-α [37]. At the same time, PS-NPs can upregulate the expression of DR5 and caspase-grade apoptotic proteins (such as caspase-3, 8, 9) and cytochrome c, thus inducing cell cycle blockage and mitochondrial dysfunction [25]. Jin et al. found that polyvinyl chloride (PVC) can also induce the aging of A549 cells through oxidative stress [38]. In Calu-3 pulmonary epithelial cells with secretory functions, polylactic acid (PLA) nanoparticles will destroy the close connection between cells, reduce mucus secretion and induce DNA damage; at the same time, it will also stimulate the excessive secretion and cell remodeling of related proteins. Interestingly, although it is also a PLA particle, it does not show significant direct lethal cytotoxicity to A549 cells, but the potential metabolic interference effect of this part of the particle still needs to be further clarified [39].

5. Current research gaps

Although advances have been made in micro/nanoplastics (MNPs) research, critical knowledge gaps remain in this field. Most current experiments adopt standard samples with high concentrations and homogeneous physicochemical properties, neglecting environmental particle heterogeneity and real-world long-term low-

dose human exposure scenarios. The release kinetics of MNPs as carcinogen carriers and their synergistic carcinogenic risks have not been fully quantified. Moreover, technical bottlenecks in nanoparticle detection greatly hinder the clarification of the epidemiological association between MNPs and lung cancer risk.

6. Conclusion and perspectives

Environmental MNPs are significant atmospheric risk factors for lung cancer. Inhaled MNPs accumulate in deep lung tissues. They exert chronic toxicity. They drive cancer progression through multiple pathways. These include oxidative stress-induced genotoxicity. They also involve pro-cancer inflammation, immune evasion, and EMT activation. These processes create a favorable niche for malignant transformation and metastasis. Their "Trojan horse" effect amplifies the toxicity of adsorbed mutagens. Clinical evidence for MNPs is still evolving. Toxicological data confirm their high carcinogenic potential. This highlights the need for multidisciplinary risk assessment. This assessment is essential to safeguard public health.

Disclosure statement

The authors declare no conflict of interest.

References

[1] Singh S, Tiwari RR, 2025, Micro/Nanoplastics and Human Health: A Review of the Evidence, Consequences, and Toxicity Assessment. Food and Chemical Toxicology, 203: 115595.

[2] Shi X, Wang X, Huang R, et al., 2022, Cytotoxicity and Genotoxicity of Polystyrene Micro- and Nanoplastics with Different Size and Surface Modification in A549 Cells. International Journal of Nanomedicine, 17: 4509–4523.

[3] Boccia P, Mondellini S, Mauro S, et al., 2024, Potential Effects of Environmental and Occupational Exposure to Microplastics: An Overview of Air Contamination. Toxics, 12(5): 320.

[4] Allen D, Allen S, Abbasi S, et al., 2022, Microplastics and Nanoplastics in the Marine-Atmosphere Environment. Nature Reviews Earth & Environment, 3(6): 393–405.

[5] Siddiqui SA, Singh S, Bahmid NA, et al., 2023, Polystyrene Microplastic Particles in the Food Chain: Characteristics and Toxicity - A Review. Science of The Total Environment, 892: 164531.

[6] Wu X, Lin L, Yan H, et al., 2025, Exposure to Environmental Xenobiotics and Lung Tissue Function: A Comprehensive Review on Biological Mechanisms and Pathways. Ecotoxicology and Environmental Safety, 308: 119438.

[7] Wang M, Kim RY, Kohonen-Corish MRJ, et al., 2025, Particulate Matter Air Pollution as a Cause of Lung Cancer: Epidemiological and Experimental Evidence. British Journal of Cancer, 132(11): 986–996.

[8] Rádis-Baptista G, 2023, Do Synthetic Fragrances in Personal Care and Household Products Impact Indoor Air Quality and Pose Health Risks? Journal of Xenobiotics, 13(1): 121–131.

[9] Anthony J, Varalakshmi S, Kumar Sekar A, et al., 2024, Microplastics Pollution in Indian Marine Environment: Sources, Effects and Solutions. Frontiers in Marine Science, 11: 1512802.

[10] Knap K, Kwiecień K, Reczyńska-Kolman K, et al., 2023, Inhalable Microparticles as Drug Delivery Systems to the Lungs in a Dry Powder Formulations. Regenerative Biomaterials, 10: rbac099.

[11] Lippmann M, Yeates DB, Albert RE, 1980, Deposition, Retention, and Clearance of Inhaled Particles.

Occupational and Environmental Medicine, 37(4): 337–362.

[12] Borgatta M, Breider F, 2024, Inhalation of Microplastics—A Toxicological Complexity. Toxics, 12(5): 358.

[13] Pauly JL, Stegmeier SJ, Allaart HA, et al., 1998, Inhaled Cellulosic and Plastic Fibers Found in Human Lung Tissue. Cancer Epidemiology, Biomarkers & Prevention, 7(5): 419–428.

[14] Zhu L, Kang Y, Ma M, et al., 2024, Tissue Accumulation of Microplastics and Potential Health Risks in Human. Science of The Total Environment, 915: 170004.

[15] Uogintė I, Vailionytė A, Skapas M, et al., 2023, New Evidence of the Presence of Micro- and Nanoplastic Particles in Bronchioalveolar Lavage Samples of Clinical Trial Subjects. Heliyon, 9(9): e19665.

[16] Chen CY, Huang KY, Chen CC, et al., 2024, The Role of PM2.5 Exposure in Lung Cancer: Mechanisms, Genetic Factors, and Clinical Implications. EMBO Molecular Medicine, 17(1): 31–40.

[17] Zha H, Xia J, Wang K, et al., 2024, Foodborne and Airborne Polyethersulfone Nanoplastics Respectively Induce Liver and Lung Injury in Mice: Comparison with Microplastics. Environment International, 183: 108350.

[18] Kadac-Czapska K, Ośko J, Knez E, et al., 2024, Microplastics and Oxidative Stress—Current Problems and Prospects. Antioxidants, 13(5): 579.

[19] Sun R, Liu M, Xiong F, et al., 2024, Polystyrene Micro- and Nanoplastics Induce Gastric Toxicity Through ROS Mediated Oxidative Stress and P62/Keap1/Nrf2 Pathway. Science of The Total Environment, 912: 169228.

[20] Zorov DB, Juhaszova M, Sollott SJ, 2014, Mitochondrial Reactive Oxygen Species (ROS) and ROS-Induced ROS Release. Physiological Reviews, 94(3): 909–950.

[21] Danso IK, Woo JH, Lee K, 2022, Pulmonary Toxicity of Polystyrene, Polypropylene, and Polyvinyl Chloride Microplastics in Mice. Molecules, 27(22): 7926.

[22] Bianchi MG, Casati L, Sauro G, et al., 2025, Biological Effects of Micro-/Nano-Plastics in Macrophages. Nanomaterials, 15(5): 394.

[23] Kim D, Kim D, Kim HK, et al., 2025, Organ-Specific Accumulation and Toxicity Analysis of Orally Administered Polyethylene Terephthalate Microplastics. Scientific Reports, 15: 6616.

[24] Wu Y, Wang J, Zhao T, et al., 2023, Polystyrene Nanoplastics Lead to Ferroptosis in the Lungs. Journal of Advanced Research, 56: 31–41.

[25] Shahzadi C, Di Serafino A, Aruffo E, et al., 2023, A549 as an In Vitro Model to Evaluate the Impact of Microplastics in the Air. Biology, 12(9): 1243.

[26] Wolff CM, Singer D, Schmidt A, et al., 2023, Immune and Inflammatory Responses of Human Macrophages, Dendritic Cells, and T-Cells in Presence of Micro- and Nanoplastic of Different Types and Sizes. Journal of Hazardous Materials, 459: 132194.

[27] Grote K, Brüstle F, Vlacil A K, 2023, Cellular and Systemic Effects of Micro- and Nanoplastics in Mammals—What We Know So Far. Materials, 16(8): 3123.

[28] Italiani P, Boraschi D, 2014, From Monocytes to M1/M2 Macrophages: Phenotypical vs. Functional Differentiation. Frontiers in Immunology, 5: 514.

[29] Orecchioni M, Ghosheh Y, Pramod A B, et al., 2019, Macrophage Polarization: Different Gene Signatures in M1(LPS+) vs. Classically and M2(LPS–) vs. Alternatively Activated Macrophages. Frontiers in Immunology, 10: 1084.

[30] He F, Liao B, Pu J, et al., 2017, Exposure to Ambient Particulate Matter Induced COPD in a Rat Model and a Description of the Underlying Mechanism. Scientific Reports, 7(1): 45666.

[31] Kasai H, Allen JT, Mason RM, et al., 2005, TGF-β1 Induces Human Alveolar Epithelial to Mesenchymal Cell

Transition (EMT). Respiratory Research, 6(1): 56.

[32] Bertoldi A, Cusumano G, Calzoni E, et al., 2025, Multi-Omic Characterization of Epithelial–Mesenchymal Transition: Lipidomic and Metabolomic Profiles as Key Markers of TGF-β-Induced Transition in Huh7 Hepatocellular Carcinoma. Cells, 14(16): 1233.

[33] Huang Y, Shang P, Li Y, et al., 2025, Lung Hazards of Microplastics and Their Toxicological Mechanisms. Environmental Pollution, 385: 127149.

[34] Nabi D, Carmona E, Menger F, et al., 2025, UV Weathering Alters Toxicity and Chemical Composition of Consumer Plastic Leachates. Journal of Hazardous Materials, 498: 139791.

[35] Lynch HN, Loftus CT, Cohen JM, et al., 2016, Weight-of-Evidence Evaluation of Associations Between Particulate Matter Exposure and Biomarkers of Lung Cancer. Regulatory Toxicology and Pharmacology, 82: 53–93.

[36] Sarkar S, Diab H, Thompson J, 2023, Microplastic Pollution: Chemical Characterization and Impact on Wildlife. International Journal of Environmental Research and Public Health, 20(3): 1745.

[37] Woo JH, Seo HJ, Lee JY, et al., 2023, Polypropylene Nanoplastic Exposure Leads to Lung Inflammation Through p38-Mediated NF-κB Pathway Due to Mitochondrial Damage. Particle and Fibre Toxicology, 20: 2.

[38] Jin W, Zhang W, Tang H, et al., 2024, Microplastics Exposure Causes the Senescence of Human Lung Epithelial Cells and Mouse Lungs by Inducing ROS Signaling. Environment International, 185: 108489.

[39] Da Luz CM, Boyles MSP, Falagan-Lotsch P, et al., 2017, Poly-Lactic Acid Nanoparticles (PLA-NP) Promote Physiological Modifications in Lung Epithelial Cells and Are Internalized by Clathrin-Coated Pits and Lipid Rafts. Journal of Nanobiotechnology, 15: 11.