

REVIEW ARTICLE

Genotoxicity and Genomic Instability Induced by Micro- and Nanoplastics: A Comprehensive Multi-Taxa Mechanistic Review

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Received: 10 November 2025 | **Revised:** 30 January 2026 | **Accepted:** 3 February 2026

Keywords: cellular processes | DNA fragmentation | genomic instability | micro-nanoplastics (MNPs) | pollutant

ABSTRACT

Micro- and nanoplastics (MNPs) are pervasive contaminants increasingly implicated in DNA damage and genomic instability across biological systems. This systematic review addresses two core questions: (1) How do MNPs induce genotoxic effects and/or genomic instability in invertebrates, vertebrates, and human cell lines? (2) Through which molecular mechanisms and cellular pathways do these particles exert genotoxic effects? To answer these questions, the review employs an analytical framework integrating mechanistic toxicology, comparative organismal evidence, and pathway-level synthesis. Using PRISMA-guided methods, data were compiled from studies assessing oxidative stress, DNA strand breaks, chromosomal alterations, and disruption of repair pathways. Across aquatic and terrestrial organisms, as well as human epithelial and fly model models, MNP exposure consistently activated oxidative stress pathways, impaired base-excision and nucleotide-excision repair, triggered inflammatory signaling (e.g., NF- κ B), and induced apoptosis or cell-cycle arrest. The framework highlights converging mechanisms—including ROS overproduction, mitochondrial dysfunction, and direct nuclear interactions—that collectively compromise genome integrity. These findings reveal a coherent pattern of genotoxicity across taxa and underscore the growing public-health and ecological risks associated with rising MNP pollution. The review identifies critical knowledge gaps, particularly in chronic low-dose exposures, polymer diversity, and environmentally aged particles, and calls for standardized mechanistic research to inform regulatory interventions.

1 | Introduction

Microplastics (MPs) are plastic particles with diameters less than 5 mm, while nanoplastics (NPs) are typically defined as particles smaller than 100 nm (Thompson et al. 2004; Anifowoshe et al. 2022, 2024, 2025). These small plastic fragments are now ubiquitous in the environment, originating from a variety of sources. Primary MPs are intentionally manufactured at microscopic scales for use in products such as personal care items

and industrial abrasives. In contrast, secondary MPs arise from the degradation and fragmentation of larger plastic debris due to environmental factors such as ultraviolet radiation, weathering, and mechanical abrasion (Andrady 2022).

The rapid proliferation of MPs in ecosystems correlates strongly with the exponential growth of global plastic production, which now reaches hundreds of millions of tons annually (Bexleitova et al. 2024). Improper disposal and inadequate waste

management have contributed significantly to the accumulation of plastic pollutants in oceans, freshwater bodies, soil, and even the atmosphere (Geyer et al. 2017). NPs, though less studied, are of increasing concern due to their ultrafine size, which enables them to cross biological membranes and potentially exert unknown toxicological effects (Gigault et al. 2018).

MPs have been detected across a wide range of environmental compartments—from remote marine ecosystems to urban air—underscoring their pervasiveness (Jolaosho et al. 2025). Their presence in aquatic ecosystems is particularly troubling due to the risk of ingestion by marine organisms, subsequent bioaccumulation, and the potential for trophic transfer, which may ultimately impact human health (Guerrera et al. 2021; Ashrafy et al. 2023; Jolaosho et al. 2025). Furthermore, micro- and NPs frequently act as vectors for other environmental contaminants, including persistent organic pollutants (POPs) and heavy metals, which adhere to their surfaces and may be transported across ecosystems (Cole et al. 2011).

NPs, owing to their small size and high surface area-to-volume ratio, may exhibit greater chemical reactivity and potential toxicity than their larger counterparts (Alimi et al. 2018; Teng et al. 2022; He and Yin 2024; Jolaosho et al. 2025). They may also penetrate cellular structures more easily, posing risks that are not yet fully understood. Preliminary research suggests that NPs can disrupt cellular function and elicit cytotoxic and genotoxic responses (Koelmans et al. 2015).

1.1 | Environmental Trends and Sources of Micro- and Nanoplastics (MNP)

MNPs have become increasingly pervasive across global ecosystems, reflecting a clear upward trend in environmental plastic contamination. The rapid increase in plastic production—now reaching hundreds of millions of tons annually—has directly accelerated the generation and environmental accumulation of micro-sized and nano-sized particles (Bexleitova et al. 2024). Inadequate waste management, improper disposal, and widespread use of single-use plastics contribute significantly to their presence in freshwater, marine, terrestrial, and atmospheric compartments (Geyer et al. 2017).

MNPs originate from primary sources, which include intentionally manufactured microbeads used in cosmetics, industrial abrasives, and biomedical applications, and secondary sources, which arise through the fragmentation of larger plastic debris via photo-oxidation, mechanical abrasion, and environmental weathering (Andrady and Neal 2011). Their occurrence has now been documented in remote marine ecosystems, urban runoff, agricultural soils, and even airborne particulate matter (Jolaosho et al. 2025), indicating their mobility and persistence.

Environmental monitoring studies highlight that MNPs frequently act as carriers for POPs, heavy metals, and other environmental contaminants due to their high surface-area-to-volume ratio and diverse surface functional groups (Cole et al. 2011). This adsorptive capacity enhances their chemical reactivity and increases ecological and human health risks. NPs, in particular, display heightened environmental behavior and toxicity due to

their ultrafine size, which facilitates transport across biological membranes and long-range movement through air and water currents (Gigault et al. 2018).

Overall, the global trends reveal a continuous rise in MNP abundance across ecosystems, driven by expanding plastic production, ineffective waste control, and the gradual breakdown of existing plastic pollution. These environmental patterns underscore the relevance of examining MNP-induced genomic instability, as the growing environmental burden increases the likelihood of organismal exposure across trophic levels.

1.2 | Biological Significance of Genotoxicity and Genomic Instability

Genotoxicity refers to acute or short-term DNA and chromosomal lesions that are measurable soon after exposure (e.g., alkaline comet tail moment, γ H2AX foci, and micronucleus frequency), often reflecting direct damage or ROS-mediated oxidative lesions and early repair responses. By contrast, genomic instability (GI) denotes sustained, heritable increases in mutation and chromosomal mis-segregation rates arising from defects in genome maintenance systems (e.g., BER/NER failure, DSB repair imbalance, centrosome amplification, and spindle-checkpoint slippage) and epigenetic drift. In this review, we classify comet/micronucleus/ γ H2AX/8-oxoG as genotoxic endpoints, and we interpret aneuploidy, chromosomal mis-segregation, persistent copy-number variation, and stable repair pathway repression as genomic-instability endpoints. We further trace a mechanistic sequence—exposure $\rightarrow$ mitochondrial ROS $\rightarrow$ DNA base/strand lesions $\rightarrow$ repair pathway saturation or suppression $\rightarrow$ checkpoint adaptation $\rightarrow$ chromosomal instability (CIN)—to anchor how short-term genotoxic signals may progress into long-term GI across models. We apply this hierarchy consistently when interpreting Tables 1–6 and Figure 2.

Genomic stability refers to the preservation of DNA sequence and chromosomal integrity over time—a fundamental requirement for cellular homeostasis, accurate cell division, and the prevention of mutations (Ferguson et al. 2015). Maintaining genomic stability is essential for avoiding diseases such as cancer, neurodegeneration, and premature aging (Negrini et al. 2010). This stability is safeguarded by a range of mechanisms, including DNA repair pathways—base excision repair (BER), nucleotide excision repair, mismatch repair, and double-strand break repair—which correct errors arising during DNA replication or caused by environmental insults (Huang and Zhou 2021).

Additionally, cell cycle checkpoints coordinate DNA repair with cell division, ensuring that damaged DNA is not propagated (Clay and Fox 2021). In stem cells and during development, robust DNA maintenance systems are vital for proper differentiation and sustained functionality (Mani et al. 2020). The accumulation of DNA damage with age contributes to tissue decline and the onset of age-related pathologies (López-Otín et al. 2023). Recent advances in genomics have shed light on the complexity of these repair networks, providing new avenues for therapeutic intervention, particularly in oncology, where targeting weaknesses in DNA repair mechanisms has become a strategy for personalized cancer treatments.

TABLE 1 | Induction of genotoxicity and/or genomic instability by micro-nano plastics (MNPs) in aquatic organisms.

Model system (organisms)	Types of microplastics	Size	Concentration	Exposure time	Relevant findings	References
Zebrafish (<i>Danio rerio</i>)	Polyisobutylene (PIB)	<2-10µm	3.0–6.0 µg/ml (larvae) 0.5–1.0 mg/L (adult)	4 days (larvae) 21 days (adult)	Zebrafish exposed to various concentrations of PIB-MPs exhibited numerous morphological and molecular changes by altering mRNA levels of genes encoding antioxidant proteins.	Anifowoshe et al. 2024
Zebrafish (<i>D. rerio</i>)	High-density polyethylene (HDPE) and polystyrene (PS) MPs	< 5 mm (mixture; manufacturer-grade)	100 and 1000 µg/L	20 days	Whole-transcriptome profiling in liver showed down-regulation of sterol/terpenoid biosynthesis and epithelial-integrity genes; histology revealed mucosal neutrophilia and lamellar fusion—consistent with stress responses that can precede genomic instability.	Limonta et al. 2019
Zebrafish (<i>D. rerio</i>)	Polystyrene MPs	~10 µm (typical spheres)	10 and 100 µg/L	(dose- and time-dependent; chronic study)	Upregulation of p53, gadd45ba, casp3b, with ROS surge and inflammatory genes (tnfa, ptgs2a) → apoptosis via ROS-mediated p53 signaling; a canonical pathway of genotoxic stress.	Umamaheswari et al. 2021
Zebrafish embryos (<i>D. rerio</i>)	Polystyrene nanoplastics	100 nm	100, 200, 400 mg/L	24–96 h	Decreased hatching/survival; suppressed locomotion; activation of Base Excision Repair (BER) genes (lig1/3, polb, parp1, xrcc1, ogg1)—a direct signature of DNA damage and repair.	Feng et al. 2022
Zebrafish embryos/larvae (<i>D. rerio</i>)	Polystyrene micro/nanoplastics	0.05–10.2 µm (six sizes)	0.0005–0.2 µg/µL	Up to 120 h (assay-dependent)	Phenotypic and neurobehavioral toxicity across sizes; uptake and organ distribution documented; decreased baseline activity—supports size-dependent developmental stress that can couple to genomic responses.	Levesque et al. 2025
Zebrafish (<i>D. rerio</i>)	Polystyrene MPs	(0.07, 0.7, 7 µm) ± Cu nanoparticles	Environmentally realistic acute setups	Acute	Cell-cycle pathway perturbation (DNA replication inhibition; S-phase/G2/M delays; chromosome arrangement/separation errors) indicating chromosomal instability; effects modulated by co-exposure to Cu-NPs.	Gao et al. 2021

(Continues)

TABLE 1 | (Continued)

Model system (organisms)	Types of microplastics	Size	Concentration	Exposure time	Relevant findings	References
Zebrafish (<i>D. rerio</i>)	Polyethylene MPs (PE-MPs; spheres)	~59 µm	Adults: 0–100 mg/L (96 h); embryos: 0–100 mg/L (96 h)	96 h (acute) + depuration follow-up	No internalization or overt genotoxicity; AChE and GST activities altered; slow GI depuration (12–15 days) in juveniles; no embryotoxicity (chorion barrier)	de Mello Pereira et al. 2023
Zebrafish (<i>D. rerio</i>)	Polystyrene NPs (size-dependent)	50 nm vs. 100 nm	(study used fluorescent PS-NPs; behavioral and EEG assays)	≤ 5–7 dpf (acute)	50 nm PS-NPs penetrated BBB → brain accumulation, abnormal behavior and EEG, disruption of dopaminergic metabolites; 100 nm much less active	Hwang et al. 2022
Zebrafish (<i>D. rerio</i>) Embryo-larvae	Polystyrene NPs (simulated environmental plastics vs. nanobeads)	~50–200 nm (SEPs and beads)	0.1 µg/L	0–6 dpf	SEPs caused delayed hatching, ↓ body length (~150 µm), ~40% ↓ locomotion, cortisol 2–3 × ↑; HPI/HPA axis genes altered—effects greater than commercial beads	Saraceni et al. 2025
Zebrafish (<i>D. rerio</i>)	Recycled PVC MPs (20 ± 5 µm)	~20 µm	5, 10, 20 µg/L	96 h	At these levels: no significant effects on survival, locomotion, or oxidative status; authors advise longer/chronic studies	de Mello Pereira et al. 2023
Japanese medaka (<i>Oryzias latipes</i>)	Polystyrene MPs (fluorescent spheres)	~10 µm	500–2000 µg/g diet	10 weeks	Ovarian output decreased; gill mucus and gut epithelial alterations; kidney and spleen changes. (While histological, these chronic stressors co-occur with pathways linked to DNA damage/repair in teleosts).	Zhu et al. 2020
Javanese medaka (<i>Oryzias javanicus</i>)	Polystyrene MPs beads	~5–10 µm	Study doses Up to mg/L range	21 days	Oxidative stress and neurotoxicity with intestinal, hepatic, renal lesions—oxidative damage is a known driver of DNA damage (linking to genotoxic endpoints in fish).	Usman et al. 2021
Mediterranean mussel (<i>Mytilus galloprovincialis</i>)	Polystyrene MPs ± fluoranthene (adsorbed)	µm-scale MPs	mg/L (experimental)	Hours–days (acute)	Comet assay showed DNA damage in haemocytes with PS MPs alone; co-exposure altered genotoxic response (Trojan-horse interactions).	Kolarević et al. 2023

(Continues)

TABLE 1 | (Continued)

Model system (organisms)	Types of microplastics	Size	Concentration	Exposure time	Relevant findings	References
Blue mussel (<i>Mytilus</i> spp.)	PE/PP MPs mix (from consumer products)	Mixture	0.008–100 µg/L	10 days exposure + 10 days depuration	Tissue-specific SOD/CAT responses and DNA-integrity changes at higher doses—multi-organ biomarker panel implicates oxidative DNA damage at realistic concentrations.	Revel et al. 2019
Sea urchin (<i>Paracentrotus lividus/Strongylocentrotus purpuratus</i>) embryos	Plastic leachates (virgin/beached pellets; PVC biobeads)	n/a (leachate studies)	Leachate equivalents	72 h leachate exposures	Severe developmental abnormalities (radialization; skeletogenesis/neurogenesis defects) linked to leachate chemicals (PAHs/PCBs; Zn), with multi-omics pointing to redox stress → genomic instability.	Rendell-Bhatti et al. 2021, Paganos et al. 2023
Common carp (<i>Cyprinus carpio</i>)	Polyethylene MPs	Various (environmental fragments)	0, 5, 25, 50 mg/L	7 and 14 days	Micronucleus frequency in erythrocytes rose concentration/time-dependently (up to 28% MN at 50 mg/L for 14 d) direct genotoxicity.	Usman et al. 2025
Freshwater leech <i>Hirudo verbana</i>	PET NPs	Average diameter of 82.48 ± 24.76 nm	0.05, 0.5, and 5 mg/L	Acute (24–72 h), Chronic (1 week–1 month)	PET nanoparticles were internalized in leech tissues and macrophage-like cells. Exposure induced time- and dose-dependent inflammation, marked by macrophage recruitment, angiogenic remodeling, and HmAIF-1 upregulation. Endothelial activation was confirmed by CD31 expression and neovascularization. Oxidative stress occurred via altered glutathione S-transferase and superoxide dismutase gene expression.	Bon et al. 2026
Silver carp	Polystyrene microspheres	4–85 µm	80 µg/L (low) 800 µg/L (high)	48 h	Low concentrations induced oxidative stress and up-regulation of TUBB4 and HSP70 genes in the intestine, with recovery observed after depuration. High concentrations caused significant damage to gills and intestines, with limited recovery even after depuration.	Zhang et al. 2021

(Continues)

TABLE 1 | (Continued)

Model system (organisms)	Types of microplastics	Size	Concentration	Exposure time	Relevant findings	References
Yellow river carp <i>Cyprinus carpio</i> var. larvae	Polyvinylchloride (PVC)	100–200 μm	10%, 20%, 30%, 40%	60 days	Affected gonadal development, oxidative stress, and immune function	Liu et al. 2023
European sea bass (<i>Dicentrarchus labrax</i>)	Polyvinylchloride (PVC) Polyethylene (PE)	104.1 $\pm$ 36.2 μm (PVC), 77.5 $\pm$ 18.3 μm (PE)	100 or 500 mg PVC or PE kg ⁻¹	3 weeks (21 days)	Oxidative stress, immune response, and histopathology	Espinosa et al. 2019
<i>Poecilia reticulata</i> (Guppy)	Particles	33–40 μm	100 and 1000 $\mu\text{g/L}$	28 days	Impaired digestive performance, stimulating immune response, and inducing microbiota dysbiosis.	Huang et al. 2020
Common carp (<i>C. carpio</i>)	Polystyrene particles	Nano (< 100 nm), micro (100 nm–5 mm), and macro (> 5 mm)	100 mg/L	15 days	Exposure to plastic particles can be associated with neurotoxicity in common carp. Exposure to all sizes of plastics led to neurotoxic effects, including retinal degeneration, necrosis, and vacuolation in retinal layers. The severity of effects varied with particle size.	Hamed et al. 2022
Japanese medaka (<i>O. latipes</i>)	Polyester and polypropylene fibers	Polyester (10–20 μm) and polypropylene fibers (50–60 μm)	10,000 microplastic fibers/L	21 days	Exposure resulted in increased mucus production, epithelial denudation on gill arches, fusion of primary lamellae, aneurysms in secondary lamellae, and morphological alterations in gill structures.	Guerrera et al. 2021
Goldfish (<i>Carassius auratus</i>)	Polyvinylchloride (PVC)	0.100–1000 μm	0.1 or 0.5 mg/L	4 days	Exposure led to fragmentation of gill filaments, indicating respiratory stress and potential impairment of gas exchange functions.	Guerrera et al. 2021
Korean bullhead (<i>Pseudobagrus fulvidraco</i>)	Polyethylene		0, 10, 20, 5000, and 10,000 mg/L	96 h	At higher concentrations (5000 and 10,000 mg/L), significant toxic effects were observed, including inhibition of acetylcholinesterase activity, increased stress indicators (heat shock protein 70 and cortisol), and decreased immune responses (lysozyme activity and immunoglobulin M levels)	Lee et al. 2025

(Continues)

TABLE 1 | (Continued)

Model system (organisms)	Types of microplastics	Size	Concentration	Exposure time	Relevant findings	References
Mrigal carp (<i>Cirrhinus mrigala</i>)	Polystyrene		0.5%, 1%, 1.5%, 2%, and 2.5% in diet	90 days	Higher concentrations of polystyrene microplastics in the diet adversely affected growth, nutrient digestibility, body composition, hematology, and histopathology of fingerlings.	Rashid et al. 2024
Red seabream (<i>Pagrus major</i>)	Polystyrene	5 and 20 µm		7 days	Accumulation of 5 µm microplastics occurred in gills, liver, and gut, whereas 20 µm microplastics were only accumulated in the gills and gut. These microplastics induced inflammation and lipid accumulation in the liver, as well as oxidative stress, with significant disturbance of lipid and energy metabolism.	Lu et al. 2016
Gilthead seabream (<i>Sparus aurata</i>)	Polystyrene	1–20 µm	25 and 250 mg/kg b.w./day	21 days	Subchronic oral exposure to polystyrene microplastics affected redox balance in the anterior and posterior intestine, leading to oxidative damage to lipids and proteins, and modulation of antioxidant defense system enzymes and heat shock proteins.	Piano et al. 2023
African catfish (<i>Clarias gariepinus</i>)	Low-density polyethylene (LDPE)	50–500 µm	0.5, 1.0, 1.5, and 2.0 g/L	4 days	Microplastics accumulated in the gastrointestinal tract in a concentration-dependent manner. Opercular respiratory rate increased with higher concentrations, and swimming performance was significantly reduced. Mortality was observed only at the highest concentration (10%).	Tongo and Erhunmwunse (2022)
Striped catfish (<i>Pangasianodon hypophthalmus</i>)	Polyamide	Small (25–50 µm), large (300 µm–2 mm), and mixed sizes	500 mg/kg of feed	28 days	Smaller microplastics led to higher ingestion rates, reduced growth, compromised feed conversion, decreased survivability, and significant hematological and intestinal histopathological abnormalities.	Shahriar et al. 2024

(Continues)

TABLE 1 | (Continued)

Model system (organisms)	Types of microplastics	Size	Concentration	Exposure time	Relevant findings	References
Adult mussels <i>M. galloprovincialis</i>	PS-MPs	1.0 µm	8.5 and 85 mg/L (EC10 and EC50, respectively)	24 h, 48 h, 72 h, 1 w	Microplastic exposure alters miRNA expression and their downstream target genes, thereby activating distinct regulatory pathways involved in immune modulation, cellular stress responses, protein interaction networks, apoptosis, and programmed cell death.	Annona et al. 2025
Marine mussels (<i>Mytilus edulis</i>)	MPs and NPs	—	0.08, 10 µg, and 100 µg·L ⁻¹	24 h	Results showed that immune response was only activated when mussels were exposed in vivo. However, cytotoxicity (hemocyte mortality) and genotoxicity (DNA damage) parameters were induced after both types of exposure, but in a dose-dependent manner after in vitro hemocyte exposure to all tested plastic conditions. These results indicate that in vitro approaches could be considered as potential predictors of in vivo exposures.	Roman et al. 2023
Mediterranean mussel <i>Mytilus Galloprovincialis</i>	PS MPs	10 µm	0, 0.02, 0.2, and 2 mg/L	21 days	Results showed a minor effect on DNA integrity but a worse physical status at higher doses.	Masiá et al. 2021
Sea urchin (<i>P. lividus</i>)	PS-MPs	1.0 µm	50 µg/mL	30 min	Results showed that PS-MPs significantly reduced sperm viability and motility without altering morphology, and induced sperm DNA fragmentation mediated by reactive oxygen species production	Mottola et al. 2024

TABLE 2 | Induction of genotoxicity and/or genomic instability by MNPs in terrestrial invertebrates.

Model system (organisms)	Types of microplastics	Size	Concentration	Exposure time	Findings (abstract)	References
<i>Buthus occitanus</i> (North African scorpion)	Polystyrene (PS)	10–100 µm	0.4% w/w in prey (insects) and environmental substrate	30 days	Elevated levels of ROS and MDA in scorpion tissues suggested that oxidative stress was a contributing factor to the observed genotoxic effects on exposure to PS-MPs	Zhang et al. 2021
<i>Silver carp</i> (<i>Hypophthalmichthys molitrix</i>)	Polystyrene (PS)	5 µm	80–800 µg/L	48 h	Low microplastic concentration (80 µg/L) induced oxidative stress and up-regulation of TUB84 and HSP70 gene in intestine, and silver carp have ability to recover after the exposure to microplastic was removed	Zhang et al. 2021
<i>Eisenia fetida</i> (Red wiggler earthworm)	Polystyrene (PS)	65–125 µm	0.5% w/w in soil	28–180 days	The results revealed significant DNA damage, evidenced by increased DNA strand breaks in earthworms exposed to PS microplastics compared to control group.	Sobhani et al. 2021
<i>Pieris rapae</i> (Cabbage white butterfly)	Polystyrene (PS)	5–50 µm	1% w/w in artificial nectar	21 days	Histopathological analysis of butterfly tissues revealed damage to the gut and reproductive organs, suggesting potential impacts on reproduction and overall health.	Tang and Yuen 2023

(Continues)

TABLE 2 | (Continued)

Model system (organisms)	Types of microplastics	Size	Concentration	Exposure time	Findings (abstract)	References
Silkworm, <i>Bombyx mori</i>	PS-NPs	0.5 µm (500 nm)	0.25 mg per 0.5 g diet (≈0.5 mg·g ⁻¹ diet)	10–21 days	Particles ingested and observed inside midgut epithelium. Malpighian tubules and haemocytes (translocation into tissues/hemolymph). Significant inhibition of SOD activity (superoxide dismutase) measured (<i>p</i> < 0.05). Behavioural perturbation (erratic movement, chemotaxis defects). No broad redox imbalance measured besides SOD inhibition; the study did not report comet/micronucleus assays for DNA strand breaks. These biochemical changes (↓SOD) are mechanistically relevant because weakened antioxidant defence can promote oxidative DNA lesions, but direct DNA-damage endpoints were not measured in this paper.	Parenti et al. 2020
Silkworm, <i>B. mori</i>	PS-MPs	—	0.125, 0.25, or 0.5 µg per diet unit (reported as µg/diet)	5-days	MPs did not strongly affect survival over the 5-day exposure but altered microbial and metabolic pathways that are plausibly linked to host detoxification and immune competence—these indirect changes can influence DNA-repair and oxidative-stress susceptibility, but no direct comet or other DNA-strand break data	Zhang et al. 2024
Silkworm (<i>B. mori</i>)	PS- MNPs	—	---	72 h	Exposure to MNPs caused alterations at physiological, biochemical, and molecular levels. PS-MPs induced a stronger immune response and hosts better survived the infection.	Muhammad et al. 2021
Earthworm (<i>E. fetida</i>)	Polyethylene (PE)	50–500 µm	0.1%–1% w/w in soil	28 days	Increased oxidative stress markers (SOD, CAT), DNA damage confirmed by comet assay, and histological changes in gut epithelium.	Lwanga et al. 2017

Abbreviation: Polyethylene terephthalate nanoplastics (PET NPs).

TABLE 3 | Induction of genotoxicity and/or genomic instability by MNPs in terrestrial vertebrates.

Model system (organisms)	Types of microplastics	Size	Concentration	Exposure time	Findings (abstract)	References
Adult female albino mice	Polyvinyl chloride (PVC)	—	0.1, 0.2, 0.4, and 0.8 mg/kg	35 days	Exposure led to increase in the number of binuclei and micronuclei formation as the dose increased, indicating increased chromosome instability. Prolonged exposure to PVC showed a positive correlation between doses with increased DNA damage and fragmentation in liver and kidney cells. PVC-MPs increased the production of reactive oxygen species (ROS), which led to cell abnormalities.	Ullah et al. 2025
Adult male Mice	Polyvinyl chloride (PVC)	2 μm	100 mg/kg	60 days	There was a marked decrease in mucus secretions in the intestine along with an increase in intestinal permeability as a result of reduced mRNA expression related to the genes responsible for mucus secretion.	Chen et al. 2022
Wistar rats	Polystyrene (PS)	0.5 μm	0.015, 0.15, and 1.5 mg/kg	90 days	Long-term exposure to PS MPs triggered the NLRP3/Caspase-1 signaling pathway through oxidative stress, leading to granulosa cell pyroptosis and apoptosis, and a decreased ovarian reserve.	Hou et al. 2021
Mice	Polystyrene (PS)	5.0 μm	0.1, 0.5, and 1 mg mL ⁻¹	28 days	MP-induced intense oxidative stress and inflammation.	Mu et al. 2022
Mice	Polystyrene (PS)	4 μm and 10 μm	20 and 40 mg/kg		MPs induced an imbalance of mTORC1 and mTORC2 pathways in the mouse testis through ROS burst and ultimately leading to blood–testis barrier integrity disruption and spermatogenesis dysfunction	Wei et al. 2021

(Continues)

TABLE 3 | (Continued)

Model system (organisms)	Types of microplastics	Size	Concentration	Exposure time	Findings (abstract)	References
Albino mice	Polyethylene (PE)	14 to 184 nm (diameter)	1.3 or 0.6 mg/kg	45 days	Higher doses of PE-MPs led to increased oxidative stress, which induced oxidative DNA damage and decreased antioxidant defenses compared to lower doses.	Majeed and Rabee 2025
Female mice	Polystyrene (PS)	0.8 μm	30 mg/kg	35 days	Increased level of ROS in oocytes, reduced level of MDA, increased IL-6 concentration in ovaries, decreased viability of oocytes and Induced inflammation of ovaries.	Liu et al. 2022
Male mice	Polystyrene (PS)	5 μm	10, 20, and 40 mg/kg	28 days	Exposure to PS-MPs significantly reduced testosterone levels through mitochondrial oxidative stress and impaired the synthesis function of testicular steroids and increased BAX/BCL2-mediated apoptosis rate.	Liu et al. 2024
Female mice	Polyethylene (PE)		0.4, 4, and 40 mg/kg	30 days	Ingestion of MPs significantly increased the ROS level in oocytes and embryos, leading to oxidative stress, mitochondrial dysfunction, and apoptosis. The mouse exposure to MPs caused DNA damage in oocytes, including spindle/chromosome morphology defects.	Zhang et al. 2023
C57BL/6Korl (WT) and leptin-KO mice	PS MPs	Not stated (PS spheres)	Oral for 9 weeks	9 weeks	Altered hepatic lipid/glucose/amino-acid pathways, increased serum lipids, adipogenesis/lipogenesis changes—metabolic stress consistent with oxidative/inflammatory signaling that can co-activate DNA-repair pathways.	Roh et al. (2024)
Kunming mice (male and female)	PVC microplastics	Not stated	4-group design; oral exposure (n = 6/group)	Study period per paper	Impaired reproductive tissue integrity, sex-dependent alterations in intestinal microflora, and intestinal structural damage—mechanistic context for systemic stress that can elevate DNA-damage risk.	Yang et al. (2024)

TABLE 4 | Induction of genotoxicity and/or genomic instability by MNPs in human cell lines and/or human.

Model system (organisms)	Types of microplastics	Size	Concentration	Exposure time	Relevant findings	References
Human cell line: HRT-18 and CMT-93 epithelial cell lines	Polystyrene	4.8–5.8 μm	1 mg/mL	6, 24, and 48 h	Exposure to polystyrene (PS-MPs) resulted in a marked increase in the expression of IL-8 and B2M genes in human HRT-18 cells, suggesting an activation of inflammatory and immune-related pathways. In contrast, no significant gene expression changes were observed in the murine CMT-93 cells, indicating a cell-type-specific response to PS-MPs.	Mattioda et al. 2023
Human Caco-2 cells	Polystyrene	5 μm	12.5–50.0 mgL ⁻¹	24 h	The Caco-2 cells exposed to different concentrations of PS-MPs changed the activity of many genes in the cells, with the biggest change happening at the highest plastic dose (50 mgL ⁻¹). The changes were linked to inflammation, immune responses, fat and energy use, and cancer-related pathways.	Wu et al. 2019
Human embryonic kidney cells and human hepatocellular liver cells	Polystyrene	1 μm	100 μg /mL	24–72 h	The cells exposed to PS-MPs showed reduced expression of the glycolytic gene GAPDH (Glyceraldehyde 3-phosphate dehydrogenase) and the antioxidant genes SOD2 (Superoxide dismutase 2) and CAT (Catalase) in both HEK 293 and Hep G2 cells. This reduction weakens the cell's ability to manage oxidative stress.	Goodman et al. 2022
Human liver cells	Oxidized polystyrene	1 and 5 μm	25–500 μg /mL	24–48 h	Exposure of HepG2 cells to oxidized polystyrene microplastics (PS-MPs _{ox}), particularly 1 μm in size, resulted in significant DNA damage. The damage was further enhanced when MPs _{ox} were loaded with benzo[a]pyrene (BaP), and significantly increased following simulated gastric pretreatment. The 1 μm MPs _{ox} -BaP caused greater genotoxic effects than 5 μm particles, likely due to their higher surface area-to-volume ratio and improved cellular uptake.	La Maestra et al. 2025

(Continues)

TABLE 4 | (Continued)

Model system (organisms)	Types of microplastics	Size	Concentration	Exposure time	Relevant findings	References
Human lung A549 cells	Industrial waste plastics	< 50 µm	100 µg/ml	48 h	After exposure, the cells showed signs of genetic damage, which include small extra pieces of DNA from broken or lost chromosomes, and small bulges from the nucleus, linked to DNA repair or gene amplification	Bengalli et al. 2021
Human intestinal cells (HT-C9)	Polystyrene	3 and 10 µm	100–1600 mgL ⁻¹	24 h and 48 days	Short-term exposure (24 h) to PS-MPs (both 3 and 10 µm sizes) caused severe DNA damage in cells, as shown by a big increase in broken DNA (29.5% for 3 µm size and 66.8% for 10 µm size) Long-term exposure (48 days) DNA damage was smaller (4.5% for 3 µm and 11.5% for 10 µm)	Visalli et al. 2021
Human colon epithelial cells H129	Polystyrene	Not specified	200 µL	24 h	Exposure to various PS-MPs materials, particularly in saline or lipid-rich environments, leads to significant DNA damage, highlighting the genotoxic potential of both marine and food-packaging plastics.	Filipkowski et al. 2022
Human adipose and bone marrow mesenchymal stromal cells (BMMSCs and AMSCs)	Polyethylene	< 1 µm and < 2.6 µm	10 µg/mL	72 h	Exposure of both sizes of MPs-PET caused persistent DNA damage in both BMMSCs and AMSCs after 48 h. An accumulation of DNA damage foci was also observed across both treatments tested indicating consistent induction of genomic stress following MPs-PET exposure.	Najahi et al. 2022
Human lymphocytes	Polystyrene	1 µm	25–200 µg/mL	20 h	Exposure to PS-MPs had a dose-dependent effect on human lymphocytes. DNA damage, indicated by the presence of micronuclei (MNI) and nuclear buds (NBUDs), was significantly increased only at the highest concentration of PS (200 µg/mL). Lower doses (25, 50, and 100 µg/mL) did not cause notable DNA damage.	Santovito et al. 2024

(Continues)

TABLE 4 | (Continued)

Model system (organisms)	Types of microplastics	Size	Concentration	Exposure time	Relevant findings	References
Human fibroblast Hs27 cell line	Polystyrene nanoplastics	100 nm	5–75 µg/mL	4, 24, 48 h	PNPs induce genotoxic effects in a dose-dependent manner, with increased DNA damage observed at higher concentrations (25 and 75 µg/mL), evidenced by elevated micronuclei and NBUD formation	Poma et al. 2019
Human hematopoietic cell lines	Polystyrene nanoplastics	0.05–0.1 µm	100 µg/mL	3, 24, and 48 h	PSNPs induced genotoxic and oxidative DNA damage in a cell-type, dose, and time-dependent manner. Raji-B and TK6 cells showed damage, especially with FPG-complemented assays, while THP-1 cells showed no effects.	Rubio et al. 2020
Human blood lymphocytes	Polystyrene nanoplastics	50 nm	500–2000 µg/mL	48 h	PSNPs caused dose-dependent genotoxic effects in human lymphocytes, as evidenced by increased micronuclei, chromosomal aberrations, and altered cell division indices. The highest genotoxicity was observed at 2000 µg/mL.	Sarma et al. 2022
Human intestinal Caco-2 cells	Polystyrene nanoplastics	50 nm	100 µ	8 weeks and 24 h	The results indicated that exposure to PSNPs for both 24 h and 8 weeks did not increase genotoxicity or oxidative DNA damage in the tested cells.	Domenech et al. 2021

TABLE 5 | Induction of genotoxicity and/or genomic instability by MNPs in Fly model (*Drosophila melanogaster*).

Model system	Types of micro/nanoplastics	Size	Concentration	Exposure time	Findings (abstract)	References
<i>D. melanogaster</i>	Polyethylene microplastics (PE-MPs)	2–10 µm	1 and 10 mg/mL in diet	Larval–adult stages	Increased ROS, reduced SOD, increased GST activity; impaired climbing/crawling; upregulation of p53, rpr, Hsp70Bc indicating oxidative stress and activation of cell-death pathways.	Ranjan et al. 2024
<i>D. melanogaster</i>	Polyethylene microplastics (PE-MPs)	2–10 µm	Noted exposures included 1–10 mg/mL	Larval–adult stages	Longevity reduction, impaired locomotion, decreased eclosion rate; increased antioxidant enzyme activity; transcriptional activation of Hsp70Bc, rpr, cat, p53, sod.	Priscilla et al. 2025
<i>D. melanogaster</i>	Polyethylene terephthalate microplastics (PET-MPs)	Not provided (MP fraction)	Higher experimental doses tested	Multistage exposure	Increased oxidative stress, reproductive toxicity, and activation of heat-shock proteins; evidence of cellular and genetic alteration.	Kauts et al. 2024
<i>D. melanogaster</i>	True-to-life PET nanoplastics (PET-NPLs)	Nanoplastic range	Environmentally realistic, lab-generated NPLs	Acute and chronic exposures	Internalization into gut tissues and hemocytes; disturbed expression of stress, antioxidant, and DNA repair genes; significant oxidative stress and DNA damage.	Alaraby et al. 2023
<i>D. melanogaster</i>	Polystyrene nanoplastics (PS-NPLs)	50, 200, 500 nm	Various ingestion doses	Larval exposures	Internalization across gut barrier; ROS induction, DNA damage (comet assay), altered expression of general stress, antioxidant, and genotoxicity-response genes; size-dependent toxicity strongest for 50 nm.	Alaraby et al. 2022
<i>D. melanogaster</i>	Polystyrene microplastics (PS-MPs)	Not specified	5 and 10 g/L	Dietary	Increased oxidative stress, reduced climbing ability, altered pupal positioning patterns; lipid peroxidation indicating oxidative DNA damage.	Raj et al. 2024
<i>D. melanogaster</i>	Polystyrene micro- and nanoplastics (PS-MPs/NPLs)	1 µm and 20 nm	0.01–100 ppm	13-day and 8-day exposures	Internalization documented; intestinal damage, impaired locomotion, size-dependent toxicity; increased activity associated with compromised nutrient absorption.	Matthews 2020
<i>D. melanogaster</i>	Polystyrene microplastic beads	2 µm	0.005–0.5 µg/mL	7–14 days	Sex-specific toxicity (males more sensitive); midgut necrosis/apoptosis; reduced starvation resistance; reproductive effects	El Kholy and Al-Naggar 2023
<i>D. melanogaster</i>	PET microplastics (PET-MPs)	MP fraction	mg/L range	Short-term (24–48 h)	Cytotoxicity in larval midgut; ↑MDA, altered SOD/CAT; heat-shock protein induction suggests cellular stress and potential genetic alteration	Kauts et al. 2024

TABLE 6 | Comparison of environmental vs. experimental exposure concentrations of MNPs.

Category	Environmental exposure concentrations (field measurements)	Experimental exposure concentrations (laboratory studies in your review)	Implications
Aquatic ecosystems	- Often reported in the low $\mu\text{g/L}$ to low mg/L range, depending on region and polymer type. - Freshwater and marine studies show concentrations typically between 0.1–10 mg/L. - Atmospheric fallout into waterbodies contributes variable loads.	- Zebrafish: 10–1000 $\mu\text{g/L}$ PS-MPs; 100–400 mg/L PS-NPs; 3–6 $\mu\text{g/mL}$ PIB-MPs. - Carp: 5–50 mg/L PE-MPs. - Mussels: 0.02–2 mg/L PS-MPs. - Medaka: 500–2000 $\mu\text{g/g}$ diet. - Leech: 0.05–5 mg/L PET-NPs.	Laboratory exposures frequently exceed environmental levels to induce measurable effects; however, environmentally aged particles may be more toxic than pristine MPs/NPs.
Terrestrial ecosystems (soil, litter, and agriculture)	- Typically mg/kg range in soils. - Agricultural soils can accumulate tens to hundreds of mg/kg from sewage sludge, mulching films, and atmospheric fallout.	- Invertebrates (centipede, mites, slugs): 0.1%–0.5% w/w in substrate (equivalent to 1000–5000 mg/kg). - Earthworms: 0.1%–1% w/w PS or PE MPs (1000–10,000 mg/kg). - Silkworms: doses mixed in diet, approx. 0.25–0.5 mg/g diet.	Experimental concentrations are often 1–2 orders of magnitude higher than typical field measurements, though hotspots near urban centers or agricultural sites can approach experimental levels.
Terrestrial vertebrates (mammals)	- Limited direct environmental quantification. - Likely dominated by dietary ingestion and airborne fallout, typically in $\mu\text{g/day}$ exposure scale.	- Mice: 0.1–100 mg/kg (PVC, PS, PE across studies). - Rats: 0.015–1.5 mg/kg PS MPs. - Chronic studies: 20–40 mg/kg or 50–500 mg/kg food PS-MPs.	Mammalian exposures in labs are standardized for mechanistic clarity but exceed environmental intake; however, humans encounter lifelong chronic low-dose exposure.
Human exposure (inhalation and ingestion)	- Indoor air: 0.3–1.5 particles/m^3 (nanoplastics) and several hundred $\mu\text{g/m}^3$ MPs in polluted areas. - Foodborne exposure: a few μg to mg per day, depending on diet (e.g., seafood, salt, and bottled water).	In vitro studies: - Human epithelial cells (HRT-18, Caco-2): 12.5–50 mg/L PS-MPs. - HEK293/HepG2: 100 $\mu\text{g/mL}$. - Human lymphocytes: 25–2000 $\mu\text{g/mL}$ PS-NPs.	In vitro concentrations must be higher to observe measurable genotoxic responses. Direct comparison with human exposure is complex due to different uptake mechanisms.
Fly model (<i>Drosophila melanogaster</i>)	- Terrestrial matrices (soils, dust, and food surfaces) often report microplastics in mg/kg ranges; airborne fallout adds particles-m^{-3}/$\mu\text{g}\cdot\text{m}^{-3}$ loads relevant to foraging flies (review syntheses). - Environmental heterogeneity and weathering (oxidation, pollutant loading) increase bio-reactivity, even at low chronic doses	- PE-MPs: 1–10 mg/mL diet; locomotor deficits, $\uparrow\text{ROS}$, $\downarrow\text{SOD}$, $\uparrow\text{GST}$; p53, rpr, Hsp70Bc upregulated (Ranjan et al. 2024; Priscilla et al. 2025). - PS-MPs: 5–10 g/L diet; $\uparrow$lipid peroxidation, $\downarrow$climbing, altered pupal positioning (Raj et al. 2024). - PS-NPLs: 50–200–500 nm (ingestion); gut translocation; size-dependent $\uparrow\text{ROS}$, DNA damage, stress/repair gene changes (Alaraby et al. 2022). - PET-NPLs (true-to-life): ingestion; internalization into enterocytes/hemocytes; $\uparrow$oxidative stress and DNA damage; altered repair/stress genes (Alaraby et al. 2023). - PET-MPs: higher experimental doses; reproductive/cellular toxicity; $\uparrow$heat-shock proteins (Kauts et al. 2024). - PS-MPs/NPs: 0.01–100 ppm; intestinal damage; sublethal locomotor effects; size-dependent toxicity (Matthews 2020).	Laboratory doses are frequently above environmental medians, yet they reveal conserved mechanisms—gut uptake, ROS surge, repair pathway modulation (BER/NER gene signals), and apoptosis/inflammation—that likely operate under chronic low-dose, weathered conditions (Alaraby et al. 2022; Alaraby et al. 2023; Ranjan et al. 2024). Aligning future designs to environmentally realistic concentrations and aged/pollutant-loaded particles will improve external validity; the fly's rapid lifecycle enables multigeneration testing of genomic instability endpoints (Priscilla et al. 2025; Matthews 2020).

Abbreviations: PE, polyethylene; PET, polyethylene terephthalate; PIB, polyisobutylene; PS, polystyrene; PVC, polyvinyl chloride.

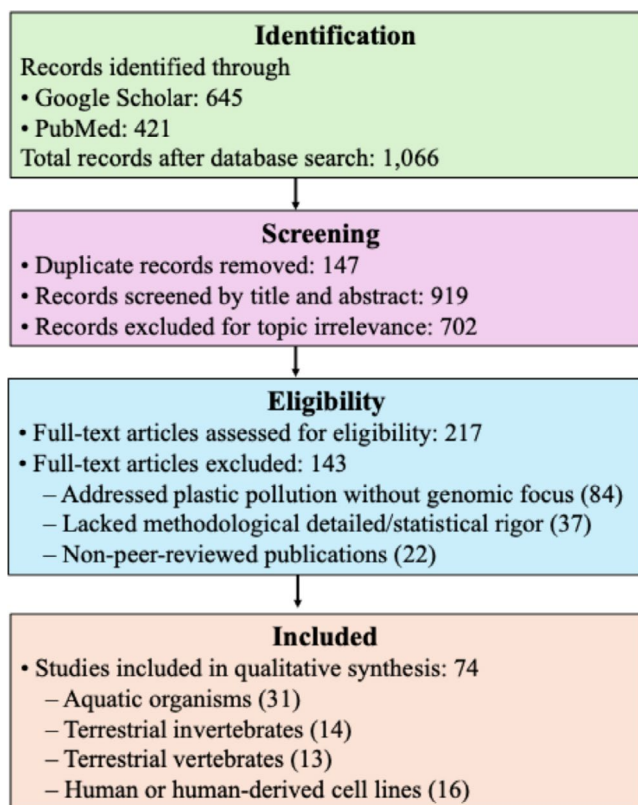


FIGURE 1 | PRISMA flow diagram of this systematic review. The flow reveals the study selection process in accordance with PRISMA 2020 guidelines. The flowchart presents the number of records ($n = 1066$) identified through database searching and other sources, the number of duplicates removed, the records screened, assessed for eligibility, and the final number of studies ($n = 74$) included in the qualitative and/or quantitative synthesis. The reasons for exclusion at each stage are documented to ensure transparency of the selection process.

1.3 | Mechanisms of DNA Damage: Oxidative Stress and Indirect Pathways

DNA is continuously exposed to damage from both endogenous and exogenous sources. Among the most common are single-strand breaks (SSBs), which occur over 10,000 times per cell per day (Hossain et al. 2018). If unrepaired, SSBs can lead to replication stress, chromosomal mutations, and eventually double-strand breaks (DSBs)—a more severe form of damage (Lai et al. 2016).

Micro/nanoplastics often induce DNA damage indirectly through oxidative stress. These particles can generate ROS via inflammatory responses and mitochondrial dysfunction, often mediated by activation of NADPH oxidase. Excessive ROS production has been observed in mammalian cell lines upon exposure to polystyrene NPs, with particle size, concentration, and exposure duration all influencing ROS levels.

Rubio et al. (2020) demonstrated increased ROS in hematopoietic cells after 3–24 h of PS-NP exposure. Smaller particles induced greater oxidative stress, a trend also supported by Kik et al. (2020) who reported significant ROS generation even at low concentrations. Kadac-Czapska et al. (2024) found that long-term NP exposure significantly altered expression of oxidative

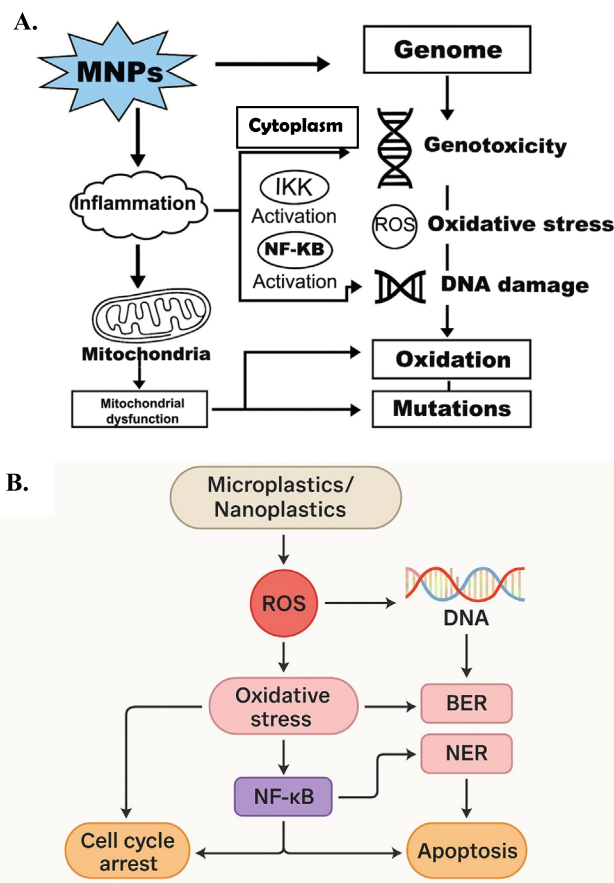


FIGURE 2 | A and B: Schematic Pathways of MNP-Induced Genotoxicity and Genomic Instability.

stress-related genes, such as *ho1* and *sod2*, in intestinal cells, despite no immediate increase in ROS levels.

Particle surface chemistry also influences toxicity. Functional groups, such as amino or carboxyl groups, can enhance the oxidative potential of MNPs. While short-term responses may be mitigated by antioxidant defenses, prolonged exposure may overwhelm detoxification systems, leading to sustained oxidative damage.

1.4 | Environmental and Health Implications

The intersection of MNP pollution and genomic stability is a critical emerging issue in environmental and health sciences. These particles not only accumulate in ecosystems but may also infiltrate biological systems and disrupt essential molecular processes. Their capacity to act as vectors for POPs and heavy metals further elevates their toxic potential (Cole et al. 2011).

From a health perspective, chronic exposure to MNPs has been linked to inflammation, cytotoxicity, and potentially carcinogenesis. Their ability to cross biological barriers—including the blood–brain barrier, placenta, and testicular tissues—raises profound concerns about systemic toxicity. Anifowoshe et al. (2024) report that exposure in animals leads to oxidative stress, membrane dysfunction, and reduced cell viability.

Ultimately, the toxic effects of MNPs are multifactorial and interlinked. Disruption of one pathway—such as oxidative balance—may cascade into broader dysfunctions, including DNA damage, apoptosis, or uncontrolled cell proliferation. As research evolves, understanding the mechanisms behind MNP-induced genomic instability will be vital for environmental risk assessment and public health policy development.

2 | Materials and Methods

A comprehensive literature search was conducted using two major scientific databases—Google Scholar and PubMed—to identify peer-reviewed studies investigating the impact of MNPs on genomic integrity across various biological systems. The search strategy employed a targeted combination of keywords, including but not limited to: “Induction of genomic instability by microplastics in aquatic organisms,” “Induction of genomic instability by microplastics in terrestrial invertebrates,” “Induction of genomic instability by microplastics in terrestrial vertebrates,” and “Induction of genomic instability by microplastics in human cell lines and/or humans.” These search terms were chosen to ensure a broad yet focused coverage of relevant literature examining both the physiological interactions and molecular impacts of MNPs on genetic material and associated cellular processes. This systematic review was conducted in adherence to the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework. PRISMA offers a structured and transparent approach to identifying, selecting, and synthesizing relevant research, ensuring the reliability and generalizability of the findings. Figure 1 represents a flow chart using the PRISMA protocol that summarizes our screening processes to obtain the inclusion.

2.1 | Inclusion Criteria

To ensure the relevance and quality of selected studies, the following inclusion criteria were applied:

1. Study scope: Articles between 2015 and 2025 were selected if they specifically investigated the induction of genomic instability caused by MNP exposure in aquatic organisms, terrestrial invertebrates or vertebrates, and human or human-derived cell lines.
2. Study type: Eligible studies included original research articles, systematic reviews, and meta-analyses that utilized in vivo animal models, in vitro cellular systems, or human subjects.
3. Publication timeframe: Preference was given to studies published within the last 20 years to incorporate the most current findings and emerging scientific trends in the field of MNP toxicology.
4. Language: Only studies published in English were included to maintain consistency in interpretation and reporting.
5. Scientific rigor: Studies were evaluated for methodological robustness, including clear experimental design, appropriate sample size, well-defined control groups, and rigorous statistical analysis.

2.2 | Exclusion Criteria

Studies were excluded based on the following criteria:

1. Topic irrelevance: Articles that addressed plastics in general without directly exploring their genomic effects in biological systems were excluded.
2. Lack of peer review: Non-peer-reviewed materials, such as conference abstracts, editorial opinions, or popular science articles, were not considered to maintain scientific integrity.
3. Redundancy: Duplicate publications or studies presenting overlapping datasets were excluded to avoid redundancy and ensure the uniqueness of the data set.
4. Insufficient methodological detail: Studies lacking comprehensive information on experimental methods, data analysis, or statistical validation were omitted to uphold the reliability and credibility of the review's conclusions.

3 | Result and Discussion

MNPs have emerged as ubiquitous environmental pollutants, infiltrating terrestrial, freshwater, and marine ecosystems. Their persistence and small size enable them to be readily ingested or absorbed by organisms across multiple trophic levels, ranging from microorganisms to vertebrates. Once internalized, MNPs can traverse biological barriers and accumulate in tissues, where they may exert toxicological effects. A growing body of evidence indicates that MNPs can induce genomic instability through multiple pathways, including the generation of reactive oxygen species (ROS), chronic inflammation, physical disruption of cellular architecture, and direct interaction with DNA and nuclear proteins. These disturbances can lead to DNA strand breaks, impaired repair mechanisms, chromosomal aberrations, and altered gene expression patterns, all of which are hallmarks of genomic instability.

Numerous in vivo and in vitro studies have demonstrated the genotoxic potential of MNPs in various organisms and cell lines, as summarized in Tables 1–4. Table 1 highlights findings from aquatic model organisms, including Zebrafish (*Danio rerio*), Silver Carp (*Hypophthalmichthys molitrix*), and Yellow River Carp (*Cyprinus carpio haematopterus*), all of which displayed cellular and molecular indicators of stress and genomic disruption following MNP exposure. In Zebrafish, for example, exposure to varying concentrations of polyisobutylene MPs (PIB-MPs) triggered significant morphological deformities and biochemical alterations. These included changes in the expression levels of genes encoding antioxidant enzymes such as catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GPx), indicating oxidative stress-mediated molecular damage (Anifowoshe et al. 2024).

Similarly, in Silver Carp, even exposure to relatively low concentrations of polystyrene microplastics (PS-MPs) led to oxidative stress and a notable upregulation of stress-related genes such as *tub84* and *hsp70* in the intestinal tissues. Although these effects were partially reversible upon cessation of exposure and

a period of depuration, the reversibility was limited at higher concentrations. Fish subjected to high-dose exposure showed irreversible damage to both gill and intestinal tissues, underscoring the dose-dependent severity of MNP toxicity (Zhang et al. 2021). These observations collectively suggest that MNPs can disrupt cellular homeostasis and promote genotoxic effects in aquatic organisms, raising significant concerns about ecological safety and potential trophic transfer effects that may also impact human health.

In terrestrial invertebrates (Table 2), microplastic exposure has also demonstrated significant genotoxic and cytotoxic effects. For instance, centipedes exposed to polypropylene MPs (PP-MPs) exhibited considerable DNA damage, which was evidenced by an increase in DNA strand breaks and the formation of micronuclei—both reliable biomarkers of genomic instability. Histopathological evaluations further revealed severe damage to the digestive system, including epithelial cell degeneration, disruption of gut tissue architecture, and altered morphology of absorptive surfaces. These structural impairments likely compromise nutrient absorption and metabolic homeostasis, leading to broader physiological dysfunction. In silkworms exposed to MNPs, no significant changes in larval body mass or survival were reported. Nevertheless, exposure led to significant alterations in the expression of immunity-related genes (cecropin A, lysozyme, SOD, and GST) and antioxidant-mediated protective response (SOD, GST, and CAT enzymes), which differed in the PS-MP and PS-NP groups.

Research on terrestrial vertebrates supports similar findings, reinforcing the concern that MNPs pose a pervasive biological threat across taxonomic boundaries. In a study involving adult female albino mice, exposure to varying concentrations of polyvinyl chloride MPs (PVC-MPs) induced a dose-dependent increase in chromosomal instability, as demonstrated by the elevated frequency of binucleated cells and micronucleus formation. Prolonged exposure exacerbated these effects, with significant DNA fragmentation and damage observed in liver and kidney cells. These genotoxic effects were closely associated with elevated levels of ROS, which are known to damage cellular components and disrupt genomic integrity (Ullah et al. 2025).

Complementary findings were reported in a study involving adult male mice exposed to PVC MPs. This study revealed gastrointestinal toxicity marked by a pronounced reduction in mucus secretion and a significant increase in intestinal permeability. These effects were linked to the downregulation of genes associated with mucus production, highlighting the molecular impact of MNPs on epithelial barrier function and host-microbiota interactions (Chen et al. 2022). These changes can facilitate systemic exposure to environmental toxins and pathogens, amplifying physiological stress and the risk of inflammation-mediated genomic damage (Table 3).

At the cellular level, MNPs have been shown to bind to components of the nuclear envelope and interact with nuclear proteins, leading to the disruption of fundamental cellular processes. Specifically, these plastics can alter gene expression profiles related to DNA repair, apoptosis, and cellular metabolism. Such

changes are primarily driven by oxidative stress, which acts as a central mechanism in mediating MNP-induced cytotoxicity and genotoxicity (Yang et al. 2024). These findings suggest a mechanistic link between MNP exposure and impaired genomic maintenance, raising serious concerns about long-term ecological and public health consequences. The ability of MNPs to interfere with genomic stability not only threatens individual organisms but also poses risks of transgenerational effects and ecosystem-level disruptions.

In human cell lines (HRT-18 and CMT-93 epithelial cell lines), exposure to PS-MPs resulted in a marked increase in the expression of IL-8 and B2M genes in human HRT-18 cells, suggesting an activation of inflammatory and immune-related pathways. In contrast, no significant gene expression changes were observed in the murine CMT-93 cells, indicating a cell-type-specific response to PS-MPs (Mattioda et al. 2023) (Table 4). Approximately 30,000 types of plastic polymers have been identified, but they share common features such as high surface area and strong binding affinity, allowing extensive interactions with various substances, including metal cations, inorganic anions, organic chemicals, and biomolecules. These interactions are facilitated through hydrophobic forces or electrostatic attractions with functional groups present on MNPs. Such extensive surface interactions can lead to complex environmental consequences and biological effects, including gene toxicity. The Caco-2 cells exposed to different concentrations of PS-MPs changed the activity of many genes in the cells, with the biggest change happening at the highest plastic dose (50 mg/L). The changes were linked to inflammation, immune responses, fat and energy use, and cancer-related pathways (Table 4).

In vitro studies involving human and animal epithelial cell lines have provided valuable insights into the cytotoxic and genotoxic effects of MNPs at the molecular level. Notably, in human colorectal epithelial HRT-18 cells and murine intestinal epithelial CMT-93 cells, differential gene expression patterns were observed following exposure to PS-MPs. Specifically, PS-MP exposure led to a marked upregulation of interleukin-8 (IL-8) and beta-2-microglobulin (B2M) genes in HRT-18 cells, indicating the activation of inflammatory and immune response pathways (Mattioda et al. 2023). IL-8 plays a critical role in neutrophil recruitment and the initiation of inflammatory cascades, while B2M is associated with immune system regulation, including antigen presentation. In contrast, the murine CMT-93 cell line did not exhibit significant changes in gene expression under similar experimental conditions, suggesting a potential species-specific or cell-type-specific response to PS-MP exposure. These findings underscore the complexity of cellular responses to MNPs and the necessity of examining multiple biological models to fully understand the scope of plastic-induced toxicity (Table 4).

The chemical and physical properties of microplastic polymers further contribute to their biological reactivity. Although approximately 30,000 distinct plastic polymers have been identified globally, they tend to share several physicochemical characteristics, including large surface area-to-volume ratios, surface functionalization, and strong binding affinities. These features enable MNPs to engage in diverse interactions with environmental and biological molecules, including metal cations, inorganic anions, POPs, proteins, and DNA. Such interactions

are primarily facilitated through hydrophobic interactions, van der Waals forces, and electrostatic attractions between the functional groups on MNP surfaces and target molecules. This binding capacity not only allows MNPs to serve as vectors for toxicants but also amplifies their potential to cause gene-level toxicity through secondary mechanisms.

Supporting this, research using the human intestinal Caco-2 epithelial cell line has shown that exposure to varying concentrations of PS-MPs results in widespread transcriptomic alterations. These changes are dose-dependent, with the most pronounced effects observed at the highest tested concentration of 50 mg/L. The altered gene expression profiles were associated with a range of biological processes, including inflammation, immune system modulation, lipid metabolism, energy homeostasis, and oncogenic signaling pathways (Table 4). The disruption of these pathways raises serious concerns, particularly regarding chronic exposure, which may predispose cells to metabolic dysregulation, inflammatory disorders, and even carcinogenesis.

The compiled studies on *Drosophila melanogaster* provide clear evidence that MNPs induce oxidative stress, disrupt physiological functions, and activate genotoxic pathways across multiple polymer types and particle sizes. Polyethylene (PE) MPs consistently elevated ROS, reduced antioxidant defences such as SOD, and upregulated stress-response and apoptosis-related genes including p53, rpr, and Hsp70Bc—demonstrating early genomic stress signals (Ranjan et al. 2024; Priscilla et al. 2025). PET MPs and NPs further intensified these responses, inducing cellular and reproductive toxicity, heat-shock protein activation, and measurable DNA damage, supporting a conserved mechanism of oxidative and genotoxic stress (Kauts et al. 2024; Alaraby et al. 2023). Polystyrene MNPs caused size-dependent internalization, ROS production, intestinal damage, impaired locomotion, and genotoxicity, with smaller nanoparticles eliciting stronger DNA damage responses (Alaraby et al. 2022; Raj et al. 2024). Across studies, sublethal impairments such as locomotor deficits and developmental abnormalities were consistent, even where mortality remained unchanged (Matthews 2020).

Table 5 summarizes studies on micro/nanoplastic exposure in *Drosophila melanogaster*. PE and polystyrene (PS) MPs (2–10 µm) at dietary concentrations of 1–10 mg/mL or small liquid doses caused oxidative stress, reduced antioxidant enzymes, impaired climbing, and activated stress and apoptosis genes (p53, Hsp70Bc). PET MPs and true-to-life PET NPs induced gut internalization, disrupted antioxidant and DNA repair gene expression, and caused intestinal and genetic damage. Size-dependent toxicity was observed for PS micro/nanoplastics (0.01–100 ppm), leading to locomotor deficits and nutrient absorption issues. Overall, findings indicate ROS overproduction, mitochondrial dysfunction, genotoxicity, and behavioral impairments across larval and adult stages, highlighting systemic toxicity of MPs in flies.

Table 6 compares real-world environmental concentrations of MNPs with the typically higher doses used in laboratory experiments. Environmental levels in water, soil, air, and food generally fall within low µg/L to mg/L or mg/kg ranges, whereas experimental studies often apply elevated concentrations to reveal mechanistic effects. This contrast highlights a key gap: laboratory

exposures may exceed natural levels, yet environmental particles are more weathered and potentially more toxic. The comparison underscores the importance of aligning experimental designs with environmentally realistic conditions to improve the ecological and human-health relevance of genotoxicity findings.

The internalization of MNPs by cells occurs predominantly through endocytosis and phagocytosis, processes that depend on particle size, surface chemistry, and cell type. Several endocytic pathways have been implicated in MNP uptake, including clathrin-mediated endocytosis (CME), caveolin-mediated endocytosis, and macropinocytosis. CME involves the formation of clathrin-coated pits (~100 nm) that internalize particles via receptor-mediated binding, followed by vesicle scission and trafficking to endosomes and lysosomes (Doherty and McMahon 2009). Caveolin-mediated endocytosis occurs in flask-shaped invaginations called caveolae and can bypass lysosomal degradation, directing internalized materials to the Golgi apparatus or endoplasmic reticulum (Barman and Drolia 2024). Macropinocytosis enables the uptake of larger vesicles (0.2–5 µm) through actin-driven membrane ruffling, often contributing to nonspecific MNP internalization (Lim and Gleeson 2011). In vitro studies with Caco-2 intestinal epithelial cells have demonstrated that polystyrene NPs are internalized through a combination of CME, caveolin-mediated pathways, macropinocytosis, and actin-dependent phagocytic-like processes, with uptake efficiency strongly influenced by particle size and surface charge (Xie et al. 2024).

Phagocytosis is specialized for larger particles (> 0.5 µm) and is primarily executed by professional phagocytes such as macrophages and neutrophils. This process involves actin cytoskeleton remodeling to form pseudopods that engulf particles into phagosomes, which subsequently fuse with lysosomes for degradation (Flannagan et al. 2012). The adsorption of serum proteins (opsonins) onto MNP surfaces—known as the biocorona—can enhance recognition and uptake by phagocytes (Nasser and Lynch 2016).

Particle size is a key determinant: NPs (< 0.5 µm) are preferentially internalized via endocytic routes, whereas MPs (> 0.5 µm) typically undergo phagocytosis. Surface charge and hydrophobicity further modulate internalization efficiency, with positively charged particles generally exhibiting higher uptake rates due to electrostatic interactions with negatively charged cell membranes (Yong et al. 2020).

A growing body of evidence indicates that MNPs induce genomic instability through the activation or impairment of multiple molecular pathways involved in DNA repair, oxidative stress regulation and mitochondrial signalling. One of the earliest cellular events observed in MNP-exposed cells is the overproduction of ROS, which not only compromises mitochondrial membrane potential but also drives oxidative lesions in DNA. Such oxidative lesions, including 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxoG), are normally processed by the BER pathway. However, excessive ROS generation can saturate BER capacity, leading to misrepair and strand breaks. In polystyrene-treated zebrafish, downregulation of Ogg1 and Apex1—two key components of the BER machinery—has been reported in parallel with increased levels of DNA strand breaks (Mu et al. 2022).

In addition to oxidative damage, several studies have demonstrated direct interference of MNPs with nucleotide excision repair (NER) pathways. For example, exposure of human epithelial cells to NPs resulted in suppressed expression of XPA, XPC, and ERCC1, which are essential for removal of bulky DNA adducts. This suggests that MNPs not only induce DNA damage but also compromise the cell's ability to repair it. Similarly, mitochondrial dysfunction and release of cytochrome-c has been described in rodent models and in vitro systems following MNP exposure (Liu et al. 2024). This mitochondrial stress activates caspase-9 and downstream caspase-3, leading to apoptotic cell death, thereby contributing to loss of genomic integrity (Hamed et al. 2022).

Transcriptomic analyses in zebrafish and mussel models further showed upregulation of pro-inflammatory and apoptotic gene networks, including TNF- α , NF- κ B, and Casp3, after MNP exposure (Annona et al. 2025; Roman et al. 2023). The activation of NF- κ B has a dual effect because, while it promotes inflammatory gene transcription, it also suppresses p53-mediated DNA repair and apoptosis, favouring survival of damaged cells (Ferguson et al. 2015; Teng et al. 2022). These findings highlight a convergence between inflammatory signalling and impaired genomic maintenance mechanisms.

Taken together, these lines of evidence indicate that the genotoxicity of MNPs is mediated not by a single molecular event but by interference with multiple pathways, including mitochondrial ROS production, BER/NER impairment, and dysregulated inflammatory signalling, ultimately resulting in chromosomal instability and cell death.

Although numerous investigations demonstrate strong genotoxic effects of MNPs, a few studies show no statistically significant DNA damage in certain cell lines under controlled exposure conditions. For example, Bengalli et al. (2021) observed that A549 human lung epithelial cells exposed to environmentally relevant concentrations (1–10 μ g/mL) of polyethylene-derived microplastic particles did not show a significant increase in DNA strand breaks as measured by alkaline comet assay. The authors suggested that cellular antioxidant systems may have compensated for the transient oxidative stress induced by the particles, preventing measurable DNA lesions.

Similarly, Poma et al. (2019) reported that polystyrene NPs did not induce statistically significant micronuclei formation in human fibroblast Hs27 cells after 24 h exposure, although slight elevations in oxidative markers were detected. These results indicate that some cell types, particularly primary fibroblasts and lung epithelial models, can maintain genomic integrity at lower MNP concentrations through DNA repair and stress-response mechanisms.

In another study, Rubio et al. (2020) found no significant changes in γ H2AX foci formation in human hematopoietic cell lines exposed to low doses (<5 μ g/mL), suggesting that DNA double-strand breaks may not occur at sub-cytotoxic concentrations. However, mild but consistent increases in ROS and subtle transcriptional changes in BER-related genes (e.g., PARP1 and OGG1) were observed, indicating early molecular responses that may precede overt DNA damage.

Thus, these results emphasize that MNP-induced genotoxicity is highly dependent on cell type, polymer type, concentration, and duration of exposure.

MNPs exert their toxic effects through multiple interconnected pathways that ultimately compromise genomic integrity (Figure 2). Upon exposure, MNPs can directly interact with cellular DNA, causing genotoxicity, or indirectly trigger inflammation, which activates signaling cascades such as IKK and NF- κ B, leading to stress responses. Concurrently, MNPs induce mitochondrial dysfunction, resulting in excessive production of ROS. Elevated ROS levels drive oxidative stress, which damages DNA through strand breaks and base modifications while impairing repair mechanisms like BER and NER. These processes collectively lead to persistent DNA damage, oxidation, and mutations, increasing the risk of carcinogenesis and transgenerational effects. The severity of these outcomes is influenced by polymer type (e.g., polystyrene, polyethylene, PVC, PET, and PIB), particle size, dose, and environmental aging or weathering, which alter surface chemistry and enhance toxicity.

The Figure 2A,B showed the proposed mechanistic model of microplastic/nanoplastic-induced genotoxic stress and genomic instability. MNP exposure disrupts mitochondrial function, causing excessive ROS production. ROS accumulation induces oxidative stress in the cytoplasm, activating NF- κ B-mediated stress signaling, and diffuses into the nucleus where it induces oxidative DNA damage. Although BER and NER pathways are engaged, sustained ROS leads to repair overload and impairment, resulting in mutations and chromosomal instability. These events ultimately activate cell-cycle arrest or apoptosis. This schematic illustrates the cellular and molecular mechanisms by which MNPs disrupt genomic integrity. MNP exposure initiates inflammation and mitochondrial dysfunction, leading to activation of IKK/NF- κ B signaling and excessive ROS production. These processes drive oxidative stress, DNA damage, and impaired repair pathways, culminating in genotoxicity, oxidation, and mutations (Figure 2A). The combined effects of direct genome interaction and indirect stress responses highlight the multifactorial nature of MNP toxicity and its potential role in carcinogenesis and transgenerational impacts. The signaling pathway diagram (landscape) showing how MNP exposure $\rightarrow$ ROS $\rightarrow$ oxidative DNA damage $\rightarrow$ BER/NER, with NF- κ B-mediated inflammation, cell-cycle arrest, and apoptosis in Figure 2B.

Species vary widely in their sensitivity to MNPs due to fundamental physiological and cellular differences that shape exposure, uptake, and genomic responses. Organisms with high metabolic rates, such as small fish, insects, and larval stages, generate more endogenous ROS and therefore experience amplified oxidative stress when exposed to MNPs, increasing the likelihood of DNA strand breaks and impaired repair. Sensitivity is further influenced by differences in antioxidant capacity: aquatic invertebrates and insects possess limited or rapidly saturable antioxidant defenses (e.g., SOD, CAT, and GST), making them more vulnerable to oxidative DNA damage than vertebrates with more robust detoxification systems.

Uptake efficiency also varies. Species with high rates of endocytosis or filtration—including mussels, daphnids, and *Drosophila*—internalize greater quantities of particles, promoting lysosomal

destabilization, mitochondrial ROS, and apoptosis. In addition, anatomical features such as permeable epithelia, developing barriers in embryos and larvae, and gill or tracheal structures facilitate deeper tissue penetration of nanoparticles.

Differences in detoxification enzyme capacity (e.g., CYP450s and glutathione pathways) influence how effectively species remove adsorbed co-pollutants. Thus, species with fast life-history cycles are more susceptible to disruptions in early cell division and germ-line stability.

4 | Strengths and Limitations

Although numerous studies report that MNPs induce genomic instability across biological systems, the strength of the evidence varies considerably depending on study design, model organism, and exposure conditions. In aquatic models such as zebrafish and mussels, most studies employ acute or sub-chronic exposures under controlled laboratory conditions; however, exposure concentrations sometimes far exceed environmentally relevant levels, which may overestimate biological impact. In addition, a large proportion of aquatic studies focus on a single polymer type (e.g., polystyrene), which does not reflect the complexity of real-world mixtures. Terrestrial invertebrate and vertebrate studies also differ markedly in routes of administration (dietary, injection, and gavage), and in some cases lack appropriate vehicle controls, complicating interpretation of dose–response relationships. Also, as reported in Table 6, median environmental concentrations generally fall in the low $\mu\text{g/L}$ – mg/L (water) and mg/kg (soil/food) ranges, whereas experimental doses used to resolve mechanisms frequently extend ≥ 1 – 2 orders of magnitude higher, particularly in short-term cell or animal studies. This creates an upward extrapolation bias if nominal mass/volume is interpreted without accounting for particle number, surface area, weathering state, and adsorbed co-pollutants.

A further limitation relates to the heterogeneity of genomic response pathways assessed across studies. Although oxidative stress and ROS-driven damage are consistently reported, downstream genomic pathways—including BER, NER, DNA double-strand break repair, p53 signaling, NF- κ B-mediated inflammation, and apoptotic pathways—are not uniformly evaluated across models. Aquatic species often emphasize oxidative DNA lesions and BER-associated gene expression, whereas terrestrial invertebrates frequently report apoptosis-related markers with limited assessment of canonical repair pathways. Mammalian studies highlight p53-dependent and inflammatory responses, yet few compare these pathways systematically or quantify cross-talk among them. This inconsistency limits the ability to draw firm conclusions about conserved or divergent genomic mechanisms across taxa.

Similarly, in vitro experiments using human or mammalian cell lines often demonstrate clear evidence of oxidative DNA damage, altered expression of DNA repair genes, and increased micronucleus formation; however, these studies frequently rely on single-time-point exposures and immortalized cell lines that may not fully recapitulate responses of primary cells. Moreover, only a few investigations include replication across laboratories or validation in physiologically relevant 3D models. Thus, although the cumulative evidence supports the capacity of MNPs

to disrupt genome integrity, the fragmented assessment of genomic pathways across studies prevents a fully systematic comparison of mechanistic responses.

4.1 | Dose Realism, Extrapolation Bias, and Ecological Risk Interpretation

While Table 6 summarizes reported exposure concentrations of MNPs across experimental systems, a critical consideration is the frequent mismatch between laboratory dosing regimens and environmentally realistic exposure levels. Environmental concentrations of MNPs in water, soil, food, and biota are typically reported in the $\mu\text{g/L}$ – mg/L or particles m^{-3} range, whereas many experimental studies employ concentrations that are one to several orders of magnitude higher to elicit measurable biological responses within short exposure windows (Vethaak and Legler 2021; Koelmans et al. 2022). Although such dosing strategies are valuable for mechanistic discovery, they introduce dose–response extrapolation bias when nominal mass concentrations are interpreted directly in an ecological or human health context.

Importantly, mass-based comparisons alone can be misleading. Particle number, surface area, size distribution, polymer type, and weathering state strongly influence biological reactivity, meaning that lower environmental doses of aged or contaminated particles may exert effects comparable to higher doses of pristine laboratory particles (Hartmann et al. 2019; Koelmans et al. 2022). Failure to account for these parameters risks either overestimating hazard from high-dose studies or underestimating risk from environmentally relevant exposures.

From an ecological risk perspective, Table 6 should therefore be interpreted as defining hazard potential rather than direct environmental risk. Robust risk assessment will require integration of time-resolved, low-dose exposures, environmentally aged particles, and dosimetry frameworks that normalize responses to particle number and surface area, alongside IVIVE-based extrapolation to realistic tissue burdens (Vethaak and Legler 2021). Such approaches will better bridge laboratory findings with real-world exposure scenarios and improve the regulatory relevance of MNP toxicology.

Therefore, the heterogeneity in experimental systems, dosing strategies, endpoints, and mechanistic pathway coverage highlights the need for standardised protocols and integrated genomic frameworks. Future work should harmonise methodologies, examine a broader range of polymers, particle sizes, and co-pollutant scenarios, and adopt pathway-based approaches that directly compare ROS generation, DNA repair pathways, inflammatory signaling, and apoptosis across models. Such alignment will strengthen causal inference and improve ecological and human health risk assessment.

4.2 | Summary

MNPs, derived from both primary (manufactured) and secondary (fragmented) sources, have become pervasive environmental contaminants. These particles infiltrate biological systems through ingestion, inhalation, and dermal contact, affecting

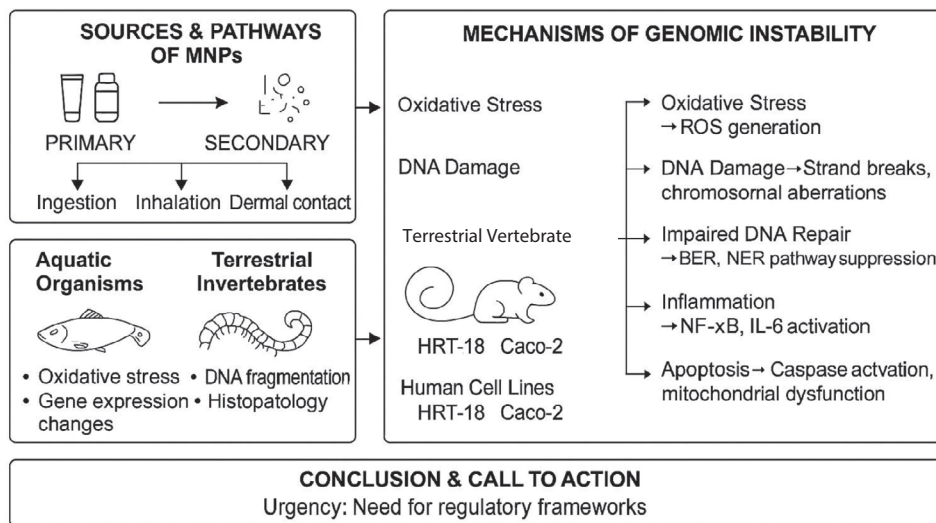


FIGURE 3 | Mechanisms of genomic instability in vertebrate, invertebrate, and human cell lines exposed to MNPs.

organisms across aquatic, terrestrial, and atmospheric ecosystems. Their small size and reactive surfaces enable cellular uptake and interaction with biomolecules, triggering a cascade of toxicological effects.

Mechanistically, MNPs induce genomic instability through several interconnected pathways. Oxidative stress is a central driver, with elevated ROS leading to DNA strand breaks and chromosomal aberrations. These particles also impair DNA repair mechanisms—particularly BER and NER—and activate inflammatory signaling pathways such as NF- κ B and IL-6. Mitochondrial dysfunction and caspase-mediated apoptosis further contribute to cellular damage and genomic disruption.

The biological impact of MNPs spans multiple taxa. Aquatic organisms like zebrafish and silver carp exhibit oxidative stress and altered gene expression. Terrestrial invertebrates such as centipedes and silkworms show DNA fragmentation and histopathological changes, while vertebrates like albino mice demonstrate chromosomal instability and organ-specific genotoxicity. Human epithelial cell lines (HRT-18, Caco-2) respond with cell-type-specific inflammation and metabolic dysregulation, highlighting the translational relevance of these findings (Figure 3).

This growing body of evidence underscores the urgent need for regulatory frameworks to mitigate the genomic and ecological risks posed by MNP exposure. As plastic pollution escalates globally, its intersection with genome integrity presents a critical challenge for environmental health and public safety. While the current body of research provides valuable insights into the genotoxic potential of MNPs, it is dominated by acute and sub-chronic exposure studies, which may not accurately reflect real-world scenarios of chronic, low-dose exposure. Furthermore, PS remains the most extensively studied polymer, creating a knowledge gap regarding other commonly encountered plastics such as PE, polyvinyl chloride (PVC), polyethylene terephthalate (PET), and polyisobutylene (PIB). To strengthen ecological and human health risk assessments, future investigations must prioritize long-term, environmentally relevant exposure models and incorporate a broader spectrum of polymer types. Additionally, the influence of aging and weathering processes

on particle physicochemical properties and toxicity warrants systematic evaluation, as these factors significantly alter surface reactivity and biological interactions. Addressing these gaps will enable a more comprehensive understanding of MNP-induced genomic instability under realistic environmental conditions.

5 | Conclusion

MNPs have become unavoidable contaminants in modern ecosystems, with documented presence in aquatic, terrestrial, and even atmospheric environments. Their small size, large surface area, and diverse chemical composition facilitate their entry into biological systems, where they are capable of interacting directly with cells and biomolecules. Evidence from aquatic organisms, terrestrial animals, and human cell models clearly demonstrates that MNP exposure can induce oxidative stress, inflammation, DNA fragmentation, and chromosomal instability. These cellular and molecular disruptions are linked to impaired antioxidant responses, altered gene expression, and reduced genomic integrity. This review highlights the intricate mechanisms by which MNPs influence gene expression and cellular behavior. They also emphasize the urgency of further research into the effects of plastic pollution at the cellular and molecular levels, especially in human-relevant models, to better assess potential health risks and inform regulatory policies.

5.1 | Recommendation and Future Directions

Given the pervasive distribution of MNPs and their capacity to induce oxidative stress, inflammation, and genomic instability across taxa, urgent action is warranted. Future research should prioritize *mechanistic investigations* that elucidate the precise cellular and molecular pathways underlying MNP-induced DNA damage, particularly in relation to oxidative stress signaling and DNA repair suppression. Additionally, *long-term* in vivo models are needed to assess chronic and transgenerational effects. We also recommend expanding studies beyond PS to include diverse polymer types and environmentally aged particles. From a practical standpoint, there is an immediate need to develop

and implement *regulatory guidelines* limiting environmental discharge of MNPs and monitoring hotspot ecosystems. In addition, future research on MNPs should adopt two complementary frameworks to strengthen mechanistic understanding and ecological relevance. First, an In Vitro-to-In Vivo Extrapolation (IVIVE) framework is needed to translate cellular-level genotoxicity—such as oxidative DNA damage, impaired BER/NER repair pathways, NF- κ B-mediated inflammation, and apoptosis—into organism-level dose equivalents. This requires harmonized particle characterization, standardized in vitro dosimetry, and physiologically based modeling of intestinal uptake and tissue accumulation. Mechanistic anchor endpoints, including 8-oxoG, micronuclei formation, and repair gene expression, should be used to develop benchmark dose estimates applicable across taxa. Second, multi-generation exposure designs (F_0 – F_2 / F_3) are essential for assessing long-term and transgenerational impacts. These studies should use environmentally realistic doses and examine developmental, reproductive, and genomic outcomes in model organisms such as zebrafish, earthworms, silkworms, and mice. Emphasis should be placed on chronic low-dose effects, persistence of DNA damage and repair suppression, inflammatory signaling, mitochondrial dysfunction, and epigenetic or miRNA-mediated inheritance. Incorporating aged or pollutant-loaded particles will improve environmental realism. Together, IVIVE modeling and multi-generation testing will provide a more accurate foundation for ecological risk assessment, regulatory guideline development, and mechanistic insight into how MNPs contribute to genomic instability across biological systems.

Therefore, we recommend systematically comparing pristine versus UV-/oxidatively aged MPs/NPs, with and without adsorbed PAHs/metals, to quantify potency shifts in ROS generation, repair gene repression (BER/NER panels), and CIN metrics. Include factorial designs to resolve additive versus synergistic effects and rank mixture-level hazard under environmentally realistic scenarios.

Pair in vitro particle dosimetry (mass, count, and surface area) with physiologically based intestinal uptake/clearance models to estimate organ burdens that reproduce observed BER/NER suppression and micronucleus benchmark doses in vivo. Report conversion factors to μ g plastic per g tissue and particles per 10^6 cells to harmonize endpoints across systems and support risk-relevant dose setting.

Use chronic low-dose exposures with aged, mixed-polymer particles, tracking: (i) genotoxic endpoints (comet/ γ H2AX/micronucleus) in F_0 tissues; (ii) genomic-instability endpoints (aneuploidy rates, segregation errors, persistent CNV by qPCR or shallow WGS) across F_1 – F_2 ; (iii) epigenetic drift (global 5-mC, selected DMRs/miRNA panels) to test inheritance. Employ ≥ 3 biological replicates per sex/timepoint and fit mixed-effects models to resolve lineage effects.

Also, in Table 6, to reduce bias, we advocate reporting mass, count, and surface-area dosimetry together; using aged/mixed-polymer particles; and prioritizing longer, low-dose exposures. Ecological risk inferences should therefore weigh environmental realism (weathered particles may be more potent per mass than pristine spheres) against the mechanistic value of higher

laboratory doses that reveal repair suppression, checkpoint adaptation, and early CIN signatures.

Finally, future work should explore bioremediation strategies, including microbial degradation and enzyme-based approaches, as sustainable methods to reduce MNP abundance in aquatic and terrestrial environments.

Acknowledgments

During the preparation of this work, the author(s) used Copilot/ChatGPT to improve language. After using this service, the author(s) reviewed and edited the content as needed and take full responsibility for the content of the publication.

Funding

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

- Alaraby, M., D. Abass, J. Domenech, A. Hernández, and R. Marcos. 2022. "Hazard Assessment of Ingested Polystyrene Nanoplastics in *Drosophila* larvae." *Environmental Science: Nano* 9: 1845–1857.
- Alaraby, M., D. Abass, A. Villacorta, A. Hernández, and R. Marcos. 2023. "The Hazardous Impact of True-to-Life PET Nanoplastics in *Drosophila*." *Science of the Total Environment* 863: 160954.
- Alimi, O. S., J. F. Budarz, L. M. Hernandez, and N. Tufenkji. 2018. "Microplastics and Nanoplastics in Aquatic Environments: Aggregation, Deposition, and Enhanced Contaminant Transport." *Environmental Science & Technology* 52, no. 4: 1704–1724.
- Andrady, A. L. 2022. "Weathering and Fragmentation of Plastic Debris in the Ocean Environment." *Marine Pollution Bulletin* 180: 113761.
- Andrady, A. L., and M. A. Neal. 2011. "Applications and Societal Benefits of Plastics." *Philosophical Transactions of the Royal Society, B: Biological Sciences* 364, no. 1526: 1977–1984.
- Anifowoshe, A. T., M. N. Akhtar, A. Majeed, A. S. Singh, T. F. Ismail, and U. Nongthomba. 2025. "Microplastics: A Threat to Fetoplacental Unit and Reproductive Systems." *Toxicology Reports* 14: 101938.
- Anifowoshe, A. T., A. Mukherjee, V. A. Ajisafe, and U. Nongthomba. 2024. "Synthesis and Characterization of Micro-Sized Polyisobutylene and Evaluation of Its Toxicological Effects on the Development and Homeostasis of Zebrafish (*Danio rerio*)." *Scientific Reports* 14: 20300.
- Anifowoshe, A. T., D. Roy, S. Dutta, and U. Nongthomba. 2022. "Evaluation of Cytogenotoxic Potential and Embryotoxicity of KRS Cauvery River Water in Zebrafish (*Danio rerio*)." *Ecotoxicology and Environmental Safety* 233: 113320. <https://doi.org/10.1016/j.ecoenv.2022.113320>.
- Annona, G., C. Montanino, B. De Felice, and P. De Luca. 2025. "Identification of MicroRNA-mRNA Regulatory Network Associated With Microplastic Exposure in *Mytilus galloprovincialis*." *Genomics* 117, no. 5: 111080.
- Ashrafy, A., A. A. Liza, M. N. Islam, et al. 2023. "Microplastics Pollution: A Brief Review of Its Source and Abundance in Different Aquatic Ecosystems." *Journal of Hazardous Materials Advances* 9: 100215.

- Barman, D., and R. Drolia. 2024. "Caveolin-Mediated Endocytosis: Bacterial Pathogen Exploitation and Host-Pathogen Interaction." *Cells* 14, no. 1: 2. <https://doi.org/10.3390/cells14010002>.
- Bengalli, R., A. Zerboni, P. Bonfanti, et al. 2021. "Characterization of Microplastics Derived From Waste Plastics and Their Bio-Interaction With Human Lung A549 Cells." *Journal of Applied Toxicology* 42: 2030–2044. <https://doi.org/10.1002/jat.4372>.
- Bexeitova, K., A. Baimenov, E. A. Varol, et al. 2024. "Microplastics in Freshwater Systems: A Review of Classification, Sources, and Environmental Impacts." *Chemical Engineering Journal Advances* 20: 100649. <https://doi.org/10.1016/j.cej.2024.100649>.
- Bon, C., L. Pulze, S. Amoroso, et al. 2026. "Inflammatory and Oxidative Responses to PET Nanoplastics in the Leech *Hirudo verbana*: A Comparative Analysis of Acute and Chronic Exposure." *Environmental Science: Nano* 13: 427–446. <https://doi.org/10.1039/D5EN00733J>.
- Chen, X., J. Zhuang, Q. Chen, L. Xu, X. Yue, and D. Qiao. 2022. "Polyvinyl Chloride Microplastics Induced Gut Barrier Dysfunction, Microbiota Dysbiosis and Metabolism Disorder in Adult." *Ecotoxicological and Environmental Safety Journal* 241: 113809.
- Clay, D. E., and D. T. Fox. 2021. "DNA Damage Responses During the Cell Cycle: Insights From Model Organisms and Beyond." *Genes* 12, no. 12: 1882. <https://doi.org/10.3390/genes12121882>.
- Cole, M., P. Lindeque, C. Halsband, and T. S. Galloway. 2011. "Microplastics as Contaminants in the Marine Environment: A Review." *Marine Pollution Bulletin* 62, no. 12: 2588–2597.
- de Mello Pereira, D., S. C. Mazon, E. J. Mendes, et al. 2023. "Recycled Polyvinyl Chloride Microplastics: Investigation of Environmentally Relevant Concentrations on Toxicity in Adult Zebrafish." *Journal of Toxicology and Environmental Health, Part A* 86, no. 11: 347–360. <https://doi.org/10.1080/15287394.2023.2203154>.
- Doherty, G. J., and H. T. McMahon. 2009. "Mechanisms of Endocytosis." *Annual Review of Biochemistry* 78, no. 1: 857–902. <https://doi.org/10.1146/annurev.biochem.78.081307.110540>.
- Domenech, J., M. de Britto, A. Velázquez, et al. 2021. "Long-Term Effects of Polystyrene Nanoplastics in Human Intestinal Caco-2 Cells." *Biomolecules* 11, no. 10: 1442. <https://doi.org/10.3390/biom11101442>.
- El Kholy, S., and Y. Al-Naggat. 2023. "Exposure to Polystyrene Microplastic Beads Causes Sex-specific Toxic Effects in the Model Insect *Drosophila melanogaster*." *Scientific Reports* 13: 204. <https://doi.org/10.1038/s41598-022-27284-7>.
- Espinosa, C., M. Á. Esteban, and A. Cuesta. 2019. "Dietary Administration of PVC and PE Microplastics Produces Histological Damage, Oxidative Stress and Immunoregulation in European Sea Bass (*Dicentrarchus labrax* L.)." *Fish & Shellfish Immunology* 95: 574–583. <https://doi.org/10.1016/j.fsi.2019.10.072>.
- Feng, M., J. Luo, Y. Wan, et al. 2022. "Polystyrene Nanoplastic Exposure Induces Developmental Toxicity by Activating the Oxidative Stress Response and Base Excision Repair Pathway in Zebrafish (*Danio rerio*)." *ACS Omega* 7, no. 37: 32153–32163. <https://doi.org/10.1021/acsomega.2c03738>.
- Ferguson, L. R., H. Chen, A. R. Collins, et al. 2015. "Genomic Instability in Human Cancer: Molecular Insights and Opportunities for Therapeutic Attack and Prevention Through Diet and Nutrition." *Seminars in Cancer Biology* 35: S5–S24.
- Filipkowski, P., C. Aleksandra, Z. Koziara, K. Parchem, L. Zedler, and J. Ryl. 2022. "Analysis of the Influence of Polystyrene Microplastics and Their Derivatives on the DNA of Human Colon Epithelial Cells HT29 With the Comet Assay." *Research Square* <https://www.researchsquare.com/article/rs-1859481/v1>.
- Flannagan, R. S., V. Jaumouillé, and S. Grinstein. 2012. "The Cell Biology of Phagocytosis." *Annual Review of Pathology: Mechanisms of Disease* 7: 61–98. <https://doi.org/10.1146/annurev-pathol-011811-132445>.
- Gao, N., Z. Huang, J. Xing, S. Zhang, and J. Hou. 2021. "Impact and Molecular Mechanism of Microplastics on Zebrafish in the Presence and Absence of Copper Nanoparticles." *Frontiers in Marine Science* 8: 762530. <https://doi.org/10.3389/fmars.2021.762530>.
- Geyer, R., J. R. Jambeck, and K. L. Law. 2017. "Production, Use, and Fate of All Plastics Ever Made." *Science Advances* 3, no. 7: 700782.
- Gigault, J., A. T. Halle, M. Baudrimont, et al. 2018. "Current Opinion: What Is a Nanoplastic?" *Environmental Pollution* 235: 1030–1034.
- Goodman, K. E., T. Hua, and Q. X. A. Sang. 2022. "Effects of Polystyrene Microplastics on Human Kidney and Liver Cell Morphology, Cellular Proliferation, and Metabolism." *ACS Omega* 7: 34136–34153.
- Guerrera, M. C., M. Aragona, C. Porcino, et al. 2021. "Micro and Nano Plastics Distribution in Fish as Model Organisms: Histopathology, Blood Response and Bioaccumulation in Different Organs." *Applied Sciences* 11, no. 13: 5768. <https://doi.org/10.3390/app11135768>.
- Hamed, M., C. J. Martyniuk, M. Naguib, J.-S. Lee, and A. E.-D. H. Sayed. 2022. "Neurotoxic Effects of Different Sizes of Plastics (Nano, Micro, and Macro) on Juvenile Common Carp (*Cyprinus carpio*)." *Frontiers in Molecular Neuroscience* 15: 1028364. <https://doi.org/10.3389/fnmol.2022.1028364>.
- Hartmann, N. B., T. Hüffer, R. C. Thompson, et al. 2019. "Are We Speaking the Same Language? Recommendations for a Definition and Categorization Framework for Plastic Debris." *Environmental Science and Technology* 53, no. 3: 1039–1047. <https://doi.org/10.1021/acs.est.8b05297>.
- He, Y., and R. Yin. 2024. "The Reproductive and Transgenerational Toxicity of Microplastics and Nanoplastics: A Threat to Mammalian Fertility in Both Sexes." *Journal of Applied Toxicology* 44, no. 1: 66–85.
- Hossain, M. A., Y. Lin, and S. Yan. 2018. "Single-Strand Break End Resection in Genome Integrity: Mechanism and Regulation by APE2." *International Journal of Molecular Sciences* 19, no. 8: 2389. <https://doi.org/10.3390/ijms19082389>.
- Hou, J., Z. Lei, L. Cui, et al. 2021. "Polystyrene Microplastics Lead to Pyroptosis and Apoptosis of Ovarian Granulosa Cells via NLRP3/Caspase-1 Signaling Pathway in Rats." *Ecotoxicology and Environmental Safety* 212: 112012.
- Huang, J. N., B. Wen, J. G. Zhu, Y. S. Zhang, J. Z. Gao, and Z. Z. Chen. 2020. "Exposure to Microplastics Impairs Digestive Performance, Stimulates Immune Response and Induces Microbiota Dysbiosis in the Gut of Juvenile Guppy (*Poecilia reticulata*)." *Science of the Total Environment* 733: 138929. <https://doi.org/10.1016/j.scitotenv.2020.138929>.
- Huang, R., and P. K. Zhou. 2021. "DNA Damage Repair: Historical Perspectives, Mechanistic Pathways and Clinical Translation for Targeted Cancer Therapy." *Signal Transduction and Targeted Therapy* 6, no. 1: 254.
- Hwang, K.-S., Y. Son, S. S. Kim, et al. 2022. "Size-Dependent Effects of Polystyrene Nanoparticles on Behaviors and Endogenous Neurochemicals in Zebrafish Larvae." *International Journal of Molecular Sciences* 23, no. 18: 10682. <https://doi.org/10.3390/ijms231810682>.
- Jolaosho, T. L., M. F. Rasah, E. V. Omotoye, et al. 2025. "Microplastics in Freshwater and Marine Ecosystems: Occurrence, Characterization, Sources, Distribution Dynamics, Fate, Transport Processes, Potential Mitigation Strategies, and Policy Interventions." *Ecotoxicology and Environmental Safety* 294: 118036.
- Kadac-Czapska, K., J. Oško, E. Knez, and M. Grembecka. 2024. "Microplastics and Oxidative Stress-Current Problems and Prospects." *Antioxidants (Basel, Switzerland)* 13, no. 5: 579. <https://doi.org/10.3390/antiox13050579>.
- Kauts, S., Y. Mishra, and M. P. Singh. 2024. "Impact of Polyethylene Terephthalate Microplastics on *Drosophila melanogaster* Biological Profiles and Heat Shock Protein Levels." *Biology* 13, no. 5: 293.

- Kik, K., B. Bukowska, and P. Sicińska. 2020. "Polystyrene Nanoparticles: Sources, Occurrence in the Environment, Distribution in Tissues, Accumulation and Toxicity to Various Organisms." *Environmental Pollution* 262: 114297.
- Koelmans, A. A., E. Besseling, and W. J. Shim. 2015. "Nanoplastics in the Aquatic Environment. Critical Review." In *Marine Anthropogenic Litter*, edited by M. Bergmann, L. Gutow, and M. Klages. Springer. https://doi.org/10.1007/978-3-319-16510-3_12.
- Koelmans, A. A., P. E. Redondo-Hasselerharm, N. H. M. Nor, V. N. de Ruijter, S. M. Mintenig, and M. Kooi. 2022. "Risk Assessment of Microplastic Particles." *Nature Reviews Materials* 7: 138–152. <https://doi.org/10.1038/s41578-021-00411-y>.
- Kolarević, S., M. Kračun-Kolarević, J. Jovanović Marić, et al. 2023. "Single and Combined Potential of Polystyrene Microparticles and Fluoranthene in the Induction of DNA Damage in Haemocytes of Mediterranean Mussel (*Mytilus galloprovincialis*)."
Mutagenesis 38, no. 1: 3–12. <https://doi.org/10.1093/mutage/geac017>.
- La Maestra, S., F. D'Agostini, M. Benvenuti, et al. 2025. "Microplastics as Benzo-a-pyrene Carriers: Genotoxicity Assessment Simulating Human Gastric Digestion." *Archives of Toxicology* 99, no. 7: 3023–3033.
- Lai, Y., Z. Jiang, J. Zhou, E. Osemota, and Y. Liu. 2016. "AP Endonuclease 1 Prevents the Extension of a T/G Mismatch by DNA Polymerase β to Prevent Mutations in CpGs During Base Excision Repair." *DNA Repair* 43: 89–97. <https://doi.org/10.1016/j.dnarep.2016.03.006>.
- Lee, J.-H., J.-H. Choi, Y. J. Kang, et al. 2025. "Toxic Effects of Microplastics (Polyethylene) Exposure on Acetylcholinesterase, Stress Indicators and Immunity in Korean Bullhead, *Pseudobagrus fulvidraco*." *Environmental Toxicology and Pharmacology* 114: 104654. <https://doi.org/10.1016/j.etap.2025.104654>.
- Levesque, B., S. Hrapovic, F. Berru  , A. Vogt, L. D. Ellis, and L. Hermabessiere. 2025. "Evaluation of Phenotypic and Behavioral Toxicity of Micro- and Nano-Plastic Polystyrene Particles in Larval Zebrafish (*Danio rerio*)."
Toxicological Sciences 205, no. 1: 154–165. <https://doi.org/10.1093/toxsci/kfaf015>.
- Lim, J. P., and P. A. Gleeson. 2011. "Macropinocytosis: An Endocytic Pathway for Internalising Large Gulp." *Immunology and Cell Biology* 89, no. 8: 836–843. <https://doi.org/10.1038/icb.2011.20>.
- Limonta, G., A. Mancina, A. Benkhalqui, et al. 2019. "Microplastics Induce Transcriptional Changes, Immune Response and Behavioral Alterations in Adult Zebrafish." *Scientific Reports* 9: 15775. <https://doi.org/10.1038/s41598-019-52292-5>.
- Liu, X., C. Liang, M. Zhou, Z. Chang, and L. Li. 2023. "Exposure of *Cyprinus carpio* var. Larvae to PVC Microplastics Reveals Significant Immunological Alterations and Irreversible Histological Organ Damage." *Ecotoxicology and Environmental Safety* 249: 114377.
- Liu, Y., X. Li, and Y. Xiong. 2024. "Chronic Polystyrene Microplastic Exposure Reduces Testosterone Levels in Mice Through Mitochondrial Oxidative Stress and BAX/BCL2-Mediated Apoptosis." *Toxics* 12, no. 8: 561–569.
- Liu, Z., Q. Zhuan, L. Zhang, L. Meng, X. Fu, and Y. Hou. 2022. "Polystyrene Microplastics Induced Female Reproductive Toxicity in Mice." *Journal of Hazardous Materials* 424, Pt C: 127629. <https://doi.org/10.1016/j.jhazmat.2021.127629>.
- L  pez-Ot  n, C., M. A. Blasco, L. Partridge, M. Serrano, and G. Kroemer. 2023. "Hallmarks of Aging: An Expanding Universe." *Cell* 186, no. 2: 243–278. <https://doi.org/10.1016/j.cell.2022.11.001>.
- Lu, Y., Y. Zhang, Y. Deng, et al. 2016. "Uptake and Accumulation of Polystyrene Microplastics in Zebrafish (*Danio rerio*) and Toxic Effects in Liver." *Environmental Science & Technology* 50, no. 7: 4054–4060. <https://doi.org/10.1021/acs.est.6b00183>.
- Lwanga, E. H., H. Gertsen, H. Gooren, et al. 2017. "Incorporation of Microplastics From Litter Into Burrows of *Lumbricus terrestris*." *Environmental Pollution* 220: 523–531. <https://doi.org/10.1016/j.envpol.2016.09.096>.
- Majeed, Z. M., and A. M. Rabee. 2025. "The Toxicity of Polyethylene Microplastics on Molecular and Biochemical Parameters in Albino Mice." *Journal of Ecological Engineering* 26, no. 3: 274–282.
- Mani, C., P. H. Reddy, and K. Palle. 2020. "DNA Repair Fidelity in Stem Cell Maintenance, Health, and Disease." *Biochimica et Biophysica Acta - Molecular Basis of Disease* 1866, no. 4: 165444. <https://doi.org/10.1016/j.bbadis.2019.03.017>.
- Masi  , P., A. Ardura, and E. Garc  a-V  zquez. 2021. "Virgin Polystyrene Microparticles Exposure Leads to Changes in Gills DNA and Physical Condition in the Mediterranean Mussel *Mytilus galloprovincialis*." *Animals* 11, no. 8: 2317. <https://doi.org/10.3390/ani11082317>.
- Matthews, S. 2020. "Evaluating the Toxicity of Microplastics and Nanoplastics to *Drosophila Melanogaster*." (Master's thesis) McGill University.
- Mattioda, V., V. Benedetti, C. Tessarolo, et al. 2023. "Pro-Inflammatory and Cytotoxic Effects of Polystyrene Microplastics on Human and Murine Intestinal Cell Lines." *Biomolecules* 13: 140.
- Mottola, F., M. Carannante, A. Barretta, I. Palmieri, and L. Rocco. 2024. "Reproductive Cytotoxic and Genotoxic Impact of Polystyrene Microplastic on *Paracentrotus lividus* Spermatozoa." *Current Research in Toxicology* 6: 100173. <https://doi.org/10.1016/j.crtox.2024.100173>.
- Mu, Y., J. Sun, Z. Li, et al. 2022. "Activation of Pyroptosis and Ferroptosis is Involved in the Hepatotoxicity Induced by Polystyrene Microplastics in Mice." *Chemosphere* 291: 132944.
- Muhammad, A., X. Zhou, J. He, et al. 2021. "Toxic Effects of Acute Exposure to Polystyrene Microplastics and Nanoplastics on the Model Insect, Silkworm *Bombyx mori*." *Environmental Pollution* 285: 117255. <https://doi.org/10.1016/j.envpol.2021.117255>.
- Najahi, H., N. Alessio, T. Squillaro, et al. 2022. "Environmental Microplastics (EMPs) Exposure Alter the Differentiation Potential of Mesenchymal Stromal Cells." *Environmental Research* 214, no. Pt 4: 114088. <https://doi.org/10.1016/j.envres.2022.114088>.
- Nasser, F., and I. Lynch. 2016. "Secreted Protein Eco-Corona Mediates Uptake and Impacts of Polystyrene Nanoparticles on *Daphnia magna*." *Journal of Proteomics* 137: 45–51. <https://doi.org/10.1016/j.jprot.2015.09.005>.
- Negrini, S., V. G. Gorgoulis, and T. D. Halazonetis. 2010. "Genomic Instability—An Evolving Hallmark of Cancer." *Nature Reviews. Molecular Cell Biology* 11, no. 3: 220–228.
- Paganos, P., C. V. Ullmann, D. Gaglio, et al. 2023. "Plastic Leachate-Induced Toxicity During Sea Urchin Embryonic Development: Insights into the Molecular Pathways Affected by PVC." *Science of the Total Environment* 864: 160901. <https://doi.org/10.1016/j.scitotenv.2022.160901>.
- Parenti, C. C., A. Binelli, S. Caccia, et al. 2020. "Ingestion and Effects of Polystyrene Nanoparticles in the Silkworm *Bombyx mori*." *Chemosphere* 257: 127203. <https://doi.org/10.1016/j.chemosphere.2020.127203>.
- Piano, D. F., A. Lama, A. Monnolo, et al. 2023. "Subchronic Exposure to Polystyrene Microplastic Differently Affects Redox Balance in the Anterior and Posterior Intestine of *Sparus aurata*." *Animals* 13, no. 4: 606. <https://doi.org/10.3390/ani13040606>.
- Poma, A., G. Vecchiotti, S. Colafarina, et al. 2019. "In Vitro Genotoxicity of Polystyrene Nanoparticles on the Human Fibroblast Hs27 Cell Line." *Nanomaterials (Basel)* 9: 1299.
- Priscilla, S., R. Nagasawa, S. Senthil Kumar, et al. 2025. "Polyethylene Microplastics Induce Behavioural and Developmental Deficits in the *Drosophila* Model." *Toxicology and Environmental Health Sciences* 17: 449–460.

- Raj, H., A. Raj, S. Ranjan, G. Azad, and S. Yasmin. 2024. "Exposure of Polystyrene Microplastics Induces Oxidative Stress and Physiological Defects in *Drosophila melanogaster*." *Asian Journal of Basic Science & Research* 1: 55–64.
- Ranjan, H., S. Senthil Kumar, S. Priscilla, S. Swaminathan, M. Umezawa, and S. S. Mohideen. 2024. "Polyethylene Microplastics Affect Behavioural, Oxidative Stress, and Molecular Responses in the *Drosophila* Model." *Environmental Science: Processes & Impacts* 26: 2203–2214.
- Rashid, E., S. M. Hussain, S. Ali, K. A. Al-Ghanim, and P. K. Sarker. 2024. "Toxicological Consequences of Polystyrene Microplastics on *Cirrhinus mrigala*: Effects on Growth, Body Composition, Nutrient Digestibility, Haematology and Histopathology." *Marine and Freshwater Research* 75: MF24055.
- Rendell-Bhatti, F., P. Paganos, A. Pouch, et al. 2021. "Developmental Toxicity of Plastic Leachates on the Sea Urchin *Paracentrotus lividus*." *Environmental Pollution* 269: 115744. <https://doi.org/10.1016/j.envpol.2020.115744>.
- Revel, M., F. Lagarde, H. Perrein-Ettajani, et al. 2019. "Tissue-Specific Biomarker Responses in the Blue Mussel *Mytilus* spp. Exposed to a Mixture of Microplastics at Environmentally Relevant Concentrations." *Frontiers in Environmental Science* 7: 33. <https://doi.org/10.3389/fenvs.2019.00033>.
- Roh, Y., J. Kim, H. Song, et al. 2024. "Impact of the Oral Administration of Polystyrene Microplastics on Hepatic Lipid, Glucose, and Amino Acid Metabolism in C57BL/6Korl and C57BL/6-Lepem1hwl/Korl Mice." *International Journal of Molecular Sciences* 25, no. 9: 4964. <https://doi.org/10.3390/ijms25094964>.
- Roman, C., P. Mahé, O. Latchere, et al. 2023. "Effect of Size Continuum from Nanoplastics to Microplastics on Marine Mussel *Mytilus edulis*: Comparison in Vitro/in Vivo Exposure Scenarios." *Comparative Biochemistry and Physiology, Part C: Toxicology & Pharmacology* 264: 109512. <https://doi.org/10.1016/j.cbpc.2022.109512>.
- Rubio, L., I. Barguilla, J. Domenech, R. Marcos, and A. Hernández. 2020. "Biological Effects, Including Oxidative Stress and Genotoxic Damage, of Polystyrene Nanoparticles in Different Human Hematopoietic Cell Lines." *Journal of Hazardous Materials* 398: 122900.
- Santovito, A., M. Lambertini, and A. Nota. 2024. "In Vitro and In Vivo Genotoxicity of Polystyrene Microplastics: Evaluation of a Possible Synergistic Action with Bisphenol A." *Journal of Xenobiotics* 14: 1415–1431.
- Saraceni, A., A. E. Rubin, Y. Wexler, Y. Gothilf, P. Bovolin, and I. Zucker. 2025. "Simulated Environmental Nanoplastics Induce Zebrafish Developmental Toxicity and Stress Response." *ACS Sustainable Chemistry & Engineering* 13: 4833–4844. <https://doi.org/10.1021/acssuschemeng.4c10847>.
- Sarma, D. K., R. Dubey, R. M. Samarth, et al. 2022. "The Biological Effects of Polystyrene Nanoplastics on Human Peripheral Blood/Lymphocytes." *Nanomaterials (Basel)* 12: 1632.
- Shahriar, S. I. M., M. M. Rahman, and M. S. Islam. 2024. "Size Dependent Ingestion and Effects of Microplastics on Survivability, Hematology and Intestinal Histopathology of Juvenile Striped Catfish (*Pangasianodon hypophthalmus*)." *Chemosphere* 356: 141827. <https://doi.org/10.1016/j.chemosphere.2024.141827>.
- Sobhani, Z., L. Panneerselvam, C. Fang, R. Naidu, and M. Megharaj. 2021. "Chronic and Transgenerational Effects of Polystyrene Microplastics at Environmentally Relevant Concentrations in Earthworms (*Eisenia fetida*)." *Environmental Toxicology and Chemistry* 40, no. 8: 2240–2246. <https://doi.org/10.1002/etc.5072>.
- Tang, K. H. D., and H. A. Yuen. 2023. "The Effects of Plastic Pollution on Insects: A Review of the Impacts of Microplastics on Insect Health and Ecological Function." *Science of the Total Environment* 850: 157857. <https://doi.org/10.1016/j.scitotenv.2022.157857>.
- Teng, M., X. Zhao, C. Wang, et al. 2022. "Polystyrene Nanoplastics Toxicity to Zebrafish: Dysregulation of the Brain–Intestine–Microbiota Axis." *ACS Nano* 16, no. 5: 8190–8204.
- Thompson, R. C., Y. Olsen, R. P. Mitchell, et al. 2004. "Lost at Sea: Where Is All the Plastic?" *Science* 304, no. 5672: 838.
- Tongo, I., and N. O. Erhunmwunse. 2022. "Effects of Ingestion of Polyethylene Microplastics on Survival Rate, Opercular Respiration Rate and Swimming Performance of African Catfish (*Clarias gariepinus*)." *Journal of Hazardous Materials* 423, Pt B: 127237. <https://doi.org/10.1016/j.jhazmat.2021.127237>.
- Ullah, N., S. Sidra, H. Hamda Azmat, and M. A. Muddassir. 2025. "Dose-Dependent Genotoxicity and Gene Expression Induced by Oral Exposure to PVC-MPs in *Mus musculus*." *Pollution and Environmental Studies Journal* 200461: 1–11.
- Umamaheswari, S., S. Priyadarshinee, K. Kadirvelu, and M. Ramesh. 2021. "Polystyrene Microplastics Induce Apoptosis via ROS-Mediated p53 Signaling Pathway in Zebrafish." *Chemico-Biological Interactions* 345: 109550. <https://doi.org/10.1016/j.cbi.2021.109550>.
- Usman, A., A. Ghani, Z. Ali, M. Salman, and A. Khan. 2025. "Eco-Toxicological Effects of Polyethylene Microplastics on DNA Damage in Erythrocytes of Common Carp (*Cyprinus carpio*)." *Pure and Applied Biology* 14, no. 4: 1191–1197. <https://doi.org/10.19045/bspub.2025.140107>.
- Usman, S., A. F. Abdull Razis, K. Shaari, et al. 2021. "Polystyrene Microplastics Exposure: An Insight Into Multiple Organ Histological Alterations, Oxidative Stress and Neurotoxicity in Javanese Medaka Fish (*Oryzias javanicus* Bleeker, 1854)." *International Journal of Environmental Research and Public Health* 18, no. 18: 9449. <https://doi.org/10.3390/ijerph18189449>.
- Vethaak, A. D., and J. Legler. 2021. "Microplastics and Human Health." *Science* 371, no. 6530: 672–674. <https://doi.org/10.1126/science.abe5041>.
- Visalli, G., A. Facciola, M. P. Ciarello, G. De Marco, M. Maisano, and A. Di Pietro. 2021. "Acute and Sub-Chronic Effects of Microplastics (3 and 10 μ m) on the Human Intestinal Cells HT-29." *International Journal of Environmental Research and Public Health* 18: 5833.
- Wei, Y., Y. Zhou, C. Long, et al. 2021. "Polystyrene Microplastics Disrupt the Blood-Testis Barrier Integrity Through ROS-Mediated Imbalance of mTORC1 and mTORC2." *Environmental Pollution Journal* 289: 117904.
- Wu, S., M. Wu, D. Tian, L. Qiu, and T. Li. 2019. "Effects of Polystyrene Microbeads on Cytotoxicity and Transcriptomic Profiles in Human Caco-2 Cells." *Environmental Toxicology* 35, no. 4: 495–506.
- Xie, Y., H. Li, X. Guo, Y. Li, and Y. Wang. 2024. "Mechanisms of Polystyrene Nanoplastic Uptake by Intestinal Epithelial Cells." *Environmental Pollution* 342: 123864. <https://doi.org/10.1016/j.envpol.2023.123864>.
- Yang, Z., G. M. DeLoid, J. Baw, H. Zarbl, and P. Demokritou. 2024. "Assessment of Ingested Micro- and Nanoplastic (MNP)-Mediated Genotoxicity in an In Vitro Model of the Small Intestinal Epithelium (SIE)." *Nanomaterials (Basel)* 14, no. 9: 807. <https://doi.org/10.3390/nano14090807>.
- Yong, C. Q. Y., S. Valiyaveetil, and B. L. Tang. 2020. "Toxicity of Microplastics and Nanoplastics in Mammalian Systems." *International Journal of Environmental Research and Public Health* 17, no. 5: 1509. <https://doi.org/10.3390/ijerph17051509>.
- Zhang, C., J. Wang, Y. Luo, X. Wang, Y. Chen, and Y. Liu. 2021. "A Dosage-Effect Assessment of Acute Toxicology Tests of Microplastic Exposure in Filter-Feeding Fish." *Fish & Shellfish Immunology* 113: 154–161.
- Zhang, X., W. Zheng, W. Shao, et al. 2024. "Environmental Concentrations of Microplastic-Induced Gut Microbiota and Metabolite Disruption in Silkworm, *Bombyx mori*." *Chemosphere* 358: 142126. <https://doi.org/10.1016/j.chemosphere.2024.142126>.

Zhang, Y., X. Wang, Y. Zhao, J. Zhao, T. Yu, and Y. Yao. 2023. "Reproductive Toxicity of Microplastics in Female Mice and Their Offspring From Induction of Oxidative Stress." *Environmental Pollution* 327: 121482.

Zhu, X., Y. Zhao, Y. Wang, and L. Zhang. 2020. "Polystyrene Microplastics Induce Gut Microbiota Dysbiosis and Hepatic Lipid Metabolism Disorder in Mice." *Aquatic Toxicology* 214: 105396. <https://doi.org/10.1016/j.aquatox.2019.105396>.