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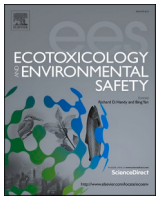

Perspective on using non-human primates in Exposome research

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ABSTRACT

The physiological and pathological changes in the human body caused by environmental pressures are collectively referred to as the Exposome. Human society is facing escalating environmental pollution, leading to a rising prevalence of associated diseases, including respiratory diseases, cardiovascular diseases, neurological disorders, reproductive development disorders, among others. Vulnerable populations to the pathogenic effects of environmental pollution include those in the prenatal, infancy, and elderly stages of life. Conducting Exposome mechanistic research and proposing effective health interventions are urgent in addressing the current severe environmental pollution. In this review, we address the core issues and bottlenecks faced by current Exposome research, specifically focusing on the most toxic ultrafine nanoparticles. We summarize multiple research models being used in Exposome research. Especially, we discuss the limitations of rodent animal models in mimicking human physiopathological phenotypes, and prospect advantages and necessity of non-human primates in Exposome research based on their evolutionary relatedness, anatomical and physiological similarities to human. Finally, we declare the initiation of NHPE (Non-Human Primate Exposome) project for conducting Exposome research using non-human primates and provide insights into its feasibility and key areas of focus.

Synopsis: Non-human primate models hold unique advantages in human Exposome research.

1. Conceptual introduction

1.1. Exposome

Since the advent of genome sequencing technology, genomic information of many biological species including human has been deciphered (Gibbs, 2020). This has allowed us to gain a deeper understanding of the operational principles of life at the genetic level and the mechanistic pathways underlying the occurrence and progression of human diseases. However, it is estimated that only about 15 % of human diseases can be entirely attributed to genetic variations. Correspondingly, approximately 85 % of human diseases do not solely rely on genetic variations but result from the interplay between genetics and the environment (Berg, 2016; Scheen and Junien, 2012). For instance, diseases such as cardiovascular disorders, tumors, and neurodegenerative diseases are not only associated with individual genetic variations but also heavily influenced by factors such as age, lifestyle, and occupational exposures in terms of their incidence and progression (Alonso-Curbelo et al., 2021; Kwo and Christiani, 2017). Therefore, a profound comprehension of the impact of environmental factors on human health and the driving mechanisms behind human diseases has become a crucial focus in post-genomic era health research.

The concept of the Exposome was introduced by Christopher Paul Wild in 2005, referring to the collective term for physiological and pathological changes in the human body caused by various environmental exposure factors throughout the entire lifespan (Wild, 2005). In

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contrast to the emphasis on the importance of genetic variations in genomic research, the Exposome underscores the role of non-genetic factors in human health. These non-genetic factors can be categorized as ecosystem disturbances, societal behaviors, lifestyles, and physical-chemical factors, among others (Vermeulen et al., 2020). Simultaneously, Exposomics encompasses a research framework spanning various levels, including the genome, transcriptome, proteome, epigenome, and metabolome, with the aim of comprehensively understanding the environmental and genetic interplays in human physiological and pathological scenarios (Wu et al., 2023). In fact, drawing inspiration from Genome-Wide Association Studies (GWAS) and Biobank databases (Patel et al., 2010), the concept of Environment-wide association study (EWAS) has been introduced (Patel et al., 2013). The construction of EWAS databases is still in its early stage. The integration of comprehensive EWAS data resources, including human-related omics data, cohort data, and those obtained from cell lines and various living organism models, requires further efforts. Moreover, while EWAS often consolidates data from short-term time points, there is a relative scarcity of long-term, continuous monitoring data from specific individuals or populations. Additionally, EWAS mega data identifies numerous genetic risk factors and environmental exposure factors, but the in-depth mechanistic understanding of these factors remain limited (Wu et al., 2023). Thus, two aspects need to be promised in current Exposome research: there is a need to prioritize the collection of long-term (*e.g.* life-long) continuous data to improve research breadth, meanwhile detailed biological mechanistic studies are essential for study depth.

1.2. Pollutome

Environmental pollution is undeniably the central focus of Exposome research. Environmental pollution can be broadly categorized into subtypes such as air pollution, water pollution, soil pollution, and occupational exposure (Fuller et al., 2022). In order to facilitate a scientific, systematic, and hierarchical understanding of environmental pollution, Philip J Landrigan and colleagues proposed the concept of the "Pollutome" in 2017 (Landrigan et al., 2018a). The Pollutome refers to the sum total of all pollutants that have detrimental effects on human health. Thus, the Pollutome constitutes a subset within the Exposome category. Based on the mechanisms of pollutants and their association with human diseases, the Pollutome is further divided into three zones (Landrigan et al., 2018a). Zone 1 comprises known pollutants with clear toxic mechanisms and well-established etiological effects on specific human diseases. Relevant data has been consolidated into the Global Burden of Disease (GBD) database (Global, 2022). Zone 2 includes emerging pollutants, where it has been recognized that these pollutants have toxic effects on human health, but the quantitative relationship with specific diseases and the resulting societal disease burden are not yet clear. Examples include PM2.5 and its relationship with diabetes, preterm birth, childhood autism, and late-life dementia (Wu et al., 2022; Malley et al., 2017; Heusinkveld et al., 2016; Kioumourtzoglou et al., 2016). Relevant data has not yet been consolidated into the GBD database. Zone 3 refers to emerging pollutants that may have strong toxic effects, but the toxic mechanisms, quantitative relationships, and the types of diseases and mechanisms they cause are currently unclear. Examples include new pesticides, herbicides, battery waste, etc. Relevant data has not been consolidated into the GBD database. The toxic mechanisms of pollutants classified in zone 1 are relatively clear, and corresponding prevention and control measures have been implemented nationally or internationally (Pascual, 2021). However, substantial detailed work is still required to understand the pathogenic mechanisms of zone 2 pollutants, as well as the identification, disease associations, toxic mechanisms, and corresponding prevention and control measures for potential pollutants in zone 3.

It is estimated that all types of environmental pollution causes approximately 9 million deaths globally per year (Landrigan et al., 2018a). Among them, the mortality and morbidity rates attributed to air pollution are particularly significant. Based on physical characteristics and composition, air pollution can be further subdivided into solid particulate pollution such as black carbon particles, microplastics, nanoplastics, tire particles, etc., and gaseous chemical pollution such as ammonia (Manisalidis et al., 2020). The escalating microplastics and nanoplastics in the oceans are major emerging pollutants that are being paid attention to in the research field (Peng et al., 2020). These substances do not exist in isolation but often exist in the form of complex multi-component aerosols. In the process of biosphere recycling, they may deposit in rivers, lakes, swamps, etc., intermingling with pollutants such as heavy metals (Nguyen et al., 2019; Ivleva, 2021), further increasing the difficulty of toxicological research on specific components.

1.3. Environmental ultrafine nanoparticles (UFPs)

Regarding pollutants grouped in zone 1 of Pollutome, there are outstanding reviews for reference (Rajagopalan et al., 2018; Landrigan et al., 2018b; Cohen et al., 2017). Here we focused on environmental ultrafine nanoparticles for further discussion. It is noteworthy that coarse particles in the atmosphere, with diameters in the tens of micrometers (PM10), tend to settle down rapidly, resulting in limited harm to human health. Micron-sized fine particles (PM2.5), when exposed through inhalation, often remain in the respiratory tract and lungs (Thomas, 2013; Brown et al., 2013). The cilia and mucosal systems in the human respiratory system can effectively clear most fine particles (Bustamante-Marin and Ostrowski, 2017). However, nanoscale ultrafine particles, characterized by small size, large quantity, and high surface area, exhibit heightened toxicity (Kwon et al., 2020a). In addition to respiratory exposure, dietary intake and skin contact are exposure pathways that require attention as well (Han et al., 2023). Ultrafine particles can enter the human circulatory system through multiple pathways such as deep lung alveoli, olfactory bulbs, digestive tract, and skin (Calderón-Garcidueñas and Ayala, 2022). It is generally believed that ultrafine particles with a diameter smaller than 240 nanometers can penetrate almost all barrier systems in the human body, including the blood-brain barrier (Heusinkveld et al., 2016; Wick et al., 2010), blood-placenta barrier (Medley et al., 2023), and blood-testis barrier (Ni et al., 2021). These kinds of particles deposit in various organs and tissues, disrupting the microenvironmental homeostasis, disturbing physiological processes as well as accelerating the progression of diseases (Ural et al., 2022). Indeed, types of UFPs were detected in multiple organs and tissues from bodies at embryonic stages (Bos et al., 2023) or adults (Zhang et al., 2024).

The body possesses inherent mechanisms for clearing ultrafine particles, such as macrophages in the immune system (Geiser et al., 2008) and lymphatic clearance systems in the brain (Schraufnagel, 2020). However, faced with escalating pollution, these clearance systems may operate under overwhelmed conditions. The glymphatic clearance system operates primarily during sleep, and individuals with sleep disorders may experience inefficiencies in clearance of ultrafine particles from brain (Hussain et al., 2023). This may explain the causal association between PM2.5 and childhood autism, as well as late-life dementia (Costa et al., 2020; Fu et al., 2019). Although we realized the toxicity of ultrafine particles, health mitigation measures remain limited. Considering that we unavoidably breathe them in continuously, and our daily diet also unavoidably exposes us to substances like nanoplastics, simple protective measures, such as wearing N95 masks (Adhikari et al., 2018) or supplementing antioxidants deliberately to counteract oxidative stress caused by ultrafine particles (Li et al., 2022a), might be quite insufficient.

Table 1
animal models in UFPs Exposome research.

Life stage	UFP subtype	Animal model	Methodology	Major conclusions	Reference
Early-stage embryos	Diesel exhaust	C57BL/6 mice	Pregnant mice exposure to UFPs at a low dose (LD, 100 mg/m3) or high dose (HD, 500 mg/m3) for 6 hours per day from gestational day 0.5–18.5	Decreased placental weights and crown to rump lengths and disturbed lipid metabolism in offspring, especially in female in the LD exposure group	(Behlen et al., 2021a)
	Polystyrene	ICR mice	Exposed pregnant mice to 0.5 and 5μm with 100 and 1000 μg/L polystyrene MPs from gestational day 0 to production day	Increased risk of fatty acid metabolism disruption in offspring: In both sexes, 5 μm particle exposure reduced β-oxidation and fatty acid synthesis. Amino acid metabolism is reduced in females	(Luo et al., 2019)
	Polystyrene	C57BL/6-mated BALB/c mice	Pregnant mice were intraperitoneally injected polystyrene at a dose of 250 μg in a 200 μL saline solution on days 5.5 and 7.5 of gestation	Elevated embryo reabsorption rate and decreased the number and diameter of uterine arterioles in PS particle exposure; disturbed maternal-fetal immune balance	(Hu et al., 2021)
	Ultrafine particles from the air	C57BL/6 J pun/pun mice	Pregnant mice were exposed by intratracheal instillation repeated six times during the gestation day 6.5, 8.5, 10.5, 12.5, 14.5 and 16.5 day, and 12 μg or 400 μg/kg	Increased embryo reabsorption, intrauterine oxidative damage and inflammation; decreased uterus, placental, and fetal weights	(Morales-Rubio et al., 2019)
	PS/100 nm and 157 ± 52 μm	Zebrafish, embryos/ larvae (Danio rerio)	μ-PS or n-PS suspended in 50 mL exposure solution	PS particles have high affinity to embryonic chorions leading to an antioxidant system disorder in the embryo, and enter the blood stream liver and brain of fish larvae after hatching.	(Duan et al., 2020)
Organ development	Polystyrene nanoparticles	Kunming mice	Pregnant mice were administered gestationally and lactationally PS-NPs dispersed in drinking water at different doses of 0, 0.1, 1 and 10 mg/L	Cause hepatic and testicular toxicity in male mouse pups.	(Huang et al., 2022a)
	Carbon black nanoparticle (CB-NP)	Pregnant ICR mice	Intranasal instillation 1 mL/kg body weight suspension of CB-NP (95 μg/kg body weight) or ultra-pure water	Dysregulation of major functional genes and mental neurotoxicity	(Onoda et al., 2018)
	Silica nanoparticles	sea urchin	Studying the sperm of the sea urchin through a multidisciplinary approach, including developmental biology, ecotoxicology, biochemistry, and microscopy analyses.	Increased undeveloped and anomalous embryos in SiO2 NPs in sea urchin offspring, SiO2 NPs exposure did not affect fertilization ability	(Gambardella et al., 2015)
	Nylon and polyethylene terephthalate	Female C57BL/6 mice	Human and murine alveolar and airway-type organoids as well as air-liquid interface cultures	Nylon microfibers inhibited airway epithelial differentiation in airway organoids	(Song et al., 2023)
Infancy	Ultrafine Particulate	C57BL/6 n	Exposed time- mated C57Bl/6 n mice to filtered air (FA) or UFPs at a low dose (LD, 55μg/m^3) and high dose (HD, 275μg/m^3) and challenged their offspring with RSV or sham (control) shortly after birth to evaluate infection responses.	Reduced Offspring body weights in response to infection in the LD RSV group, particularly females. Increased levels of oxidative stress and inflammation related genes in HD exposed male offspring in RSV-infected groups.	(Lau et al., 2022)
	Ultrafine Particulate	C57BL/6 J mice	Exposed to ultrafine elemental carbon at 50 μg/m^3 from postnatal days 4–7 and 10–13 for 4 hours per day	No significant differences in anogenital distance, body weight, central nervous system pathological markers, novel object recognition, and elevated plus maze performance	(Morris-Schaffer et al., 2019)
	Polystyrene nanoparticles	NRVMs from rat	Intracellular distribution of PS NPs at the single-cell level at 0, 5, 15, 30, and 60 min	Impaired collective contractility of neonatal cardiomyocytes under electrical synchronization.	(Roshanzadeh et al., 2021)
Adult	Polystyrene	BALB/c mice (Male, 6 weeks)	100 μL PS, PS-COOH and PS NH2 NPs (10 mg/mL) by gavage once a day (1 mg/day) for 28 day	Hematological system injury and lipid metabolism disorder; Induced cell apoptosis, inflammation, and structure disorder in mice spleen, lung, kidney, small intestine, large intestine, testis, and brain.	(Xu et al., 2021)
	Graphene oxide	Xenopus laevis (X. laevis) tadpoles	Exposed to various concentrations of typical pyrethroid, either alone or in combination with graphene oxide (GO), for 21 days	Disruption of neurotransmitter systems and interference in metamorphic development	(Li et al., 2020)
	Diesel exhaust particles, iron oxide (Fe_2O_3) or silica(SiO_2)	Pregnant, eight-week-old C57BL/6 J mice	Exposed intranasally to 50 mg in 50 μL of saline, or saline alone, on gestational day (E) 7.5, E12.5 and E17.5. Groups of non-pregnant mice were exposed on day (D)0, D5 and D10	Changed the inflammatory response to silica and altered the immune response to DEP.	(Thaver et al., 2019)
Gerontic stage	Fluorescently-labeled pristine polystyrene	C57BL/6 J mice	Young (4-month-old) and old (21-month-old) C57BL/6 J female mice were exposed to polystyrene particles and assessed using behavioral assays,	Short-term exposure to polystyrene particles induces both behavioral changes and alterations in immune markers in liver and brain tissues.	(Gaspar et al., 2023)
	SiO_2	Rat, 3 weeks (65 g), 8 weeks (265 g), and 20 months	Young, adult, and old rats physiologically inhaled air containing aerosol of SiO_2 nanoparticles (24.1 mg/m3; 40 min/day) for four weeks.	Pulmonary and cardiovascular alterations in old rats, yet less change in young and adult rats, including pulmonary inflammation, myocardial ischemic damage, atrio-ventricular blockage, and increasing in fibrinogen concentration and blood viscosity.	(Chen et al., 2008)
	Ultrafine particles from the air	Rat	Isolated Langendorff-perfused rat hearts from young adult and aged rats were perfused with buffer only and UFPs	Ultrafine particles instilled directly into the cardiac vasculature were equally cardiotoxic in young adult and old rat hearts.	(Simkhovich et al., 2007)

2. Threats of UFPs on human health and diseases

2.1. Physiological

As mentioned above, ultrafine particles could penetrate various barriers in the human body and enter the circulatory system, diffusing and depositing in various corners of the body. Therefore, it is essential to perceive ultrafine particles from the perspective of systemic toxicology rather than simply respiratory toxicology (Terzano et al., 2010). Combining data from epidemiological investigations, meteorological monitoring, and pathology testing in clinical samples, along with experiments conducted in cell lines and animal models, we have realized the toxic effects of ultrafine particles at multiple levels or from different angles. Regarding animal models, zebrafish, Xenopus, mice, rats, etc., have been employed in environmental toxicology research (Table 1). Emerging models, such as pluripotent stem cell derived organoids, are also beginning to be applied in UFPs toxic studies (Chandy et al., 2022; Hua et al., 2022).

UFPs disrupt the microenvironmental homeostasis under normal physiological conditions in tissues such as the cardiovascular system, central nervous system, respiratory system, digestive system, and reproductive system (Kan et al., 2018) (Sawicki et al., 2019; Li et al., 2022b). The vulnerability of two specific groups, infants and the elderly, makes the mortality and morbidity rates caused by UFPs particularly high (Zhang et al., 2016). Even fetuses within the uterus, before their first breath, are already facing with exposure to carbon nanoparticles through blood exchange between mother and fetus (Bongaerts et al., 2022).

2.2. Pathological

Besides physiological conditions, ultrafine nanoparticles also alter the progression of certain diseases such as tumors and neurodegenerative disorders (Table 2). For instance, chronic exposure to carbon nanoparticles reshapes macrophage metabolism and accelerates lung cancer progression (Chang et al., 2022). The delayed toxicity following exposure to carbon nanotubes has an impact on tumor occurrence and progression in distant organs or tissues beyond the lungs, leading to the multiple metastases of *in situ* breast tumors (Lu et al., 2019). In addition, PM2.5 is considered a significant inducer of neurodegenerative diseases (Zhu et al., 2020). This highlights the necessity for effective daily protection against ultrafine particles for patients particularly, through which potentially improve therapeutic outcomes.

2.3. Mechanism research

In terms of molecular mechanisms, it is currently understood that ultrafine particles have the capability to enter the interior of cells and deposit within the cytoplasm or nucleus. For instance, Cytoplasmic UFPs alter the morphology and functions of endoplasmic reticulum (Calderón-Garcidueñas and Ayala, 2022) and mitochondria (Xia et al., 2004), while nuclear UFPs induce DNA damage and genomic instability (Quezada-Maldonado et al., 2021; Mroz et al., 2008). UFPs interact with biomolecules closely with the form of protein coronas. Other biological components such as RNAs may also be contained in corona complex with unknown functions (Nel et al., 2009). Research on protein coronas is a focal point in understanding the toxicological mechanisms of ultrafine particles, but UFPs purification from biosamples is still challenging. For ultrafine particles containing iron oxide components, purification can be achieved through magnetic adsorption (Böhmert et al., 2020). However, for non-magnetic ultrafine particles like nano-carbon particles or nanoplastics, purification is often only possible through density gradient centrifugation, and the resulting purity and specificity cannot be guaranteed (Cai et al., 2021). In summary, ultrafine particles may disrupt cellular homeostasis through physical and/or chemical means. Methodological innovations are required to purify UFPs from biological samples for deep examination

2.4. Current issues in UFPs Exposome research

Based on the above mention, we believe that there are several important issues to be addressed in the following Exposome research field focusing on UFPs:

I. Animal Models: Although various animal models such as zebrafish,

Table 2
influences of UFPs on occurrence and progression of human diseases.

Disease	UFP subtype	Methodology	Major conclusions	Reference
Lung cancer	Carbon black ultrafine (nCB) particles	Mouse models with non–small cell lung cancers chronic exposure to nCB	nCB exposure metabolically rewires lung macrophages to promote immunosuppression and accelerates the development of lung cancer	(Chang et al., 2022)
	Carbon black nanoparticles	An *ex vivo* biosensor assay and transcriptome change of primary bronchial epithelial cells from workers with long-term occupational carbon black exposure history.	Carbon black exposure increased lung cancer risk by affecting the cell cycle via circulatory inflammation	(Zhang et al., 2022a)
Ovarian cancer	Polystyrene nanoplastics (PS-NPs)	Human EOC cell line HEY as an *in vitro* cell model and mice as a mammalian model exposure to PS-NPs	PS-NPs exposure accelerates ovarian cancer development in mice by altering the tumor microenvironment	(Chen et al., 2024)
Breast cancer	Multi-walled carbon nanotubes (MWCNTs)	The timeline of MWCNT exposure, establishment of tumor allografts, tumor excision and detection of tumor metastasis	A single pulmonary exposure to MWCNT dramatically enhances angiogenesis and the invasiveness of orthotopically implanted mammary carcinoma, leading to metastasis and rapid colonization of the lungs and other organs	(Lu et al., 2019)
	SiO_2 nanoparticles	SiO_2 nanoparticles exposure to breast cancer mouse model	SiO_2 nanoparticles injection increased lung metastasis of breast cancer cells compared to the untreated mice	(Dai et al., 2022)
Neurodegenerative disease	Polystyrene nanoplastic particles	*In vitro*, nanoplastic exposure with α-synuclein fibrils; In vivo, nanoplastic and α-synuclein fibrils intracranial injections and tissue staining	Nanoplastics promote Parkinson's disease–slows the degradation of aggregated α-synuclein	(Liu et al., 2023)
	Silica oxide nanoparticles (SiO_2 NPs)	SiO_2 NPs exposure to SH-SY5Y cells, different cellular and molecular assays were performed to reveal the α-syn amyloid fibrils-associated cytotoxicity	Acceleration of α-synuclein fibril formation and associated cytotoxicity stimulated by silica nanoparticles	(Pang et al., 2021)
	Ultrafine black carbon (uBC)	Cytotoxicity and oxidative stress increased in SH-SY5Y cells by uBC	uBC initiated progressive development of Alzheimer's disease (AD) associated features, including neuro-inflammation and phosphorylation of tau protein (p-Tau) accumulation.	(Shang et al., 2019)

Table 3
Summary of molecular mechanism research of UFPs.

UFP subtype	Research model	Methodology	Major conclusions	Reference
Carbon black nanoparticle 14 nm (average)	A549 cell line	Cellular exposure	Induce DNA damage, activate P53 and DNA repair proteins and proinflammatory transcription factor	(Mroz et al., 2007)
Polystyrene (PS) 100 nm	Rats	Inhalation	Activate TGF-β and TNF-α signaling in the lung tissue, and promote fibrosis and inflammation	(Lim et al., 2021)
Polystyrene (PS) 23 nm	Swiss mice	Intraperitoneal injection	Induce DNA damage and cognitive impairment	(Estrela et al., 2021)
Road traffic 45 nm (average)	*Ldlr*$^{-/-}$ mice	Whole-body exposure	Activate the NF-κB signaling Induce vascular calcification and atherosclerosis	(Li et al., 2013)
Polyethylene (PE) 65 nm	RAW 264.7 cell line	Cellular exposure	Down-regulate SIRT1, enhance ER stress and promote osteoclastogenesis and osteolysis	(Zhang et al., 2018)
Carbon black nanoparticle 35 nm (average)	C57BL/6 mice	Intravenous injection	Induce oxidative DNA damage and hepatic genotoxicity	(Shukla et al., 2013)
Ambient sampling 66 nm (average)	C57BL/6 mice	Whole-body exposure	Activate the FXR/LXR and Hnf4a Signaling and induce Lipid metabolism disorders	(Behlen et al., 2021b)
SiO_2 NPs 15, 30 and 100 nm	HUVECs cell line	Cellular exposure	Activation of NLRP3 inflammasome and HMGB1/TLR4/MYD88/NF-κB signaling pathway	(Liu et al., 2021)
SiO_2 NPs 15 nm	Sprague–Dawley rats	Intravitreal injection	Induce oxidative stress and retinal toxicity	(Zhang et al., 2022b)
Diesel Exhaust <100 nm	Fischer rats	Whole-body exposure	Increase TNFα, α-Synuclein, Aβ42 Tau hyperphosphorylation, Neuroinflammation	(Levesque et al., 2011)
Polystyrene (PS) 20 nm	A549 cell line	Cellular exposure	Disrupt cell membrane and interaction with chromosome	(Kihara et al., 2021)
Polyethylene terephthalate (PET) 100 nm	Caco−2 cell line	Cellular exposure	Destroy the integrity of cell membrane, and stimulate inflammatory adipocytokines	(Magrì et al., 2018)
Polypropylene (PP)	ICR mice	Intratracheal instillation	Up-regulate p38 and NF-κB signaling and induce infammation and ROS production in the lung tissues	(Woo et al., 2023)
Polyethylene terephthalate (PET) 100 nm	Zebrafish	Whole-body exposure	Affect the embryonic development of zebrafish including hatchability, heart rate and ROS production	(Ji et al., 2020)

mice, and rats have been used in Exposome research, these species hold inherent evolutionary and genetic differences from humans (Ernst and Carvunis, 2018; Seok et al., 2013; Twigger, 2004; Davis et al., 2014). For example, commonly used mice models hold substantial differences in brain structure and lack advanced cognitive functions (Davis et al., 2014). Therefore, these models may be unable to phenocopy structural or behavioral changes in human brain accurately in Exposome studies. UFPs induce cardiac arrhythmias (Zhu et al., 2023). However, the differences of the ventricular action potential and ionic currents between human and mouse hearts need to be pay attention to (Blackwell et al., 2022). In addition, mice lack respiratory bronchiole structure in lungs, while this structure is abundant in human lungs (Basil et al., 2022). Mice also display dramatic difference in spermatogenesis from humans (Chen et al., 2021). Considering the accumulative effects of UFP derived toxicity, common used rodent models hold much shorter timescale compared to human regarding gestational age or lifespan. For instance, the gestational age in mouse or rat is around 3 weeks, while around 40 weeks in human (Rokas et al., 2020). In addition, human hold around 75 years longevity on average, while mouse has 4 years lifespan maximum (Cremer et al., 2022). All these divergences make mice not ideal enough in UFPs Exposome research. So developing more suitable animal models should be a crucial consideration in Exposome research.

II. Long-term Monitoring and Data Collection: Recent studies suggest that humans are exposed to UFPs such as carbon nanoparticles since the fetal stage (Bongaerts et al., 2022), reminding that Exposome research on UFPs should adopt a lifelong perspective. In addition, human diseases such as cognitive decline Alzheimer's disease, respiratory and cardiovascular illnesses have been associated with aging (Pandics et al., 2023). However, published studies always set up short-term acute exposure procedures or selected a few time points for sampling within exposure periods ranging from several days to months (Table 1). These studies may not be able to answer the entire lifespan toxic dynamics of experimental animals. On the cellular level, the proliferating cells might undermine UFP deposition through cell division. However, some long-lived post-mitotic cell types, such as neurons, adult cardiomyocytes and skeletal myofibers, may have to face UFP toxicity in their whole long life if under UFP exposure (Rodriguez et al., 2010). Therefore, understanding the systematic toxic effects of UFPs from a lifelong perspective remains a critical area that requires the establishment of continuous monitoring databases. However, neither using small nor large animal models for life-long exposure assay is easy. To this goal, we may need to modify or upgrade facility equipment, a long period of time (years to decades), high-cost to collect samples and multi-omics analysis. This seems to be impracticable. Alternatively, it could be a better choice to leverage on cutting-edge artificial intelligence and machine learning to integrate cohort tracing database to achieve human life-long Exposome research (Merino Martinez et al., 2021).

III. Molecular Mechanism Studies: UFPs cause cellular toxicity either through indirect ways such as reactive oxygen species (ROS) (Durga et al., 2014), or through direct interaction with biomolecules (Hadjidemetriou and Kostarelos, 2017). The absorbance of biomolecules on UFPs surface has been defined as corona. The corona structure contains proteins, nucleic acids, glycans, lipids, among others (Mahmoudi et al., 2023). Furthermore, the corona structure is separated into solid layer (biomolecules stably combining onto UFPs surface) and soft layer (incompact binding, dynamically attach to or detach from UFPs surface) (García-Álvarez and Vallet-Regí, 2021). Mass spectrometry analysis revealed that proteins involving cytoskeleton, gene transcription, translation, epigenetic modification, chromatin remodeling, DNA repair pathways have been identified in corona purification (da Costa Marques et al., 2023). In addition, UFPs induced ROS also influence the pathways mentioned above (Yu et al., 2020; Hussain et al., 2014). Therefore, the impact of UFPs on the genome, transcriptome, epigenome, proteome, and metabolome should be studied comprehensively crossing multiple levels. The components and status of corona depends on cell types and microenvironmental context (Mahmoudi et al., 2023). The same UFPs may hold different corona components in different cell types, which remind us the cell type heterogeneity should be taken into account when studying UFPs toxicity. Single-cell multi-omics technologies may serve as ideal tools to address these questions. Understanding what and how biomolecules interact with UFPs, including proteins, nucleic acids, lipids, and sugars in the toxicological processes are crucial (Saptarshi

et al., 2013; Engin et al., 2017). Single-cell RNA and ATAC sequencing have been used broadly in recent biomedical studies by far (Baysoy et al., 2023). However, other techs such as single-cell proteomics, single-cell epigenomic sequencing, or single-cell metabolism are still at initiated stages (Perkel, 2021). Furthermore, there will be an upgraded challenge to integrate above single-cell techs in one cell simultaneous detection, which needs elaborate optimization to achieve real comprehensive understanding of UFP toxicity at the single-cell level.

Single-cell omics and EWAS/ GWAS database may provide us the macroscopic molecular landscape of UFP toxicity. We also require exploring one more layer that the interaction modules of UFPs and key nodes through cellular and biochemical assays to understand the UFPs endowed etiology deeply. For example, TDP-43 is a key node of amyotrophic lateral sclerosis (ALS) disease. Polystyrene plastics (PS) UFPs were found to interact with cytoplasmic TDP-43 to form a complex with PS UFPs. This complex promotes the condensation and solidification of TDP-43, triggering ALS-like characteristics (Sun et al., 2024). β-amyloid (Aβ) deposition is the main cause of Alzheimer's disease. Silica nanoparticles could pass through blood-brain barrier and promote Aβ influx to the brain, leading to Aβ burden in the brain (Wei et al., 2024). These studies provide direct connection between environmental pollution and neurodegenerative disorders. In these studies, either wildtype or gene edited mice models were used. For instance, *ApoE* knockout ($ApoE^{-/-}$) mice provided a ready-to-use model to examine silica nanoparticle induced phenotypes in the context of Alzheimer's disease, making the phenotypic analysis more easily and concentrated than using than wildtype (Wei et al., 2024). Similar strategies were also used in UFPs and cancer crossover studies (Chang et al., 2022; Lu et al., 2019), Besides, cutting-edge in vitro organoids have been discussed to be novel models in Exposome research (Chandy et al., 2022). For example, human pluripotent stem cell derived cerebral organoids or retinal organoids have been used to evaluate particulate matter toxicity (Bilinovich et al., 2020; Zeng et al., 2021). Although organoids models display plenty of advantages in terms of three-dimensional structure, cell-type diversity, large-scale screening and dynamic monitoring, some limitations still need to be considered when using organoids in UFPs exposure research, such as lack of blood and immune microenvironment, organoids heterogeneity and data reproducibility. All these limitation rely on the methodological progress of organoids field to be overcome. Undoubtedly, organoids provide us good tools to fast screen potential pollutants as well as identify toxicological mechanism integrating single-cell omic techs.

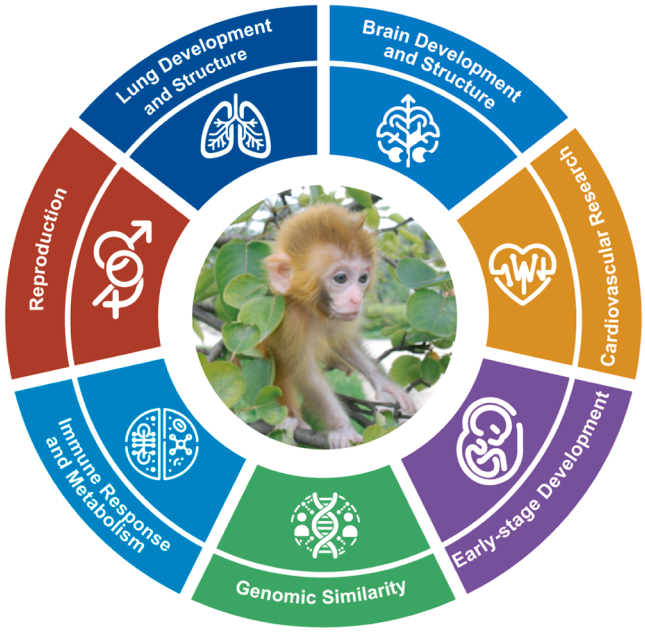

Fig. 1. Advantages of non-human primates in human biomedical research. This illustration enumerates the seven advantages in non-human primates versus rodent models in the context of human biomedical studies.

IV. Health Intervention: Regarding persistent entering of UFPs into human circulatory system, research is needed to develop practical measures for clearing or neutralizing their toxicity. UFPs in human tracheobronchial tree could be clear out through cilia movement and mucus. However, UFPs in deep alveoli would not be clear out through mucosa system, finally penetrate into human blood stream (Chen et al., 2016). In addition, UFPs may also enter into human circulatory system through gastrointestinal tract, skin or olfactory nerve (Calderón-Garcidueñas and Ayala, 2022; Kwon et al., 2020b), and macrophages could transfer ingested UFPs in circulation along with their mitigation (Wieland et al., 2024). Oxidative stress is common in UFPs toxicity. However, it has been revealed that not all UFP types lead to oxidative stress (Horie and Tabei, 2021). Lu *et.al.* used chemical multi-fingerprinting technology to quantify exogenous UFPs in human serum and pleural effusion samples (Lu et al., 2020), providing a feasible avenue to measure UFPs dosage in human individuals. Indeed, UFPs in human circulatory system displayed much complexed manners regarding their size, chemical constitution, organ/tissue distribution and translocation. So it is still difficult to achieve accurate measurement of UFPs in human bodies at present.

In terms of human health intervention under UFPs exposure, some dietary strategies have been proposed including daily addition of vitamin C/E, omega-3 fatty acids or metformin to neutralize oxidative stress, inhibit inflammation or rewire metabolic status (Aryal et al., 2021). These health protection strategies might be passive, but not active enough. While there are some commercial products available for protecting against atmospheric UFPs, such as N95 and N100 masks, and air purifiers dealing with indoor air pollution (Adanur and Jayswal, 2020). Several reviews discussed the intervention effects of air purifiers or masks (Allen and Barn, 2020; Bard et al., 2019; Carlsten et al., 2020). For example, commercial high-efficiency particulate air/arresting (HEPA) filter air purifier was confirmed to be able to reduce indoor PM2.5 concentration from 60 to 24 $\mu g/m^3$ to more than 50 % over periods of two weeks, reducing systemic inflammation but not affect lung function, blood pressure or heart rate variability (Shao et al., 2017). In UGAAR (Ulaanbaatar Gestation and Air Pollution Research) cohort study, portable HEPA filter air purifier was evaluated in pregnancy on fetal growth and childhood development (Barn et al., 2018). HEPA air purifiers dramatically reduced indoor PM2.5 concentrations during pregnancy by 29 % (from 25 to 17 $\mu g/m^3$), and improved fetal growth (birth weight increased by 85 g) (Barn et al., 2018). This indicated that air purifiers could benefit susceptible subpopulations under UFPs exposure. In addition, well-fitting facemasks such as N95 (KN95 in China) were reported to attenuate pollution-induced effects on airway inflammation, but no effects on systemic oxidative stress (Guan et al., 2018). The efficiency of other types of masks in reducing UFPs exposure is highly variable. Overall, these studies were conducted in short-term timescale (from days to weeks), we still need long-term evaluation of face coverings and air purifiers in improving subclinical or even clinical human health (Allen and Barn, 2020).

Rapid urbanization is an important element needing to be taken into consideration in UFPs pollution abatement. Currently, the total UFPs levels in megacities all over the world are still above World Health Organization (WHO) guideline (de Jesus et al., 2019; Kumar et al., 2014). In addition to elevated construction dust, industrial development and new technologies are also changing UFPs composition and ratios when remodeling human lifestyle. For instance, electric vehicle (EV) usage may help to decrease traditional diesel burning produced UFPs, but may increase tire wearing derived rubber and carbon black nanoparticles (Kim et al., 2021; Alanazi, 2023). Along with lithium battery application in EV industry, the process covering recycling, disassembling, and deep processing of scrapped lithium battery would cause new contaminants

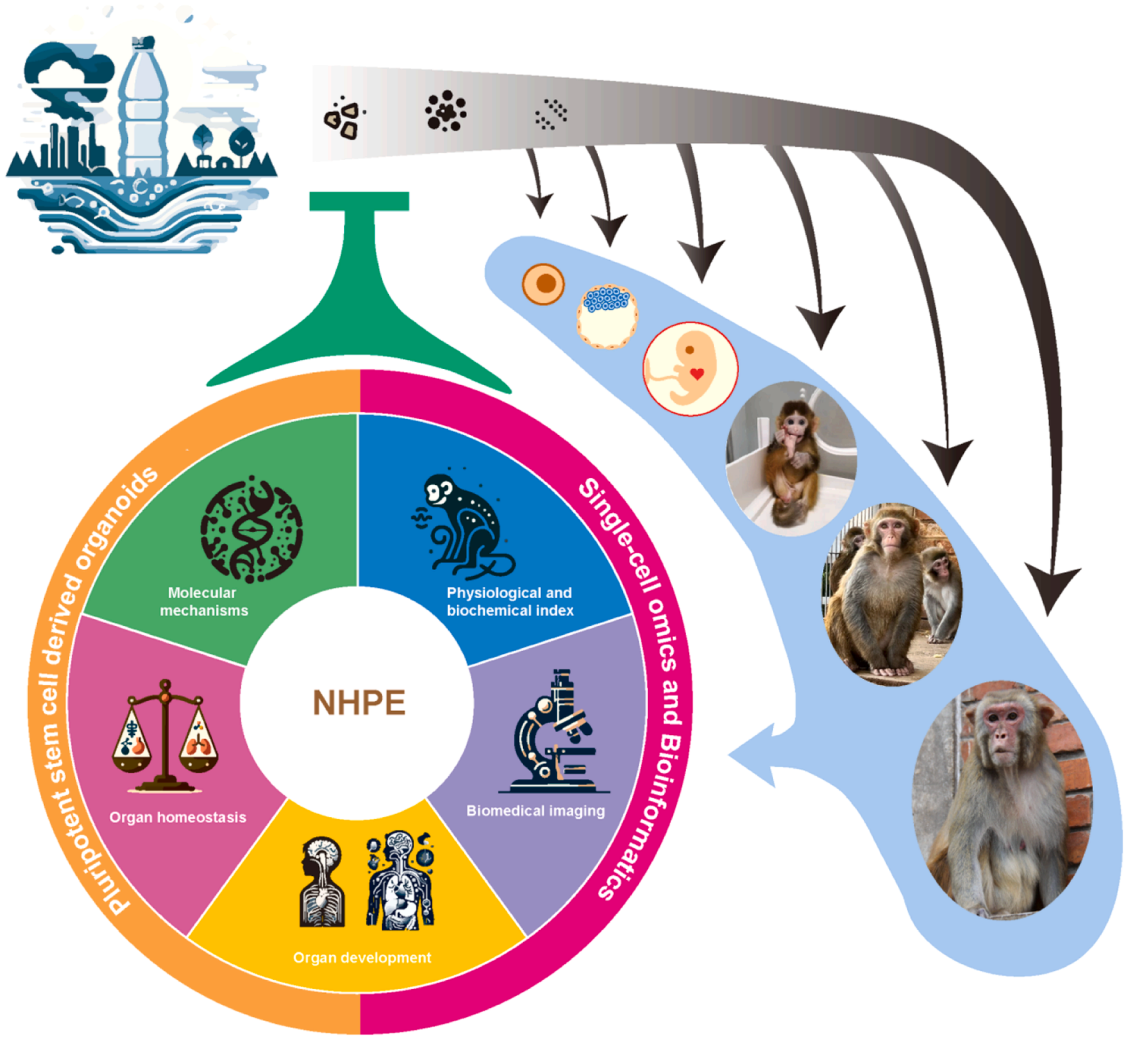

Fig. 2. Graphic summary of Non-Human Primate Exposome (NHPE) project. This illustration encompasses the designed modules in NHEP. Briefly, rhesus macaques will be categorized into groups spanning from prenatal to infancy (pregnancy to four years old), youth (seven to ten years old), and elderly (15 years old and above). We will conduct exposure experiments involving UFPs including nano-plastics (through dietary and water intake pathways) and carbon black nanoparticles (via respiratory pathways). At the organ and tissue level, we will engage in phased monitoring and analysis of physiological and biochemical parameters, biomedical imaging, tissue pathology, and other assessments. On the cellular and molecular level, we will employ single-cell multi-omics and bioinformatics techniques to scrutinize alterations in organs such as the central nervous system, cardiovascular system, respiratory system, and reproductive system. Focusing on significant variances in molecular pathways and key factors, we will utilize corresponding organoids systems to dissect functional mechanisms.

including UFPs (Mrozik et al., 2021; Grabow et al., 2023). Currently, the public policies and government actions still lag behind emerging pollution situations, with lacking legal procedures to promise the environmental safety. Moreover, with the rapid development of the fast-food and delivery industries, the harm caused by microplastics and nanoplastics from plastic packages in daily diet should also be considered (Sánchez et al., 2022). Urban forests have been investigated to intercept atmospheric microplastics (12,593 n/m^2 of fibers and 347.69 kg of microplastics for one year), supporting the notion that urban afforestation should be improved in government and public health agencies (Huang et al., 2022b). Regarding citizen personal lifestyle, compared to drivers, the median life expectancy losses in active commuter population were up to 1 year lower, indicating that the benefits outweighed the negative effects of ambient pollution (Cepeda et al., 2017). In summary, both urban planning policies and personal behaviors should be considered seriously to improve health intervention following current pollution episode.

3. Rationale of using non-human primates (NHPs) in UFPs Exposome research

3.1. Non-human primates in biomedical research

There are more than 500 species of non-human primates distributed worldwide, with a few species such as macaques, crab-eating monkeys, and marmosets being applied in biomedical research (Ardith, 2008; Hannibal et al., 2017). In comparison to commonly used animal models in Exposome research such as mice, rats, and zebrafish, non-human primates offer unique advantages in the following aspects (Fig. 1):

I. Genomic Similarity: Non-human primates possess a functional genome more similar to humans, facilitating a more accurate analysis of gene function and genomic regulatory patterns (Enard et al., 2010; Harding, 2013).

II. Early-stage Development: The embryonic development process of non-human primates, especially at the peri-implantation embryonic stage, exhibits structures, cell composition and gene expression dynamics highly similar to humans (Zhai et al., 2022).

III. Cardiovascular Research: Non-human primates are better suited

for cardiovascular toxicology, as well as microvascular degradation studies (Heyen and Vargas, 2015; Cox et al., 2017).

IV. Brain Development and Function: Non-human primates share similarities with humans in terms of gyrus structure, functional zoning, projection pathways, and the unique phenomenon of neoteny (Niu and Palomero-Gallagher, 2023; Zhang et al., 2023; Linker et al., 2022). In addition, non-human primates hold unique advantages in advanced behavior testing (Stephan et al., 2019).

V. Lung Development and Structure: Non-human primates closely resemble humans in respiratory bronchiole structure, which is absent in mice (Basil et al., 2022; Miller et al., 2017).

VI. Reproduction: Non-human primates and humans share a conservative spermatogenesis process (Murat et al., 2023), and female monkeys have menstrual and ovulation cycles (Hunnell et al., 2007). The placental structure during pregnancy is also more similar to humans compared to mice (Matsumoto et al., 2023).

VII. Immune Response and Metabolism: Non-human primates exhibit high similarity to humans in infection immunity and metabolism, both crucial aspects of population Exposome research (Bjornson-Hooper et al., 2022).

Despite these advantages, utilizing non-human primates in scientific research still poses several challenges: limited animal resources, high labor, time, and economic costs, the need for specialized personnel and technology for the care, maintenance, and quarantine of non-human primates, requirement for experimental instrument modifications, and stringent biomedical ethical scrutiny (Cauvin et al., 2015). These limitations hinder the widespread use of non-human primates in Exposome research.

3.2. Initiation of NHPE (Non-Human Primate Exposome) project

Leveraging non-human primates may prove to be a more suitable animal model for Exposome research. To our knowledge, there are no published Exposome studies performed in NHP models by far. Here we propose the NHPE project, which is being performed relying on National Research Facility for Phenotypic and Genetic Analysis of Primate Model Animals in China (referred to as the Primate Facility). The Primate Facility is a state-level support platform established at the Kunming Institute of Zoology, Chinese Academy of Sciences, dedicated to conducting biomedical research on non-human primates (Yao and K.I.Z.P.F, 2022). This facility encompasses modules for non-human primate breeding, phenotype determination, genetic analysis, imaging, pathology, toxicology, and biomedical mega data integration. It features scalability, standardization, precision, automation, and intelligence. The Primate Facility enables a systematic and accurate description of non-human primate phenotypes, genotypes, and their responses to environmental changes. This aids in understanding the regulatory states and mechanisms of life, supporting research on human diseases and the regulation of animal life processes accurately.

We have equipped the facility with several key instruments for conducting Exposome research on non-human primates, including non-human primate respiratory exposure system, metabolic monitoring system, and devices for embryonic manipulation, infant daycare, physiological analysis, biochemical analysis, behavioral test, and medical imaging. Leveraging the non-human primates, we aim to conduct lifelong (from early embryonic stages to old) Exposome research of UFPs carbon nanoparticles, nanoplastics among others on non-human primates. Besides routine whole-body physiological and biochemical index monitoring, our research will place extra emphasis on the toxicological effects of UFPs on NHPs' cardiovascular system, central nervous system, respiratory system, and reproductive system. Combining cutting-edge single-cell multi-omics and pluripotent stem cell derived organoids technologies, we will establish a comprehensive Exposome biobanking database, conduct in-depth mechanistic studies, and develop effective strategies for human health interventions (Fig. 2).

4. Conclusions

Here we summarize the conceptual scope, current state, and several key issues that need to be addressed in the Exposome research on UFPs. We discuss the feasibility of conducting Exposome research using non-human primates as models rely on the national primate facility in China. We raise the NHPE project through which will enrich EWAS datasets, strengthen the study of the toxicological mechanisms of environmental UFPs, and inspire new health intervention strategies.

Ethics approval and consent to participate

The "Exposome research of ultrafine particulate pollutants in rhesus macaque models" was established following the guidelines of Institutional Animal Care and Use Committee of Kunming Institute of Zoology, Chinese Academy of Sciences. All experiments conducted on animals were approved by the Institutional Animal Care and Use Committee of Kunming Institute of Zoology, Chinese Academy of Sciences (Approval No: IACUC-PE-2024–01–004 for prenatal/infancy group, approval date was January 10, 2024; IACUC-PE-2024–01–002 for youth/elderly group, approval date was January 03, 2024).

Declaration of AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used Chat GPT in order to improve English language and readability. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

CRediT authorship contribution statement

Bo Zhao: Writing – review & editing, Writing – original draft, Supervision, Project administration, Funding acquisition, Conceptualization. **Qiu Tu:** Writing – original draft, Investigation. **Jiao Zhang:** Writing – original draft, Investigation. **Wenxian Xiao:** Investigation. **Gaojing Liu:** Writing – original draft, Investigation. **Xiuyun Liu:** Writing – original draft, Investigation. **Longbao Lv:** Writing – review & editing, Supervision, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Declaration of competing interest

The authors declare no competing interests.

Data Availability

No data was used for the research described in the article.

References

Adanur, S., Jayswal, A., 2020. Filtration mechanisms and manufacturing methods of face masks: an overview. J. Ind. Text. 51 (3_suppl), 3683S–3717S.

Adhikari, A., et al., 2018. Field evaluation of N95 filtering facepiece respirators on construction jobsites for protection against airborne ultrafine particles. Int J. Environ. Res Public Health 15 (9).

Alanazi, F., 2023. Electric vehicles: benefits, challenges, and potential solutions for widespread adaptation. Appl. Sci. 13 (10), 6016.

Allen, R.W., Barn, P., 2020. Individual- and household-level interventions to reduce air pollution exposures and health risks: a review of the recent literature. Curr. Environ. Health Rep. 7 (4), 424–440.

Alonso-Curbelo, D., et al., 2021. A gene-environment-induced epigenetic program initiates tumorigenesis. Nature 590 (7847), 642–648.

Ardith, A.E., 2008. The Crab-Eating Macaque (Macaca fascicularis): widespread and Rapidly Declining. Primate Conserv. 23 (1), 129–132.

Aryal, A., Harmon, A.C., Dugas, T.R., 2021. Particulate matter air pollutants and cardiovascular disease: strategies for intervention. Pharm. Ther. 223, 107890.

Bard, R.L., et al., 2019. Interventions to reduce personal exposures to air pollution: a primer for health care providers. Glob. Heart 14 (1), 47–60.

Barn, P., et al., 2018. The effect of portable HEPA filter air cleaner use during pregnancy on fetal growth: The UGAAR randomized controlled trial. Environ. Int 121 (Pt 1), 981–989.

Basil, M.C., et al., 2022. Human distal airways contain a multipotent secretory cell that can regenerate alveoli. Nature 604 (7904), 120–126.

Baysoy, A., et al., 2023. The technological landscape and applications of single-cell multi-omics. Nat. Rev. Mol. Cell Biol. 24 (10), 695–713.

Behlen, J.C., et al., 2021b. Gestational Exposure to Ultrafine Particles Reveals Sex- and Dose-Specific Changes in Offspring Birth Outcomes, Placental Morphology, and Gene Networks. Toxicol. Sci. 184 (2), 204–213.

Behlen, J.C., et al., 2021a. Gestational exposure to ultrafine particles reveals sex- and dose-specific changes in offspring birth outcomes, placental morphology, and gene networks. Toxicol. Sci. 184 (2), 204–213.

Berg, J., 2016. Gene-environment interplay. Science 354 (6308)), 15.

Bilinovich, S.M., et al., 2020. Integrated RNA sequencing reveals epigenetic impacts of diesel particulate matter exposure in human cerebral organoids. Dev. Neurosci. 42 (5-6), 195–207.

Bjornson-Hooper, Z.B., et al., 2022. A COmprehensive Atlas of Immunological Differences between Humans, Mice, and Non-human Primates. Front. Immunol. 13.

Blackwell, D.J., Schmeckpeper, J., Knollmann, B.C., 2022. Animal models to study cardiac arrhythmias. Circ. Res 130 (12), 1926–1964.

Böhmert, L., et al., 2020. Isolation methods for particle protein corona complexes from protein-rich matrices. Nanoscale Adv. 2 (2), 563–582.

Bongaerts, E., et al., 2022. Maternal exposure to ambient black carbon particles and their presence in maternal and fetal circulation and organs: an analysis of two independent population-based observational studies. Lancet Planet Health 6 (10), e804–e811.

Bos, B., et al., 2023. Prenatal exposure to air pollution is associated with structural changes in the neonatal brain. Environ. Int 174, 107921.

Brown, J.S., et al., 2013. Thoracic and respirable particle definitions for human health risk assessment. Part Fibre Toxicol. 10, 12.

Bustamante-Marin, X.M., Ostrowski, L.E., 2017. Cilia and mucociliary clearance. Cold Spring Harb. Perspect. Biol. 9 (4).

Cai, H., et al., 2021. Separation and enrichment of nanoplastics in environmental water samples via ultracentrifugation. Water Res. 203, 117509.

Calderón-Garcidueñas, L., Ayala, A., 2022. Air pollution, ultrafine particles, and your brain: are combustion nanoparticle emissions and engineered nanoparticles causing preventable fatal neurodegenerative diseases and common neuropsychiatric outcomes? Environ. Sci. Technol. 56 (11), 6847–6856.

Carlsten, C., et al., 2020. Personal strategies to minimise effects of air pollution on respiratory health: advice for providers, patients and the public. Eur. Respir. J. 55 (6).

Cauvin, A.J., Peters, C., Brennan, F., 2015. Advantages and Limitations of Commonly Used Nonhuman Primate Species in Research and Development of Biopharmaceuticals. Nonhum. Primate Nonclinical Drug Dev. Saf. Assess. 379–395. https://doi.org/10.1016/B978-0-12-417144-2.00019-6. Epub 2015 Mar 20.

Cepeda, M., et al., 2017. Levels of ambient air pollution according to mode of transport: a systematic review. Lancet Public Health 2 (1), e23–e34.

Chandy, M., Obal, D., Wu, J.C., 2022. Elucidating effects of environmental exposure using human-induced pluripotent stem cell disease modeling. EMBO Mol. Med 14 (11), e13260.

Chang, C.Y., et al., 2022. Chronic exposure to carbon black ultrafine particles reprograms macrophage metabolism and accelerates lung cancer. Sci. Adv. 8 (46), eabq0615.

Chen, G., et al., 2024. Polystyrene nanoparticle exposure accelerates ovarian cancer development in mice by altering the tumor microenvironment. Sci. Total Environ. 906, 167592.

Chen, H., et al., 2021. Dissecting mammalian spermatogenesis using spatial transcriptomics. Cell Rep. 37 (5), 109915.

Chen, R., et al., 2016. Beyond PM2.5: The role of ultrafine particles on adverse health effects of air pollution. Biochim Biophys. Acta 1860 (12), 2844–2855.

Chen, Z., et al., 2008. Age-related differences in pulmonary and cardiovascular responses to SiO2 nanoparticle inhalation: nanotoxicity has susceptible population. Environ. Sci. Technol. 42 (23), 8985–8992.

Cohen, A.J., et al., 2017. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. Lancet 389 (10082), 1907–1918.

Costa, L.G., et al., 2020. Effects of air pollution on the nervous system and its possible role in neurodevelopmental and neurodegenerative disorders. Pharm. Ther. 210, 107523.

da Costa Marques, R., et al., 2023. Proteomics reveals time-dependent protein corona changes in the intracellular pathway. Acta Biomater. 172, 355–368.

Cox, L.A., et al., 2017. Nonhuman Primates and Translational Research—Cardiovascular Disease. ILAR J. 58 (2), 235–250.

Cremer, A., Abplanalp, W.T., Rieger, M.A., 2022. Time's up: mutation rate and lifespan. Signal Transduct. Target Ther. 7 (1), 282.

Dai, H., et al., 2022. Systemically administered silica nanoparticles result in diminished T cell response in lung. Nano Today 42, 101332.

Davis, E.E., Frangakis, S., Katsanis, N., 2014. Interpreting human genetic variation with in vivo zebrafish assays. Biochim Biophys. Acta 1842 (10), 1960–1970.

Duan, Z., et al., 2020. Barrier function of zebrafish embryonic chorions against microplastics and nanoplastics and its impact on embryo development. J. Hazard Mater. 395, 122621.

Durga, M., et al., 2014. Effects of ultrafine petrol exhaust particles on cytotoxicity, oxidative stress generation, DNA damage and inflammation in human A549 lung cells and murine RAW 264.7 macrophages. Environ. Toxicol. Pharm. 38 (2), 518–530.

Enard, D., Depaulis, F., Roest Crollius, H., 2010. Human and Non-Human Primate Genomes Share Hotspots of Positive Selection. PLOS Genet. 6 (2), e1000840.

Engin, A.B., et al., 2017. Mechanistic understanding of nanoparticles' interactions with extracellular matrix: the cell and immune system. Part. Fibre Toxicol. 14 (1), 22.

Ernst, P.B., Carvunis, A.R., 2018. Of mice, men and immunity: a case for evolutionary systems biology. Nat. Immunol. 19 (5), 421–425.

Estrela, F.N., et al., 2021. Toxicity of polystyrene nanoplastics and zinc oxide to mice. Chemosphere 271, 129476.

Fu, P., et al., 2019. The association between PM(2.5) exposure and neurological disorders: A systematic review and meta-analysis. Sci. Total Environ. 655, 1240–1248.

Fuller, R., et al., 2022. Pollution and health: a progress update. Lancet Planet Health 6 (6), e535–e547.

Gambardella, C., et al., 2015. Multidisciplinary screening of toxicity induced by silica nanoparticles during sea urchin development. Chemosphere 139, 486–495.

García-Álvarez, R., Vallet-Regí, M., 2021. Hard and soft protein corona of nanomaterials: analysis and relevance. Nanomater. (Basel) 11 (4).

Gaspar, L., et al., 2023. Acute exposure to microplastics induced changes in behavior and inflammation in young and old mice. Int. J. Mol. Sci. 24 (15).

Geiser, M., et al., 2008. The role of macrophages in the clearance of inhaled ultrafine titanium dioxide particles. Am. J. Respir. Cell Mol. Biol. 38 (3), 371–376.

Gibbs, R.A., 2020. The human genome project changed everything. Nat. Rev. Genet 21 (10), 575–576.

Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Psychiatry, 2022. 9(2): p. 137-150.

Grabow, J., et al., 2023. Particle Contamination in Commercial Lithium-Ion Cells—Risk Assessment with Focus on Internal Short Circuits and Replication by Currently Discussed Trigger Methods. Batteries 9 (1), 9.

Guan, T., et al., 2018. The effects of facemasks on airway inflammation and endothelial dysfunction in healthy young adults: a double-blind, randomized, controlled crossover study. Part Fibre Toxicol. 15 (1), 30.

Hadjidemetriou, M., Kostarelos, K., 2017. Nanomedicine: Evolution of the nanoparticle corona. Nat. Nanotechnol. 12 (4), 288–290.

Han, D., et al., 2023. The bio-distribution, clearance pathways, and toxicity mechanisms of ambient ultrafine particles. Eco-Environ. Health 2 (3), 95–106.

Hannibal, D.L., et al., 2017. Laboratory rhesus macaque social housing and social changes: Implications for research. Am. J. Prima 79 (1), 1–14.

Harding, J.D., 2013. Progress in genetics and genomics of nonhuman primates. ILAR J. 54 (2), 77–81.

Heusinkveld, H.J., et al., 2016. Neurodegenerative and neurological disorders by small inhaled particles. Neurotoxicology 56, 94–106.

Heyen, J., Vargas, H., 2015. The Use of Nonhuman Primates in Cardiovascular Safety Assessment. Nonhum. Primate Nonclinical Drug Dev. Saf. Assess. 551–578.

Horie, M., Tabei, Y., 2021. Role of oxidative stress in nanoparticles toxicity. Free Radic. Res 55 (4), 331–342.

Hu, J., et al., 2021. Polystyrene microplastics disturb maternal-fetal immune balance and cause reproductive toxicity in pregnant mice. Reprod. Toxicol. 106, 42–50.

Hua, T., et al., 2022. Microplastics exposure affects neural development of human pluripotent stem cell-derived cortical spheroids. J. Hazard Mater. 435, 128884.

Huang, T., et al., 2022a. Maternal exposure to polystyrene nanoplastics during gestation and lactation induces hepatic and testicular toxicity in male mouse offspring. Food Chem. Toxicol. 160, 112803.

Huang, X., et al., 2022b. Are we ignoring the role of urban forests in intercepting atmospheric microplastics? J. Hazard Mater. 436, 129096.

Hunnell, N.A., et al., 2007. Physical activity of adult female rhesus monkeys (Macaca mulatta) across the menstrual cycle. Am. J. Physiol. Endocrinol. Metab. 292 (6), E1520–E1525.

Hussain, R., et al., 2023. Air pollution, glymphatic impairment, and Alzheimer's disease. Trends Neurosci. 46 (11), 901–911.

Hussain, S., et al., 2014. Intracellular signal modulation by nanomaterials. Adv. Exp. Med Biol. 811, 111–134.

Ivleva, N.P., 2021. Chemical analysis of microplastics and nanoplastics: challenges, advanced methods, and perspectives. Chem. Rev. 121 (19), 11886–11936.

de Jesus, A.L., et al., 2019. Ultrafine particles and PM2.5 in the air of cities around the world: Are they representative of each other? Environ. Int. 129, 118–135.

Ji, Y., et al., 2020. Realistic polyethylene terephthalate nanoplastics and the size- and surface coating-dependent toxicological impacts on zebrafish embryos. Environ. Sci.: Nano 7 (8), 2313–2324.
Kan, H., Pan, D., Castranova, V., 2018. Engineered nanoparticle exposure and cardiovascular effects: the role of a neuronal-regulated pathway. Inhal. Toxicol. 30 (9-10), 335–342.
Kihara, S., et al., 2021. Cellular interactions with polystyrene nanoplastics—The role of particle size and protein corona. Biointerphases 16 (4), 041001.
Kim, J., et al., 2021. Potential release of nano-carbon black from tire-wear particles through the weathering effect. J. Ind. Eng. Chem. 96, 322–329.
Kioumourtzoglou, M.A., et al., 2016. Long-term PM2.5 Exposure and Neurological Hospital Admissions in the Northeastern United States. Environ. Health Perspect. 124 (1), 23–29.
Kumar, P., et al., 2014. Ultrafine particles in cities. Environ. Int. 66, 1–10.
Kwo, E., Christiani, D., 2017. The role of gene-environment interplay in occupational and environmental diseases: current concepts and knowledge gaps. Curr. Opin. Pulm. Med 23 (2), 173–176.
Kwon, H.S., Ryu, M.H., Carlsten, C., 2020a. Ultrafine particles: unique physicochemical properties relevant to health and disease. Exp. Mol. Med 52 (3), 318–328.
Kwon, H.-S., Ryu, M.H., Carlsten, C., 2020b. Ultrafine particles: unique physicochemical properties relevant to health and disease. Exp. Mol. Med. 52 (3), 318–328.
Landrigan, P.J., et al., 2018a. The Lancet Commission on pollution and health. Lancet 391 (10119), 462–512.
Landrigan, P.J., et al., 2018b. Pollution and Global Health – An Agenda for Prevention. Environ. Health Perspect. 126 (8), 084501.
Lau, C., et al., 2022. In utero ultrafine particulate exposure yields sex- and dose-specific responses to neonatal respiratory syncytial virus infection. Environ. Sci. Technol. 56 (16), 11527–11535.
Levesque, S., et al., 2011. Air pollution & the brain: subchronic diesel exhaust exposure causes neuroinflammation and elevates early markers of neurodegenerative disease. J. Neuroinflamm. 8 (1), 105.
Li, H., et al., 2022a. Is dietary intake of antioxidant vitamins associated with reduced adverse effects of air pollution on diabetes? Findings from a large cohort study. Ecotoxicol. Environ. Saf. 246, 114182.
Li, M., et al., 2020. Coexposure to environmental concentrations of cis-bifenthrin and graphene oxide: Adverse effects on the nervous system during metamorphic development of Xenopus laevis. J. Hazard Mater. 381, 120995.
Li, R., et al., 2013. Ambient ultrafine particles alter lipid metabolism and HDL anti-oxidant capacity in LDLR-null mice. J. Lipid Res. 54 (6), 1608–1615.
Li, T., et al., 2022b. A comprehensive understanding of ambient particulate matter and its components on the adverse health effects based from epidemiological and laboratory evidence. Part. Fibre Toxicol. 19 (1), 67.
Lim, D., et al., 2021. Inhalation toxicity of polystyrene micro(nano)plastics using modified OECD TG 412. Chemosphere 262, 128330.
Linker, S.B., et al., 2022. Human-specific regulation of neural maturation identified by cross-primate transcriptomics. Curr. Biol. 32 (22), 4797–4807.e5.
Liu, X., et al., 2021. Amorphous silica nanoparticles induce inflammation via activation of NLRP3 inflammasome and HMGB1/TLR4/MYD88/NF-kb signaling pathway in HUVEC cells. J. Hazard. Mater. 404, 124050.
Liu, Z., et al., 2023. Anionic nanoplastic contaminants promote Parkinson's disease-associated α-synuclein aggregation. Sci. Adv. 9 (46), eadi8716.
Lu, D., et al., 2020. Chemical multi-fingerprinting of exogenous ultrafine particles in human serum and pleural effusion. Nat. Commun. 11 (1), 2567.
Lu, X., et al., 2019. Long-term pulmonary exposure to multi-walled carbon nanotubes promotes breast cancer metastatic cascades. Nat. Nanotechnol. 14 (7), 719–727.
Luo, T., et al., 2019. Maternal exposure to different sizes of polystyrene microplastics during gestation causes metabolic disorders in their offspring. Environ. Pollut. 255 (Pt 1)), 113122.
Magrì, D., et al., 2018. Laser Ablation as a Versatile Tool To Mimic Polyethylene Terephthalate Nanoplastic Pollutants: Characterization and Toxicology Assessment. ACS Nano 12 (8), 7690–7700.
Mahmoudi, M., et al., 2023. The protein corona from nanomedicine to environmental science. Nat. Rev. Mater. 1–17.
Malley, C.S., et al., 2017. Preterm birth associated with maternal fine particulate matter exposure: A global, regional and national assessment. Environ. Int 101, 173–182.
Manisalidis, I., et al., 2020. Environmental and Health Impacts of Air Pollution: A Review. Front Public Health 8, 14.
Matsumoto, S., et al., 2023. Similarities and differences in placental development between humans and cynomolgus monkeys. Reprod. Med Biol. 22 (1), e12522.
Medley, E.A., et al., 2023. A systematic review of the placental translocation of micro- and nanoplastics. Curr. Environ. Health Rep. 10 (2), 99–111.
Merino Martinez, R., et al., 2021. Human exposome assessment platform. Environ. Epidemiol. 5 (6), e182.
Miller, L.A., et al., 2017. Nonhuman Primate Models of Respiratory Disease: Past, Present, and Future. Ilar J. 58 (2), 269–280.
Morales-Rubio, R.A., et al., 2019. In utero exposure to ultrafine particles promotes placental stress-induced programming of renin-angiotensin system-related elements in the offspring results in altered blood pressure in adult mice. Part Fibre Toxicol. 16 (1), 7.
Morris-Schaffer, K., et al., 2019. Effects of neonatal inhalation exposure to ultrafine carbon particles on pathology and behavioral outcomes in C57BL/6J mice. Part Fibre Toxicol. 16 (1), 10.
Mroz, R.M., et al., 2007. Nanoparticle carbon black driven DNA damage induces growth arrest and AP-1 and NFkappaB DNA binding in lung epithelial A549 cell line. J. Physiol. Pharm. 58 (Suppl 5), 461–470. Pt 2.
Mroz, R.M., et al., 2008. Nanoparticle-driven DNA damage mimics irradiation-related carcinogenesis pathways. Eur. Respir. J. 31 (2), 241.
Mrozik, W., et al., 2021. Environmental impacts, pollution sources and pathways of spent lithium-ion batteries. Energy Environ. Sci. 14 (12), 6099–6121.
Murat, F., et al., 2023. The molecular evolution of spermatogenesis across mammals. Nature 613 (7943), 308–316.
Nel, A.E., et al., 2009. Understanding biophysicochemical interactions at the nano-bio interface. Nat. Mater. 8 (7), 543–557.
Nguyen, B., et al., 2019. Separation and Analysis of Microplastics and Nanoplastics in Complex Environmental Samples. Acc. Chem. Res 52 (4), 858–866.
Ni, D.Q., et al., 2021. Titanium dioxide nanoparticles perturb the blood-testis barrier via disruption of actin-based cell adhesive function. Aging (Albany NY) 13 (23), 25440–25452.
Niu, M., Palomero-Gallagher, N., 2023. Architecture and connectivity of the human angular gyrus and of its homolog region in the macaque brain. Brain Struct. Funct. 228 (1), 47–61.
Onoda, A., Takeda, K., Umezawa, M., 2018. Dysregulation of major functional genes in frontal cortex by maternal exposure to carbon black nanoparticle is not ameliorated by ascorbic acid pretreatment. Sci. Total Environ. 634, 1126–1135.
Pandics, T., et al., 2023. Exposome and unhealthy aging: environmental drivers from air pollution to occupational exposures. Geroscience 45 (6), 3381–3408.
Pang, C., Zhang, N., Falahati, M., 2021. Acceleration of α-synuclein fibril formation and associated cytotoxicity stimulated by silica nanoparticles as a model of neurodegenerative diseases. Int J. Biol. Macromol. 169, 532–540.
Pascual, F., 2021. Potential Mechanisms behind Air Pollution Toxicity: Findings from Real-World Chronic Exposures. Environ. Health Perspect. 129 (2), 24001.
Patel, C.J., et al., 2013. Systematic identification of interaction effects between genome- and environment-wide associations in type 2 diabetes mellitus. Hum. Genet 132 (5), 495–508.
Patel, C.J., Bhattacharya, J., Butte, A.J., 2010. An Environment-Wide Association Study (EWAS) on type 2 diabetes mellitus. PLoS One 5 (5), e10746.
Peng, L., et al., 2020. Micro- and nano-plastics in marine environment: Source, distribution and threats - A review. Sci. Total Environ. 698, 134254.
Perkel, J.M., 2021. Single-cell proteomics takes centre stage. Nature 597 (7877), 580–582.
Quezada-Maldonado, E.M., et al., 2021. Airborne particulate matter induces oxidative damage, DNA adduct formation and alterations in DNA repair pathways. Environ. Pollut. 287, 117313.
Rajagopalan, S., Al-Kindi, S.G., Brook, R.D., 2018. Air Pollution and Cardiovascular Disease: JACC State-of-the-Art Review. J. Am. Coll. Cardiol. 72 (17), 2054–2070.
Rodriguez, K.A., Gaczynska, M., Osmulski, P.A., 2010. Molecular mechanisms of proteasome plasticity in aging. Mech. Ageing Dev. 131 (2), 144–155.
Rokas, A., et al., 2020. Developing a theoretical evolutionary framework to solve the mystery of parturition initiation. Elife 9.
Roshanzadeh, A., et al., 2021. Exposure to nanoplastics impairs collective contractility of neonatal cardiomyocytes under electrical synchronization. Biomaterials 278, 121175.
Sánchez, A., et al., 2022. Dietary microplastics: occurrence, exposure and health implications. Environ. Res. 212, 113150.
Saptarshi, S.R., Duschl, A., Lopata, A.L., 2013. Interaction of nanoparticles with proteins: relation to bio-reactivity of the nanoparticle. J. Nanobiotechnol. 11, 26.
Sawicki, K., et al., 2019. Toxicity of metallic nanoparticles in the central nervous system, 8 (1), 175–200.
Scheen, A.J., Junien, C., 2012. [Epigenetics, interface between environment and genes: role in complex diseases]. Rev. Med Liege 67 (5-6), 250–257.
Schraufnagel, D.E., 2020. The health effects of ultrafine particles. Exp. Mol. Med 52 (3), 311–317.
Seok, J., et al., 2013. Genomic responses in mouse models poorly mimic human inflammatory diseases. Proc. Natl. Acad. Sci. USA 110 (9), 3507–3512.
Shang, Y., et al., 2019. Modifications of autophagy influenced the Alzheimer-like changes in SH-SY5Y cells promoted by ultrafine black carbon. Environ. Pollut. 246, 763–771.
Shao, D., et al., 2017. Cardiorespiratory responses of air filtration: a randomized crossover intervention trial in seniors living in Beijing: Beijing Indoor Air Purifier StudY, BIAPSY. Sci. Total Environ. 603-604, 541–549.
Shukla, R.K., et al., 2013. Titanium dioxide nanoparticle-induced oxidative stress triggers DNA damage and hepatic injury in mice. Nanomedicine 9 (9), 1423–1434.
Simkhovich, B.Z., et al., 2007. Direct and acute cardiotoxicity of ultrafine particles in young adult and old rat hearts. Basic Res Cardiol. 102 (6), 467–475.
Song, S., et al., 2023. Inhalable textile microplastic fibers impair airway epithelial differentiation. Am. J. Respir. Crit. Care Med.
Stephan, M., Volkmann, P., Rossner, M.J., 2019. Assessing behavior and cognition in rodents, nonhuman primates, and humans: where are the limits of translation? Dialog-. Clin. Neurosci. 21 (3), 249–259.
Sun, H., et al., 2024. Polystyrene nanoparticles trigger aberrant condensation of TDP-43 and amyotrophic lateral sclerosis-like symptoms. Nat. Nanotechnol.
Terzano, C., et al., 2010. Air pollution ultrafine particles: toxicity beyond the lung. Eur. Rev. Med Pharm. Sci. 14 (10), 809–821.
Thaver, S., et al., 2019. Pregnancy protects against the pro-inflammatory respiratory responses induced by particulate matter exposure. Chemosphere 225, 796–802.
Thomas, R.J., 2013. Particle size and pathogenicity in the respiratory tract. Virulence 4 (8), 847–858.
Twigger, S.N., 2004. Of rats and men. Genome Biol. 5 (3), 314.
Ural, B.B., et al., 2022. Inhaled particulate accumulation with age impairs immune function and architecture in human lung lymph nodes. Nat. Med 28 (12), 2622–2632.

Vermeulen, R., et al., 2020. The exposome and health: where chemistry meets biology. Science 367 (6476), 392–396.
Wei, W., et al., 2024. Silica nanoparticle exposure implicates β-Amyloid (1-42) Inbound and the Accelerating Alzheimer's disease progression in mice overexpressing mutated forms of human amyloid precursor protein and presenilin 1 genes. Chem. Res Toxicol. 37 (2), 429–438.
Wick, P., et al., 2010. Barrier capacity of human placenta for nanosized materials. Environ. Health Perspect. 118 (3), 432–436.
Wieland, S., et al., 2024. Nominally identical microplastic models differ greatly in their particle-cell interactions. Nat. Commun. 15 (1), 922.
Wild, C.P., 2005. Complementing the genome with an "exposome": the outstanding challenge of environmental exposure measurement in molecular epidemiology. Cancer Epidemiol. Biomark. Prev. 14 (8), 1847–1850.
Woo, J.H., et al., 2023. Polypropylene nanoplastic exposure leads to lung inflammation through p38-mediated NF-κB pathway due to mitochondrial damage. Part Fibre Toxicol. 20 (1), 2.
Wu, H., Eckhardt, C.M., Baccarelli, A.A., 2023. Molecular mechanisms of environmental exposures and human disease. Nat. Rev. Genet 24 (5), 332–344.
Wu, Y., et al., 2022. Ambient air pollution associated with incidence and dynamic progression of type 2 diabetes: a trajectory analysis of a population-based cohort. BMC Med 20 (1), 375.
Xia, T., et al., 2004. Quinones and aromatic chemical compounds in particulate matter induce mitochondrial dysfunction: implications for ultrafine particle toxicity. Environ. Health Perspect. 112 (14), 1347–1358.
Xu, D., et al., 2021. Systematic toxicity evaluation of polystyrene nanoplastics on mice and molecular mechanism investigation about their internalization into Caco-2 cells. J. Hazard Mater. 417, 126092.
Yao, Y.G., K.I.Z.P.F, 2022. Construction Team of the, Towards the peak: the 10-year journey of the National Research Facility for Phenotypic and Genetic Analysis of Model Animals (Primate Facility) and a call for international collaboration in non-human primate research. Zool. Res 43 (2), 237–240.
Yu, Z., et al., 2020. Reactive oxygen species-related nanoparticle toxicity in the biomedical field. Nanoscale Res. Lett. 15 (1), 115.
Zeng, Y., et al., 2021. The impact of particulate matter (PM2.5) on human retinal development in hESC-derived retinal organoids. Front Cell Dev. Biol. 9, 607341.
Zhai, J., et al., 2022. Primate gastrulation and early organogenesis at single-cell resolution. Nature 612 (7941), 732–738.
Zhang, J., et al., 2022a. Chronic carbon black nanoparticles exposure increases lung cancer risk by affecting the cell cycle via circulatory inflammation. Environ. Pollut. 305, 119293.
Zhang, J., et al., 2024. Adverse effects of exposure to fine particles and ultrafine particles in the environment on different organs of organisms. J. Environ. Sci. (China) 135, 449–473.
Zhang, L., et al., 2018. Particle-induced SIRT1 downregulation promotes osteoclastogenesis and osteolysis through ER stress regulation. Biomed. Pharmacother. 104, 300–306.
Zhang, R., et al., 2023. Neurogenesis in primates versus rodents and the value of non-human primate models. Natl. Sci. Rev. 10 (11), nwad248.
Zhang, S., et al., 2016. Interventions to reduce individual exposure of elderly individuals and children to haze: a review. J. Thorac. Dis. 8 (1), E62–E68.
Zhang, Z., et al., 2022b. Mechanistic study of silica nanoparticles on the size-dependent retinal toxicity in vitro and in vivo. J. Nanobiotechnol. 20 (1), 146.
Zhu, X., et al., 2020. Recent advances in understanding the mechanisms of PM2.5-mediated neurodegenerative diseases. Toxicol. Lett. 329, 31–37.
Zhu, X., et al., 2023. Micro- and nanoplastics: a new cardiovascular risk factor? Environ. Int 171, 107662.