We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900
Open access books available

185,000
International authors and editors

200M
Downloads

Our authors are among the

154
Countries delivered to

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



Chapter

Particulate Matter Exposure: Genomic Instability, Disease, and Cancer Risk

Lyda Espitia-Pérez, Luisa Jiménez-Vidal and Pedro Espitia-Pérez

Abstract

The United Nations Environment Programme (UNEP/WHO) defines particulate matter (PM) as a mixture of solid or liquid particles suspended and dispersed in the air. Constituted by a complex mixture of organic and inorganic components like metals, acids, soil, and dust is considered a major human carcinogen present in air pollution. When inhaled, PM particles penetrate the respiratory tract, where they affect different organs and systems depending on their aerodynamic size and chemical properties. In the organism, this cocktail-like mixture can interact with cellular mechanisms related to the production of reactive oxygen species (ROS) and can cause damage to important macromolecules such as DNA, lipids, and proteins. Additionally, PM induces a variety of effects at a cellular level, such as inflammation, DNA damage, and genomic instability, acting as a driving force of carcinogenic processes and increasing the incidence of respiratory, cardiopulmonary, neurogenerative, and neurodevelopment disorders. This book chapter reviews the main characteristics of PM, its effects on health, and its role in genomic instability and associated molecular mechanisms. Additionally, we explore different biomarkers associated with PM exposure, DNA damage, and the influence of PM-related oxidative stress in disease development.

Keywords: $PM_{1.0}$, $PM_{2.5}$, PM_{10}, cancer, genomic instability

1. Introduction

Air pollution represents a worldwide problem with a significant impact on ecosystems and human health. According to the World Health Organization (WHO), air pollution poses the main environmental risk to health [1]. According to the International Agency for Research on Cancer (IARC), exposure to particulate matter (PM) in air pollution is considered as a human carcinogen [2]. PM is constituted by a heterogeneous mixture of a large variety of small particles of solids and liquids of both organic and inorganic nature, derived from natural and anthropogenic sources. PM size is an important factor that influences how it is deposited in the respiratory tract and affects human health. Large particles are generally filtered in the nose and throat and do not necessarily cause problems. An important fraction of PM is referred to as PM_{10}, composed of particles ≤10 μm. PM_{10} is generally subdivided into a fraction of finer particles ≤2.5 μm ($PM_{2.5}$) and a coarser fraction of particles >2.5

and <10 μm ($PM_{2.5–10}$). $PM_{2.5}$ is dominated by products of combustion and secondary particles, while $PM_{2.5–10}$ consists mainly of crustal, biological, and fine particle fraction components [3]. Thus, smaller PM particles can penetrate deeply in the lungs, activating molecular mechanisms of epithelial and defense cells [4].

Exposure to PM, especially around industrial zones and mining systems, has been associated with an increase in the morbidity of respiratory diseases, certain types of allergies, cardiopulmonary diseases, neurological disorders, and some types of cancer [5]. The biological mechanisms behind these associations are not entirely known, but the results of toxicological studies in vitro and in vivo have shown that PM induces several adverse cellular effects due to the synergistic generation of reactive oxygen species (ROS), which includes genotoxicity, mutagenicity, oxidative stress, inflammation, and increased DNA damage potentially associated with genomic instability [6].

Genomic instability is defined as a cell's increased likelihood to develop and accumulate genome alterations (mutations, chromosomal alterations, epigenetic/posttranscriptional modifications, and changes in gene expression). The frequency of these alterations is related to the loss of fidelity in mechanisms such as DNA replication, chromosomal segregation, DNA repair, and cell cycle progression [7]. These alterations are capable of acting as a driving force of the carcinogenic process, a reason why PM exposures are associated with an increase in cancer risk [6]. This cancer risk can be evaluated through measurable changes (biochemical, physiological, or morphological) that associate with toxic exposure or any early biochemical alteration. The identification of these genome damage biomarkers is useful by defining a pathogenesis state, such as cancer. It is also of vital importance for disease prevention [8]. Consequently, the toxicological investigation of complex mixtures such as PM is one of the main objectives of recent research in toxicology and cancer [9]. In order to elucidate how genomic background and PM exposure can interact, this book chapter focuses on reviewing relevant information based on the three main aspects: *(I) the characteristics of PM as an environmental pollutant and its effects on health*, *(II) the molecular mechanisms of the cellular effects associated with genomic instability by PM exposure*, and *(III) the use of different risk biomarkers based on the determination of chromosomal instability for estimation of cancer risk in populations exposed to PM*.

2. Environmental air pollution, PM, and health effects

Environmental air pollution is defined as the presence in the atmosphere of contaminating elements that alter its composition and that affect any component of the ecosystem [10]. Air pollution is constituted by an extremely complex mixture that includes inorganic components (sulfates, nitrates, ammonium, chloride, and trace metals), elemental and organic carbon, biological components (bacteria, spores, and pollens), and adsorbed volatile and semi-volatile organic compounds. Besides, environmental particles, when mixed with atmospheric gases (ozone, sulfur nitric oxides, and carbon monoxide) can generate environmental aerosols or PM [11].

PM is a complex mixture of solid and liquid particles of different origin, size, shape, and chemical composition [12]. Atmospheric PM comes from a variety of emission sources, including natural and anthropogenic sources. In addition, the particulate material can be emitted directly into the atmosphere (primary particles) or formed in the atmosphere from gaseous precursors (secondary particles) [13]. Among the emission sources, industries are considered one of the most significant anthropogenic sources of trace metals [14, 15] although traffic emissions could also be regarded as an important source of PM and metals in urban atmospheres [16, 17].

The size of the PM is of great interest to understand their mobility and their impact on health. The respiratory system is the primary intake route of PM in the body, and the deposition of particles in different parts of the human body depends on the size, shape, and density of the particles, as well as on the individual's breathing (nasal or oral) [10]. Such health effects induced in the organism depend on the granulometry, morphology, time of exposure, individual susceptibility, and finally the chemical composition of the particles [18]. In terms of size, PM is categorized according to aerodynamic size and is divided into three main groups: the first group is large particles, which are generally filtered in the nose and throat and do not necessarily cause problems. The second group is PM_{10}, an essential fraction of PM mostly produced by mechanical processes and with sizes between 2.5 and 10 micrometers (μm). PM_{10} is also called "coarse fraction" or "breathable fraction" because of its ability to enter the respiratory tract [19]. Finally, the third group is $PM_{2.5}$ or "fine fraction" whose aerodynamic diameter is ≤2.5 μm. $PM_{2.5}$ is mainly derived from combustion sources, such as automobiles, trucks, and other vehicle exhausts, as well as from stationary combustion sources [19]. $PM_{2.5}$ can easily reach the terminal bronchioles and alveoli, from where can be phagocytosed by alveolar macrophages and cross the capillary-alveolar barrier to be transported to other organs by blood circulation [20].

Recently, "ultrafine" particles have been described with aerodynamic size <0.1 μm; these particles are generated by photochemical processes and combustion, also from various natural and anthropogenic sources, and can go directly from the alveoli to the bloodstream [21]. Besides, their smaller size and higher surface/mass ratio may allow them to have more bioavailability for bioreactive chemicals in their large surface, allowing greater access to the contact points of the cells, increasing its toxicity.

Chemically, PM mainly comprises ions, reactive gases, salts (sulfates, nitrates), organic compounds such as polycyclic and/or inorganic aromatic hydrocarbons (PAHs), heavy metals (i.e., Fe, Cu, Mo, V, and those with high toxicity such as Pb, Cd, and Ni), and carbon core particle [22] compounds with known genotoxic, mutagenic, and/or carcinogenic activity. However, the chemical composition of PM varies greatly and depends on numerous geographical, meteorological, and source-specific variables [11]. PM can absorb and transfer a myriad of pollutants which results in its variable composition, so depending on the source and composition of the PM, different subsets of components may be found on different fractions. PM_{10} and $PM_{2.5}$ are dominated by mechanically abraded or grinded particles including finely divided minerals such as oxides of aluminum silicate, iron, calcium, and potassium [23]. $PM_{2.5}$ comprises the soot-rich fraction and other particles within the atmospheric gas phase resulting in subsequent agglomeration of PM and producing inorganic ions such as sulfate, nitrate, and ammonia, as well as carbon combustion residues, organic aerosols, metals, and other combustion products. Unlike inorganic elements that can be present in both $PM_{2.5}$ and PM_{10} fractions, PAHs show a strong association with the $PM_{2.5}$ fraction. Several studies have reported that 87–95% of PAHs can be found in the $PM_{2.5}$ fraction [24]. The latter correlation seems to be stronger for the heavier and more carcinogenic PAHs with five and six aromatic rings.

Also, coarse and fine fractions differ with ultrafine particles in composition regarding various heavy metals and possibly a higher content of compounds with redox activity, such as prooxidant PAHs (dibenzo (a,l) pyrene) [25] (**Table 1**).

Health effects caused by PM exposure are supported by increasingly a growing number of scientific evidences. The latter comes from a variety of epidemiological studies using both population and occupational approach for assessing PM exposure, alongside with toxicological studies and human-controlled exposure experiments. Results support the causal relationship between PM and premature death, increased morbidity from respiratory diseases [26], lung cancer [27], and cardiopulmonary diseases [28]. In fact, several health-related studies indicate a strong association of

Study area	Population description	Area description	Analyzed pollutants	Reference
Aracaju, Brazil	Urban	Metropolitan	PM, SO_2, and elements (Cu, Fe, Mn, Ni, V, and Ti)	[33]
Beijing, China	Urban	Metropolitan	PM (PM2.5), NOx, SO_2, volatile organic compounds (HAPs), ozone, nitrate	[34, 35]
Guajira, Colombia	Ethnical	Semi-arid	PM (PM10 and PM2.5), extractable organic matter (apolar and polar fractions), and elements (Al, Cl, Cr, Cu, K, Mg, Mn, Na, P, S, Si, Ti, and Zn)	[36]
Houston, USA	Urban	Metropolitan	PM2.5, NOx, volatile organic compounds (light alkenes), ozone, sulfate	[37, 38]
Huelva, Spain	Urban	Industrial	PM (PM10, PM2.5 and PM1), phosphate, and As	[2]
Los Angeles, USA	Urban	Metropolitan	PM (PM2.5), NOx, volatile organic compounds (HAPs), ozone, nitrate	[39, 40]
	Urban	Metropolitan	PM2.5, organic carbon, ammonium, nitrate, sulfate, and elements (Al, Br, Ca, Cl, Cu, Fe, K, Mn, Na, Ni, Pb, Si, V, Zn)	[41, 42]
Mexico City, Mexico	Urban	Metropolitan	PM (PM2.5), NOx, volatile organic compounds (alkanes, HAPs), ozone, sulfate	[43–45]
Sao Paulo and Piracicaiba, Brazil	Urban	Metropolitan	PM (PM10 and PM2.5), sulphate, nitrate, ammonium, elemental carbon, and particulate organic material	[46]

Table 1.
Particulate matter characterization from several cohort studies worldwide.

airborne PM generated around coal mines with adverse impacts such as increased cardiovascular disease and other pathologies such as pneumoconiosis, neurogenerative and neurodevelopment disorders, and different types of cancer [21].

Particularly, it has been described that PM_{10} exposure can cause deterioration of the respiratory function in a short term, whereas in the long term, it is associated with the development of chronic diseases, cancer, or premature death. On the other hand, $PM_{2.5}$ exhibits a strong association with increased risk of respiratory disease, cardiovascular disorders, type II diabetes mellitus, and even autism spectrum disorders [29–31]. Finally, ultrafine particles may be the most active in terms of the induction of systemic effects; in fact, studies describe the role of ultrafine particles in the increased risk of cardiac hospitalization due to early myocardial infarction and increased frequency of readmissions for patients who have survived myocardial infarction and heart failure, which allows to consider $PM_{2.5}$ as a risk factor for cardiovascular disease [32].

3. Genomic instability by PM exposure and its relation with carcinogenesis

Several studies have examined in different experimental models in vivo and in vitro the effects of exposure to coarse, fine, and ultrafine PM. These studies

provide biological support to epidemiological studies that show an association between acute exposure to PM and health effects. The relationship between disease and air pollution is well established, but the molecular mechanism regarding their relationship is yet to be fully explored.

The interaction of PM with the cellular plasma membrane and its receptors and ion channels may directly trigger a biological response. The most important pathophysiological mechanism that has been proposed to explain the association of PM exposure and occurrence of respiratory infections, cancer, and chronic cardiopulmonary diseases is oxidative stress through the generation of ROS. ROS are oxygen-related compounds able to induce changes in cellular redox cycle and therefore triggering a series of events in cascade such as inflammation, apoptosis, and oxidative damage to macromolecules such as proteins, lipids, and nucleic acids [33]. Under the name of ROS, several species derived from the reduction of molecular oxygen (O_2) are included, mainly superoxide anion (O^{2-}), hydrogen peroxide (H_2O_2), and hydroxyl radical (OH^-), all of which are highly reactive and capable of causing damage in the cell. These reactive species can be generated naturally by exhibiting a relevant function in cell biology or by inducing oxidizing agents in the medium [34].

Oxidative stress in the cell is caused by an imbalance between the production of ROS and the ability of the system to detoxify them or repair the resulting damage [35]. In the lungs, a particular target of PM, oxidative stress initiates the synthesis of mediators of pulmonary inflammation in lung epithelial cells triggering the activation of carcinogenic mechanisms (**Figure 1**). Inflammatory cells are particularly effective in generating most of the ROS. The activation of the redox metabolism of inflammatory cells generates a highly oxidative environment within an organ for aerobic organisms. ROS-mediated inflammation teams with another type of chemical species such as reactive nitrogen species (RNS) which also causes oxidative damage to cellular components. Many proinflammatory mediators, especially cytokines, chemokines, and prostaglandins, turn on the angiogenesis switches mainly

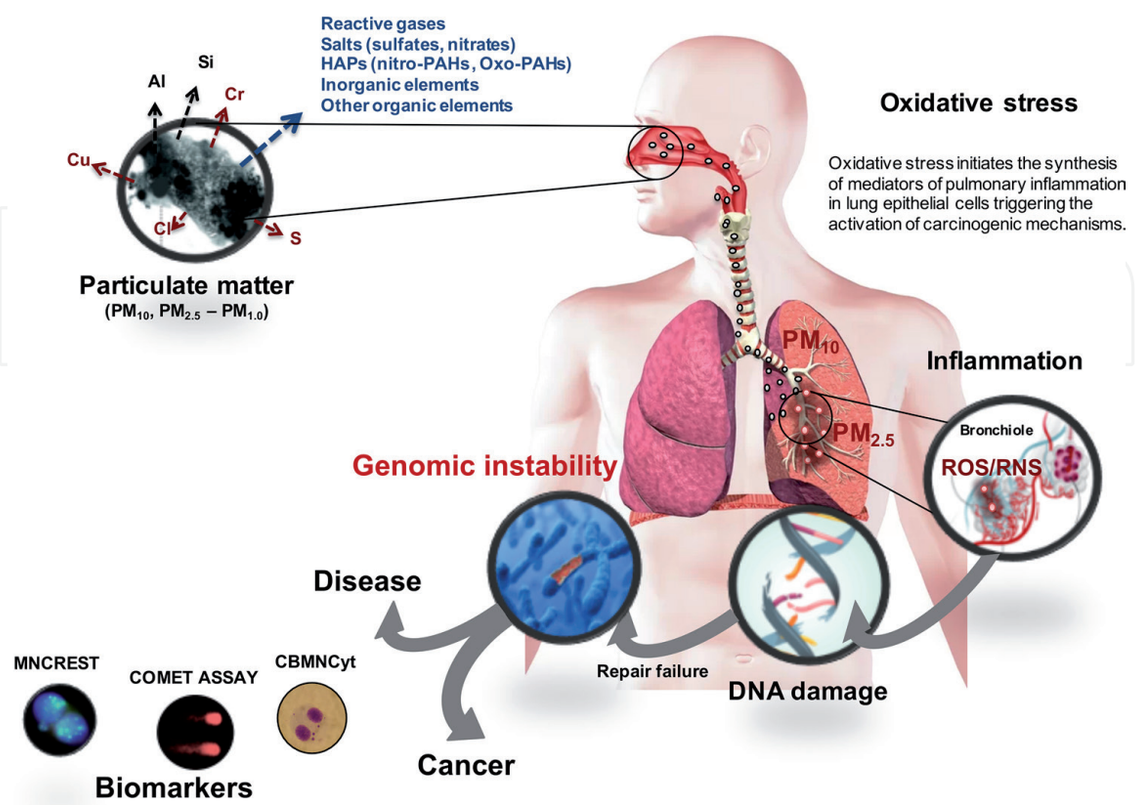


Figure 1.
Main processes and biomarkers associated with genomic instability, inflammation and cancer risk induced by particulate matter exposure.

controlled by vascular endothelial growth factors [36, 37]. The possible mechanisms by which inflammation can contribute to carcinogenesis include genomic instability, alterations in epigenetic events and subsequent inappropriate gene expression, enhanced proliferation of initiated cells, resistance to apoptosis, aggressive tumor neovascularization, invasion through the tumor-associated basement membrane, angiogenesis, and metastasis [36].

Oxidative damage generated by both ROS and RNS species in DNA is considered one of the most harmful effects for the cell since they can produce irreversible changes in the genome. Chemical modifications in DNA structure include strand breaks, sugar moiety modification, nitrogenous base oxidation, and generation of apurinic/apyrimidinic sites (AP sites) [38]. This type of DNA damage can be generated with frequencies between 104 and 105 DNA mutations per cell/day. This DNA damage can also produce several chromosomal alterations such as deletions, insertions, or translocations increasing the toxic spectrum for the cell. Accumulation of these genomic alterations may cause dysregulation of cell division, the imbalance between cell growth and death, and cancer [18].

The use of biological monitoring procedures, or biomonitoring, through specific biomarkers can assess the effects of PM exposure and its possible impact on the organism. Early biomonitoring allows detection of the first alterations during the non-malignant phase, including the measurable changes (biochemical, physiological, or morphological) that associate a toxic exposure with any early biochemical alteration.

3.1 Molecular mechanisms associate with genomic instability and cancer by PM exposure

The International Agency for Research on Cancer (IARC) has classified exposure to PM in air pollution as a human carcinogen [2]. The molecular reactions induced by the PM exposure are often initiated by reactive PM constituents including metals and various PAHs and PAH's derivatives like nitro-PAHs and various oxo-PAHs (quinones). These substances are potent oxidants, either through direct effects on proteins, lipids, mitochondrial or nuclear DNA or indirectly through the generation of free radicals and activation of intracellular oxidant pathways [11, 39]. Correspondingly, several studies have shown that other transition metals (Fe, Cu, Cr, and V) with catalytic activity during Fenton's reaction ($Fe^{2+} + H_2O_2 + H^+ \rightarrow Fe^{3+} + OH^{\cdot} + H_2O$) generate the highly reactive hydroxyl radical able to induce oxidative DNA damage, oxidative stress, and inflammatory responses [11].

Depending on its structure, PAHs show carcinogenic potential. IARC classifies these compounds as a human carcinogen (group 1), probably carcinogenic (group 2A), possibly carcinogenic (group 2B), and not classified as carcinogenic (group 3). Particularly, The HAPs that have angulated structures typically react with adenine residues and are related to a higher carcinogenic activity compared to those with a linear and more condensed structure, which usually react with guanine residues [40].

Many of the biological effects of PAHs, including oxidative stress and DNA damage, are believed to be mediated by activation of the aryl hydrocarbon receptor (AhR) and subsequent induction metabolism by cytochrome P450 (CYP) enzymes [41–43]. The binding of PAH metabolites to DNA and the associated effects that occur as a consequence are considered the main mechanisms of mutagenicity and carcinogenicity attributed to PAHs. Additionally, it is believed that the formation of redox-active quinones is catalyzed by dihydrodiol dehydrogenases, also contributing to PAH carcinogenesis and tumor promotion [44].

At least three distinct molecular mechanisms have been proposed to explain the process of tumor initiation by exposure to PAHs. These models include the formation of (1) diol-epoxide, (2) radical cations, and (3) o-quinones. The metabolism

of PAHs into diol-epoxide may lead to the formation of DNA adducts, mainly in guanines and adenines, generating mutations in proto-oncogenes and tumor suppressor genes. The radical cation leads to the formation of adducts of DNA, generating AP sites. Finally, o-quinones can generate ROS and potentially cause mutations in TP53 and other tumor suppressor genes and/or proto-oncogenes [45].

On the other hand, oxy- and nitro-PAHs, which consist of oxygen and nitrogen derivatives of PAHs, respectively, play an important role in the mutagenicity attributed to PM. Studies with *Salmonella* strains (YG1041) sensitive to this group of organic compounds indicated a mutagenic activity for a fraction of nitro-PAHs, whereas oxy-PAHs can generate DNA adducts [46].

Besides, transition metal ions with redox potential, which are presented in PM (adsorbed at high concentrations inside particle cavities), can contribute to ROS overproduction and play an important role in oxidative DNA and protein damage [47]. Soluble metals on inhaled particles, such as Fe, Ni, V, Co, Cu, and Cr, were associated with increased ROS production, followed by cellular oxidative stress in airway epithelial cells [48]. Studies have identified certain metals as responsible for oxidant effects and inflammation in experimental animals, by using diverse metal chelators (such as EDTA, which increase the redox reactivity of some metals) and antioxidants (which scavenge oxygen-free radicals) for metal assessment [44].

The different types of particles in PM, their extracts, as well as single obtained components, all have demonstrated genotoxic effects in human and animal studies both in vivo and in vitro [23]. Several studies have shown that cells may be arrested in various parts of the cell cycle [49, 50]. Most often, such effects have been linked to DNA damage, and following PM exposure, this DNA damage includes mainly DNA single-strand breaks, alkali-labile single-strand DNA breaks, and various forms of oxidative DNA damage including oxidized guanines measured as 8-oxo-7,8-dihydroguanine (8-oxoGua) adducts and lesions detected as formamidopyrimidine DNA glycosylase (FPG) sites by the comet assay [51]. Often this type of damage is associated with chromosomal damage induction. These biomarkers are used to assess genotoxic effects on human populations exposed to complex mixtures of chemicals.

3.2 Risk biomarkers based on the determination of genomic instability for estimation of cancer risk

Exposure biomarkers reflect human exposure on different routes. Biological monitoring of PAHs is restricted because of the few PAHs for which metabolites are available as standards. However, this limitation is partially overcome by the use of metabolite markers of total exposure to PAHs, such as 1-hydroxypyrene (1-OHP) [48, 52]. Several studies have shown that urinary 1-OHP is a useful biomarker of both environmental and occupational exposures to PAHs and shows a correlation with genotoxic effect biomarkers measured in peripheral blood lymphocytes [53, 54].

In addition to these biochemical markers, other cytogenetic biomarkers have been suggested for the identification of cancer risk; the most generalized and best-characterized biomarker for evaluating the mutagenic effects and possible cancer risk in populations exposed to PM is the assessment of micronuclei (MN) frequency in vivo. MN is an effect biomarker consisting of small nuclear masses of genetic material separate from the main nucleus and arising in the dividing cells. They are measured 1/3 to 1/16 of the size of the nucleus and are delimited by a nuclear membrane. MNs are derived from chromosomal breaks (clastogenic origin) and/or whole chromosomes (aneugenic origin). MN composed of fragments of

chromosomes (clastogenic) can result from the direct breaking of the double strand of DNA, conversion from single-stranded to double-stranded strand after cell replication or inhibition of DNA synthesis. The MN formed by whole chromosomes (aneugenic) is mainly caused by defects in the mechanism of chromosomal segregation, such as deficiencies in the control of cell cycle genes, mitotic spindle faults, kinetochore, or other parts of the mitotic apparatus, mechanical rupture, or hypomethylation of centromeric DNA [55–58]. For MN assessment the used protocol is the cytokinesis-block cytome micronucleus assay (CBMNCyt), whereas for rapid chromosomal break evaluation, the micronucleus assay with CREST immunostaining (MNCREST) is often used.

CBMNCyt used in primary cultured cells such as lymphocytes allows measuring not only genotoxicity parameters (solely MN frequency) but also cytokinesis defects (binucleate cells) and includes MNBN (MN in binucleated or cytokinesis blocked cells), a biomarker of chromosome breakage and/or whole chromosome loss; MNMONO (MN in mononucleated cells), a biomarker of chromosomal damage induced and expressed in vivo before the start of the CBMN assay culture; NPBs (nucleoplasmic bridges), a biomarker of DNA misrepair and/or telomere end-fusions; and NBUDs (or "nuclear buds"), a biomarker of elimination of amplified DNA and/or DNA repair complexes [55]. In addition, the assay allows measuring the proliferative potential (basal cells) and various forms of cell death (pyknotic, karyolytic, karyorrhexis, and chromatin condensation). So, the application of this approach provides information on genotoxic, cytotoxic, and cytostatic effects increasing the predictive capacity of the bioassay [59]. However, it is worth emphasizing that only the frequency of MN has been associated with an increased risk of cancer development, neurodegenerative diseases, and acceleration of aging [56, 60]. MNMONO frequencies may give an estimation of the genome instability accumulated over many years in stem cells and circulating T lymphocytes long before the blood was sampled, whereas MNBN cells provide an additional measure of lesions that have accumulated in DNA or key proteins [61].

In a study developed by our laboratory, we assessed PM exposure in populations with residential proximity to open-pit coal mine in Northern Colombia and investigated the correlation between chromosomal damage and genetic instability evaluated by CBMNcyt in isolated lymphocytes of individuals with residential proximity to the coal mining corridor and its relation with measured PM_{10} and $PM_{2,5}$ levels. Our results revealed a significant increase in MNBN and MNMONO cells in individuals with residential proximity to open-pit coal mines. Additionally, correlation analysis demonstrated a highly significant association between $PM_{2.5}$ levels, MNBN frequencies, and CREST+ micronucleus induction in exposed residents. These results suggest that $PM_{2.5}$ fraction generated in coal mining activities may induce whole chromosome loss (aneuploidy) preferentially, although there are also chromosome breaks. This aneugenic effect may be associated with an oxidative stress status inside the cell, potentially capable of causing mitotic arrest (elevated MNMONO frequency), centromere damage, kinetochore malfunction, or disruption of the mitotic spindle [18].

Other types of MN assessment use exfoliated buccal cells isolated from exposed individuals. The micronucleus test in oral mucosal cells or buccal MN cytome assay (BMCyt) has been widely used in studies of populations exposed environmentally or occupationally to genotoxic agents. Previous work from our laboratory demonstrated MN formation in exfoliated buccal cells of workers occupationally exposed to open coal mining residues, which correlated with PM increased levels detected by BMCyt assay [62]. This technique is particularly attractive because oral mucosal cells can be collected in a minimally invasive manner [63, 64].

4. Conclusions

Sufficient evidence has been accumulated from epidemiological studies that support the fact that a broad spectrum of health outcome variables may come from short-term exposure to coarse, fine, and ultrafine PM. This association is consistent with experimental evidence that identifies different mechanisms of damage at a cellular level: inflammation, oxidative stress, cytotoxicity, alterations of autonomic nervous system, and coagulation. In relation to chronic effects on health, studies are less numerous, and the evidence is still inconsistent. Previous work suggests that PM exerts its genotoxic and carcinogenic effects through the generation of DNA damage and chromosomal instability. The biological mechanisms behind these associations are not fully understood, but toxicological results in vitro have shown that PM induces several types of adverse cellular effects.

Author details

Lyda Espitia-Pérez*, Luisa Jiménez-Vidal and Pedro Espitia-Pérez
Grupo de Investigaciones Biomedicas y Biología Molecular, Universidad del Sinú, Montería, Córdoba, Colombia

*Address all correspondence to: lydaespitia@unisinu.edu.co

IntechOpen

© 2019 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/3.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. CC BY

References

[1] Prüss-Üstün A, Corvalán C. Preventing disease through healthy environments: A global assessment of the burden of disease from environmental risks. Geneva: World Health Organization; 2016

[2] Loomis D, Grosse Y, Lauby-Secretan B, Ghissassi FE, Bouvard V, Benbrahim-Tallaa L, et al. The carcinogenicity of outdoor air pollution. The Lancet Oncology. 2013;**14**(13):1262-1263

[3] EPA USEPA. Executive summary. In: Air Quality Criteria for Particulate Matter. Vol. I. Publication No. EPA/600/P-95/001/aF; National Center for Environmental Assessment; Research Triangle Park. 1996. pp. 1-21

[4] Andreau K, Leroux M, Bouharrour A. Health and cellular impacts of air pollutants: From cytoprotection to cytotoxicity. Biochemistry Research International. 2012;**2012**:1-18

[5] Pope CA 3rd, Burnett RT, Thun MJ, Calle EE, Krewski D, Ito K, et al. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. Journal of the American Medical Association. 2002;**287**(9):1132-1141

[6] Santibáñez-Andrade M, Quezada-Maldonado EM, Osornio-Vargas Á, Sánchez-Pérez Y, García-Cuellar CM. Air pollution and genomic instability: The role of particulate matter in lung carcinogenesis. Environmental Pollution. 2017;**229**:412-422

[7] Broustas CG, Lieberman HB. DNA damage response genes and the development of cancer metastasis. Radiation Research. 2014;**181**(2):111-130

[8] Benford D, Hanley B, Bottrill K, Oehlschlager S, Balls M, Branca F, et al. Biomarkers as predictive tools in toxicity testing. Alternatives to Laboratory Animals. 2000;**28**:119-131

[9] Hu Z, Brooks SA, Dormoy V, Hsu CW, Hsu HY, Lin LT, et al. Assessing the carcinogenic potential of low-dose exposures to chemical mixtures in the environment: Focus on the cancer hallmark of tumor angiogenesis. Carcinogenesis. 2015;**36**(Suppl 1): S184-S202

[10] Vallero D. Air pollution decision tools. In: Fundamentals of Air Pollution. 5th ed. Amsterdam: Academic Press; 2014. pp. 83-109

[11] Lodovici M, Bigagli E. Oxidative stress and air pollution exposure. Journal of Toxicology. 2011;**2011**:1-9

[12] Grantz DA, Garner JHB, Johnson DW. Ecological effects of particulate matter. Environment International. 2003;**29**(2-3):213-239

[13] Pey J, Rodríguez S, Querol X, Alastuey A, Moreno T, Putaud JP, et al. Variations of urban aerosols in the western mediterranean. Atmospheric Environment. 2008;**42**(40):9052-9062

[14] Zheng N, Liu J, Wang Q, Liang Z. Health risk assessment of heavy metal exposure to street dust in the zinc smelting district, northeast of China. Science of the Total Environment. 2010;**408**(4):726-733

[15] Zhou S, Yuan Q, Li W, Lu Y, Zhang Y, Wang W. Trace metals in atmospheric fine particles in one industrial urban city: Spatial variations, sources, and health implications. Journal of Environmental Sciences. 2014;**26**(1):205-213

[16] Johansson C, Norman M, Burman L. Road traffic emission factors for heavy metals. Atmospheric Environment. 2009;**43**(31):4681-4688

[17] Lough GC, Schauer JJ, Park JS, Shafer MM, Deminter JT, Weinstein JP. Emissions of metals associated

with motor vehicle roadways. Environmental Science & Technology. 2005;**39**(3):826-836

[18] Espitia-Perez L, da Silva J, Espitia-Perez P, Brango H, Salcedo-Arteaga S, Hoyos-Giraldo LS, et al. Cytogenetic instability in populations with residential proximity to open-pit coal mine in northern Colombia in relation to PM10 and PM2. 5 levels. Ecotoxicology and Environmental Safety. 2018;**148**:453-466

[19] Campagna M, Pilia I, Marcias G, Frattolillo A, Pili S, Bernabei M, et al. Ultrafine particle distribution and chemical composition assessment during military operative trainings. International Journal of Environmental Research and Public Health. 2017;**14**(6):579

[20] Lu F, Xu D, Cheng Y, Dong S, Guo C, Jiang X, et al. Systematic review and meta-analysis of the adverse health effects of ambient PM2.5 and PM10 pollution in the Chinese population. Environmental Research. 2015;**136**:196-204

[21] Baldauf R, Devlin R, Gehr P, Giannelli R, Hassett-Sipple B, Jung H, et al. Ultrafine particle metrics and research considerations: Review of the 2015 UFP workshop. International Journal of Environmental Research and Public Health. 2016;**13**(11):1054

[22] Cheng H, Gong W, Wang Z, Zhang F, Wang X, Lv X, et al. Ionic composition of submicron particles (PM1.0) during the long-lasting haze period in January 2013 in Wuhan, Central China. Journal of Environmental Sciences. 2014;**26**(4):810-817

[23] Nemmar A, Holme JA, Rosas I, Schwarze PE, Alfaro-Moreno E. Recent advances in particulate matter and nanoparticle toxicology: A review of the *in vivo* and *in vitro* studies. BioMed Research International. 2013;**2013**:279371

[24] Kawanaka Y, Matsumoto E, Sakamoto K, Wang N, Yun S-J. Size distributions of mutagenic compounds and mutagenicity in atmospheric particulate matter collected with a low-pressure cascade impactor. Atmospheric Environment. 2004;**38**(14):2125-2132

[25] Araujo JA, Nel AE. Particulate matter and atherosclerosis: Role of particle size, composition and oxidative stress. Particle and Fibre Toxicology. 2009;**6**:24

[26] Weichenthal SA, Godri-Pollitt K, Villeneuve PJ. PM2.5, oxidant defence and cardiorespiratory health: A review. Environmental Health. 2013;**12**:40

[27] Kurth L, Kolker A, Engle M, Geboy N, Hendryx M, Orem W, et al. Atmospheric particulate matter in proximity to mountaintop coal mines: Sources and potential environmental and human health impacts. Environmental Geochemistry and Health. 2015;**37**(3):529-544

[28] Brook RD, Rajagopalan S, Pope CA 3rd, Brook JR, Bhatnagar A, Diez-Roux AV, et al. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. Circulation. 2010;**121**(21):2331-2378

[29] Achilleos S, Kioumourtzoglou MA, Wu CD, Schwartz JD, Koutrakis P, Papatheodorou SI. Acute effects of fine particulate matter constituents on mortality: A systematic review and meta-regression analysis. Environment International. 2017;**109**:89-100

[30] Morales-Suarez-Varela M, Peraita-Costa I, Llopis-Gonzalez A. Systematic review of the association between particulate matter exposure and autism spectrum disorders. Environmental Research. 2017;**153**:150-160

[31] Weinmayr G, Hennig F, Fuks K, Nonnemacher M, Jakobs H, Mohlenkamp S, et al. Long-term exposure to fine particulate matter and incidence of type 2 diabetes mellitus in a cohort study: Effects of total and traffic-specific air pollution. Environmental Health. 2015;**14**:53

[32] Heusinkveld HJ, Wahle T, Campbell A, Westerink RHS, Tran L, Johnston H, et al. Neurodegenerative and neurological disorders by small inhaled particles. Neurotoxicology. 2016;**56**:94-106

[33] Li N, Xia T, Nel AE. The role of oxidative stress in ambient particulate matter-induced lung diseases and its implications in the toxicity of engineered nanoparticles. Free Radical Biology & Medicine. 2008;**44**(9):1689-1699

[34] Juan ER. Papel del Estrés Oxidativo Sobre la Estabilidad Genética y la Bioseguridad de las Células Madre Mesenquimales Humanas Adultas. Universidad Autónoma de Madrid; 2012

[35] Griendling KK, FitzGerald GA. Oxidative stress and cardiovascular injury. Circulation. 2003;**108**(16):1912-1916

[36] Valavanidis A, Vlachogianni T, Fiotakis K, Loridas S. Pulmonary oxidative stress, inflammation and cancer: Respirable particulate matter, fibrous dusts and ozone as major causes of lung carcinogenesis through reactive oxygen species mechanisms. International Journal of Environmental Research and Public Health. 2013;**10**(9):3886-3907

[37] Costa C, Incio J, Soares R. Angiogenesis and chronic inflammation: Cause or consequence? Angiogenesis. 2007;**10**(3):149-166

[38] Gajewski TF, Schreiber H, Fu YX. Innate and adaptive immune cells in the tumor microenvironment. Nature Immunology. 2013;**14**(10):1014-1022

[39] Moller P, Loft S. Oxidative damage to DNA and lipids as biomarkers of exposure to air pollution. Environmental Health Perspectives. 2010;**118**(8):1126-1136

[40] Galvão DO. Avaliação do Potencial Genotóxico e Citotóxico Associado a Queima Artesanal da Castanha de Caju. Universidade Federal do Rio Grande do Norte; 2011

[41] Jarvis IW, Dreij K, Mattsson A, Jernstrom B, Stenius U. Interactions between polycyclic aromatic hydrocarbons in complex mixtures and implications for cancer risk assessment. Toxicology. 2014;**321**:27-39

[42] Jarvis IW, Bergvall C, Bottai M, Westerholm R, Stenius U, Dreij K. Persistent activation of DNA damage signaling in response to complex mixtures of PAHs in air particulate matter. Toxicology and Applied Pharmacology. 2013;**266**(3):408-418

[43] Murray IA, Patterson AD, Perdew GH. Aryl hydrocarbon receptor ligands in cancer friend and foe. Nature Reviews. Cancer. 2014;**14**(12):801-814

[44] Valavanidis A, Fiotakis K, Vlachogianni T. Airborne particulate matter and human health: Toxicological assessment and importance of size and composition of particles for oxidative damage and carcinogenic mechanisms. Journal of Environmental Science and Health Part C Environmental Carcinogenesis & Ecotoxicology Reviews. 2008;**26**(4):339-362

[45] EPA. Development of a Relative Potency Factor (RPF) Approach for Polycyclic Aromatic Hydrocarbon (PAH) Mixtures. 2010

[46] Umbuzeiro GA, Franco A, Martins MH, Kummrow F, Carvalho L, Schmeiser HH, et al. Mutagenicity and DNA adduct formation of PAH, nitro-PAH, and oxy-PAH fractions of

atmospheric particulate matter from Sao Paulo, Brazil. Mutation Research. 2008;**652**(1):72-80

[47] Valko M, Rhodes CJ, Moncol J, Izakovic M, Mazur M. Free radicals, metals and antioxidants in oxidative stress-induced cancer. Chemico-Biological Interactions. 2006;**160**(1):1-40

[48] Yuan TH, Shie RH, Chin YY, Chan CC. Assessment of the levels of urinary 1-hydroxypyrene and air polycyclic aromatic hydrocarbon in PM2.5 for adult exposure to the petrochemical complex emissions. Environmental Research. 2015;**136**:219-226

[49] Gualtieri M, Ovrevik J, Mollerup S, Asare N, Longhin E, Dahlman HJ, et al. Airborne urban particles (Milan winter-PM2.5) cause mitotic arrest and cell death: Effects on DNA, mitochondria, AhR binding and spindle organization. Mutation Research. 2011;**713**(1-2):18-31

[50] Danielsen PH, Loft S, Kocbach A, Schwarze PE, Moller P. Oxidative damage to DNA and repair induced by Norwegian wood smoke particles in human A549 and THP-1 cell lines. Mutation Research. 2009;**674**(1-2):116-122

[51] Dubinett SM, Lee JM, Sharma S, Mule JJ. Chemokines: Can effector cells be redirected to the site of the tumor? Cancer Journal. 2010;**16**(4):325-335

[52] Hansen AM, Mathiesen L, Pedersen M, Knudsen LE. Urinary 1-hydroxypyrene (1-HP) in environmental and occupational studies—A review. International Journal of Hygiene and Environmental Health. 2008;**211**(5-6):471-503

[53] Duan H, Leng S, Pan Z, Dai Y, Niu Y, Huang C, et al. Biomarkers measured by cytokinesis-block micronucleus cytome assay for evaluating genetic damages induced by polycyclic aromatic hydrocarbons. Mutation Research. 2009;**677**(1-2):93-99

[54] Leng S, Dai Y, Niu Y, Pan Z, Li X, Cheng J, et al. Effects of genetic polymorphisms of metabolic enzymes on cytokinesis-block micronucleus in peripheral blood lymphoc. Cancer Epidemiology, Biomarkers & Prevention. 2004;**13**(10):1631-1639

[55] Fenech M. Cytokinesis-block micronucleus assay evolves into a "cytome" assay of chromosomal instability, mitotic dysfunction and cell death. Mutation Research. 2006;**600**(1-2):58-66

[56] Bolognesi C, Knasmueller S, Nersesyan A, Thomas P, Fenech M. The HUMNxl scoring criteria for different cell types and nuclear anomalies in the buccal micronucleus cytome assay—An update and expanded photogallery. Mutation Research. 2013;**753**(2):100-113

[57] Terradas M, Martin M, Genesca A. Impaired nuclear functions in micronuclei results in genome instability and chromothripsis. Archives of Toxicology. 2016;**90**(11):2657-2667

[58] Iarmarcovai G, Botta A, Orsiere T. Number of centromeric signals in micronuclei and mechanisms of aneuploidy. Toxicology Letters. 2006;**166**(1):1-10

[59] Bolognesi C, Bonassi S, Knasmueller S, Fenech M, Bruzzone M, Lando C, et al. Clinical application of micronucleus test in exfoliated buccal cells: A systematic review and metanalysis. Mutation Research, Reviews in Mutation Research. 2015;**766**:20-31

[60] Bonassi S, Znaor A, Ceppi M, Lando C, Chang WP, Holland N, et al. An increased micronucleus frequency in peripheral blood lymphocytes

predicts the risk of cancer in humans. Carcinogenesis. 2007;**28**(3):625-631

[61] Kirsch-Voldersa M, Bonassi S, Knasmueller S, Holland N, Bolognesi C, Fenech FM. Commentary critical questions, misconceptions and a road map for improving the use of the lymphocyte cytokinesis-block micronucleus assay for *in vivo* biomonitoring of human exposure to genotoxic chemicals—A HUMN project perspective. Mutation Research. 2014;**759**:49-58

[62] Leon-Mejia G, Quintana M, Debastiani R, Dias J, Espitia-Perez L, Hartmann A, et al. Genetic damage in coal miners evaluated by buccal micronucleus cytome assay. Ecotoxicology and Environmental Safety. 2014;**107**:133-139

[63] Thomas P, Holland N, Bolognesi C, Kirsch-Volders M, Bonassi S, Zeiger E, et al. Buccal micronucleus cytome assay. Nature Protocols. 2009;**4**(6):825-837

[64] Doherty A, Steven MB, Jeffrey C. Bemis. The in vitro micronucleus assay. Genetic Toxicology Testing. Academic Press; 2016. pp. 161-205

IntechOpen