UNIVERSITI PUTRA MALAYSIA

INFLUENCE OF POLYCYCLIC AROMATIC HYDROCARBON AND GENETIC POLYMORPHISMS (CYP1A1, GSTM1, GSTT1) ON PYRENE METABOLITE AND DNA DAMAGE AMONG CHILDREN IN THE KLANG VALLEY, MALAYSIA

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Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia in Fulfilment of the Requirements for the Degree of Doctor of Philosophy

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June 2022

Chairman : Juliana Jalaludin, PhD
Faculty : Medicine and Health Sciences

Polycyclic Aromatic Hydrocarbon (PAHs) are hazardous particulate matter bound-organic compound found in urban atmospheric environment. Exposure to PAHs is of great concern to public health especially for children, due to their ubiquitous presence in the environment and well-recognised carcinogenicity, teratogenicity and genotoxicity to human health. This study aimed to assess the association of particulate PAHs exposure on biomarker of PAHs exposure, urinary 1-hydroxypyrene (1-OHP) and DNA damage among children in the vicinity of heavy traffic areas in the Klang Valley. In addition, this study investigated the effects of genetic polymorphisms of PAHs metabolising enzymes on the concentrations of pyrene metabolite, the urinary 1-OHP level, and on DNA damage in children. This cross-sectional comparative study was conducted at eight primary schools in high traffic (HT) and low traffic (LT) areas in Klang Valley, Malaysia. A validated questionnaire on socio-demographic, health status, personal exposure and dietary intake was distributed to randomly selected children. The indoor and outdoor samples of particulate matter $PM_{2.5}$-bound PAHs were collected using a MiniVol portable air sampler for 24 h. PAHs concentration was quantified using Gas Chromatography-Mass Spectrometry (GC-MS). Source diagnostic ratio was applied to determine the source of PAHs emission. DNA damage in buccal cells were evaluated using Comet Assay, while urinary 1-OHP was assessed using High-Performance Liquid Chromatography (HPLC). Genes encoding three PAHs-metabolising enzymes *CYP1A1*, *GSTT1* and *GSTM1* were studied for polymorphisms using PCR-RFLP and multiplex PCR. The results showed that the total outdoor PAHs was higher (range between 1.36-5.76 ng/m^3) than indoor environments (range between 1.25-5.58 ng/m^3). The concentration of total PAHs was higher at HT compared to LT area. Based on the source diagnostic ratio, PAHs in the HT area is pyrogenic, mainly from high combustion activity (vehicular emission). Meanwhile, the urinary 1-OHP concentration was significantly higher among children in HT as compared to LT (0.07 vs 0.04 µmol/mol-creatinine). The DNA damage was obviously higher among children in HT as compared to LT. A

significant association were found between environmental PAHs exposure with urinary 1-OHP and DNA damage. It was observed that there was no significant effect of *CYP1A1*, *GSTM1* and *GSTT1* genotypes on urinary 1-OHP and DNA damage levels. The 95th percentile of the incremental lifetime cancer risk (ILCR) using Monte Carlo simulation showed that the inhalation risk for the children in HT and LT area were 2.80×10^{-7} and 1.43×10^{-7}, respectively. After controlling the possible confounders, the result from multiple linear regression showed that PAHs exposure was the most significant factor associated with urinary 1-OHP and DNA damage among children. This study provided evidence that children living near heavy traffic area are more likely to be exposed to environmental PAHs and have a higher risk of DNA damage than children living in low traffic areas. Findings from this study will be able to help in minimising the potential health effect related to traffic related air pollution in urban area by designing a mitigation plan for school.

Keywords: PAHs, children, urinary 1-OHP, DNA damage, genetic polymorphisms

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

PENGARUH HIDROKARBON AROMATIK POLISIKLIK DAN POLIMORFISME GENETIK (*CYP1A1, GSTM1, GSTT1*) PADA METABOLIT PIRENA DAN KEROSAKAN DNA DALAM KALANGAN KANAK-KANAK DI LEMBAH KLANG, MALAYSIA

Oleh

NUR HAZIRAH BINTI HISAMUDDIN

Jun 2022

Pengerusi : Juliana Jalaludin, PhD
Fakulti : Perubatan dan Sains Kesihatan

Hidrokarbon Aromatik Polisiklik (HAP) ialah sebatian organik terikat zarah berbahaya yang terdapat dalam persekitaran atmosfera bandar. Pendedahan kepada HAP amat membimbangkan kesihatan awam terutamanya kepada kanak-kanak, kerana kehadirannya di alam sekitar dan sifat karsinogenik, teratogenik dan genotoksik kepada kesihatan manusia. Kajian ini bertujuan untuk menilai hubungan pendedahan HAP partikulat terhadap penanda biologi HAP, urin 1-hidroksipirena (1-OHP) dan kerosakan DNA dalam kalangan kanak-kanak di sekitar kawasan trafik tinggi di Lembah Klang. Sebagai tambahan, kajian ini menilai kesan polimorfisme genetik enzim metabolisme HAP terhadap kepekatan metabolit pirena iaitu urin 1-OHP dan kerosakan DNA pada kanak-kanak. Kajian keratan rentas perbandingan ini dilakukan di lapan buah sekolah rendah di kawasan trafik tinggi (HT) dan kawasan trafik rendah (LT) di Lembah Klang. Borang soal selidik yang telah divalidasi berkaitan sosiodemografi, status kesihatan, pendedahan individu dan pemakanan telah diedarkan kepada kanak-kanak yang dipilih secara rawak. Sampel partikulat $PM_{2.5}$ (dalaman dan luaran) dikumpulkan menggunakan pensampel udara mudah alih MiniVol selama 24 jam. Kepekatan HAP diukur menggunakan Kromatografi Gas Spektroskopi Jisim. Nisbah sumber diagnostik digunakan untuk menentukan punca emisi HAP. Kerosakan DNA pada sel pipi dinilai menggunakan analisis komet, sementara urin 1-OHP dinilai menggunakan Kromatografi Cecair Prestasi Tinggi. Gen enzim metabolisme HAP, *CYP1A1*, *GSTT1* dan *GSTM1* dikaji untuk polimorfisme menggunakan PCR-RFLP dan multipleks PCR. Hasil kajian menunjukkan bahawa kepekatan HAP luaran lebih tinggi (julat antara 1.36-5.76 ng/m^3) berbanding kepekatan dalaman (julat antara 1.25-5.58 ng/m^3). Kepekatan keseluruhan HAP lebih tinggi di kawasan HT berbanding di kawasan LT. Berdasarkan nisbah sumber diagnostik, HAP di kawasan HT adalah pirogenik, berpunca daripada aktiviti pembakaran tinggi (pelepasan kenderaan). Sementara itu, kepekatan urin 1-OHP adalah lebih tinggi dalam kalangan kanak-kanak di HT berbanding LT (0.07 vs 0.04 µmol /mol-kreatinin). Kerosakan DNA jelas lebih tinggi dalam kalangan kanak-kanak di HT

berbanding LT. Terdapat hubungan yang signifikan antara pendedahan HAP persekitaran dengan kerosakan DNA dan urin 1-OHP. Tiada kesan yang signifikan dari gen *CYP1A1*, *GSTT1* dan *GSTM1* terhadap urin 1-OHP dan kerosakan DNA. Berdasarkan model Risiko Kanser Seumur Hidup (ILCR) menggunakan simulasi Monte Carlo, risiko kanser bagi kanak-anak di kawasan HT dan LT adalah 2.80×10^{-7} dan 1.43×10^{-7}. Hasil dari Regresi Linier Berganda menunjukkan bahawa pendedahan kepada HAP adalah faktor yang paling signifikan yang berkait dengan urin 1-OHP dan kerosakan DNA, setelah mengawal faktor-faktor pembauran yang berkemungkinan. Kajian ini menunjukkan bahawa kanak-kanak yang tinggal berhampiran trafik tinggi lebih cenderung terdedah kepada HAP dan mempunyai risiko kerosakan DNA yang lebih tinggi berbanding kanak-kanak yang tinggal di kawasan trafik rendah. Penemuan dari kajian ini akan dapat membantu meminimumkan potensi kesan kesihatan dari pencemaran udara berkaitan trafik di kawasan bandar dengan merancang pelan mitigasi strategik untuk sekolah.

Kata kunci: PAHs, kanak-kanak, kerosakan DNA, urin 1-hidroksipirena, polimorfisme genetik

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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Doctor of Philosophy. The members of the Supervisory Committee were as follows:

Juliana binti Jalaludin, PhD
Professor
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Chairman)

Suhaili binti Abu Bakar@Jamaludin, PhD
Senior Lecturer
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Member)

Mohd Talib bin Latif, PhD
Professor
Faculty of Science and Technology
Universiti Kebangsaan Malaysia
(Member)

ZALILAH MOHD SHARIFF, PhD
Professor and Dean
School of Graduate Studies
Universiti Putra Malaysia

Date: 11 August 2022

Declaration by Members of Supervisory Committee

This is to confirm that:

- the research conducted and the writing of this thesis was under our supervision;
- supervision responsibilities as stated in the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) are adhered to.

Signature: _____

Name of Chairman of Supervisory Committee: Professor Dr. Juliana binti Jalaludin

Signature: _____

Name of Member of Supervisory Committee: Dr. Suhaili binti Abu Bakar@Jamaludin

Signature: _____

Name of Member of Supervisory Committee: Professor Dr. Mohd Talib bin Latif

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LIST OF ABBREVIATIONS

<	Less than
>	More than
≥	At least
%	Per cent
°C	Degree celsius
∑	Summation
∑PAHs	Total PAHs
χ^2	Chi square
x g	Times gravity
µL	Microlitre
µm	Micrometre
µM	Micromolar
µg/m^3	Microgram per metre cubic
µmol/mol	Micromol per mol
1-OHP	1-hydroxypyrene
ACP	Acenaphthene
ACY	Acenaphthelyne
ADT	Average daily traffic
ANT	Anthracene
ANOVA	Analysis of variance
AT	Averaging time
ATS	American Thoracic Society

ATSDR	Agency for Toxic Substances and Disease Registry
Avg	Average
BaA	Benzo[a]anthracene
BaP	Benzo[a]pyrene
BeP	Benzo[e]pyrene
BaPeq	BaP-equivalent concentration
BbF	Benzo[b]fluoranthene
BkF	Benzo[k]fluoranthene
BgP	Benzo[g,h,i]perylene
BMI	Body mass index
BW	Body weight
cf	Conversion factor
CI	Confidence interval
cPAHs	Carcinogenic PAHs
CSF	Cancer slope factor
CYP	Cytochrome P450
CYR	Chrysene
CYP1A1	*Cytochrome P450 1A1*
DhA	Dibenzo(a,h)anthracene
DNA	Deoxyribonucleic acid
DOE	Department of Environment
ED	Exposure duration
EDTA	Ethylenediaminetetraacetic acid
EF	Exposure frequency

ETS	Environmental tobacco smoke
FLR	Fluorene
FLT	Fluoranthene
g/L	Gram per litre
GC-MS	Gas Chromatography-mass spectrometry
GM	Geometric mean
GST	*Glutathione S-transferase*
GSTM1	*Glutathione S-transferase Mu 1*
GSTT1	*Glutathione S-transferase Theta 1*
h	Hours
HMW	High molecular weight
HPLC	High-performance liquid chromatography
HT	High traffic
IARC	International Agency for Research on Cancer
IcP	Indeno(1,2,3-cd)pyrene
ILCR	Incremental lifetime cancer risk
IQR	Interquartile range
IR	Inhalation rate
L/min	Litre per minute
LMW	Low molecular weight
LOD	Limit of detection
LT	Low traffic
M	Molar
m/s	Metre per second

Max	Maximum
Min	Minimum
MLR	Multiple linear regression
MOE	Ministry of Education
N	Total population
n	Number of samples
NAP	Naphthalene
ncPAHs	Non-carcinogenic PAHs
ng/g	Nanogram per gram
ng/m^3	Nanogram per metre cubic
PAHs	Polycyclic aromatic hydrocarbons
PBS	Phosphate buffer solution
PCR	Polymerase chain reaction
PHE	Phenanthrene
ppb	Part per billion
ppm	Part per million
PM	Particulate matter
PM_1	Particulate matter below 1 micrometre aerodynamic diameter
$PM_{2.5}$	Particulate matter below 2.5 micrometres aerodynamic diameter
PM_{10}	Particulate matter below 10 micrometres aerodynamic diameter
PYR	Pyrene
RH	Relative humidity
ROS	Reactive oxygen species

rpm	Rotation per minute
SE	Standard error
SD	Standard deviation
SLR	Simple linear regression
TEQ	Toxicity equivalent concentration
TEF	Toxic equivalent factor
tPAHs	Total PAHs (Carcinogenic and Non-carcinogenic)
USEPA	United States Environmental Protection Agency
V	Volt
WHO	World Health Organization
WS	Wind speed

CHAPTER 1

INTRODUCTION

1.1 Study Background

Urbanisation and economic growth are closely related to increased transportation demand and number of road vehicles in cities (Nagpure et al. 2016, Azhari, Latif, and Mohamed 2018). Pollutants from traffic emissions, also known as traffic-related air pollution (TRAP), are the main contributor to air pollution in Malaysia, especially in urban areas (Awang et al., 2020; Mohd Shafie & Mahmud, 2020). Klang Valley, the most densely populated area in Malaysia, accounts for a large fraction of the anthropogenic sources that have contributed to the worsening of air quality in recent years (Latif et al., 2021). Air quality in Klang Valley frequently has been studied for many years as it is recognised as the central pollutant emission source area in Malaysia, especially particulate matter (PM) pollution (Amil et al., 2016; Juneng et al., 2011; Khan et al., 2015; Latif et al., 2014).

Polycyclic aromatic hydrocarbons (PAHs) are one of the most significant organic groups bound to PM in terms of health risk (Jakovljević et al., 2020). PAHs are ubiquitous, semi-volatile and persistent organic pollutants generated mainly during the incomplete combustion of organic materials (Sulong et al., 2019; Suradi et al., 2021; Urbancova et al., 2020). Due to their resistance to degradation processes, especially when bound to particles, they are subjected to the long-range atmospheric transport and could be detected even in remote areas (Liu et al., 2018). Previous studies have shown the contribution of vehicles emission on PAHs level in urban areas (Bahry et al., 2009; Omar et al., 2006; Omar et al., 2002). The impact of PAHs on the environment and public health are of great concern due to their mutagenic and carcinogenic properties (IARC, 2010, 2021). PAHs congeners are ranked 9th out of 275 hazardous chemicals on the Agency for Toxic Substances and Disease Registry's (ATSDR) priority list, indicating a severe health risk to humans and the environment (ATSDR, 2020). Exposure to PAHs have been associated with various toxicological effects, including immunotoxicity, reproductive and developmental toxicity and carcinogenic and genotoxic effects (Huang et al., 2019). In particular, human exposure to PAHs has been linked to many diseases including cancer, diabetes, cardiovascular disease and hypertension (Fernández et al., 2021).

The application of biomarkers to investigate the effects of PAH exposure helped researchers understand the contribution of environmental exposure to cancer risk, particularly in areas with moderate or low air pollution (Sopian et al., 2021; Suhaimi & Jalaludin, 2015). Biomarkers are divided into three main categories; biomarkers of exposure, effect, and susceptibility (Ladeira & Viegas, 2016; World Health Organization, 1993). Urinary 1-hydroxypyrene, PAH-DNA and PAH-protein adducts are frequently used as a biological marker of PAHs exposure (Jeng & Pan, 2014; Jongeneelen, 2001; Li et al., 2017). Besides, biomarker of effects such as DNA damage,

sister chromatid exchanges, chromosomal aberrations and micronuclei are widely used to assess the association of PAHs exposure and genotoxic effects in human (Ladeira & Viegas, 2016; Zare Jeddi et al., 2021).

Apart from the carcinogenicity of PAHs, the factor of interindividual variation may also lead to adverse health effects. The metabolic pathways of PAHs involved genes encoding xenobiotic metabolizing enzymes such as phase I cytochrome P450s; cytochrome P450 1A1 (*CYP1A1*), and phase II detoxifying enzymes; glutathione S-transferase Mu 1 (*GSTM1*) and glutathione S-transferase Theta 1 (*GSTT1*), which involve in the activation and elimination of carcinogenic PAHs (Sreeja et al., 2005). Enzyme coding genes were considered a risk factor in contributing to changes in the internal dose of PAHs exposure and causing alteration of normal cell function such as DNA damage. Although individuals may be exposed to similar environmental exposures, genetic differences in metabolism may result in markedly different doses at the target site and thus in a different response (World Health Organization, 1993). Biological differences or genetic polymorphisms may exist that cause some individuals to be more susceptible to environmental diseases and serve as markers of susceptibility (USEPA, 2004). Figure 1.1 shows a series of biomarkers which can be applied to enhance the understanding on the entire disease continuum, from exposure to effect, or disease outcome (USEPA, 2004).

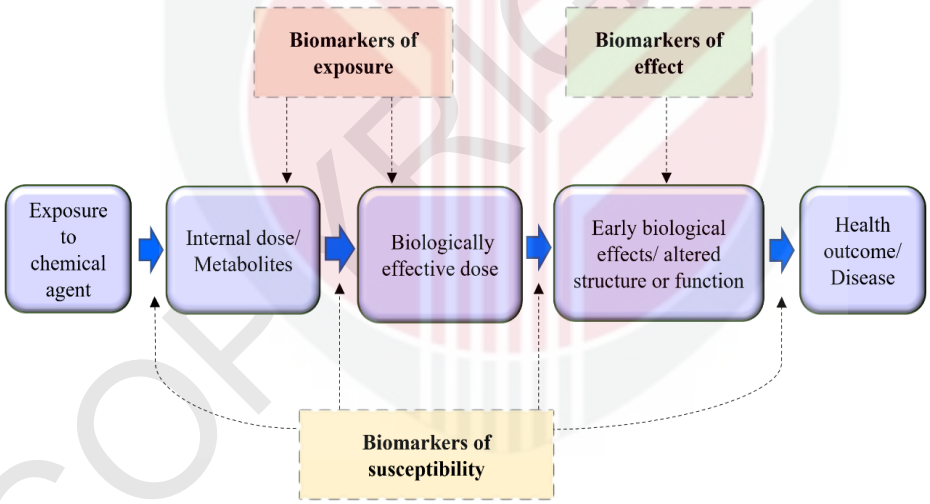

Figure 1.1: Exposure-disease Continuum Involving Biomarkers of Susceptibility, Exposure and Effects [Adapted from USEPA, 2004]

1.2 Problem Statement

The rapid urbanisation, industrial activities, population growth and high traffic volume have resulted in the Klang Valley being constantly exposed to air quality problems. Recent studies in the city of Kuala Lumpur, Malaysia have shown that PM pollution in

this area is greatly contributed by vehicular emissions (Azhari et al., 2021; Suhaimi et al., 2021). According to the Ministry of Transport Malaysia (2019) data, Klang Valley ranked first in the total number of motor vehicles by state in 2019. In addition, the number of newly registered vehicles in Kuala Lumpur increased by 10.95% from 109,365 units in 2018 to 121,340 units in 2019 (Ministry of Transport Malaysia, 2019). Air pollution in the city of Klang Valley is expected to increase as most cities in Malaysia are dominated by private vehicles such as cars and motorcycles (Figure 1.2), which may increase pollutant emissions.

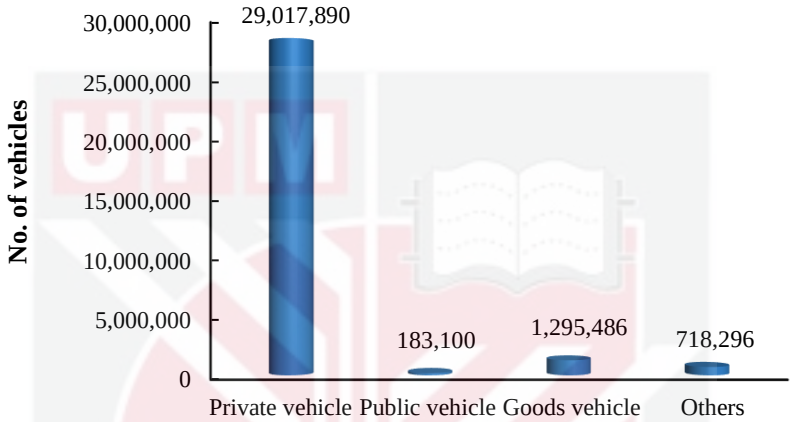

Figure 1.2: Total Motor Vehicles by Type in Malaysia as recorded until 31 Disember 2019 [Adapted from Ministry of Transport Malaysia, 2019].

Malaysia's climate is categorised as an equatorial with uniform temperature and is hot and humid throughout the year (Norazman et al., 2021). Urban schools in Malaysia typically use natural ventilation systems to introduce fresh outdoor air into the classroom as a practical approach to improve the indoor environment. However, the natural ventilation through door and window openings has brought the particles and other air pollutants into the classroom simultaneously. It has been suggested that school located in urban areas with high vehicle densities may contribute to poor indoor air quality in the classrooms (Othman et al., 2022; Zhang et al., 2019). School located nearby heavy traffic area may have high concentrations of outdoor pollutants which can be transferred to the indoor environment via ventilation intake, open doors and windows (Mohammadyan et al., 2017), air exchange rate (Yang et al., 2017) and cracks in the building (Srithawirat et al., 2016). Previous local studies indicated that proximity to traffic affects indoor air quality (IAQ) in classrooms where the outdoor air pollutants could penetrate the indoor environment (Jalaludin et al., 2014; Othman et al., 2019; Suhaimi et al., 2021).

PAHs are associated with carcinogenic effects, among the most important concerns and adverse health effects in humans. The International Agency for Research on Cancer (IARC) classifies benzo[a]pyrene (BaP) as Group 1 (carcinogenic to humans) and

several other PAHs as Group 2A (probably carcinogenic to humans) and 2B (possibly carcinogenic to humans) (IARC, 2021). Exposure to carcinogenic compounds at a young age may pose a significant health risk by causing genetic damage that may increase cancer risk later in life. Previous studies reported that environmental PAHs exposure leads to increased DNA damage in children who attended schools within 500 m of high traffic roads than children who went to rural school in Thailand (Ruchirawat et al., 2007; Tuntawiroon et al., 2007). Genetic damage that occurs early in life may give impact to the risk of carcinogenesis and other chronic diseases in adulthood more than later damage (Zani et al., 2020). Children have a longer lifespan and are more likely to develop chronic diseases that can be triggered by early exposure. Chronic diseases and cancer caused by environmental toxicants are thought to evolve in phases that take years or even decades to develop from their initiation to clinical manifestation. Carcinogenic and toxic exposures in early childhood seem more likely to lead to disease than similar exposures later in life (Mielzyńska et al., 2006; Suk et al., 2003).

Pyrene is one of the major components of PAHs and its urinary metabolites, urinary 1-hydroxypyrene (1-OHP) is the most employed biomarker of exposure to total PAHs (Miri et al., 2018; Sochacka-Tatara et al., 2018; Urbancova et al., 2017). Available evidence showed that children in the youngest age group (6-11 years) had nearly 30% higher urinary 1-OHP levels than adults under the same conditions, suggesting that children appear to be more susceptible to PAHs and have a higher potential health risk (Huang et al., 2006). Changes in the internal PAHs metabolites and the occurrence of DNA damage have the potential to reflect the main effects of PAHs exposure and genetic susceptibility. Apart from the PAHs exposure, genetic polymorphism may be one of the factors leading to differences in internal dose of PAHs excreted, DNA damage and further increased cancer risk. The study of genetic polymorphisms of enzymes that activate and detoxify PAHs helps to identify the individuals who are susceptible to PAHs toxicity.

To the best of our knowledge, none of the study has been conducted on the gene-environment interactions in relation to environmental exposure to PAHs in Malaysia. To date, only three studies have been conducted on the effect of genetic polymorphisms on biomarker of exposure and effects among children population in other countries. However, understanding of the gene-environment interaction for the ambient levels of PAHs exposure among children population is still limited due to inconsistencies findings. In a study by Mielzynska-Svach et al. (2013), no effect of *GSTM1* polymorphism on the level of 1-OHP concentration was found in Polish children, whereas in Mexican children with the *GSTM1* null polymorphism, the risk of high urinary 1-OHP concentrations was five times higher (Sánchez-Guerra et al., 2012). The inconsistencies in the previous literatures seem to indicate that further studies are needed to extend the knowledge of gene-environment interactions in relation to environmental exposure to PAHs, particularly in Malaysian children. In addition, *CYP1A1*, *GSTM1* and *GSTT1* polymorphisms and their modifying effects on children have not been fully elucidated, especially at low levels of PAHs exposure (Nerurkar et al., 2000). Genetic polymorphisms may have different modulation effects at low doses than at high doses (Vineis et al., 2000).

1.3 Study Justification

Investigation on PAHs in the school environment can serve as a baseline data on microenvironmental exposure to PAHs for children in urban traffic area, Klang Valley. Educational buildings like preschools, primary or elementary schools are some of the most important buildings where children typically spend up to 1/3 of their time (around 7–8 h) at these places (Oliveira et al., 2017). According to the current school list from the Ministry of Education Malaysia, 5895 (57.7%) of the 10,218 national primary and secondary schools in Malaysia are located in urban areas. Of these, 851 (90.5%) out of 940 schools are located in urban areas in Selangor and 295 schools (100.0%) are located in Kuala Lumpur. Given these figures for schools in urban areas, special attention should be given to air quality in school buildings, especially for schools located near busy roads. Therefore, understanding the exposure to health-relevant air pollutants in schools has become a priority to the scientific community, in line with the fourth target of the Sustainable Development Goals (SDGs), "excellent education," which requires a focus on educational buildings (Jasso-Pineda et al., 2015; Ochoa-Martinez et al., 2016; Oliveira et al., 2017).

To assess the health risks resulting from exposure to PAHs, it is also necessary to quantify the actual dose entering the body and the resulting changes using various biomarkers (Tuntawiroon et al., 2007). Incorporating biomarker assessment into studies is particularly important in children because the absorbed dose at a given external exposure may be very different from adult due to differences in metabolism, physiology and behaviours (hand-to-mouth activity, playing on the floor) (Oliveira et al., 2017). Previous studies on PAHs exposure in the Klang Valley mainly focused on calculating incremental lifetime cancer risk to estimate the potential health risk of PAHs exposure to the general population (Jamhari et al., 2014; Khan et al., 2015; Omar et al., 2002; Sulong et al., 2019; Suradi et al., 2021). The present study was conducted to fill the knowledge gap on traffic PAHs emission and health effect concerning DNA damage among children living near heavy traffic areas. The concentrations of internal PAHs metabolites (urinary 1-OHP) and DNA damage (assessed by tail moment) were evaluated to investigate the influence of low PAHs concentrations on both biomarkers.

Several epidemiological studies in other countries have reported the association of PAHs exposure with biomarkers of exposure and effects in children population. However, the susceptibility markers involved in PAHs metabolism is still less known, especially among children population, with the fluctuation results were obtained. Therefore, the extension information is needed, especially among the population of Malaysian children. It is important to note that genetic background influence an individual's response to environmental pollutants; thus, studying polymorphisms in human populations is necessary for correct interpretations. The combination assessment of the biomarker of early effects, exposure and susceptibility represent a valuable tool for assessing the potential health effects in the exposed subjects which will provide a comprehensive characterisation of human exposure to PAHs (Alhamdow et al., 2017; Barth et al., 2017; Oliveira et al., 2020). Therefore, this study was conducted to extend the knowledge of gene-environment interactions in relation to environmental PAHs exposure particularly in Malaysian children. In addition, the modifying effects of *CYP1A1*, *GSTT1* and *GSTM1*

polymorphisms on PAHs marker exposure (urinary 1-OHP) and DNA damage were investigated to understand the health risk posed by children exposed to environmental PAHs.

Scientific findings on the characterisation of air pollutants can provide useful information for policymakers to develop underlying action and implement mitigation plans to protect the public, especially children. The findings of this study will not just be beneficial to children but also to those communities living near the heavy traffic areas that might be continuously exposed to traffic emission. More importantly, it is intended that the study's findings would aid in the development of a comprehensive action plan for managing air quality in schools. This research also would help in giving the primary prevention of health specifically in promoting awareness among school children, school staff, parents and other school communities on the risk of air pollution on children's health. The mitigation strategies to reduce air pollution in the schools should begin within the nearby community, school management, as well as local authorities to ensure a clean environment for children.

1.4 Conceptual Framework

A conceptual framework is depicted in Figure 1.3.

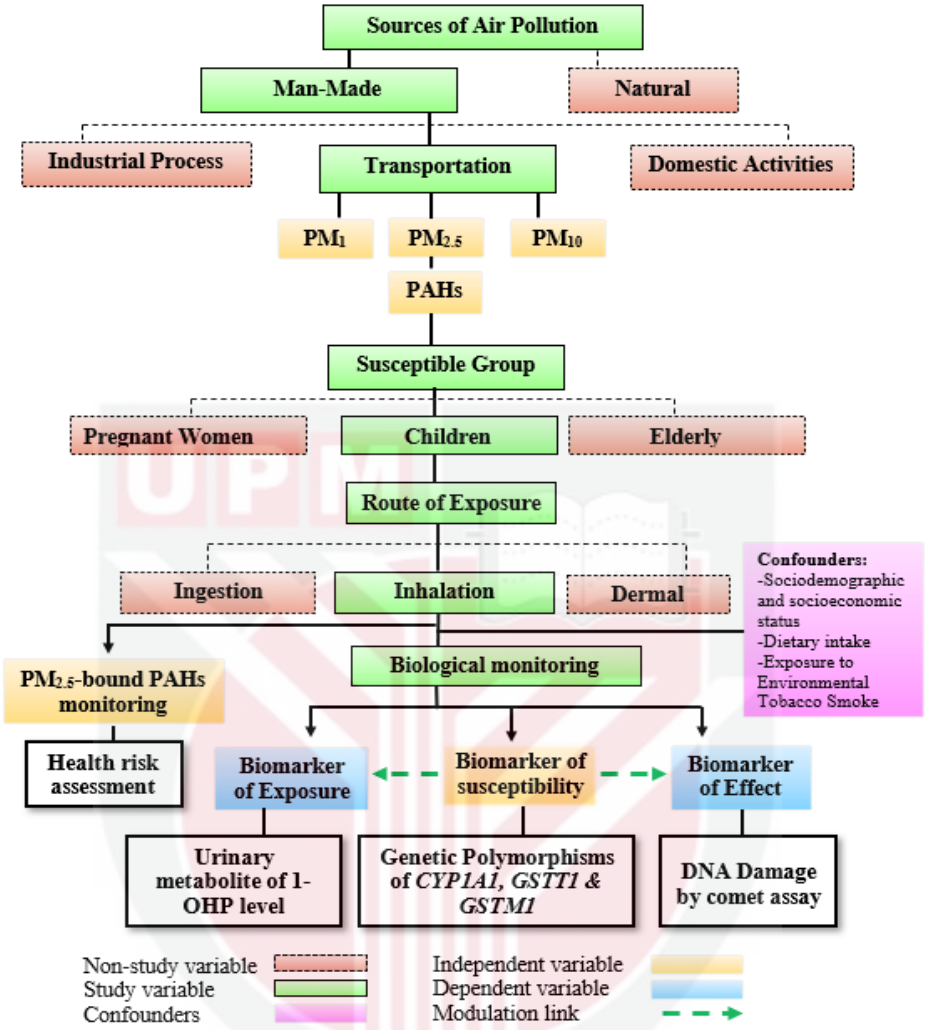

Figure 1.3: **Conceptual Framework**

This study focused on air pollution emitted from transportation, mainly PM and PAHs in urban city of the Klang Valley. Klang Valley is recognised as one of the most polluted areas in Malaysia. Vehicle emissions significantly contribute to PM pollutants in urban areas. $PM_{2.5}$ is a significant constituent of polluted air and is being intensively studied along with the carcinogenic PAHs bound to it. The particle-associated PAHs are more harmful to human health than gaseous PAHs as they are inhalable and can deposit in the human respiratory system. Route of exposure to PAHs in human occurs via inhalation, ingestion, and dermally from air particles. However, exposure to PAHs from tiny inhalable particles is mainly through inhalation (Suradi et al., 2021). The susceptible population, such as children, is believed to be exposed to a high level of PAHs, especially for those who live and attend schools near high traffic areas. The environmental monitoring of PM and PAHs was carried out among primary school children who were

divided into the high-traffic and low-traffic groups. Environmental monitoring was conducted to evaluate the external doses of PAHs exposed to children. The concentrations of PAHs measured can assist the assessment of carcinogenic risk via health risk assessment using the USEPA approach. In line, biological monitoring was performed to assess the biomarker of exposure, effect and susceptibility with respect to PAHs exposure.

PAHs is rapidly metabolised and conjugated prior to the excretion into urine in the form of urinary metabolites. Urinary 1-OHP is urinary metabolites derived from inhaled PAHs and a specific marker of exposure to PAHs. The genotoxicity impact of exposure to PAHs can be assessed by using biomarker of effects. In this study, the measurement of early biological effects was assessed by evaluating DNA damage using comet assay. The comet assay is reliable method and widely used to evaluate the genotoxic effects of PAHs exposure among children population (Gamboa et al., 2008; Jasso-Pineda et al., 2015; Ruchirawat et al., 2007; Sánchez-Guerra et al., 2012). The biomarker of susceptibility in this study refers to the genetic polymorphisms in individual with respect to expsoure to PAHs. This genetic polymorphism could modulate the effect of environmental exposures to genotoxic agents and cause some individuals to be more susceptible to environmentally induced diseases. In this tudy, the modifying effects of *CYP1A1*, *GSTT1* and *GSTM1* polymorphisms on the biomarker of exposure and effects were investigated. There were linkage studies of *CYP1A1*, *GSTT1* and *GSTM1* polymorphism with the internal dose of 1-OHP and DNA damage (Mielzynska-Svach et al., 2013; Sánchez-Guerra et al., 2012). In this study, confounders that may affect the study's dependent variables such as sociodemographic information, socioeconomic status, dietary intake and exposure to environmental tobacco smoke were also assessed.

1.5 Research Objectives

1.5.1 General Objective

To determine the influence of PAHs and *CYP1A1*, *GSTT1* and *GSTT1* polymorphisms on the PAHs marker exposure (urinary 1-hydroxypyrene) and DNA damage (tail moment) among children in the vicinity of heavy traffic areas in Klang Valley, Malaysia.

1.5.2 Specific Objectives

i. To determine sociodemographic and socioeconomic information, background of residences, home environment and dietary intake among children in heavy and low traffic areas.

ii. To evaluate the concentration of PM and PAHs at schools and residences nearby heavy and low traffic areas.

iii. To evaluate the carcinogenic risk of PAHs by inhalation exposure using the incremental lifetime cancer risk (ILCR) model.

iv. To compare the concentration of urinary 1-hydroxypyrene (1-OHP), extent of DNA damage and genotype distributions (*CYP1A1, GSTT1, GSTM1*) among children living nearby heavy and low traffic areas.

v. To determine the association between PAHs exposure with urinary 1-OHP level and extent of DNA damage among school children.

vi. To determine the influence of genetic polymorphisms (*CYP1A1*, *GSTT1*, *GSTM1*) on urinary 1-OHP and DNA damage.

vii. To evaluate the factors that influence the concentration of urinary 1-OHP and DNA damage after controlling the confounders.

1.6 Research Hypothesis

i. There are significant differences in socio-demographic and socio-economic information, background of residences, home environment and dietary intake between children in heavy and low traffic areas.

ii. There are significant differences in the concentration of PM and PAHs in schools and residences between heavy and low traffic areas.

iii. Children in heavy traffic areas had a substantially higher cancer risk than the children in low traffic areas.

iv. There are significant differences in concentration of urinary 1-OHP, extent of DNA damage and genotype distributions among children between heavy and low traffic areas.

v. There are significant associations between PAHs exposure with urinary 1-OHP and DNA damage among children.

vi. There are significant influences of genetic polymorphism (*CYP1A1*, *GSTT1*, *GSTM1*) on urinary 1-OHP and DNA damage among children.

vii. PAHs exposure is the main factor influencing concentration of urinary 1-OHP and DNA damage among children after controlling the confounders.

1.7 Definition of Variables

1.7.1 Conceptual Definition

1.7.1.1 High and low traffic area

High traffic area are defined as area within 500 m on either side of highways with an Average Daily Traffic (ADT) volume of ≥18,000 vehicles, or within 100 m on either

side of major urban roads with ADT volume of ≥15,000 vehicles (Brauer et al., 2013). Low traffic area refers to area located at 5 km away from highways, major roadways and industrial sites in Selangor.

1.7.1.2 PM_1

PM_1 is a respirable PM with an aerodynamic diameter of 1 µm or less. PM_1 may even pass through the bloodstream (USEPA, 2021).

1.7.1.3 $PM_{2.5}$

$PM_{2.5}$ is defined as fine inhalable particles with a diameters of 2.5 µm and smaller (USEPA, 2021). $PM_{2.5}$ is more harmful than coarse particles because it could easily penetrate the respiratory tract and reach the circulatory system (Kim et al., 2015).

1.7.1.4 PM_{10}

PM_{10} is defined as inhalable coarse particulate matter with an aerodynamic diameter of 10 µm or less (USEPA, 2021)

1.7.1.5 Polycyclic aromatic hydrocarbon

Polycyclic aromatic hydrocarbons (PAHs) are persistent organic pollutants (POPs) containing hydrogen and carbon with two or more fused aromatic rings (Abdel-Shafy & Mansour, 2016; Famiyeh et al., 2021). PAHs originate mainly from anthropogenic sources including motor vehicle emissions, fossil fuel burning, coal combustion, oil refining, waste incineration and the coke and steel industries (Khan et al., 2015).

1.7.1.6 Urinary 1-hydroxypyrene

1-hydroxypyrene (1-OHP) is a metabolite of PAH pyrene, a compound that is typically abundant in all PAHs mixtures (Li et al., 2017). Pyrene is one of the main components of PAHs mixture in the air. Pyrene is absorbed into the body by inhalation, skin absorption or ingestion, and then metabolised to 1-OHP, which is ultimately excreted in urine. Urinary 1-OHP has been widely used as a biological marker of PAHs exposure (Jeng & Pan, 2014).

1.7.1.7 DNA damage

DNA damage is an alteration in the chemical structure of DNA that modifies its coding properties and disrupts the cell functions. A major cause of DNA damage is oxidative stress, which is an imbalance between the production of reactive oxygen species (ROS) and an organism's ability to detoxify the reactive intermediates. Environmental factors such as air pollution can induce DNA damage through oxidative stress. DNA strand breaks, which can be detected using a comet assay, are among the main type of DNA damage (Gonzalez-Hunt et al., 2018). DNA damage could serve as a biomarker of early effects of carcinogenic compound exposure.

1.7.1.8 Genetic polymorphism

Genetic polymorphisms are described as variations in DNA sequence that are observed in 1% or more of the population (Norppa, 2004). The biomarkers of susceptibility most frequently used are the genetic polymorphisms of phase I and II metabolizing enzymes (Poblete-Naredo & Albores, 2016). Identifying polymorphisms is crucial in understanding the correlation between genetic variation and susceptibility to toxic exposures (Ramos & Bojang, 2018).

1.7.1.9 *CYP1A1*

The cytochrome P450 (CYP) are the major enzymes involved in phase I metabolism of PAHs. Enzyme CYP P450 1A1, which is encoded by the *CYP1A1* gene is responsible for the metabolic activation of PAHs into reactive metabolites (Stading et al., 2021). There are three genotypes of *CYP1A1* polymorphism wild-type (TT), heterozygous variant (TC) and homozygous variant (CC). The variant of *CYP1A1* genotypes (heterozygous and homozygous) has been associated with elevated induction of the enzyme, and thus increased levels of PAHs reactive metabolites (Xie et al., 2016).

1.7.1.10 *GSTT1* and *GSTM1*

Glutathione s-transferases (GSTs) are key enzymes in phase II metabolism that help the body detoxify various carcinogenic metabolites. GST class theta-1 (*GSTT1*) and GST class mu-1 (*GSTM1*) are the genes encoding for the GST isoenzymes (Wan Rashidi & Bakar, 2019). The deletion polymorphism in *GSTT1* and *GSTM1 (*null genotype*)* is associated with depleted enzyme function, thus increased the toxic metabolites in the body (Abubakar & Sanusi, 2020).

1.7.2 Operational Definition

1.7.2.1 Particulate matter

The real-time sampling of PM_1, $PM_{2.5}$ and PM_{10} (6 hours) was measured using TSI DustrakTM DRX Aerosol Monitor 8534, which is based on the light scattering principle. The TSI Dust-TRAK DRX Aerosol Monitor 8534 are battery-operated with data logging that gives a real-time aerosol mass reading. This instrument can measure aerosol concentrations between 0.001 to 150 mg/m^3. For 24 h gravimetric measurement of $PM_{2.5}$, a low volume sampler (Airmetrics MiniVol) was used, with a flow rate of 5.0 L/min

1.7.2.2 Polycyclic aromatic hydrocarbon

PAHs were determined from the filter paper containing $PM_{2.5}$. The filter paper, Quartz microfibre filters (47 mm diameter size), were digested and cleaned-up using solid-phase extraction (SPE) technique. PAHs samples were quantified using gas chromatography-mass spectrometry (GC-MS). The GC-MS instrument was calibrated with standard mixtures of PAHs.

1.7.2.3 Urinary 1-hydroxypyrene

Urine samples were collected earliest in the morning. Determination of urinary 1-OHP was conducted using solid-phase extraction and high-performance liquid chromatography (HPLC) with fluorescence detection. The concentration of urinary 1-OHP was adjusted with creatinine concentration, and the final concentration was expressed in µmol/mol creatinine.

1.7.2.4 DNA damage

The gold standard for measuring DNA strand breaks is the comet assay (Gonzalez-Hunt et al., 2018). Buccal epithelial cell were used to assess DNA damage using the comet assay. The degree of DNA damage was expressed as tail moment using OpenComet software. Tail moment is defined as the product of tail length and the percentage of DNA in the tail (Hong et al., 2020).

1.7.2.5 Genetic polymorphism

Genomic DNA were extracted from buccal epithelial cells. Genotyping of three PAHs-metabolising enzymes *CYP1A1*, *GSTT1* and *GSTM1* were done by polymerase chain reaction (PCR). *CYP1A1* genotypes were characterised by PCR restriction fragment length polymorphism (PCR-RFLP). *GSTT1* and *GSTM1* null genotypes were determined by conducting multiplex PCR to amplify both genes simultaneously.

REFERENCES

Abdel-Shafy, H. I., & Mansour, M. S. M. (2016). A review on polycyclic aromatic hydrocarbons: Source, environmental impact, effect on human health and remediation. *Egyptian Journal of Petroleum*, *25*(1), 107–123. https://doi.org/10.1016/J.EJPE.2015.03.011

Abubakar, M. B., & Sanusi, K. O. (2020). Influence of GSTM1 and GSTT1 genetic polymorphisms on petrol-induced toxicities: A systematic review. *Meta Gene*, *26*, 100796. https://doi.org/10.1016/J.MGENE.2020.100796

Ada, A. O., Yilmazer, M., Suzen, S., Demiroglu, C., Demirbag, A. E., Efe, S., Alemdar, Y., Burgaz, S., & Iscan, M. (2007). Cytochrome P450 (CYP) and glutathione S-transferases (GST) polymorphisms (CYP1A1, CYP1B1, GSTM1, GSTP1 and GSTT1) and urinary levels of 1-hydroxypyrene in Turkish coke oven workers. *Genetics and Molecular Biology*, *30*(3), 511–519. https://doi.org/10.1590/s1415-47572007000400002

Adli, A., Hosseini, S. M., Lari Najafi, M., Behmanesh, M., Ghezi, E., Rasti, M., Kazemi, A. A., Rad, A., Falanji, F., Mohammadzadeh, M., Miri, M., & Dadvand, P. (2021). Polycyclic aromatic hydrocarbons exposures and telomere length: A cross-sectional study on preschool children. *Environmental Research*, *195*, 110757. https://doi.org/10.1016/J.ENVRES.2021.110757

Adonis, M., Martínez, V., Riquelme, R., Ancic, P., González, G., Tapia, R., Castro, M., Lucas, D., Berthou, F., & Gil, L. (2003). Susceptibility and exposure biomarkers in people exposed to PAHs from diesel exhaust. *Toxicology Letters*, *144*(1), 3–15. https://doi.org/10.1016/S0378-4274(03)00225-X

Afroz, R., Hassan, M. N., & Ibrahim, N. A. (2003). Review of air pollution and health impacts in Malaysia. *Environmental Research*, *92*(2), 71–77. https://doi.org/10.1016/S0013-9351(02)00059-2

Akyüz, M., & Çabuk, H. (2010). Gas–particle partitioning and seasonal variation of polycyclic aromatic hydrocarbons in the atmosphere of Zonguldak, Turkey. *Science of The Total Environment*, *408*(22), 5550–5558. https://doi.org/10.1016/J.SCITOTENV.2010.07.063

Alahabadi, A., Ehrampoush, M. H., Miri, M., Aval, H. E., Yousefzadeh, S., Ghaffari, H. R., Ahmadi, E., Talebi, P., Fathabadi, Z. A., Babai, F., Nikoonahad, A., Sharafi, K., & Hosseini-Bandegharaei, A. (2017). A comparative study on capability of different tree species in accumulating heavy metals from soil and ambient air. *Chemosphere*, *172*, 459–467. https://doi.org/10.1016/j.chemosphere.2017.01.045

Alexandrie, A. K., Warholm, M., Carstensen, U., Axmon, A., Hagmar, L., Levin, J. O., Stman, C. O. ¨, & Rannug, A. (2000). CYP1A1 and GSTM1 polymorphisms affect urinary 1-hydroxypyrene levels after PAH exposure. *Carcinogenesis*, *21*(4), 669–676.

Alghamdi, M. A., Alam, M. S., Stark, C., Mohammed, N., Harrison, R. M., Shamy, M., Khoder, M. I., Shabbaj, I. I., & Göen, T. (2015). Urinary metabolites of polycyclic aromatic hydrocarbons in Saudi Arabian schoolchildren in relation to sources of exposure. *Environmental Research*, *140*, 495–501. https://doi.org/10.1016/j.envres.2015.04.023

Alhamdow, A., Lindh, C., Albin, M., Gustavsson, P., Tinnerberg, H., & Broberg, K. (2017). Early markers of cardiovascular disease are associated with occupational exposure to polycyclic aromatic hydrocarbons. *Scientific Reports 2017 7:1*, *7*(1), 1–11. https://doi.org/10.1038/s41598-017-09956-x

Alshagga, M. A., Mohamed, N., Suhid, A. N., Ibrahim, I. A. A., & Zakaria, S. Z. S. (2011). Frequencies of glutathione s-transferase (GSTM1, GSTM3 and GSTT1) polymorphisms in a Malaysian population. *Archives of Medical Science*, *7*(4), 572–578. https://doi.org/10.5114/aoms.2011.24123

Alshagga, M. a, Mohamed, N., Shuid, A. N., Zulkifli, S., & Zakaria, S. (2014). Xenobiotic Metabolising Enzymes (CYP1A1 , CYP2E1 and NAT2) Gene Polymorphism in Malaysian Students. *Research Updates in Medical Sciences*, *2*(2), 61–69.

Alvarado-Cruz, I., Sánchez-Guerra, M., Hernández-Cadena, L., De Vizcaya-Ruiz, A., Mugica, V., Pelallo-Martínez, N. A., Solís-Heredia, M. de J., Byun, H. M., Baccarelli, A., & Quintanilla-Vega, B. (2017). Increased methylation of repetitive elements and DNA repair genes is associated with higher DNA oxidation in children in an urbanized, industrial environment. *Mutation Research - Genetic Toxicology and Environmental Mutagenesis*, *813*, 27–36. https://doi.org/10.1016/j.mrgentox.2016.11.007

Alvarado, A. T., Muñoz, A. M., Bartra, M. S., Valderrama-Wong, M., González, D., Quiñones, L. A., Varela, N., Bendezú, M. R., García, J. A., & Loja-Herrera, B. (2021). Frequency of CYP1A1*2A polymorphisms and deletion of the GSMT1 gene in a Peruvian mestizo population. *Pharmacia 68(4): 747-754*, *68*(4), 747–754. https://doi.org/10.3897/PHARMACIA.68.E71621

Amil, N., Latif, M. T., Khan, F., & Mohamad, M. (2016). Seasonal variability of PM 2.5 composition and sources in the Klang Valley urban-industrial environment. *Atmospheric Chemistry and Physics*, *16*, 5357–5381. https://doi.org/10.5194/acp-16-5357-2016

Apostoli, P., Neri, G., Lucas, D., Manno, M., & Berthou, F. (2003). Influence of genetic polymorphisms of CYP1A1 and GSTM1 on the urinary levels of 1-hydroxypyrene. *Toxicology Letters*, *144*(1), 27–34. https://doi.org/10.1016/S0378-4274(03)00227-3

Ariffin, M., & Wan Yacoob, W. N. A. (2017). Assessment of knowledge, attitude and practice of solid waste open burning in Terengganu, Malaysia. *EnvironmentAsia*, *10*(2), 25–32. https://doi.org/10.14456/ea.2017.18

Arifuddin, A. A., Jalaludin, J., & Hisamuddin, N. H. (2019). Air pollutants exposure with

respiratory symptoms and lung function among primary school children nearby heavy traffic area in Kajang. *Asian Journal of Atmospheric Environment*, *13*(1), 21–29. https://doi.org/10.5572/ajae.2019.13.1.021

Asmi, E., Antola, M., Yli-Tuomi, T., Jantunen, M., Aarnio, P., Mäkelä, T., Hillamo, R., & Hämeri, K. (2009). Driver and passenger exposure to aerosol particles in buses and trams in Helsinki, Finland. *Science of The Total Environment*, *407*(8), 2860–2867. https://doi.org/10.1016/J.SCITOTENV.2009.01.004

ATSDR. (2020). *Substance Priority List*. https://www.atsdr.cdc.gov/spl/index.html

Autrup, H. (2000). Genetic polymorphisms in human xenobiotica metabolizing enzymes as susceptibility factors in toxic response. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis*, *464*(1), 65–76. https://doi.org/10.1016/S1383-5718(99)00167-9

Awang, M. F., Jalaludin, J., Bakar, S. A., Latif, M. T., Fandi, N. F. M., & Hamid, H. H. A. (2020). Assessment of micronucleus frequency and respiratory health symptoms among traffic policemen exposed to BTEX and PM2.5 in Klang Valley, Malaysia. *Jurnal Teknologi*, *82*(4), 71–80. https://doi.org/10.11113/JT.V82.14493

Azhari, A., Halim, N. D. A., Mohtar, A. A. A., Aiyub, K., Latif, M. T., & Ketzel, M. (2021). Evaluation and prediction of PM10 and PM2.5 from road source emissions in Kuala Lumpur city centre. *Sustainability (Switzerland)*, *13*(10). https://doi.org/10.3390/su13105402

Azqueta, A., Ladeira, C., Giovannelli, L., Boutet-Robinet, E., Bonassi, S., Neri, M., Gajski, G., Duthie, S., Del Bo', C., Riso, P., Koppen, G., Basaran, N., Collins, A., & Møller, P. (2020). Application of the comet assay in human biomonitoring: An hCOMET perspective. *Mutation Research/Reviews in Mutation Research*, *783*, 108288. https://doi.org/10.1016/J.MRREV.2019.108288

Bahry, P. S., Zakaria, M. P., Abdullah, A. M. Bin, Abdullah, D. K., Sakari, M., Chandru, K., & Shahbazi, A. (2009). Forensic characterization of polycyclic aromatic hydrocarbons and hopanes in aerosols from Peninsular Malaysia. *Environmental Forensics*, *10*(3), 240–252. https://doi.org/10.1080/15275920903140387

Bai, H., Wu, M., Zhang, H., & Tang, G. (2017). Chronic polycyclic aromatic hydrocarbon exposure causes DNA damage and genomic instability in lung epithelial cells. *Oncotarget*, *8*(45), 79034. https://doi.org/10.18632/ONCOTARGET.20891

Barnes, N. M., Ng, T. W., Ma, K. K., & Lai, K. M. (2018). In-Cabin air quality during driving and engine idling in air-conditioned private vehicles in Hong Kong. *International Journal of Environmental Research and Public Health*, *15*(4). https://doi.org/10.3390/IJERPH15040611

Barraza-Villarreal, A., Escamilla-Nuñez, M. C., Schilmann, A., Hernandez-Cadena, L., Li, Z., Romanoff, L., Sjödin, A., Del Río-Navarro, B. E., Díaz-Sanchez, D., Díaz-Barriga, F., Sly, P., & Romieu, I. (2014). Lung function, airway inflammation, and

Polycyclic Aromatic Hydrocarbons exposure in Mexican schoolchildren: A pilot study. *Journal of Occupational and Environmental Medicine*, *56*(4), 415–419. https://doi.org/10.1097/JOM.0000000000000111

Barraza, C. F. (2017). *Human exposure assessment related to oil activities in Ecuador: From the air quality monitoring to the study of metallic contaminants transfer in the soil-plant continuum* [Universite Toulouse 3 Paul Sabatier]. https://tel.archives-ouvertes.fr/tel-01668502

Barth, A., Brucker, N., Moro, A., Nascimento, S., Goethel, G., Souto, C., Fracasso, R., Sauer, E., Altknecht, L., da Costa, B., Duarte, M., Menezes, C., Tasca, T., Arbo, M., & Garcia, S. (2017). Association between inflammation processes, DNA damage, and exposure to environmental pollutants. *Environmental Science and Pollution Research International*, *24*(1), 353–362. https://doi.org/10.1007/S11356-016-7772-0

Bateson, T. F., & Schwartz, J. (2008). Children's response to air pollutants. *Journal of Toxicology and Environmental Health - Part A: Current Issues*, *71*(3), 238–243. https://doi.org/10.1080/15287390701598234

Benrazavi, R. S., Binti Dola, K., Ujang, N., & Sadat Benrazavi, N. (2016). Effect of pavement materials on surface temperatures in tropical environment. *Sustainable Cities and Society*, *22*, 94–103. https://doi.org/10.1016/J.SCS.2016.01.011

Beyoglu, D., Ozkozaci, T., Akici, N., Omurtag, G. Z., Akici, A., Ceran, O., & Sardas, S. (2010). Assessment of DNA damage in children exposed to indoor tobacco smoke. *International Journal of Hygiene and Environmental Health*, *213*(1), 40–43. https://doi.org/10.1016/J.IJHEH.2009.10.001

Borrego-Soto, G., Ortiz-López, R., & Rojas-Martínez, A. (2015). Ionizing radiation-induced DNA injury and damage detection in patientswith breast cancer. *Genetics and Molecular Biology*, *38*(4), 420. https://doi.org/10.1590/S1415-475738420150019

Bosso, R. M. do V., Amorim, L. M. F., Andrade, S. J., Rossini, A., de Marchi, M. R. R., de Leon, A. P., Carareto, C. M. A., & Conforti-Froes, N. D. T. (2006). Effects of genetic polymorphisms CYP1A1, GSTM1, GSTT1 and GSTP1 on urinary 1-hydroxypyrene levels in sugarcane workers. *Science of the Total Environment*, *370*(2–3), 382–390. https://doi.org/10.1016/j.scitotenv.2006.07.025

Both, A. F., Westerdahl, D., Fruin, S., Haryanto, B., & Marshall, J. D. (2013). Exposure to carbon monoxide, fine particle mass, and ultrafine particle number in Jakarta, Indonesia: Effect of commute mode. *Science of the Total Environment*, *443*, 965–972. https://doi.org/10.1016/j.scitotenv.2012.10.082

Brauer, M., Reynolds, C., & Hystad, P. (2013). Traffic-related air pollution and health in Canada. In *CMAJ* (Vol. 185, Issue 18, pp. 1557–1558). Canadian Medical Association. https://doi.org/10.1503/cmaj.121568

Brookes, A. J. (1999). The essence of SNPs. *Gene*, *234*(2), 177–186.

https://doi.org/10.1016/S0378-1119(99)00219-X

Calderón-Garcidueñas, L., Wen-Wang, L., Zhang, Y. J., Rodriguez-Alcaraz, A., Osnaya, N., Villarreal-Calderón, A., & Santella, R. M. (1999). 8-hydroxy-2'-deoxyguanosine, a major mutagenic oxidative DNA lesion, and DNA strand breaks in nasal respiratory epithelium of children exposed to urban pollution. *Environmental Health Perspectives*, *107*(6), 469–474. https://doi.org/10.1289/ehp.107-1566580

Carroquino, M. J., Posada, M., & Landrigan, P. J. (2013). Environmental Toxicology: Children at Risk. *Environmental Toxicology*, 239. https://doi.org/10.1007/978-1-4614-5764-0_11

Cascorbi, I., Brockmoller, J., & Roots, I. (1996). A C4887A polymorphism in exon 7 of human CYP1A1: Population frequency, mutation linkages, and impact on lung cancer susceptibility. *Cancer Research*, *56*(21), 4965–4969.

Chang, J., Liu, W., Hu, Y., Zou, Z., Shen, L., Wang, X., Cai, J., Sun, C., & Huang, C. (2017). Associations between heavy traffic near residence and childhood health outcomes as modified by bedroom floor level and bedroom ventilation. *Building and Environment*, *114*, 56–67. https://doi.org/10.1016/j.buildenv.2016.12.014

Chen, B., Hu, Y., Jin, T., Lu, D., Shao, M., Zheng, L., Wang, Q., Shen, Y., Liu, H., Liu, Y., & Zhou, Y. (2007). The influence of metabolic gene polymorphisms on urinary 1-hydroxypyrene concentrations in Chinese coke oven workers. *Science of the Total Environment*, *381*, 38–46. https://doi.org/10.1016/j.scitotenv.2007.02.021

Chen, H. C., Hu, W. X., Liu, Q. X., Li, W. K., Chen, F. Z., Rao, Z. Z., Liu, X. F., Luo, Y. P., & Cao, Y. F. (2008). Genetic polymorphisms of metabolic enzymes CYP1A1, CYP2D6, GSTM1 and GSTT1 and leukemia susceptibility. *European Journal of Cancer Prevention*, *17*(3), 251–258. https://doi.org/10.1097/CEJ.0b013e3282b72093

Chen, L., Hu, G., Fan, R., Lv, Y., Dai, Y., & Xu, Z. (2018). Association of PAHs and BTEX exposure with lung function and respiratory symptoms among a nonoccupational population near the coal chemical industry in Northern China. *Environment International*, *120*(August), 480–488. https://doi.org/10.1016/j.envint.2018.08.004

Chen, Y., Bai, Y., Yuan, J., Chen, W., Sun, J., Wang, H., Liang, H., Guo, L., Yang, X., Tan, H., Su, Y., Wei, Q., & Wu, T. (2006). Association of polymorphisms in AhR, CYP1A1, GSTM1, and GSTT1 Genes with levels of DNA damage in peripheral blood lymphocytes among coke-oven workers. *Cancer Epidemiology and Prevention Biomarkers*, *15*(9), 1703–1707. https://doi.org/10.1158/1055-9965.EPI-06-0291

Chen, Y. T., Huang, Y. K., Luvsan, M. E., Gombojav, E., Ochir, C., Bulgan, J., & Chan, C. C. (2015). The influence of season and living environment on children's urinary 1-hydroxypyrene levels in Ulaanbaatar, Mongolia. *Environmental Research*, *137*, 170–175. https://doi.org/10.1016/j.envres.2014.11.022

Clément, N., Muresan, B., Hedde, M., & François, D. (2015). PAH dynamics in roadside environments: Influence on the consistency of diagnostic ratio values and ecosystem contamination assessments. *Science of The Total Environment*, *538*, 997–1009. https://doi.org/10.1016/J.SCITOTENV.2015.08.072

Crist, K. C., Liu, B., Kim, M., Deshpande, S. R., & John, K. (2008). Characterization of fine particulate matter in Ohio: Indoor, outdoor, and personal exposures. *Environmental Research*, *106*(1), 62–71. https://doi.org/10.1016/J.ENVRES.2007.06.008

Dadvand, P., Rivas, I., Basagaña, X., Alvarez-Pedrerol, M., Su, J., De Castro Pascual, M., Amato, F., Jerret, M., Querol, X., Sunyer, J., & Nieuwenhuijsen, M. J. (2015). The association between greenness and traffic-related air pollution at schools. *Science of The Total Environment*, *523*, 59–63. https://doi.org/10.1016/j.scitotenv.2015.03.103

Dasari, S., Ganjayi, M. S., Yellanurkonda, P., Basha, S., & Meriga, B. (2018). Role of glutathione S-transferases in detoxification of a polycyclic aromatic hydrocarbon, methylcholanthrene. *Chemico-Biological Interactions*, *294*, 81–90. https://doi.org/10.1016/J.CBI.2018.08.023

Dat, N. D., & Chang, M. B. (2017). Review on characteristics of PAHs in atmosphere, anthropogenic sources and control technologies. *Science of the Total Environment*, *609*, 682–693. https://doi.org/10.1016/j.scitotenv.2017.07.204

De Craemer, S., Croes, K., van Larebeke, N., Sioen, I., Schoeters, G., Loots, I., Nawrot, T., Nelen, V., Campo, L., Fustinoni, S., & Baeyens, W. (2016). Investigating unmetabolized polycyclic aromatic hydrocarbons in adolescents' urine as biomarkers of environmental exposure. *Chemosphere*, *155*, 48–56. https://doi.org/10.1016/J.CHEMOSPHERE.2016.04.017

de Nazelle, A., Fruin, S., Westerdahl, D., Martinez, D., Ripoll, A., Kubesch, N., & Nieuwenhuijsen, M. (2012). A travel mode comparison of commuters' exposures to air pollutants in Barcelona. *Atmospheric Environment*, *59*, 151–159. https://doi.org/10.1016/j.atmosenv.2012.05.013

Department of Statistics Malaysia. (2020). *Household Income & Basic Amenities Survey Report 2019*. https://www.dosm.gov.my/v1/index.php?r=column/cthemeByCat&cat=120&bul_id=TU00TmRhQ1N5TUxHVWN0T2VjbXJYZz09&menu_id=amVoWU54UTl0a21NWmdhMjFMMWcyZz09

Dobraca, D., Lum, R., Sjödin, A., Calafat, A. M., Laurent, C. A., Kushi, L. H., & Windham, G. C. (2018). Urinary biomarkers of polycyclic aromatic hydrocarbons in pre- and peri-pubertal girls in Northern California: Predictors of exposure and temporal variability. *Environmental Research*, *165*, 46–54. https://doi.org/10.1016/J.ENVRES.2017.11.011

Domingo, J. L., & Nadal, M. (2015). Human dietary exposure to polycyclic aromatic hydrocarbons: A review of the scientific literature. In *Food and Chemical*

Toxicology (Vol. 86, pp. 144–153). Elsevier Ltd. https://doi.org/10.1016/j.fct.2015.10.002

Drwal, E., Rak, A., & Gregoraszczuk, E. L. (2019). Review: Polycyclic aromatic hydrocarbons (PAHs)—Action on placental function and health risks in future life of newborns. In *Toxicology* (Vol. 411, pp. 133–142). Elsevier Ireland Ltd. https://doi.org/10.1016/j.tox.2018.10.003

Dusinska, M., & Collins, A. R. (2008). The comet assay in human biomonitoring: gene–environment interactions. *Mutagenesis*, *23*(3), 191–205. https://doi.org/10.1093/MUTAGE/GEN007

Dusinska, M., Staruchova, M., Horska, A., Smolkova, B., Collins, A., Bonassi, S., & Volkovova, K. (2012). Are glutathione S transferases involved in DNA damage signalling? Interactions with DNA damage and repair revealed from molecular epidemiology studies. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis*, *736*(1–2), 130–137. https://doi.org/10.1016/J.MRFMMM.2012.03.003

Emmanuel, M. R. (2005). *An Urban Approach to Climate-Sensitive Design*. Taylor & Francis.

Espitia-Pérez, L., Jiménez-Vidal, L., & Espitia-Pérez, P. (2019). Particulate matter exposure: Genomic instability, disease, and cancer risk. *Environmental Health - Management and Prevention Practices*. https://doi.org/10.5772/INTECHOPEN.86536

Espitia-Pérez, L., Sosa, M. Q., Salcedo-Arteaga, S., León-Mejía, G., Hoyos-Giraldo, L. S., Brango, H., Kvitko, K., da Silva, J., & Henriques, J. A. P. (2016). Polymorphisms in metabolism and repair genes affects DNA damage caused by open-cast coal mining exposure. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis*, *808*, 38–51. https://doi.org/10.1016/J.MRGENTOX.2016.08.003

Ewa, B., & Danuta, M.-Š. (2017). Polycyclic aromatic hydrocarbons and PAH-related DNA adducts. *Journal of Applied Genetics*, *58*(3), 321. https://doi.org/10.1007/S13353-016-0380-3

Fadzir, N. A. S., & Jalaludin, J. (2013). Indoor Particulate Matter 2.5 (PM2.5) and lung function among children living near busy road in Cheras, Kuala Lumpur. *Health and the Environment Journal*, *4*(2), 1–19.

Famiyeh, Lord, Chen, K., Xu, J., Sun, Y., Guo, Q., Wang, C., Lv, J., Tang, Y. T., Yu, H., Snape, C., & He, J. (2021). A review on analysis methods, source identification, and cancer risk evaluation of atmospheric polycyclic aromatic hydrocarbons. *Science of The Total Environment*, *789*, 147741. https://doi.org/10.1016/J.SCITOTENV.2021.147741

Fan, R., Wang, D., Mao, C., Ou, S., Lian, Z., Huang, S., Lin, Q., Ding, R., & She, J. (2012). Preliminary study of children's exposure to PAHs and its association with

8-hydroxy-2'-deoxyguanosine in Guangzhou, China. *Environment International*, *42*(1), 53–58. https://doi.org/10.1016/j.envint.2011.03.021

Fandi, N. F. M., Jalaludin, J., Latif, M. T., Hamid, H. H. A., & Awang, M. F. (2020). BTEX exposure assessment and inhalation health risks to traffic policemen in the Klang valley region, malaysia. *Aerosol and Air Quality Research*, *20*(9), 1922–1937. https://doi.org/10.4209/aaqr.2019.11.0574

Fang, G.-C., Wu, Y.-S., Chen, M.-H., Ho, T.-T., Huang, S.-H., & Rau, J.-Y. (2004). Polycyclic aromatic hydrocarbons study in Taichung, Taiwan, during 2002-2003. *Atmospheric Environment*, *21*(38), 3385–3391. https://doi.org/10.1016/J.ATMOSENV.2004.03.036

Feng, S., Gao, D., Liao, F., Zhou, F., & Wang, X. (2016). The health effects of ambient PM2.5 and potential mechanisms. *Ecotoxicology and Environmental Safety*, *128*, 67–74. https://doi.org/10.1016/j.ecoenv.2016.01.030

Ferguson, L., Taylor, J., Davies, M., Shrubsole, C., Symonds, P., & Dimitroulopoulou, S. (2020). Exposure to indoor air pollution across socio-economic groups in high-income countries: A scoping review of the literature and a modelling methodology. *Environment International*, *143*, 105748. https://doi.org/10.1016/J.ENVINT.2020.105748

Fernández, S. F., Pardo, O., Hernández, C. S., Garlito, B., & Yusà, V. (2021). Children's exposure to polycyclic aromatic hydrocarbons in the Valencian Region (Spain): Urinary levels, predictors of exposure and risk assessment. *Environment International*, *153*, 106535. https://doi.org/https://doi.org/10.1016/j.envint.2021.106535

Fiala, Z., Vyskocil, A., Krajak, V., Viau, C., Ettlerova, E., Bukac, J., Fialova, D., & Emminger, S. (2001). Environmental exposure of small children to polycyclic aromatic hydrocarbons. *International Archives of Occupational and Environmental Health*, *74*(6), 411–420. https://doi.org/10.1007/s004200100239

Franco, R., Schoneveld, O., Georgakilas, A. G., & Panayiotidis, M. I. (2008). Oxidative stress, DNA methylation and carcinogenesis. In *Cancer Letters* (Vol. 266, Issue 1, pp. 6–11). https://doi.org/10.1016/j.canlet.2008.02.026

Freire, C., Abril, A., Fernández, M. F., Ramos, R., Estarlich, M., Manrique, A., Aguirre, A., Ibarluzea, J., & Olea, N. (2009). Urinary 1-hydroxypyrene and PAH exposure in 4-year-old Spanish children. *Science of The Total Environment*, *407*(5), 1562–1569. https://doi.org/10.1016/J.SCITOTENV.2008.10.068

Frohlich, A., Jaqueline Moura, D., & Coelho Andre, L. (2018). Genotoxicity and cytotoxicity evaluation applied to environmental health, research of polycyclic aromatic hydrocarbons. *International Journal of Scientific Research in Environmental Science and Toxicology*, *3*(2), 1–13.

Gajewski, T. F., Schreiber, H., & Fu, Y.-X. (2013). Innate and adaptive immune cells in the tumor microenvironment. *Nature Immunology*, *14*(10), 1014.

https://doi.org/10.1038/NI.2703

Gajski, G., Gerić, M., OreŠčanin, V. Š., & Garaj-Vrhovac, V. (2013). Cytogenetic status of healthy children assessed with the alkaline comet assay and the cytokinesis-block micronucleus cytome assay. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis*, *750*(1–2), 55–62. https://doi.org/10.1016/J.MRGENTOX.2012.09.011

Gamboa, R. T., Gamboa, A. R., Bravo, A. H., & Ostrosky, W. P. (2008). Genotoxicity in child populations exposed to Polycyclic Aromatic Hydrocarbons (PAHs) in the air from Tabasco, Mexico. *International Journal of Environmental Research and Public Health*, *5*(5), 349–355. https://doi.org/10.3390/ijerph5050349

Gandhi, G., & Kaur, G. (2012). Assessment of DNA damage in obese individuals assessment of DNA damage in obese individuals. *Research Journal of Biology*, *2*(2).

Gao, P., da Silva, E., Hou, L., Denslow, N. D., Xiang, P., & Ma, L. Q. (2018). Human exposure to polycyclic aromatic hydrocarbons: Metabolomics perspective. In *Environment International* (Vol. 119, pp. 466–477). Elsevier Ltd. https://doi.org/10.1016/j.envint.2018.07.017

Gao, P., Li, H., Wilson, C. P., Townsend, T. G., Xiang, P., Liu, Y., & Ma, L. Q. (2018). Source identification of PAHs in soils based on stable carbon isotopic signatures. *Critical Reviews in Environmental Science and Technology*, *48*(13–15), 923–948. https://doi.org/10.1080/10643389.2018.1495983

Gao, Y., Guo, X., Ji, H., Li, C., Ding, H., Briki, M., Tang, L., & Zhang, Y. (2016). Potential threat of heavy metals and PAHs in PM2.5 in different urban functional areas of Beijing. In *Atmospheric Research* (Vols. 178–179). Elsevier B.V. https://doi.org/10.1016/j.atmosres.2016.03.015

Ghosal, D., Ghosh, S., Dutta, T. K., & Ahn, Y. (2016). Current state of knowledge in microbial degradation of polycyclic aromatic hydrocarbons (PAHs): A review. *Frontiers in Microbiology*, *7*(AUG). https://doi.org/10.3389/FMICB.2016.01369

Gonzalez-Hunt, C. P., Wadhwa, M., & Sanders, L. H. (2018). DNA damage by oxidative stress: Measurement strategies for two genomes. *Current Opinion in Toxicology*, *7*, 87–94. https://doi.org/10.1016/J.COTOX.2017.11.001

Gyori, B. M., Venkatachalam, G., Thiagarajan, P. S., Hsu, D., & Clement, M.-V. (2014). OpenComet: An automated tool for comet assay image analysis. *Redox Biology*, *2*, 457–465. https://doi.org/10.1016/j.redox.2013.12.020

Hammond, D., Jones, S., & Lalor, M. (2007). In-vehicle Measurement of Ultrafine Particles on Compressed Natural Gas, Conventional Diesel, and Oxidation-catalyst Diesel Heavy-duty Transit Buses. *Environmental Monitoring and Assessment 2007 125:1*, *125*(1), 239–246. https://doi.org/10.1007/S10661-006-9515-Z

Hayes, J. D., & McLellan, L. I. (2009). Glutathione and glutathione-dependent enzymes

represent a co-ordinately regulated defence against oxidative stress. *Https://Doi.Org/10.1080/10715769900300851*, *31*(4), 273–300. https://doi.org/10.1080/10715769900300851

Hayes, J. D., & Strange, R. C. (2000). Glutathione S-transferase polymorphisms and their biological consequences. *Pharmacology*, *61*(3), 154–166. https://doi.org/10.1159/000028396

Heath, J. A., Smibert, E., Algar, E. M., Dite, G. S., & Hopper, J. L. (2014). Cancer risks for relatives of children with cancer. *Journal of Cancer Epidemiology*, *2014*. https://doi.org/10.1155/2014/806076

Hong, Y., Han, H. J., Lee, H., Lee, D., Ko, J., Hong, Z. yu, Lee, J. Y., Seok, J. H., Lim, H. S., Son, W. C., & Sohn, I. (2020). Deep learning method for comet segmentation and comet assay image analysis. *Scientific Reports 2020*, *10*(1), 1–12. https://doi.org/10.1038/s41598-020-75592-7

Hoseini, M., Nabizadeh, R., Delgado-Saborit, J. M., Rafiee, A., Yaghmaeian, K., Parmy, S., Faridi, S., Hassanvand, M. S., Yunesian, M., & Naddafi, K. (2018). Environmental and lifestyle factors affecting exposure to polycyclic aromatic hydrocarbons in the general population in a Middle Eastern area. *Environmental Pollution*, *240*, 781–792. https://doi.org/10.1016/J.ENVPOL.2018.04.077

How, V., Hashim, Z., Ismail, P., Md Said, S., Omar, D., & Tamrin, S. B. M. (2014). Exploring cancer development in adulthood: Cholinesterase depression and genotoxic effect from chronic exposure to organophosphate pesticides among rural farm children. *Journal of Agromedicine*, *19*(1), 35–43. https://doi.org/10.1080/1059924X.2013.866917

Hsieh, C. M., & Huang, H. C. (2016). Mitigating urban heat islands: A method to identify potential wind corridor for cooling and ventilation. *Computers, Environment and Urban Systems*, *57*, 130–143. https://doi.org/10.1016/J.COMPENVURBSYS.2016.02.005

Hu, S. W., Chan, Y. J., Hsu, H. T., Wu, K. Y., ChangChien, G. P., Shie, R. H., & Chan, C. C. (2011). Urinary levels of 1-hydroxypyrene in children residing near a coal-fired power plant. *Environmental Research*, *111*(8), 1185–1191. https://doi.org/10.1016/j.envres.2011.07.004

Huang, C. H., Tsai, H. H., & Chen, H. C. (2020). Influence of weather factors on thermal comfort in subtropical urban environments. *Sustainability (Switzerland)*, *12*(5). https://doi.org/10.3390/su12052001

Huang, H.-B., Lai, C.-H., Chen, G.-W., Lin, Y.-Y., Jaakkola, J. J. K., Liou, S.-H., & Wang, S.-L. (2012). Traffic-related air pollution and DNA damage: A longitudinal study in Taiwanese traffic conductors. *PLoS ONE*, *7*(5), e37412. https://doi.org/10.1371/journal.pone.0037412

Huang, W., Caudill, S. P., Grainger, J., Needham, L. L., & Patterson, D. G. (2006). Levels of 1-hydroxypyrene and other monohydroxy polycyclic aromatic

hydrocarbons in children: A study based on U.S. reference range values. *Toxicology Letters*, *163*(1), 10–19. https://doi.org/10.1016/j.toxlet.2005.08.003

Huang, X., Deng, X., Li, W., Liu, S., Chen, Y., Yang, B., & Liu, Q. (2019). Internal exposure levels of polycyclic aromatic hydrocarbons in children and adolescents: A systematic review and meta-analysis. *Environmental Health and Preventive Medicine*, *24*(1), 1–15. https://doi.org/10.1186/s12199-019-0805-9

IARC. (2010). *Some Non-heterocyclic Polycyclic Aromatic Hydrocarbons and Some Related Exposures*. https://www.ncbi.nlm.nih.gov/books/NBK321712/

IARC. (2021). *List of Classifications – IARC Monographs on the Identification of Carcinogenic Hazards to Humans*. https://monographs.iarc.who.int/list-of-classifications

Iarmarcovai, G., Bonassi, S., Botta, A., Baan, R. A., & Orsière, T. (2008). Genetic polymorphisms and micronucleus formation: A review of the literature. *Mutation Research - Reviews in Mutation Research*, *658*(3), 215–233. https://doi.org/10.1016/j.mrrev.2007.10.001

Ifegwu, C., Osunjaye, K., Fashogbon, F., Oke, K., Adeniyi, A., & Anyakora, C. (2012). Urinary 1-Hydroxypyrene as a biomarker to carcinogenic polycyclic aromatic hydrocarbon exposure. *Biomarkers in Cancer*, *4*, BIC.S10065. https://doi.org/10.4137/bic.s10065

Ismail, I. N., Jalaludin, J., Bakar, S. A., Hisamuddin, N. H., & Suhaimi, N. F. (2019). Association of Traffic-Related Air Pollution (TRAP) with DNA damage and respiratory health symptoms among primary school children in Selangor. *Asian Journal of Atmospheric Environment*, *13*(2), 107–116. https://doi.org/10.5572/AJAE.2019.13.2.106

Ismail, M. F., Fadzil, M. F., Tahir, N. M., Latif, M. T., & Mohamad, N. (2019). Preliminary assessment of the distribution of PM2.5-bound polycyclic aromatic hydrocarbons in primary school environments in Kuala Lumpur. *Universiti Malaysia Terengganu Journal of Undergraduate Research*, *1*(2), 51–58.

Jain, R. B. (2020). Contributions of dietary, demographic, disease, lifestyle and other factors in explaining variabilities in concentrations of selected monohydroxylated polycyclic aromatic hydrocarbons in urine: Data for US children, adolescents, and adults. *Environmental Pollution*, *266*, 115178. https://doi.org/10.1016/J.ENVPOL.2020.115178

Jakovljević, I., Štrukil, Z. S., Godec, R., Bešlić, I., Davila, S., Lovrić, M., & Pehnec, G. (2020). Pollution sources and carcinogenic risk of PAHs in PM1 particle fraction in an urban area. *International Journal of Environmental Research and Public Health*, *17*(24), 9587. https://doi.org/10.3390/IJERPH17249587

Jalaludin, J., Noh, S. N. S., Suhaimi, N. F., & Akim, A. M. (2014). Tumor necrosis factor-alpha as biomarkers of exposure to indoor pollutants among primary school children in Klang Valley. *American Journal of Applied Sciences*, *11*(9), 1616–

1630. https://doi.org/10.3844/AJASSP.2014.1616.1630

Jamhari, A. A., Latif, M. T., Wahab, M. I. A., Othman, M., Hamid, H. H. A., Tekasakul, P., Hata, M., Furuchi, M., & Rajab, N. F. (2021). Size-segregated atmospheric polycyclic aromatic hydrocarbons down to PM0.1 in urban tropical environment: Temporal distribution, potential sources and human health risk. *Urban Climate*, *40*, 100996. https://doi.org/10.1016/J.UCLIM.2021.100996

Jamhari, A. A., Sahani, M., Latif, M. T., Chan, K. M., Tan, H. S., Khan, M. F., & Mohd Tahir, N. (2014). Concentration and source identification of polycyclic aromatic hydrocarbons (PAHs) in PM10 of urban, industrial and semi-urban areas in Malaysia. *Atmospheric Environment*, *86*, 16–27. https://doi.org/10.1016/j.atmosenv.2013.12.019

Jasso-Pineda, Y., Díaz-Barriga, F., Yáñez-Estrada, L., Pérez-Vázquez, F. J., & Pérez-Maldonado, I. N. (2015). DNA damage in Mexican children living in high-risk contaminated scenarios. *Science of the Total Environment*, *518–519*, 38–48. https://doi.org/10.1016/j.scitotenv.2015.02.073

Jeng, H. A., & Pan, C.-H. (2014). 1-Hydroxypyrene as a biomarker for environmental health. In *General Methods in Biomarker Research and their Applications* (pp. 1–15). Springer Netherlands. https://doi.org/10.1007/978-94-007-7740-8_49-1

Jeong, S. H., Jang, B. N., Kang, S. H., Joo, J. H., & Park, E. C. (2021). Association between parents' smoking status and tobacco exposure in school-age children: assessment using major urine biomarkers. *Scientific Reports 2021 11:1*, *11*(1), 1–9. https://doi.org/10.1038/s41598-021-84017-y

Ji, J.-H. (2020). Size distributions of suspended fine particles during cleaning in an office. *Aerosol and Air Quality Research*, *20*(1), 53–60. https://doi.org/10.4209/AAQR.2019.10.0511

Jiao, K., Xu, M., & Liu, M. (2018). Health status and air pollution related socioeconomic concerns in urban China. *International Journal for Equity in Health*, *17*(1), 1–11. https://doi.org/10.1186/s12939-018-0719-y

Jongeneelen, F. J. (2001). Benchmark guideline for urinary 1-hydroxypyrene as biomarker of occupational exposure to polycyclic aromatic hydrocarbons. *Annals of Occupational Hygiene*, *45*(1), 3–13. https://doi.org/10.1016/S0003-4878(00)00009-0

Juneng, L., Latif, M. T., & Tangang, F. (2011). Factors influencing the variations of PM10 aerosol dust in Klang Valley, Malaysia during the summer. *Atmospheric Environment*, *45*(26), 4370–4378. https://doi.org/10.1016/J.ATMOSENV.2011.05.045

Jyethi, D. S., Khillare, P. S., & Sarkar, S. (2014). Risk assessment of inhalation exposure to polycyclic aromatic hydrocarbons in school children. *Environmental Science and Pollution Research*, *21*(1), 366–378. https://doi.org/10.1007/s11356-013-1912-6

Kam, W., Liacos, J. W., Schauer, J. J., Delfino, R. J., & Sioutas, C. (2012). Size-segregated composition of particulate matter (PM) in major roadways and surface streets. *Atmospheric Environment*, *55*, 90–97. https://doi.org/10.1016/J.ATMOSENV.2012.03.028

Katsoyiannis, A., Sweetman, A. J., & Jones, K. C. (2011). PAH molecular diagnostic ratios applied to atmospheric sources: A critical evaluation using two decades of source inventory and air concentration data from the UK. *Environmental Science and Technology*, *45*(20), 8897–8906. https://doi.org/10.1021/ES202277U

Keir, J. L. A., Cakmak, S., Blais, J. M., & White, P. A. (2020). The influence of demographic and lifestyle factors on urinary levels of PAH metabolites-empirical analyses of Cycle 2 (2009-2011) CHMS data. *Journal of Exposure Science & Environmental Epidemiology*, *31*(2), 386–397. https://doi.org/10.1038/S41370-020-0208-4

Khan, M. F., Hwa, S. W., Hou, L. C., Mustaffa, N. I. H., Amil, N., Mohamad, N., Sahani, M., Jaafar, S. A., Nadzir, M. S. M., & Latif, M. T. (2017). Influences of inorganic and polycyclic aromatic hydrocarbons on the sources of PM2.5 in the Southeast Asian urban sites. *Air Quality, Atmosphere & Health 2017 10:8*, *10*(8), 999–1013. https://doi.org/10.1007/S11869-017-0489-5

Khan, M. F., Latif, M. T., Juneng, L., Amil, N., Nadzir, M. S. M., & Hoque, H. M. S. (2015). Physicochemical factors and sources of particulate matter at residential urban environment in Kuala Lumpur. *Journal of the Air and Waste Management Association*, *65*(8), 958–969. https://doi.org/10.1080/10962247.2015.1042094

Khan, M. F., Latif, M. T., Lim, C. H., Amil, N., Jaafar, S. A., Dominick, D., Mohd Nadzir, M. S., Sahani, M., & Tahir, N. M. (2015). Seasonal effect and source apportionment of polycyclic aromatic hydrocarbons in PM2.5. *Atmospheric Environment*, *106*, 178–190. https://doi.org/10.1016/j.atmosenv.2015.01.077

Kim, K. H., Jahan, S. A., Kabir, E., & Brown, R. J. C. (2013). A review of airborne polycyclic aromatic hydrocarbons (PAHs) and their human health effects. In *Environment International* (Vol. 60, pp. 71–80). Elsevier Ltd. https://doi.org/10.1016/j.envint.2013.07.019

Kim, K. H., Kabir, E., & Kabir, S. (2015). A review on the human health impact of airborne particulate matter. In *Environment International* (Vol. 74, pp. 136–143). Elsevier Ltd. https://doi.org/10.1016/j.envint.2014.10.005

Kim, S. S., Vuong, A. M., Dietrich, K. N., & Chen, A. (2021). Proximity to traffic and exposure to polycyclic aromatic hydrocarbons in relation to Attention Deficit Hyperactivity Disorder and conduct disorder in U.S. children. *International Journal of Hygiene and Environmental Health*, *232*, 113686. https://doi.org/10.1016/J.IJHEH.2020.113686

Krugly, E., Martuzevicius, D., Sidaraviciute, R., Ciuzas, D., Prasauskas, T., Kauneliene, V., Stasiulaitiene, I., & Kliucininkas, L. (2014). Characterization of particulate and vapor phase polycyclic aromatic hydrocarbons in indoor and outdoor air of primary

schools. *Atmospheric Environment*, *82*, 298–306. https://doi.org/10.1016/j.atmosenv.2013.10.042

Kubo, T., Bai, W., Nagae, M., & Takao, Y. (2020). Seasonal fluctuation of polycyclic aromatic hydrocarbons and aerosol genotoxicity in long-range transported air mass observed at the western end of Japan. *International Journal of Environmental Research and Public Health 2020, Vol. 17, Page 1210*, *17*(4), 1210. https://doi.org/10.3390/IJERPH17041210

Kuljukka-Rabb, T., Nylund, L., Vaaranrinta, R., Savela, K., Mutanen, P., Veidebaum, T., Sorsa, M., Rannug, A., & Peltonen, K. (2002). The effect of relevant genotypes on PAH exposure-related biomarkers. *Journal of Exposure Science & Environmental Epidemiology*, *12*(1), 81–91. https://doi.org/10.1038/sj.jea.7500204

Kumar, P., Omidvarborna, H., Barwise, Y., & Tiwari, A. (2020). *Mitigating Exposure to Traffic Pollution In and Around Schools: Guidance for Children, Schools and Local Communities*. 24. https://zenodo.org/record/3754131#.XtjBd0VKjcv

Ladeira, C., & Smajdova, L. (2017). The use of genotoxicity biomarkers in molecular epidemiology: applications in environmental, occupational and dietary studies. *AIMS Genetics*, *04*(03), 166–191. https://doi.org/10.3934/genet.2017.3.166

Ladeira, C., & Viegas, S. (2016). Human biomonitoring – An overview on biomarkers and their application in occupational and environmental health. *Biomonitoring*, *3*(1), 15–24. https://doi.org/10.1515/bimo-2016-0003

Lam, Y. W. F., & Cavallari, L. H. (2013). Principles of pharmacogenomics: Pharmacokinetic, pharmacodynamic, and clinical implications. *Pharmacogenomics*, 1–44. https://doi.org/10.1016/B978-0-12-391918-2.00001-9

Landi, M. T., Bertazzi, P. A., Shields, P. G., Clark, G., Lucier, G. W., Garte, S. J., Cosma, G., & Caporaso, N. E. (1994). Association between CYP1A1 genotype, mRNA expression and enzymatic activity in humans. *Pharmacogenetics*, *4*(5), 242–246. https://doi.org/10.1097/00008571-199410000-00002

Larsen, K. (1972). Creatinine assay by a reaction-kinetic principle. *Clinica Chimica Acta*, *41*(C), 209–217. https://doi.org/10.1016/0009-8981(72)90513-X

Larson, B. (2015). *Automated Imaging and Analysis of a Novel Comet Assay to Enable High Throughput Genotoxicity Testing*. https://www.agilent.com/cs/library/applications/automated-comet-assay-genotoxicity-5994-2597EN-agilent.pdf

Latif, M. T., Dominick, D., Ahamad, F., Khan, M. F., Juneng, L., Hamzah, F. M., & Nadzir, M. S. M. (2014). Long term assessment of air quality from a background station on the Malaysian Peninsula. *Science of The Total Environment*, *482–483*(1), 336–348. https://doi.org/10.1016/J.SCITOTENV.2014.02.132

Latif, M. T., Dominick, D., Hawari, N. S. S. L., Mohtar, A. A. A., & Othman, M. (2021).

The concentration of major air pollutants during the movement control order due to the COVID-19 pandemic in the Klang Valley, Malaysia. *Sustainable Cities and Society*, *66*, 102660. https://doi.org/10.1016/j.scs.2020.102660

Lee, B.-K., & Vu, V. T. (2010). Sources, distribution and toxicity of polyaromatic hydrocarbons (PAHs) in particulate matter. *Air Pollution, May 2014*. https://doi.org/10.5772/10045

Lee, M.-S., Eum, K.-D., Zoh, K.-D., Kim, T.-S., Pak, Y.-S., & Paek, D. (2007). 1-Hydroxypyrene as a biomarker of PAH exposure among subjects living in two separate regions from a steel mill. *International Archives of Occupational and Environmental Health 2007 80:8*, *80*(8), 671–678. https://doi.org/10.1007/S00420-007-0178-Z

Lemeshow, S., Hosmer, D. W., Klar, J., Lwanga, S. K., & Organization, W. H. (1990). *Adequacy of sample size in health studies*. https://apps.who.int/iris/bitstream/handle/10665/41607/0471925179_eng.pdf?sequence=1&isAllowed=y

Letter, C., & Jäger, G. (2019). Simulating the potential of trees to reduce particulate matter pollution in urban areas throughout the year. *Environment, Development and Sustainability 2019 22:5*, *22*(5), 4311–4321. https://doi.org/10.1007/S10668-019-00385-6

Leung, D. Y. C. (2015). Outdoor-indoor air pollution in urban environment: Challenges and opportunity. *Frontiers in Environmental Science*, *2*(JAN), 69. https://doi.org/10.3389/FENVS.2014.00069/BIBTEX

Li, D., Wang, B., Feng, G., Xie, M., Wang, L., & Gao, R. (2017). Effect of the GSTM1 genotype on the biomarkers of exposure to polycyclic aromatic hydrocarbons: Meta-analysis. *International Journal of Occupational Medicine and Environmental Health*, *30*(2), 177–201. https://doi.org/10.13075/ijomeh.1896.01054

Li, P., Wang, Y., Li, Y., Wang, Z., Zhang, H., Xu, P., & Wang, W. (2010). Characterization of polycyclic aromatic hydrocarbons deposition in PM2.5 and cloud/fog water at Mount Taishan (China). *Atmospheric Environment*, *16*(44), 1996–2003. https://doi.org/10.1016/J.ATMOSENV.2010.02.031

Li, Z., Sandau, C. D., Romanoff, L. C., Caudill, S. P., Sjodin, A., Needham, L. L., & Patterson, D. G. (2008). Concentration and profile of 22 urinary polycyclic aromatic hydrocarbon metabolites in the US population. *Environmental Research*, *107*(3), 320–331. https://doi.org/10.1016/j.envres.2008.01.013

Link, B., Gabrio, T., Zoellner, I., Piechotowski, I., Paepke, O., Herrmann, T., Felder-Kennel, A., Maisner, V., Schick, K. H., Schrimpf, M., Schwenk, M., & Wuthe, J. (2005). Biomonitoring of persistent organochlorine pesticides, PCDD/PCDFs and dioxin-like PCBs in blood of children from South West Germany (Baden-Wuerttemberg) from 1993 to 2003. *Chemosphere*, *58*(9), 1185–1201. https://doi.org/10.1016/J.CHEMOSPHERE.2004.09.061

Liu, G. R., Peng, X., Wang, R. K., Tian, Y. Z., Shi, G. L., Wu, J. H., Zhang, P., Zhou, L. D., & Feng, Y. C. (2015). A new receptor model-incremental lifetime cancer risk method to quantify the carcinogenic risks associated with sources of particle-bound polycyclic aromatic hydrocarbons from Chengdu in China. *Journal of Hazardous Materials*, *283*, 462–468. https://doi.org/10.1016/J.JHAZMAT.2014.09.062

Liu, J., Wang, Y., Li, P. H., Shou, Y. P., Li, T., Yang, M. M., Wang, L., Yue, J. J., Yi, X. L., & Guo, L. Q. (2017). Polycyclic aromatic hydrocarbons (PAHs) at high mountain site in North China: Concentration, source and health risk assessment. *Aerosol and Air Quality Research*, *17*(11), 2867–2877. https://doi.org/10.4209/AAQR.2017.08.0288

Liu, S., Liu, Q., Ostbye, T., Story, M., Deng, X., Chen, Y., Li, W., Wang, H., Qiu, J., & Zhang, J. (2017). Levels and risk factors for urinary metabolites of polycyclic aromatic hydrocarbons in children living in Chongqing, China. *Science of the Total Environment*, *598*, 553–561. https://doi.org/10.1016/j.scitotenv.2017.04.103

Liu, Yankun, Yu, Y., Liu, M., Lu, M., Ge, R., Li, S., Liu, X., Dong, W., & Qadeer, A. (2018). Characterization and source identification of PM2.5-bound polycyclic aromatic hydrocarbons (PAHs) in different seasons from Shanghai, China. *Science of the Total Environment*, *644*, 725–735. https://doi.org/10.1016/j.scitotenv.2018.07.049

Liu, Ying, Chen, L., Huang, Q. hui, Li, W. ying, Tang, Y. jian, & Zhao, J. fu. (2009). Source apportionment of polycyclic aromatic hydrocarbons (PAHs) in surface sediments of the Huangpu River, Shanghai, China. *Science of The Total Environment*, *407*(8), 2931–2938. https://doi.org/10.1016/J.SCITOTENV.2008.12.046

Locken-Castilla, A., Pacheco-Pantoja, E. L., Rodríguez-Brito, F., May-Kim, S., López-Rivas, V., & Ceballos-Cruz, A. (2019). Smoking index, lifestyle factors, and genomic instability assessed by single-cell gel electrophoresis: a cross-sectional study in subjects from Yucatan, Mexico. *Clinical Epigenetics*, *11*(1). https://doi.org/10.1186/S13148-019-0745-7

Lonati, G., Cernuschi, S., Giugliano, M., & Grosso, M. (2007). Health risk analysis of PCDD/F emissions from MSW incineration: comparison of probabilistic and deterministic approaches. *Chemosphere*, *67*(9), S334–S343. https://doi.org/10.1016/J.CHEMOSPHERE.2006.05.139

Long, C. M., & Sarnat, J. A. (2010). Indoor-outdoor relationships and infiltration behavior of elemental components of outdoor PM2.5 for Boston-area homes. *Aerosol Science and Technology*, *38*(2), 91–104. https://doi.org/https://doi.org/10.1080/027868290502281

Lu, S., Fan, R., Yu, Z., Sheng, G., & Fu, J. (2012). An improved method for the determination of urinary 1-hydroxypyrene by high-performance liquid chromatography with fluorescence detection. *Journal of Liquid Chromatography and Related Technologies*, *35*(11), 1528–1537.

https://doi.org/10.1080/10826076.2011.619041

Ma, X., Longley, I., Gao, J., & Salmond, J. (2020). Assessing schoolchildren's exposure to air pollution during the daily commute - A systematic review. *Science of The Total Environment*, *737*, 140389. https://doi.org/10.1016/J.SCITOTENV.2020.140389

Makpol, S., Mamat, S., Ahmad, Z., & Ngah, W. Z. W. (2008). Genetic polymorphisms in CYP1A1 (m1), (m2), (m4) and CYP2A6 and susceptibility to hepatocellular carcinoma in a Malaysian study population. *Malaysian Journal of Biochemistry and Molecular Biology*, *Volume 11*(Issue 1), 31–40.

Manisalidis, I., Stavropoulou, E., Stavropoulos, A., & Bezirtzoglou, E. (2020). Environmental and health impacts of air pollution: A review. *Frontiers in Public Health*, *0*, 14. https://doi.org/10.3389/FPUBH.2020.00014

Manogaran, S., Ali, M., Yusof, K. M., & Suhaili, R. (2017). Analysis of vehicular traffic flow in the major areas of Kuala Lumpur utilizing open-traffic. *AIP Conference Proceedings*, *1883*(September 2017). https://doi.org/10.1063/1.5002031

Marinković, N., Pašalić, D., & Potočki, S. (2013). Polymorphisms of genes involved in polycyclic aromatic hydrocarbons' biotransformation and atherosclerosis. *Biochemia Medica*, *23*(3), 255–265. https://doi.org/10.11613/BM.2013.032

Masson, L. F., Sharp, L., Cotton, S. C., & Little, J. (2005). Cytochrome P-450 1A1 gene polymorphisms and rtisk of breast cancer: A HuGE review. *American Journal of Epidemiology*, *161*(10), 901–915. https://doi.org/10.1093/AJE/KWI121

Mathiarasan, S., & Hüls, A. (2021). Impact of environmental injustice on children's health—Interaction between air pollution and socioeconomic status. *International Journal of Environmental Research and Public Health 2021, Vol. 18, Page 795*, *18*(2), 795. https://doi.org/10.3390/IJERPH18020795

Mcnamara, M. L., Noonan, C. W., & Ward, T. J. (2011). Correction factor for continuous monitoring of wood smoke fine particulate matter. *Aerosol and Air Quality Research*, *11*, 315–322. https://doi.org/10.4209/aaqr.2010.08.0072

Merlo, F., Andreassen, Å., Weston, A., Pan, C. F., Haugen, A., Valerio, F., Reggiardo, G., Fontana, V., Garte, S., Puntoni, R., & Abbondandolo, A. (1998). Urinary excretion of 1-hydroxypyrene as a marker for exposure to urban air levels of polycyclic aromatic hydrocarbons. *Cancer Epidemiology Biomarkers and Prevention*, *7*(2), 147–155.

Mielzynska-Svach, D., Blaszczyk, E., Butkiewicz, D., Durzynska, J., & Rydzanicz, M. (2013). Influence of genetic polymorphisms on biomarkers of exposure and effects in children living in Upper Silesia. *Mutagenesis*, *28*(5), 591–599. https://doi.org/10.1093/mutage/get037

Mielzyńska, D., Siwińska, E., Kapka, L., Szyfter, K., Knudsen, L. E., & Merlo, D. F. (2006). The influence of environmental exposure to complex mixtures including

PAHs and lead on genotoxic effects in children living in Upper Silesia, Poland. *Mutagenesis*, *21*(5), 295–304. https://doi.org/10.1093/mutage/gel037

Milić, M., Ceppi, M., Bruzzone, M., Azqueta, A., Brunborg, G., Godschalk, R., Koppen, G., Langie, S., Møller, P., Teixeira, J. P., Alija, A., Anderson, D., Andrade, V., Andreoli, C., Asllani, F., Bangkoglu, E. E., Barančoková, M., Basaran, N., Boutet-Robinet, E., … Bonassi, S. (2021). The hCOMET project: International database comparison of results with the comet assay in human biomonitoring. Baseline frequency of DNA damage and effect of main confounders. *Mutation Research. Reviews in Mutation Research*, *787*, 108371. https://doi.org/10.1016/J.MRREV.2021.108371

Ministry of Health Malaysia. (2021). *Priority List Of Environmental Health Issues In Malaysia*. http://nehapmalaysia.moh.gov.my/priority-list-of-environmental-health-issues-in-malaysia/?fbclid=IwAR0dsDSA9ZphfLil5oVkKGZKdSgKEiJ0N894HSsO-g_Q-QGU7ndlJo89v7c

Ministry of Transport Malaysia. (2019). *Malaysia transportation statistics 2019*. https://www.mot.gov.my/en/Statistik Tahunan Pengangkutan/Transport Statistics Malaysia 2019.pdf

Miri, M., Alahabadi, A., Ehrampoush, M. H., Ghaffari, H. R., Sakhvidi, M. J. Z., Eskandari, M., Rad, A., Lotfi, M. H., & Sheikhha, M. H. (2018). Environmental determinants of polycyclic aromatic hydrocarbons exposure at home, at kindergartens and during a commute. *Environment International*, *118*, 266–273. https://doi.org/10.1016/j.envint.2018.06.006

Mohammadyan, M., Alizadeh-Larimi, A., Etemadinejad, S., Latif, M. T., Heibati, B., Yetilmezsoy, K., Abdul-Wahab, S. A., & Dadvand, P. (2017). Particulate air pollution at schools: Indoor-outdoor relationship and determinants of indoor concentrations. *Aerosol and Air Quality Research*, *17*(3), 857–864. https://doi.org/10.4209/AAQR.2016.03.0128

Mohd Shafie, S. H., & Mahmud, M. (2020). Urban air pollutant from motor vehicle emissions in Kuala Lumpur, Malaysia. *Aerosol and Air Quality Research*, *20*, 2793–2804. https://doi.org/10.4209/aaqr.2020.02.0074

Møller, P., Loft, S., Ersson, C., Koppen, G., Dusinska, M., & Collins, A. (2014). On the search for an intelligible comet assay descriptor. *Frontiers in Genetics*, *5*(JUL). https://doi.org/10.3389/FGENE.2014.00217

Moorthy, B., Chu, C., & Carlin, D. J. (2015). Polycyclic aromatic hydrocarbons: From metabolism to lung cancer. *Toxicological Sciences*, *145*(1), 5–15. https://doi.org/10.1093/toxsci/kfv040

Morakinyo, T. E., Balogun, A. A., & Adegun, O. B. (2013). Comparing the effect of trees on thermal conditions of two typical urban buildings. *Urban Climate*, *3*, 76–93. https://doi.org/10.1016/J.UCLIM.2013.04.002

Morawska, L., Afshari, A., Bae, G. N., Buonanno, G., Chao, C. Y. H., Hänninen, O., Hofmann, W., Isaxon, C., Jayaratne, E. R., Pasanen, P., Salthammer, T., Waring, M., & Wierzbicka, A. (2013). Indoor aerosols: from personal exposure to risk assessment. *Indoor Air*, *23*(6), 462–487. https://doi.org/10.1111/INA.12044

Moretti, M., Dell'Omo, M., Villarini, M., Pastorelli, R., Muzi, G., Airoldi, L., & Pasquini, R. (2007). Primary DNA damage and genetic polymorphisms for CYP1A1, EPHX and GSTM1 in workers at a graphite electrode manufacturing plant. *BMC Public Health*, *7*(1), 270. https://doi.org/10.1186/1471-2458-7-270

Mori, T., Yoshinaga, J., Suzuki, K., Mizoi, M., Adachi, S. ichi, Tao, H., Nakazato, T., Li, Y. S., Kawai, K., & Kasai, H. (2011). Exposure to polycyclic aromatic hydrocarbons, arsenic and environmental tobacco smoke, nutrient intake, and oxidative stress in Japanese preschool children. *Science of the Total Environment*, *409*(15), 2881–2887. https://doi.org/10.1016/j.scitotenv.2011.04.028

Mucha, A. P., Hryhorczuk, D., Serdyuk, A., Nakonechny, J., Zvinchuk, A., Erdal, S., Caudill, M., Scheff, P., Lukyanova, E., Shrkiryak-Nyzhnyk, Z., & Chislovska, N. (2006). Urinary 1-hydroxypyrene as a biomarker of PAH exposure in 3-year-old Ukrainian children. *Environmental Health Perspectives*, *114*(4), 603–609. https://doi.org/10.1289/ehp.7898

Murawski, A., Roth, A., Schwedler, G., Schmied-Tobies, M. I. H., Rucic, E., Pluym, N., Scherer, M., Scherer, G., Conrad, A., & Kolossa-Gehring, M. (2020). Polycyclic aromatic hydrocarbons (PAH) in urine of children and adolescents in Germany - human biomonitoring results of the German Environmental Survey 2014-2017 (GerES V). *Undefined*, *226*. https://doi.org/10.1016/J.IJHEH.2020.113491

Nagpure, A. S., Gurjar, B. R., Kumar, V., & Kumar, P. (2016). Estimation of exhaust and non-exhaust gaseous, particulate matter and air toxics emissions from on-road vehicles in Delhi. *Atmospheric Environment*, *127*, 118–124. https://doi.org/10.1016/J.ATMOSENV.2015.12.026

Naksen, W., Kawichai, S., Srinual, N., Salrasee, W., & Prapamontol, T. (2017). First evidence of high urinary 1-hydroxypyrene level among rural school children during smoke haze episode in Chiang Mai Province, Thailand. *Atmospheric Pollution Research*, *8*(3), 418–427. https://doi.org/10.1016/j.apr.2016.11.002

Nerurkar, P. V, Okinaka, L., Aoki, C., Seifried, A., Lum-Jones, A., Wilkens, L. R., Loı¨c, L., & Marchand, L. (2000). CYP1A1, GSTM1, and GSTP1 genetic polymorphisms and urinary 1-hydroxypyrene excretion in non-occupationally exposed individuals. *Cancer Epidemiology, Biomarkers & Prevention*, *9*, 1119–1122.

NIOSH. (1998). *NMAM 0600: Particulates Not Otherwise Regulated, Respirable*.

Nisbet, I. C. T., & LaGoy, P. K. (1992). Toxic equivalency factors (TEFs) for polycyclic aromatic hydrocarbons (PAHs). *Regulatory Toxicology and Pharmacology*, *16*(3), 290–300. https://doi.org/10.1016/0273-2300(92)90009-X

Norazman, N., Che Ani, A. I., Ismail, W. N. W., Hussain, A. H., & Abdul Maulud, K. N. (2021). Indoor environmental quality towards classrooms' comforts level: Case study at Malaysian secondary school building. *Applied Sciences*, *11*(13), 5866. https://doi.org/10.3390/app11135866

Norppa, H. (2004). Cytogenetic biomarkers and genetic polymorphisms. *Toxicology Letters*, *149*, 309–334. https://doi.org/10.1016/j.toxlet.2003.12.042

Ochoa-Martinez, A. C., Orta-Garcia, S. T., Rico-Escobar, E. M., Carrizales-Yañez, L., Del Campo, J. D. M., Pruneda-Alvarez, L. G., Ruiz-Vera, T., Gonzalez-Palomo, A. K., Piña-Lopez, I. G., Torres-Dosal, A., & Pérez-Maldonado, I. N. (2016). Exposure assessment to environmental chemicals in children from Ciudad Juarez, Chihuahua, Mexico. *Archives of Environmental Contamination and Toxicology*, *70*(4), 657–670. https://doi.org/10.1007/s00244-016-0273-9

Olive, P. L., Banáth, J. P., & Durand, R. E. (1990). Heterogeneity in radiation-induced DNA damage and repair in tumor and normal cells measured using the comet assay. *Radiation Research*, *122*, 86–94. https://doi.org/10.1667/RRAV04.1

Oliveira, M., Costa, S., Vaz, J., Fernandes, A., Slezakova, K., Delerue-Matos, C., Teixeira, J. P., Carmo Pereira, M., & Morais, S. (2020). Firefighters exposure to fire emissions: Impact on levels of biomarkers of exposure to polycyclic aromatic hydrocarbons and genotoxic/oxidative-effects. *Journal of Hazardous Materials*, *383*, 121179. https://doi.org/10.1016/J.JHAZMAT.2019.121179

Oliveira, M., Slezakova, K., Delerue-Matos, C., do Carmo Pereira, M., & Morais, S. (2017). Assessment of exposure to polycyclic aromatic hydrocarbons in preschool children: Levels and impact of preschool indoor air on excretion of main urinary monohydroxyl metabolites. *Journal of Hazardous Materials*, *322*, 357–369. https://doi.org/10.1016/j.jhazmat.2016.10.004

Oliveira, M., Slezakova, K., Delerue-Matos, C., Pereira, M. C., & Morais, S. (2019). Children environmental exposure to particulate matter and polycyclic aromatic hydrocarbons and biomonitoring in school environments: A review on indoor and outdoor exposure levels, major sources and health impacts. *Environment International*, *124*, 180–204. https://doi.org/10.1016/J.ENVINT.2018.12.052

Oliveira, M., Slezakova, K., Delerue-Matos, C., Pereira, M. D. C., & Morais, S. (2016). Assessment of polycyclic aromatic hydrocarbons in indoor and outdoor air of preschool environments (3–5 years old children). *Environmental Pollution*, *208*, 382–394. https://doi.org/10.1016/J.ENVPOL.2015.10.004

Oliveira, M., Slezakova, K., Delerue-Matos, C., Pereira, M. do C., & Morais, S. (2015). Exposure to polycyclic aromatic hydrocarbons and assessment of potential risks in preschool children. *Environmental Science and Pollution Research 2015 22:18*, *22*(18), 13892–13902. https://doi.org/10.1007/S11356-015-4588-2

Omar, N. Y. M. ., Mon, T. C., Noorsaadah, A. R., & Abas, M. R. B. (2006). Distributions and health risks of polycyclic aromatic hydrocarbons (PAHs) in atmospheric aerosols of Kuala Lumpur, Malaysia. *The Science of the Total Environment*,

369(1–3), 76–81. https://doi.org/10.1016/J.SCITOTENV.2006.04.032

Omar, N. Y. M. J., Abas, M. R., Ketuly, K. A., & Tahir, N. M. (2002). Concentrations of PAHs in atmospheric particles (PM-10) and roadside soil particles collected in Kuala Lumpur, Malaysia. *Atmospheric Environment*, *36*(2), 247–254. https://doi.org/10.1016/S1352-2310(01)00425-3

Othman, M., Latif, M. T., Jamhari, A. A., Abd Hamid, H. H., Uning, R., Khan, M. F., Mohd Nadzir, M. S., Sahani, M., Abdul Wahab, M. I., & Chan, K. M. (2021). Spatial distribution of fine and coarse particulate matter during a southwest monsoon in Peninsular Malaysia. *Chemosphere*, *262*, 127767. https://doi.org/10.1016/J.CHEMOSPHERE.2020.127767

Othman, M., Latif, M. T., & Matsumi, Y. (2019). The exposure of children to PM2.5 and dust in indoor and outdoor school classrooms in Kuala Lumpur City Centre. *Ecotoxicology and Environmental Safety*, *170*, 739–749. https://doi.org/10.1016/j.ecoenv.2018.12.042

Othman, M., Latif, M. T., Mohd Naim, N. N., Mohamed Zain, S. M. S., Khan, M. F., Sahani, M., A Wahab, M. I., Md Sofwan, N., Abd Hamid, H. H., & Mohamed, A. F. (2022). Children's exposure to PM2.5 and its chemical constituents in indoor and outdoor schools urban environment. *Atmospheric Environment*, *273*, 118963. https://doi.org/10.1016/J.ATMOSENV.2022.118963

Ouyang, R., Yang, S., & Xu, L. (2020). Analysis and risk assessment of PM2.5-bound PAHs in a comparison of indoor and outdoor environments in a middle school: A case study in Beijing, China. *Atmosphere*, *11*(9). https://doi.org/10.3390/ATMOS11090904

Palazzi, P., Hardy, E. M., & Appenzeller, B. M. R. (2019). Biomonitoring of children exposure to urban pollution and environmental tobacco smoke with hair analysis – A pilot study on children living in Paris and Yeu Island, France. *Science of The Total Environment*, *665*, 864–872. https://doi.org/10.1016/J.SCITOTENV.2019.02.177

Pandey, P. K., Patel, K. S., & Lenicek, J. (1999). Polycyclic aromatic hydrocarbons: Need for assessment of health risks in India? *Environmental Monitoring and Assessment*, *59*(3), 287–319. https://doi.org/10.1023/A:1006169605672

Pandey, P., Patel, D. K., Khan, A. H., Barman, S. C., Murthy, R. C., & Kisku, G. C. (2013). Temporal distribution of fine particulates (PM2.5, PM10), potentially toxic metals, PAHs and Metal-bound carcinogenic risk in the population of Lucknow City, India. *Journal of Environmental Science and Health, Part A*, *48*(7), 730–745. https://doi.org/10.1080/10934529.2013.744613

Panko, J. M., Hitchcock, K. M., Fuller, G. W., & Green, D. (2019). Evaluation of Tire Wear Contribution to PM2.5 in Urban Environments. *Atmosphere 2019, Vol. 10, Page 99*, *10*(2), 99. https://doi.org/10.3390/ATMOS10020099

Pant, P., & Harrison, R. M. (2013). Estimation of the contribution of road traffic

emissions to particulate matter concentrations from field measurements: A review. *Atmospheric Environment*, *77*, 78–97. https://doi.org/10.1016/J.ATMOSENV.2013.04.028

Park, J. S., Wade, T. L., & Sweet, S. (2001). Atmospheric distribution of polycyclic aromatic hydrocarbons and deposition to Galveston Bay, Texas, USA. *Atmospheric Environment*, *35*(19), 3241–3249. https://doi.org/10.1016/S1352-2310(01)00080-2

Petchpoung, K., Kaojarern, S., Yoovathaworn, K., Sura, T., & Sirivarasai, J. (2011). The influence of metabolic gene polymorphisms on urinary 1-hydroxypyrene concentration in Thai bus drivers. *Environmental Toxicology and Pharmacology*, *31*(1), 160–164. https://doi.org/10.1016/J.ETAP.2010.10.006

Phillips, D. H. (1999). Polycyclic aromatic hydrocarbons in the diet. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis*, *443*(1–2), 139–147. https://doi.org/10.1016/S1383-5742(99)00016-2

Pies, C., Hoffmann, B., Petrowsky, J., Yang, Y., Ternes, T. A., & Hofmann, T. (2008). Characterization and source identification of polycyclic aromatic hydrocarbons (PAHs) in river bank soils. *Chemosphere*, *72*(10), 1594–1601. https://doi.org/10.1016/J.CHEMOSPHERE.2008.04.021

Piperakis, S. M., Kontogianni, K., Karanastasi, G., Iakovidou-Kritsi, Z., & Piperakis, M. M. (2009). The use of comet assay in measuring DNA damage and repair efficiency in child, adult, and old age populations. *Cell Biology and Toxicology*, *25*(1), 65–71. https://doi.org/10.1007/S10565-007-9046-6/FIGURES/1

Poblete-Naredo, I., & Albores, A. (2016). Molecular biomarkers to assess health risks due to environmental contaminants exposure. *Biomédica Molecular Biomarkers Assays TOPIC REVIEW Biomédica*, *3636*, 309–35309. https://doi.org/10.7705/biomedica.v36i3.2998

Protano, C., Guidotti, M., Manini, P., Petyx, M., La Torre, G., & Vitali, M. (2010). Benzene exposure in childhood: Role of living environments and assessment of available tools. *Environment International*, *36*(7), 779–787. https://doi.org/10.1016/J.ENVINT.2010.06.003

Purcaro, G., Moret, S., & Conte, L. S. (2013). Overview on polycyclic aromatic hydrocarbons: Occurrence, legislation and innovative determination in foods. *Talanta*, *105*, 292–305. https://doi.org/10.1016/J.TALANTA.2012.10.041

Qaid, A., Bin Lamit, H., Ossen, D. R., & Raja Shahminan, R. N. (2016). Urban heat island and thermal comfort conditions at micro-climate scale in a tropical planned city. *Energy and Buildings*, *133*, 577–595. https://doi.org/10.1016/J.ENBUILD.2016.10.006

Ramos, K. S., & Bojang Jr, P. (2018). Genetic and epigenetic determinants of environmental injury and disease. *Comprehensive Toxicology*, 463–474. https://doi.org/10.1016/B978-0-12-801238-3.99175-X

Ravindra, K., Bencs, L., Wauters, E., De Hoog, J., Deutsch, F., Roekens, E., Bleux, N., Berghmans, P., & Van Grieken, R. (2006). Seasonal and site-specific variation in vapour and aerosol phase PAHs over Flanders (Belgium) and their relation with anthropogenic activities. *Atmospheric Environment*, *40*(4), 771–785. https://doi.org/10.1016/J.ATMOSENV.2005.10.011

Ravindra, K., Sokhi, R., & Van Grieken, R. (2008). Atmospheric polycyclic aromatic hydrocarbons: Source attribution, emission factors and regulation. In *Atmospheric Environment* (Vol. 42, Issue 13, pp. 2895–2921). https://doi.org/10.1016/j.atmosenv.2007.12.010

Recio-Vega, R., Olivas-Calderon, E., Michel-Ramirez, G., Martinez-Salinas, R. I., Gallegos-Arreola, M. P., Ocampo-Gomez, G. L., & Perez-Morales, R. (2018). Associations between sperm quality, DNA damage, and CYP1A1, GSTT1 and GSTM1 polymorphisms with 1-hydroxypyrene urinary levels in men occupationally exposed to polycyclic aromatic hydrocarbons. *International Archives of Occupational and Environmental Health*, *91*(6), 725–734. https://doi.org/10.1007/S00420-018-1320-9/TABLES/5

Rengarajan, T., Rajendran, P., Nandakumar, N., Lokeshkumar, B., Rajendran, P., & Nishigaki, I. (2015). Exposure to polycyclic aromatic hydrocarbons with special focus on cancer. *Asian Pacific Journal of Tropical Biomedicine*, *5*(3), 182–189. https://doi.org/10.1016/S2221-1691(15)30003-4

Risom, L., Møller, P., & Loft, S. (2005). Oxidative stress-induced DNA damage by particulate air pollution. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis*, *592*(1–2), 119–137. https://doi.org/10.1016/J.MRFMMM.2005.06.012

Rivas, I., Donaire-Gonzalez, D., Bouso, L., Esnaola, M., Pandolfi, M., de Castro, M., Viana, M., Àlvarez-Pedrerol, M., Nieuwenhuijsen, M., Alastuey, A., Sunyer, J., & Querol, X. (2016). Spatiotemporally resolved black carbon concentration, schoolchildren's exposure and dose in Barcelona. *Indoor Air*, *26*(3), 391. https://doi.org/10.1111/INA.12214

Rivas, Ioar, Querol, X., Wright, J., & Sunyer, J. (2018). How to protect school children from the neurodevelopmental harms of air pollution by interventions in the school environment in the urban context. *Environment International*, *121*, 199–206. https://doi.org/10.1016/J.ENVINT.2018.08.063

Road Traffic Volume Malaysia. (2017). *Kuala Lumpur: Highway Planning Division, Ministry of Works Malaysia*.

Rojas, E., Lorenzo, Y., Haug, K., Nicolaissen, B., & Valverde, M. (2014). Epithelial cells as alternative human biomatrices for comet assay. *Frontiers in Genetics*, *0*(NOV), 386. https://doi.org/10.3389/FGENE.2014.00386

Ruchirawat, M., Settachan, D., Navasumrit, P., Tuntawiroon, J., & Autrup, H. (2007). Assessment of potential cancer risk in children exposed to urban air pollution in Bangkok, Thailand. *Toxicology Letters*, *168*, 200–209.

https://doi.org/10.1016/j.toxlet.2006.09.013

Saitou, M., & Ishida, T. (2015). Distributions of the GSTM1 and GSTT1 null genotypes worldwide are characterized by latitudinal clines. *Asian Pacific Journal of Cancer Prevention : APJCP*, *16*(1), 355–361. https://doi.org/10.7314/APJCP.2015.16.1.355

Salvi, S. (2007). Health effects of ambient air pollution in children. *Paediatric Respiratory Reviews*, *8*(4), 275–280. https://doi.org/10.1016/J.PRRV.2007.08.008

Sánchez-Alarcón, J., Milić, M., Gómez-Arroyo, S., Montiel-González, J. M. R., & Valencia-Quintana, R. (2016). Assessment of DNA damage by comet assay in buccal epithelial cells: Problems, achievement, perspectives. *Environmental Health Risk - Hazardous Factors to Living Species*. https://doi.org/10.5772/62760

Sánchez-Guerra, M., Pelallo-Martínez, N., Díaz-Barriga, F., Rothenberg, S. J., Hernández-Cadena, L., Faugeron, S., Oropeza-Hernández, L. F., Guaderrama-Díaz, M., & Quintanilla-Vega, B. (2012). Environmental polycyclic aromatic hydrocarbon (PAH) exposure and DNA damage in Mexican children. *Mutation Research - Genetic Toxicology and Environmental Mutagenesis*, *742*(1–2), 66–71. https://doi.org/10.1016/j.mrgentox.2011.12.006

Setayesh, T., Nersesyan, A., Mišík, M., Ferk, F., Langie, S., Andrade, V. M., Haslberger, A., & Knasmüller, S. (2018). Impact of obesity and overweight on DNA stability: Few facts and many hypotheses. In *Mutation Research - Reviews in Mutation Research* (Vol. 777, pp. 64–91). https://doi.org/10.1016/j.mrrev.2018.07.001

Shahsavani, S., Dehghani, M., Hoseini, M., & Fararouei, M. (2017). Biological monitoring of urinary 1-hydroxypyrene by PAHs exposure among primary school students in Shiraz, Iran. *International Archives of Occupational and Environmental Health*, *90*(2), 179–187. https://doi.org/10.1007/s00420-016-1184-9

Shankar, K., & Mehendale, H. M. (2014). Cytochrome P450. *Encyclopedia of Toxicology: Third Edition*, 1125–1127. https://doi.org/10.1016/B978-0-12-386454-3.00299-2

Sharma, A., Pandey, A., Sardana, S., Ashok, S., & Sharma, J. K. (2012). Genetic polymorphisms of GSTM1 and GSTT1 genes in Delhi and comparison with other Indian and global populations. *Asian Pacific Journal of Cancer Prevention*, *13*(11), 5647–5652. https://doi.org/10.7314/APJCP.2012.13.11.5647

Shen, G., Chen, Y., Du, W., Lin, N., Wang, X., Cheng, H., Liu, J., Xue, C., Liu, G., Zeng, E. Y., Xing, B., & Tao, S. (2016). Exposure and size distribution of nitrated and oxygenated polycyclic aromatic hydrocarbons among the population using different household fuels. *Environmental Pollution*, *216*, 935–942. https://doi.org/10.1016/J.ENVPOL.2016.07.002

Silva, C. S. D., Rossato, J. M., Vaz Rocha, J. A., & Vargas, V. M. F. (2015). Characterization of an area of reference for inhalable particulate matter (PM2.5)

associated with genetic biomonitoring in children. *Mutation Research - Genetic Toxicology and Environmental Mutagenesis*, *778*, 44–55. https://doi.org/10.1016/j.mrgentox.2014.11.006

Slezakova, K., Oliveira, M., Madureira, J., Fernandes, E. de O., Delerue-Matos, C., Morais, S., & Pereira, M. do C. (2017). Polycyclic aromatic hydrocarbons (PAH) in Portuguese educational settings: a comparison between preschools and elementary schools. *Journal of Toxicology and Environmental Health - Part A: Current Issues*, *80*(13–15), 630–640. https://doi.org/10.1080/15287394.2017.1286931

Sochacka-Tatara, E., Majewska, R., Perera, F. P., Camann, D., Spengler, J., Wheelock, K., Sowa, A., Jacek, R., Mróz, E., & Pac, A. (2018). Urinary polycyclic aromatic hydrocarbon metabolites among 3-year-old children from Krakow, Poland. *Environmental Research*, *164*, 212–220. https://doi.org/10.1016/J.ENVRES.2018.02.032

Sofia, D., Gioiella, F., Lotrecchiano, N., & Giuliano, A. (2020). Mitigation strategies for reducing air pollution. *Environmental Science and Pollution Research 2020 27:16*, *27*(16), 19226–19235. https://doi.org/10.1007/S11356-020-08647-X

Sopian, N. A., Jalaludin, J., Bakar, S. A., Hamedon, T. R., & Latif, M. T. (2021). Exposure to particulate PAHs on potential genotoxicity and cancer risk among school children living near the petrochemical industry. *International Journal of Environmental Research and Public Health*, *18*(5), 1–21. https://doi.org/10.3390/ijerph18052575

Sreeja, L., Syamala, V., Hariharan, S., Madhavan, J., Devan, S. C., & Ankathil, R. (2005). Possible risk modification by CYP1A1, GSTM1 and GSTT1 gene polymorphisms in lung cancer susceptibility in a South Indian population. *Journal of Human Genetics 2005 50:12*, *50*(12), 618–627. https://doi.org/10.1007/s10038-005-0303-3

Srithawirat, T., Latif, M. T., & Sulaiman, F. R. (2016). Indoor PM10 and its heavy metal composition at a roadside residential environment, Phitsanulok, Thailand. *Atmósfera*, *29*(4), 311–322. https://doi.org/10.20937/ATM.2016.29.04.03

Stading, R., Gastelum, G., Chu, C., Jiang, W., & Moorthy, B. (2021). Molecular mechanisms of pulmonary carcinogenesis by polycyclic aromatic hydrocarbons (PAHs): Implications for human lung cancer. *Seminars in Cancer Biology*. https://doi.org/10.1016/J.SEMCANCER.2021.07.001

Suhaimi, N. F., & Jalaludin, J. (2015). Biomarker as a research tool in linking exposure to air particles and respiratory health. *BioMed Research International*, *2015*. https://doi.org/10.1155/2015/962853

Suhaimi, N. F., Jalaludin, J., & Bakar, S. A. (2021). The influence of Traffic-Related Air Pollution (TRAP) in primary schools and residential proximity to traffic sources on Histone H3 level in selected Malaysian children. *International Journal of Environmental Research and Public Health*, *18*(15), 7995.

https://doi.org/10.3390/IJERPH18157995

Suk, W. A., Murray, K., & Avakian, M. D. (2003). Environmental hazards to children's health in the modern world. *Mutation Research/Reviews in Mutation Research*, *544*(2–3), 235–242. https://doi.org/10.1016/J.MRREV.2003.06.007

Sulong, N. A., Latif, M. T., Sahani, M., Khan, M. F., Fadzil, M. F., Tahir, N. M., Mohamad, N., Sakai, N., Fujii, Y., Othman, M., & Tohno, S. (2019). Distribution, sources and potential health risks of polycyclic aromatic hydrocarbons (PAHs) in PM2.5 collected during different monsoon seasons and haze episode in Kuala Lumpur. *Chemosphere*, *219*, 1–14. https://doi.org/10.1016/j.chemosphere.2018.11.195

Suradi, H., Khan, M. F., Sairi, N. A., Rahim, H. A., Yusoff, S., Fujii, Y., Qin, K., Bari, M. A., Othman, M., & Latif, M. T. (2021). Ambient levels, emission sources and health effect of pm2.5-bound carbonaceous particles and polycyclic aromatic hydrocarbons in the city of Kuala Lumpur, Malaysia. *Atmosphere*, *12*(5), 549. https://doi.org/10.3390/atmos12050549

Tarafdar, A., Oh, M.-J., Nguyen-Phuong, Q., & Kwon, J.-H. (2019). Profiling and potential cancer risk assessment on children exposed to PAHs in playground dust/soil: a comparative study on poured rubber surfaced and classical soil playgrounds in Seoul. *Environmental Geochemistry and Health 2019 42:6*, *42*(6), 1691–1704. https://doi.org/10.1007/S10653-019-00334-2

Terzaghi, E., De Nicola, F., Cerabolini, B. E. L., Posada-Baquero, R., Ortega-Calvo, J. J., & Di Guardo, A. (2020). Role of photo- and biodegradation of two PAHs on leaves: Modelling the impact on air quality ecosystem services provided by urban trees. *Science of The Total Environment*, *739*, 139893. https://doi.org/10.1016/J.SCITOTENV.2020.139893

Thai, P. K., Heffernan, A. L., Toms, L. M. L., Li, Z., Calafat, A. M., Hobson, P., Broomhall, S., & Mueller, J. F. (2016). Monitoring exposure to polycyclic aromatic hydrocarbons in an Australian population using pooled urine samples. *Environment International*, *88*, 30–35. https://doi.org/10.1016/J.ENVINT.2015.11.019

Tobiszewski, M., & Namieśnik, J. (2012). PAH diagnostic ratios for the identification of pollution emission sources. *Environmental Pollution*, *162*, 110–119. https://doi.org/10.1016/J.ENVPOL.2011.10.025

Tong, Z., Baldauf, R. W., Isakov, V., Deshmukh, P., & Max Zhang, K. (2016). Roadside vegetation barrier designs to mitigate near-road air pollution impacts. *Science of The Total Environment*, *541*, 920–927. https://doi.org/10.1016/J.SCITOTENV.2015.09.067

Trasande, L., Urbina, E. M., Khoder, M., Alghamdi, M., Shabaj, I., Alam, M. S., Harrison, R. M., & Shamy, M. (2015). Polycyclic aromatic hydrocarbons, brachial artery distensibility and blood pressure among children residing near an oil refinery. *Environmental Research*, *136*, 133–140.

https://doi.org/10.1016/j.envres.2014.08.038

Tuntawiroon, J., Mahidol, C., Navasumrit, P., Autrup, H., & Ruchirawat, M. (2007). Increased health risk in Bangkok children exposed to polycyclic aromatic hydrocarbons from traffic-related sources. *Carcinogenesis*, *28*(4), 816–822. https://doi.org/10.1093/carcin/bgl175

United Nation. (2018). *World Urbanization Prospects The 2018 Revision*.

Urbancova, K., Dvorakova, D., Gramblicka, T., Sram, R. J., Hajslova, J., & Pulkrabova, J. (2020). Comparison of polycyclic aromatic hydrocarbon metabolite concentrations in urine of mothers and their newborns. *Science of The Total Environment*, *723*, 138116. https://doi.org/10.1016/J.SCITOTENV.2020.138116

Urbancova, K., Lankova, D., Rossner, P., Rossnerova, A., Svecova, V., Tomaniova, M., Veleminsky, M., Sram, R. J., Hajslova, J., & Pulkrabova, J. (2017). Evaluation of 11 polycyclic aromatic hydrocarbon metabolites in urine of Czech mothers and newborns. *Science of The Total Environment*, *577*, 212–219. https://doi.org/10.1016/J.SCITOTENV.2016.10.165

US EPA. (2011). *Exposure Factors Handbook Chapter 6 | US EPA*. https://www.epa.gov/expobox/exposure-factors-handbook-chapter-6

US EPA. (2015). *Best Practices for Reducing Near-Road Pollution Exposure at Schools*. https://scholarassoc.org/wp-content/uploads/2017/05/Best-Practices-for-Reducing-Near-Road-Pollution-Exposure-at-Schools-2015.pdf

USEPA. (2004). *Application of Biomarkers to Environmental Health and Risk Assessment (2004)*. https://cfpub.epa.gov/ncer_abstracts/index.cfm/fuseaction/display.rfatext/rfa_id/376

USEPA. (2005). *Environmental Protection Agency. Guidelines for carcinogen risk assessment. March*. http://www.epa.gov/sites/production/files/2013-09/documents/cancer_guidelines_final_3-25-05.pdf

USEPA. (2008). *Polycyclic aromatic hydrocarbons (PAHs) Fact Sheet*. 495. https://doi.org/10.1007/978-94-017-8801-4_25

USEPA. (2021). *Particulate Matter (PM) Basics | US EPA*. https://www.epa.gov/pm-pollution/particulate-matter-pm-basics

Valavanidis, A, Vlachogianni, T., Fiotakis, K., & Loridas, S. (2013). 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*, *10*(9), 3886. https://doi.org/10.3390/IJERPH10093886

Valavanidis, Athanasios, Fiotakis, K., & Vlachogianni, T. (2008). Airborne particulate matter and human health: Toxicological assessment and importance of size and

composition of particles for oxidative damage and carcinogenic mechanisms. In *Journal of Environmental Science and Health - Part C Environmental Carcinogenesis and Ecotoxicology Reviews* (Vol. 26, Issue 4, pp. 339–362). https://doi.org/10.1080/10590500802494538

van Drooge, B. L., Rivas, I., Querol, X., Sunyer, J., & Grimalt, J. O. (2020). Organic air quality markers of indoor and outdoor pm2.5 aerosols in primary schools from barcelona. *International Journal of Environmental Research and Public Health*, *17*(10). https://doi.org/10.3390/ijerph17103685

Venkataraman, C., Lyons, J. M., & Friedlander, S. K. (1994). Size distributions of polycyclic aromatic hydrocarbons and elemental carbon. 1. Sampling, measurement methods, and source characterization. *Environmental Science and Technology*, *28*(4), 555–562. https://doi.org/10.1021/ES00053A005

Vergara, A. G., Watson, C. J. W., Chen, G., & Lazarus, P. (2020). UDP-glycosyltransferase 3A metabolism of polycyclic aromatic hydrocarbons: Potential importance in aerodigestive tract tissues. *Drug Metabolism and Disposition*, *48*(3), 160–168. https://doi.org/10.1124/DMD.119.089284/-/DC1

Villarini, M., Moretti, M., Fatigoni, C., Agea, E., Dominici, L., Mattioli, A., Volpi, R., & Pasquini, R. (2008). Evaluation of primary DNA damage, cytogenetic biomarkers and genetic polymorphisms for CYP1A1 and GSTM1 in road tunnel construction workers. *Journal of Toxicology and Environmental Health, Part A*, *71*(21), 1430–1439. https://doi.org/10.1080/15287390802328580

Vineis, P., Kogevinas, M., Simonato, L., Brennan, P., & Boffetta, P. (2000). Levelling-off of the risk of lung and bladder cancer in heavy smokers: an analysis based on multicentric case-control studies and a metabolic interpretation. *Mutation Research*, *463*, 103–110. https://doi.org/10.1016/S1383-5742(00)00002-8

Vornanen-Winqvist, C., Salonen, H., Järvi, K., Andersson, M. A., Mikkola, R., Marik, T., Kredics, L., & Kurnitski, J. (2018). Effects of ventilation improvement on measured and perceived indoor air quality in a school building with a hybrid ventilation system. *International Journal of Environmental Research and Public Health*, *15*(7). https://doi.org/10.3390/IJERPH15071414

Wan Rashidi, W. N., & Bakar, S. A. (2019). Glutathione S-transferase: An overview on distribution of GSTM1 and GSTT1 polymorphisms in Malaysian and other populations. *Malaysian Journal of Medicine and Health Sciences*, *15*(July), 85–95.

Wang, G., Jiang, R., Zhao, Z., & Song, W. (2013). Effects of ozone and fine particulate matter (PM2.5) on rat system inflammation and cardiac function. *Toxicology Letters*, *217*(1), 23–33. https://doi.org/10.1016/J.TOXLET.2012.11.009

Wang, I. J., Karmaus, W. J. J., & Yang, C. C. (2017). Polycyclic aromatic hydrocarbons exposure, oxidative stress, and asthma in children. *International Archives of Occupational and Environmental Health*, *90*(3), 297–303. https://doi.org/10.1007/s00420-017-1198-y

Wang, J., Guinot, B., Dong, Z., Li, X., Xu, H., Xiao, S., Ho, S. S. H., Liu, S., & Cao, J. (2017). PM2.5-bound polycyclic aromatic hydrocarbons (PAHs), Oxygenated-PAHs and Phthalate esters (PAEs) inside and outside middle school classrooms in Xi'an, China: Concentration, characteristics and health risk assessment. *Aerosol and Air Quality Research*, *17*(7), 1811–1824. https://doi.org/10.4209/AAQR.2017.03.0109

Wang, J., Xu, H., Guinot, B., Li, L., Ho, S. S. H., Liu, S., Li, X., & Cao, J. (2017). Concentrations, sources and health effects of parent, oxygenated- and nitrated-polycyclic aromatic hydrocarbons (PAHs) in middle-school air in Xi'an, China. *Atmospheric Research*, *192*, 1–10. https://doi.org/10.1016/J.ATMOSRES.2017.03.006

Wang, M., Jia, S., Lee, S. H., Chow, A., & Fang, M. (2021). Polycyclic aromatic hydrocarbons (PAHs) in indoor environments are still imposing carcinogenic risk. *Journal of Hazardous Materials*, *409*, 124531. https://doi.org/10.1016/j.jhazmat.2020.124531

Wang, Q., Dong, Z., Guo, Y., Yu, F., Zhang, Z., & Zhang, R. (2020). Characterization of PM 2.5-bound polycyclic aromatic hydrocarbons at two central China cities: Seasonal variation, sources, and health risk assessment. *Archives of Environmental Contamination and Toxicology*, *78*(1), 20–33. https://doi.org/10.1007/S00244-019-00671-4

Wang, W., Ding, X., Turap, Y., Tursun, Y., Abulizi, A., Wang, X., Shao, L., Talifu, D., An, J., Zhang, X., Zhang, Y., & Liu, H. (2020). Distribution, sources, risks, and vitro DNA oxidative damage of PM2.5-bound atmospheric polycyclic aromatic hydrocarbons in Urumqi, NW China. *Science of the Total Environment*, *739*, 139518. https://doi.org/10.1016/j.scitotenv.2020.139518

WHO. (2006). WHO's global air-quality guidelines. *The Lancet*, *368*(9544), 1302. https://doi.org/10.1016/S0140-6736(06)69530-5

WHO. (2010). *Guidelines for Indoor Air Quality: Selected Pollutants*. https://www.euro.who.int/__data/assets/pdf_file/0009/128169/e94535.pdf

Wilhelm, M., Eberwein, G., Hölzer, J., Gladtke, D., Angerer, J., Marczynski, B., Behrendt, H., Ring, J., Sugiri, D., & Ranft, U. (2007). Influence of industrial sources on children's health - Hot spot studies in North Rhine Westphalia, Germany. *International Journal of Hygiene and Environmental Health*, *210*(5), 591–599. https://doi.org/10.1016/j.ijheh.2007.02.007

Wong, L. P., Alias, H., Aghamohammadi, N., Ghadimi, A., & Sulaiman, N. M. N. (2017). Control measures and health effects of air pollution: A survey among public transportation commuters in malaysia. *Sustainability (Switzerland)*, *9*(9), 1616. https://doi.org/10.3390/su9091616

World Health Organization. (1993). Biomarkers and risk assessment: concepts and principles. Environmental Health Criteria 155. *Environmental Health Criteria*, *155*, 82.

http://www.inchem.org/documents/ehc/ehc/ehc155.htm#SectionNumber:1.1

World Health Organization. (1996). *Biological monitoring of chemical exposure in the workplace: Guidelines.* (Vol. 1). http://apps.who.int/iris/bitstream/10665/41856/1/WHO_HPR_OCH_96.1.pdf

Wu, Y., Salamova, A., & Venier, M. (2021). Using diagnostic ratios to characterize sources of polycyclic aromatic hydrocarbons in the Great Lakes atmosphere. *Science of The Total Environment*, *761*, 143240. https://doi.org/10.1016/J.SCITOTENV.2020.143240

Xie, S., Luo, C., Shan, X., Zhao, S., He, J., & Cai, Z. (2016). CYP1A1 MspI polymorphism and the risk of oral squamous cell carcinoma: Evidence from a meta-analysis. *Molecular and Clinical Oncology*, *4*(4), 660–666. https://doi.org/10.3892/MCO.2016.768

Xing, Y.-F., Xu, Y.-H., Shi, M.-H., & Lian, Y.-X. (2016). The impact of PM2.5 on the human respiratory system. *Journal of Thoracic Disease*, *8*(1), E69. https://doi.org/10.3978/J.ISSN.2072-1439.2016.01.19

Yang, L., Hou, X.-Y., Wei, Y., Thai, P., & Chai, F. (2017). Biomarkers of the health outcomes associated with ambient particulate matter exposure. *Science of the Total Environment*, *579*, 1446–1459. https://doi.org/10.1016/j.scitotenv.2016.11.146

Yang, M., Jang, J. Y., Kim, S., Lee, S. M., Chang, S. S., Cheong, H. K., Lee, E., Kang, D., Kim, H., Kawamoto, T., & Doo Shin, H. (2003). Genetic effects on urinary 1-hydroxypyrene levels in a Korean population. *Carcinogenesis*, *24*(6), 1085–1089. https://doi.org/10.1093/CARCIN/BGG054

Yang Razali, N. Y., Latif, M. T., Dominick, D., Mohamad, N., Sulaiman, F. R., & Srithawirat, T. (2015). Concentration of particulate matter, CO and CO2 in selected schools inMalaysia. *Building and Environment*, *87*, 108–116. https://doi.org/10.1016/j.buildenv.2015.01.015

Yu, Yingxin, Peng, M., Liu, Y., Ma, J., Wang, N., Ma, S., Feng, N., & Lu, S. (2021). Co-exposure to polycyclic aromatic hydrocarbons and phthalates and their associations with oxidative stress damage in school children from South China. *Journal of Hazardous Materials*, *401*, 123390. https://doi.org/10.1016/j.jhazmat.2020.123390

Yu, Yunjiang, Wang, Q., Li, L., Liu, Z., Sun, P., Zhang, Y., Lin, H., Xiang, M., Li, H., & Lin, B. (2016). Particle-associated ambient benzo[a]pyrene and levels of urinary 1-hydroxypyrene in a non-occupationally exposed population of adults and children in Lanzhou, China. *Bulletin of Environmental Contamination and Toxicology*, *96*. https://doi.org/10.1007/s00128-016-1741-7

Yuan, T. H., Shie, R. H., Chin, Y. Y., & Chan, C. C. (2015). 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*, *136*, 219–226. https://doi.org/10.1016/J.ENVRES.2014.10.007

Yunker, M. B., Macdonald, R. W., Vingarzan, R., Mitchell, R. H., Goyette, D., & Sylvestre, S. (2002). PAHs in the Fraser River basin: a critical appraisal of PAH ratios as indicators of PAH source and composition. *Organic Geochemistry*, *33*(4), 489–515. https://doi.org/10.1016/S0146-6380(02)00002-5

Zając, J., Gomółka, E., & Szot, W. (2018). Urinary 1-hydroxypyrene in occupationally-exposed and non-exposed individuals in Silesia, Poland. *Annals of Agricultural and Environmental Medicine*, *25*(4), 625–629. https://doi.org/10.26444/aaem/75940

Zaki, S. A., Azid, N. S., Shahidan, M. F., Hassan, M. Z., Md Daud, M. Y., Abu Bakar, N. A., Ali, M. S. M., & Yakub, F. (2020). Analysis of urban morphological effect on the microclimate of the urban residential area of Kampung Baru in Kuala Lumpur using a geospatial approach. *Sustainability 2020, Vol. 12, Page 7301*, *12*(18), 7301. https://doi.org/10.3390/SU12187301

Zalata, A., Yahia, S., El-Bakary, A., & Elsheikha, H. M. (2007). Increased DNA damage in children caused by passive smoking as assessed by comet assay and oxidative stress. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis*, *629*(2), 140–147. https://doi.org/10.1016/J.MRGENTOX.2007.02.001

Zani, C., Ceretti, E., Zerbini, I., Viola, G. C. V., Donato, F., Gelatti, U., & Feretti, D. (2020). Comet test in saliva leukocytes of pre-school children exposed to air pollution in North Italy: The respira study. *International Journal of Environmental Research and Public Health*, *17*(9). https://doi.org/10.3390/ijerph17093276

Zare Jeddi, M., Hopf, N. B., Viegas, S., Price, A. B., Paini, A., van Thriel, C., Benfenati, E., Ndaw, S., Bessems, J., Behnisch, P. A., Leng, G., Duca, R. C., Verhagen, H., Cubadda, F., Brennan, L., Ali, I., David, A., Mustieles, V., Fernandez, M. F., … Pasanen-Kase, R. (2021). Towards a systematic use of effect biomarkers in population and occupational biomonitoring. *Environment International*, *146*, 106257. https://doi.org/10.1016/J.ENVINT.2020.106257

Zare, M., Shahtaheri, S. J., Mehdipur, P., Abedinejad, M., & Zare, S. (2013). The influence of CYP1A1 and GSTM1 polymorphism on the concentration of urinary 1-hydroxypyrene in cPAHs exposed Iranian anode plant workers. *Molecular & Cellular Toxicology 2013 9:3*, *9*(3), 303–309. https://doi.org/10.1007/S13273-013-0038-8

Zhang, Li, Jin, Y., Huang, M., & Penning, T. M. (2012). The role of human aldo-keto reductases in the metabolic activation and detoxication of polycyclic aromatic hydrocarbons: Interconversion of PAH catechols and PAH o-quinones. *Frontiers in Pharmacology*, *3 NOV*(February 2014). https://doi.org/10.3389/fphar.2012.00193

Zhang, Lulu, Morisaki, H., Wei, Y., Li, Z., Yang, L., Zhou, Q., Zhang, X., Xing, W., Hu, M., Shima, M., Toriba, A., Hayakawa, K., & Tang, N. (2019). Characteristics of air pollutants inside and outside a primary school classroom in Beijing and respiratory health impact on children. *Environmental Pollution*, *255*, 113147. https://doi.org/10.1016/J.ENVPOL.2019.113147

Zhang, W., Zhang, S., Wan, C., Yue, D., Ye, Y., & Wang, X. (2008). Source diagnostics of polycyclic aromatic hydrocarbons in urban road runoff, dust, rain and canopy throughfall. *Environmental Pollution*, *153*(3), 594–601. https://doi.org/10.1016/J.ENVPOL.2007.09.004

Zhao, B., Lee, E. J. D., Wong, J. Y. Y., Yeoh, P. N., & Gong, N. H. (1995). Frequency of mutant CYP1A1, NAT2 and GSTM1 alleles in normal indians and malays. *Pharmacogenetics*, *5*(5), 275–280. https://doi.org/10.1097/00008571-199510000-00002

Zuurbier, M., Hoek, G., Oldenwening, M., Lenters, V., Meliefste, K., van den Hazel, P., & Brunekreef, B. (2010). Commuters' Exposure to Particulate Matter Air Pollution Is Affected by Mode of Transport, Fuel Type, and Route. *Environmental Health Perspectives*, *118*(6), 783–789. https://doi.org/10.1289/EHP.0901622