**UNIVERSITI PUTRA MALAYSIA**

# *INFLUENCE OF TRAFFIC-RELATED AIR POLLUTION EXPOSURE ON RESPIRATORY HEALTH, TNFa AND CYP1A1 GENE AND HISTONE MODIFICATIONS AMONG SCHOOL CHILDREN IN THE KLANG VALLEY, MALAYSIA*

**NUR FASEEHA BINTI SUHAIMI**

**FPSK(p) 2021 14**

**INFLUENCE OF TRAFFIC-RELATED AIR POLLUTION EXPOSURE ON RESPIRATORY HEALTH, *TNFα* AND *CYP1A1* GENE AND HISTONE MODIFICATIONS AMONG SCHOOL CHILDREN IN THE KLANG VALLEY, MALAYSIA**

By

**NUR FASEEHA BINTI SUHAIMI**

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

**June 2021**

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Doctor of Philosophy

# INFLUENCE OF TRAFFIC-RELATED AIR POLLUTION EXPOSURE ON RESPIRATORY HEALTH, *TNFα* AND *CYP1A1* GENE AND HISTONE MODIFICATIONS AMONG SCHOOL CHILDREN IN THE KLANG VALLEY, MALAYSIA

By

**NUR FASEEHA BINTI SUHAIMI**

**June 2021**

**Chair: Juliana Jalaludin, PhD**
**Faculty: Medicine and Health Sciences**

Traffic-related air pollution (TRAP) is a complex mixture of many pollutants, which has adverse health impacts, especially on children who live near heavily-travelled roads. This cross-sectional comparative study was conducted at eight schools in high traffic (HT) and low traffic (LT) areas to investigate the potential risks from TRAP exposure to respiratory health among children with the incorporation of histone H3 level and deoxyribonucleic acid methylation (DNAm) status of *Tumour Necrosis Factor Alpha (TNFα)* and *Cytochrome P450 Family 1 Subfamily A Member 1 (CYP1A1)*. Respondents' background information, personal exposure to TRAP, and respiratory symptoms were obtained from validated questionnaires distributed to randomly selected 7 to 11-year-old children to be filled in by parents or guardians. Portable instruments equipped with integrated sensors for real-time monitoring were used for 6-h measurements of coarse particulate matter ($PM_{10}$), fine particulate matter ($PM_{2.5}$), extremely fine particulate matter ($PM_1$), nitrogen dioxide ($NO_2$), sulphur dioxide ($SO_2$), ozone ($O_3$), carbon monoxide (CO), and total volatile organic compounds (TVOC). Meanwhile, 24-h measurements of $PM_{2.5}$-bound black carbon (BC) in schools and particulate matters in residences were performed using air sampling pumps that utilise the gravimetric method. Data from local air quality monitoring stations were also compared to validate the school findings and proceeded with Principal Component Analysis (PCA) to identify pollution sources. A lung function test was conducted using a spirometer to measure lung performance. Histone H3 modification was captured using an enzyme-linked immunosorbent assay (ELISA) kit, whereas DNAm was quantified using a methylation-specific polymerase chain reaction (MS-PCR) kit on bisulphite-treated DNA; both from saliva samples. The results indicate that HT area had significantly higher concentrations of $PM_{10}$ ($p$<0.001), $PM_{2.5}$ ($p$<0.001), $PM_1$ ($p$<0.001), BC ($p$<0.001), $NO_2$ ($p$<0.001), $SO_2$ ($p$<0.001), $O_3$ ($p$<0.001), CO ($p$<0.001) and TVOC ($p$<0.001) than LT area. The PCA results highlighted that the air quality in the HT area had been affected by the combustion of fuel engines. Children who attended schools in the HT area were more prone to get cough (OR=3.0), phlegm (OR=2.3), wheezing (OR=2.3), impairment in forced vital capacity (FVC%)($z$= -5.23), impairment in forced expiratory volume in 1 second ($FEV_1$%)($z$= -5.01), higher histone H3 level ($z$= -5.13), methylated *TNFα* (OR=2.0) and methylated *CYP1A1* (OR=1.7). After controlling the possible confounders, findings from multiple logistic regression show that methylated *TNFα* and *CYP1A1* were mostly influenced by exposure to $NO_2$ (OR=3.0) and BC (OR=2.0), respectively. Meanwhile, results from multiple linear regression revealed that BC and $NO_2$ were the most significant factors influencing the FVC% (adjusted $R^2$=0.405, $p$<0.001, $f^2$=0.68) among children. $FEV_1$% were mostly influenced by BC, $PM_1$ and $PM_{2.5}$ (adjusted $R^2$=0.412, $p$<0.001, $f^2$=0.70), whereas $NO_2$ was the most significant factor that influenced the histone H3 level (adjusted $R^2$=0.337, $p$<0.001, $f^2$=0.51) among children. In conclusion, epigenetic mechanisms may govern the relationships between TRAP exposures and respiratory health by acting as mediators. This study also provides the groundwork for future preventive interventions, particularly developing mitigation plans to reduce TRAP exposure in Malaysia.

Keywords: TRAP, children, epigenetic modifications, respiratory health.

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

**PENGARUH PENDEDAHAN KEPADA PENCEMARAN UDARA BERKAITAN TRAFIK KE ATAS KESIHATAN RESPIRATORI, MODIFIKASI HISTON DAN GEN *TNFα* DAN *CYP1A1* DALAM KALANGAN KANAK-KANAK SEKOLAH DI LEMBAH KLANG, MALAYSIA**

Oleh

**NUR FASEEHA BINTI SUHAIMI**

**Jun 2021**

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

Pencemaran Udara Berkaitan Trafik (TRAP) merupakan campuran kompleks beberapa pencemar yang boleh mengakibatkan kesan kesihatan yang buruk, terutamanya terhadap kanak-kanak yang tinggal berhampiran jalan yang sibuk. Kajian perbandingan keratan rentas ini dijalankan di lapan sekolah di kawasan trafik tinggi (HT) dan trafik rendah (LT) untuk menentukan potensi risiko pendedahan TRAP terhadap kesihatan pernafasan dalam kalangan kanak-kanak dengan penggabungan paras histon H3 dan status pemetilan asid deoksiribonukleik (DNAm) *Tumour Necrosis Factor Alpha (TNFα)* dan *Cytochrome P450 Family 1 Subfamily A Member 1 (CYP1A1)*. Maklumat latar belakang responden, pendedahan peribadi terhadap TRAP dan gejala pernafasan telah diperoleh daripada soal selidik yang diedarkan kepada kanak-kanak berusia 7 hingga 11 tahun yang dipilih secara rawak untuk diisi oleh ibu bapa atau penjaga. Instrumen mudah alih yang dilengkapkan dengan sensor bersepadu untuk pemantauan masa nyata digunakan untuk pengukuran bahan zarahan terampai ($PM_{10}$), bahan zarahan halus ($PM_{2.5}$), bahan zarahan sangat halus ($PM_1$), nitrogen dioksida ($NO_2$), sulfur dioksida ($SO_2$), ozon ($O_3$), karbon monoksida (CO), dan sebatian organik meruap sepenuhnya (TVOC) selama 6 jam. Sementara itu, pengukuran karbon hitam (BC) pada $PM_{2.5}$ di sekolah, dan bahan zarahan di kediaman dijalankan dengan menggunakan pam pensampelan udara yang menggunakan kaedah gravimetrik. Data dari stesen pemantauan kualiti udara tempatan telah dibandingkan untuk mengesahkan hasil penemuan di sekolah. Analisis Komponen Utama (PCA) telah digunakan untuk mengenal pasti punca pencemaran. Ujian fungsi paru-paru dilakukan dengan menggunakan spirometer untuk mengukur keupayaan paru-paru. Modifikasi histon H3 telah dikesan menggunakan kit imunosorben berkaitan enzim (ELISA), sementara DNAm telah dikesan dengan menggunakan kit tindak balas berantai polimerase spesifik untuk pemetilan (MS-PCR) pada DNA yang diubah suai dengan bisulfit; kedua-duanya daripada sampel air liur. Hasilnya menunjukkan bahawa kawasan HT mempunyai kepekatan $PM_{10}$ ($p$<0.001), $PM_{2.5}$ ($p$<0.001), $PM_1$ ($p$<0.001), BC ($p$<0.001), $NO_2$ ($p$<0.001), $SO_2$ ($p$<0.001), $O_3$ ($p$<0.001), CO ($p$<0.001) dan TVOC ($p$<0.001) yang jauh lebih tinggi berbanding dengan kawasan LT. Hasil PCA mendapati bahawa kualiti udara di kawasan HT telah dipengaruhi oleh pembakaran enjin bahan api. Kanak-kanak yang bersekolah di kawasan HT lebih mudah mendapat batuk (OR=3.0), kahak (OR=2.3), nafas berdehit (OR=2.3), pengurangan kapasiti vital terpaksa (FVC%) ($z$= -5.23), pengurangan isipadu ekspirasi paksa dalam 1 saat ($FEV_1$%) ($z$= -5.01), paras histon H3 lebih tinggi ($z$= -5.13), pemetilan *TNFα* (OR=2.0) dan pemetilan *CYP1A1* (OR=1.7). Setelah mengawal kemungkinan wujudnya risiko sampingan, penemuan daripada regresi logistik berganda menunjukkan bahawa pemetilan *TNFα* dan *CYP1A1* kebanyakannya dipengaruhi oleh pendedahan terhadap $NO_2$ (OR=3.0) dan BC (OR=2.0). Sementara itu, hasil regresi linear berganda menunjukkan bahawa BC dan $NO_2$ adalah faktor paling signifikan yang mempengaruhi FVC% ($R^2$ diubah=0.405, $p$<0.001, $f^2$=0.68) dalam kalangan kanak-kanak. $FEV_1$% adalah paling dipengaruhi oleh BC, $PM_1$ dan $PM_{2.5}$ ($R^2$ diubah=0.412, $p$<0.001, $f^2$=0.70), manakala $NO_2$ adalah faktor yang paling signifikan yang mempengaruhi paras Histon H3 ($R^2$ diubah=0.337, $p$<0.001, $f^2$=0.51) dalam kalangan kanak-kanak. Secara ringkasnya, mekanisme epigenetik berkemungkinan terlibat dalam hubungan antara pendedahan TRAP dan kesihatan pernafasan dengan bertindak sebagai pengantara. Kajian ini juga menyediakan panduan untuk intervensi pencegahan di masa depan, terutamanya pelan tindakan mitigasi untuk mengurangkan pendedahan kepada TRAP di Malaysia.

Kata Kunci: TRAP, kanak-kanak, perubahan epigenetik, kesihatan pernafasan.

# ACKNOWLEDGEMENTS

In the name of Allah, the Most Gracious and the Most Merciful.

Alhamdulillah, all praises to the Almighty Allah for granting me His blessings in every beat of my heart, good health, and great vitality in completing my PhD journey. I would like to acknowledge and extend my gazillion thanks to many people who had been there with me during the whole process of this research, making it possible for me to complete this research successfully. I am grateful to have had the privilege of contributing to the nation.

I wish to express my profound appreciation to my supervisor, Prof. Dr Juliana Jalaludin, for guiding me in this adventure. She generously granted me time to learn new subjects related to my study and is always available during and after office hours for consultations, despite her busy work schedule. Her significant expertise, supportive advice, continuous encouragement, and productive criticism have shaped me with the right mould in this field. My special gratitude also goes to my co-supervisors, Dr Suhaili Abu Bakar, Dr Nor Eliani Ezani and Prof. Dr Mohd. Talib Latif for sharing their useful knowledge and constructive comments throughout my research venture.

Besides that, I am indebted to these bodies for financial supports; the Ministry of Higher Education Malaysia for the FRGS grant in funding my research project, the Ministry of Higher Education Malaysia and Universiti Putra Malaysia for full scholarships in financing my PhD study. Many thanks are also extended to the Study Leave Section, Registrar Office of UPM, for enormous supports and sponsored workshops during my candidacy.

Furthermore, I appreciate my fellow graduate friends who cannot be all named here. Thank you for making my research journey more enjoyable, supporting me through thick and thin, and inspiring me at all times. Many thanks to Nur Hazirah Hisamuddin, Ernie Syazween Junaidi, Aina Nadirah Yusof, Muhammad Afif Mohd Juhari, Nur Intan Shafiqah Roslan, Nur Ain Danisya Mohd Yusri, Syhidatul Farhana Othman and Faris Syahmi Mohd Shahidin for accompanying me during data collection. Special thanks also go to Dr Nor Ashikin Sopian, Dr Noor Fatihah Mohd Fandi and Dr Noor Haziqah Kamaludin for their assistance in data analysis.

Moreover, I would like to give my most profound appreciation to all dear respondents, their parents and guardians, the school teachers, and the management of primary schools for their willingness and support to engage in this research despite the inconvenience they had experienced.

My sincere gratitude also goes to these laboratory and support staffs for providing me worthy information and excellent assistance while handling the research samples and instruments, also while performing the laboratory works; from the Department of Environmental and Occupational Health, and Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, UPM; from Faculty of Forestry and Environment, UPM; from Faculty of Science and Technology, UKM; from Institute of Oceanography and Environment, UMT.

Last but not least, I am very grateful to my beloved family members who have been very understanding with my commitments, always helping me to look after my daughter, continuously praying to Allah for my success, and continually motivating me throughout my life from the moment I was born; my mother Ms Normayati Sulaiman, my father Mr Suhaimi Hasan, my sister Nur Azeema Suhaimi, my mother-in-law Ms Asiah Idris, and all of my family members. My special gratitude to my supportive husband, Mr Muhammad Fauzi Idris, for his endless love, patience, companionship and motivation throughout this doctoral journey. To my adorable daughter Fauzana Aneesa, you have been an excellent source of love and relief from my scholarly endeavour. To my son and PhD baby Fauzan Ameen, having you during the final year of my PhD journey is a blessing. I love you all to the moon and back.

Not to forget my sincere gratitude to those who contributed either directly or indirectly to complete my research. May Allah rewards all of you.

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)

**Nor Eliani binti Ezani, PhD**
Senior Lecturer
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Member)

**Mohd Talib 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: 14 October 2021

**Declaration by Graduate Student**

I hereby confirm that:

- this thesis is my original work;
- quotations, illustrations and citations have been duly referenced;
- this thesis has not been submitted previously or concurrently for any other degree at any other institutions;
- intellectual property from the thesis and copyright of thesis are fully owned by Universiti Putra Malaysia, as according to the Universiti Putra Malaysia (Research) Rules 2012;
- written permission must be obtained from the supervisor and the office of Deputy Vice-Chancellor (Research and Innovation) before the thesis is published (in the form of written, printed or in electronic form), including books, journals, modules, proceedings, popular writings, seminar papers, manuscripts, posters, reports, lecture notes, learning modules or any other materials as stated in the Universiti Putra Malaysia (Research) Rules 2012;
- there is no plagiarism or data falsification/fabrication in the thesis, and scholarly integrity is upheld as according to the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) and the Universiti Putra Malaysia (Research) Rules 2012. The thesis has undergone plagiarism detection software.

Signature: ____________________________ Date: ____________________

Name and Matric No.: Nur Faseeha binti Suhaimi, GS50755

**Declaration by Members of Supervisory Committee**

This is to confirm that:

- this research conducted and the writing of this thesis was under our supervision;
- the 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: Prof. Dr Juliana binti Jalaludin

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

Signature: ______________________
Name of Member of Supervisory Committee: Dr Nor Eliani binti Ezani

Signature: ______________________
Name of Member of Supervisory Committee: Prof. Dr Mohd. Talib Latif

## TABLE OF CONTENTS


| | | | Page |
|---|---|---|---|
| **ABSTRACT** | | | i |
| ***ABSTRAK*** | | | iii |
| **ACKNOWLEDGEMENTS** | | | v |
| **APPROVAL** | | | vii |
| **DECLARATION** | | | ix |
| **LIST OF TABLES** | | | xv |
| **LIST OF FIGURES** | | | xviii |
| **LIST OF ABBREVIATIONS** | | | xxii |
| **CHAPTER** | | | |
| **1** | **INTRODUCTION** | | 1 |
| | 1.1 | Background | 1 |
| | 1.2 | Problem Statement | 2 |
| | 1.3 | Study Justifications | 4 |
| | 1.4 | Conceptual Framework | 7 |
| | 1.5 | Study Objectives | 9 |
| | | 1.5.1 General Objective | 9 |
| | | 1.5.2 Specific Objectives | 9 |
| | 1.6 | Hypotheses | 9 |
| | 1.7 | Definition of Variables | 10 |
| | | 1.7.1 Conceptual Definitions | 10 |
| | | 1.7.2 Operational Definitions | 13 |
| **2** | **LITERATURE REVIEW** | | 17 |
| | 2.1 | Traffic-Related Air Pollution (TRAP) | 17 |
| | | 2.1.1 TRAP in Klang Valley | 18 |
| | | 2.1.2 Children as A Population at Risk for Exposure to TRAP | 20 |
| | | 2.1.3 Guidelines and Government Policies | 20 |
| | 2.2 | Monitoring Exposure to Air Pollution in Schools and Residences | 22 |
| | 2.3 | Deposition of TRAP in Respiratory System | 28 |
| | 2.4 | Lung Function Test | 29 |
| | | 2.4.1 Interpretation of Lung Function Test | 29 |
| | | 2.4.2 Lung Function Test as An Indicator of Respiratory Health | 30 |
| | 2.5 | Epigenetics | 30 |
| | | 2.5.1 Basics of Histone Modifications and DNA Methylation (DNAm) | 30 |
| | | 2.5.2 Histone H3 Modification | 31 |
| | | 2.5.3 DNA Methylation (DNAm) | 32 |
| | 2.6 | Associations between TRAP and Epigenetic Mechanisms | 32 |

3 **METHODOLOGY** 35
3.1 Study Design 35
3.2 Study Location 35
3.3 Study Sampling 40
3.3.1 Sampling Duration 40
3.3.2 Target Population 40
3.3.3 Sampling Frame 40
3.3.4 Sampling Unit 40
3.3.5 Sampling Method 41
3.3.6 Sample Size 41
3.4 Data Collection and Instrumentations 44
3.4.1 Questionnaires 44
3.4.2 Air Quality 45
3.4.3 Human Samples 53
3.4.4 Statistical Analyses 63
3.4.5 Quality Control 64
3.4.6 Study Ethics 65

4 **RESULTS AND DISCUSSION** 67
4.1 Characteristics of Respondents 67
4.1.1 Response Rate 67
4.1.2 Sociodemographic and Socioeconomic Information 68
4.1.3 House Conditions and Locations 72
4.1.4 Dietary Intake 73
4.2 Air Pollutants 75
4.2.1 Respondents' Daily Activities 75
4.2.2 Respondents' Traffic Exposure at Residences 77
4.2.3 Sources of IAQ in Residences 80
4.2.4 Traffic Counts (TC) in Schools 82
4.2.5 Concentrations of Air Pollutants in Schools 85
4.2.6 Concentrations of Air Pollutants in Residences 109
4.2.7 Indoor/Outdoor (I/O) Ratios 110
4.2.8 Correlations between TRAP Concentrations and Traffic Counts (TC) 111
4.2.9 Associations between Residential TRAP Concentrations and Air Pollutants Sources at Residences 113
4.2.10 The Trend of Air Pollutants in Nearby Continuous Air Quality Monitoring (CAQM) Stations 116
4.2.11 Principal Component Analysis (PCA) of Air Pollutants 124
4.3 Health Impacts 129
4.3.1 Reported Respiratory Symptoms 129
4.3.2 Lung Function Status 131

| | | | |
|---|---|---|---|
| | 4.3.3 | Level of Histone H3 Modification | 134 |
| | 4.3.4 | DNA Methylation (DNAm) Status | 135 |
| 4.4 | Relationships between Air Pollutants and Health Impacts | | 139 |
| | 4.4.1 | Relationships between Respondents' Daily Activities and Health Impacts | 139 |
| | 4.4.2 | Relationships between Children's Mode of Transport to Schools and Health Impacts | 142 |
| | 4.4.3 | Correlations between TRAP Concentrations, Lung Function Status and Histone H3 Level | 144 |
| | 4.4.4 | Relationships between TRAP Concentrations, Reported Respiratory Symptoms and DNAm Status | 145 |
| | 4.4.5 | Relationships between Air Pollutant Sources at Residences and Health Impacts | 149 |
| | 4.4.6 | Relationships between Reported Respiratory Symptoms and Epigenetic Modifications | 155 |
| | 4.4.7 | Relationships between Dietary Intake and Epigenetic Modifications | 156 |
| 4.5 | Multivariate Analyses | | 157 |
| | 4.5.1 | Multiple Logistic Regressions | 157 |
| | 4.5.2 | Multiple Linear Regressions | 160 |
| **5** | **SUMMARY, CONCLUSION, LIMITATIONS AND RECOMMENDATIONS** | | 164 |
| 5.1 | Summary | | 164 |
| | 5.1.1 | Measurements of Indoor TRAP and Physical Parameters | 165 |
| | 5.1.2 | Measurements of Outdoor TRAP and Meteorological Parameters | 165 |
| | 5.1.3 | Measurements of Indoor Particulate Matter in Residences | 166 |
| | 5.1.4 | Indoor/Outdoor (I/O) Ratios | 166 |
| | 5.1.5 | Trends in Nearby CAQM Stations | 167 |
| | 5.1.6 | Principal Component Analysis (PCA) | 167 |
| | 5.1.7 | Reported Respiratory Symptoms | 167 |
| | 5.1.8 | DNA Methylation (DNAm) Status | 167 |
| | 5.1.9 | Lung Function Status | 168 |
| | 5.1.10 | Histone H3 Level | 168 |
| | 5.1.11 | Relationships between TRAP Exposure and Health Impacts | 168 |
| 5.2 | Conclusion | | 169 |
| 5.3 | Limitations | | 170 |
| 5.4 | Recommendations | | 171 |

**REFERENCES** 180
**APPENDICES** 208
**BIODATA OF STUDENT** 232
**LIST OF PUBLICATIONS** 233

## LIST OF TABLES


| Table | | Page |
|---|---|---|
| 2.1 | Previous research on TRAP in Southeast Asia | 17 |
| 2.2 | Previous research on TRAP in Klang Valley | 19 |
| 2.3 | Comparison of ambient air quality guidelines | 21 |
| 2.4 | Relevant government policies | 21 |
| 2.5 | Compilation of measurements of air pollutants by previous research | 23 |
| 2.6 | Previous research that links TRAP with epigenetic mechanisms | 33 |
| 3.1 | List of selected primary schools | 36 |
| 3.2 | Physical characterisation of classrooms in both areas and surrounding local activities | 39 |
| 3.3 | The sample size of each stratum in the HT group | 44 |
| 3.4 | The sample size of each stratum in the LT group | 44 |
| 3.5 | Reference values of lung function test among Malay children (Source: Azizi & Henry, 1994) | 55 |
| 3.6 | Lung function test interpretation (Source: Pellegrino et al., 2005) | 55 |
| 3.7 | The severity of lung function test abnormality (Source: Pellegrino et al., 2005) | 55 |
| 3.8 | Primers for DNAm analysis | 61 |
| 3.9 | Statistical tests involved in this study | 63 |
| 4.1 | Sociodemographic background of respondents | 70 |
| 4.2 | Socioeconomic background of respondents | 71 |
| 4.3 | Household income categories of respondents | 71 |
| 4.4 | Comparison of residential background information | 72 |
| 4.5 | Comparison of dietary intake between both groups | 74 |

| | | |
|---|---|---|
| 4.6 | Comparison of sources of residential IAQ between both groups | 81 |
| 4.7 | Indoor TRAP and physical parameters of selected schools | 86 |
| 4.8 | Outdoor TRAP and meteorological factors of selected schools and nearby CAQM stations | 87 |
| 4.9 | Indoor particulate matter concentrations in residences | 109 |
| 4.10 | Associations between $PM_{10}$ inside residences and air pollutant sources at residences | 114 |
| 4.11 | Associations between $PM_{2.5}$ inside residences and air pollutant sources at residences | 115 |
| 4.12 | The Kaiser-Meyer-Olkin and Bartlett's test result of air monitoring in selected schools | 125 |
| 4.13 | The Kaiser-Meyer-Olkin and Bartlett's test result of nearby CAQM stations | 125 |
| 4.14 | Factor loadings after PCA-varimax rotation of selected schools | 126 |
| 4.15 | Factor loadings after PCA-varimax rotation of nearby CAQM stations | 126 |
| 4.16 | Reported respiratory symptoms among children in each school | 130 |
| 4.17 | Comparison of anthropometry data between two groups of respondents | 131 |
| 4.18 | Comparison of lung function status between two groups of respondents | 132 |
| 4.19 | Comparison of lung function abnormality between two groups of respondents | 133 |
| 4.20 | Lung function abnormality among children in each school | 133 |
| 4.21 | Histone H3 level among children in each school | 135 |
| 4.22 | Comparison of DNAm status between the two groups | 138 |
| 4.23 | DNAm status among children in each school | 138 |
| 4.24 | Hours spent at home according to group | 140 |

| | | |
|---|---|---|
| 4.25 | Associations between hours spent at home on weekdays and health impacts | 140 |
| 4.26 | Associations between hours spent at home on weekends and health impacts | 141 |
| 4.27 | Comparisons between children's mode of transport to schools and health impacts | 142 |
| 4.28 | Associations between children's mode of transport to schools and health impacts | 143 |
| 4.29 | Travel period from children's residences to schools | 143 |
| 4.30 | Associations of TRAP concentrations in schools with reported respiratory symptoms | 146 |
| 4.31 | Associations of TRAP concentrations in schools with DNAm of *TNFα* and *CYP1A1* | 148 |
| 4.32 | Associations between air pollutant sources at residences and reported respiratory symptoms | 150 |
| 4.33 | Associations between air pollutant sources at residences and lung function status | 152 |
| 4.34 | Associations between air pollutant sources at residences and histone H3 level | 153 |
| 4.35 | Associations between air pollutant sources at residences and DNAm status | 154 |
| 4.36 | Associations between reported respiratory symptoms and epigenetic modifications | 155 |
| 4.37 | Associations between dietary intake and epigenetic modifications | 156 |
| 4.38 | Factors that influenced respiratory symptoms among children after controlling the confounders | 158 |
| 4.39 | Factors that influenced DNAm among children after controlling the confounders | 160 |
| 4.40 | Multiple linear regression for the association between TRAP and lung function abnormality among children | 161 |
| 4.41 | Multiple linear regression for the association between $NO_2$ and histone H3 level among children | 163 |
| 5.1 | Mitigation strategies for reducing TRAP exposure at schools in Malaysia | 172 |

# LIST OF FIGURES


| Figure | | Page |
|---|---|---|
| 1.1 | A classroom in a national school in Malaysia | 3 |
| 1.2 | A network of a few mechanisms connecting respiratory health effects and exposure to air pollution | 6 |
| 1.3 | Conceptual framework | 8 |
| 2.1 | Diagrammatic representation of deposition of TRAP in the respiratory system of a child (adapted from Nucleus Medical Media, 2016) | 29 |
| 2.2 | The organisational network of epigenetic components in the cells | 31 |
| 2.3 | Potential mechanisms linking environmental exposures to epigenetic effects (adapted from Baccarelli & Bollati, 2009) | 32 |
| 3.1 | Locations of the selected primary schools | 36 |
| 3.2 | Locations of the selected primary schools and nearby CAQM stations as generated by Google Earth | 37 |
| 3.3 | HT schools and surrounding local environment as generated by Google Earth (a) H1, (b) H2, (c) H3, (d) H4 | 37 |
| 3.4 | LT schools and surrounding local environment as generated by Google Earth (a) L1, (b) L2, (c) L3, (d) L4 | 38 |
| 3.5 | Q-Trak IAQ Monitor | 46 |
| 3.6 | VelociCalc Multifunction Ventilation Meter | 46 |
| 3.7 | The placement of the instruments indoors | 46 |
| 3.8 | DustTrak DRX Aerosol Monitor | 47 |
| 3.9 | Aeroqual Air Quality Monitor | 47 |
| 3.10 | PpbRAE 3000 | 47 |
| 3.11 | The placement of the instruments outdoors | 48 |
| 3.12 | MiniVol Air Sampler | 49 |
| 3.13 | Smoke Stain Reflectometer | 50 |
| 3.14 | Escort Personal Sampling Pump | 51 |

| | | |
|---|---|---|
| 3.15 | Traffic counts in the morning | 52 |
| 3.16 | Traffic counts in the afternoon | 52 |
| 3.17 | Anthropometry measurements | 53 |
| 3.18 | Spirometer | 54 |
| 3.19 | Spirometry test | 54 |
| 3.20 | Collection of saliva samples | 56 |
| 3.21 | One of the steps in ELISA using a multichannel pipette | 57 |
| 3.22 | ELISA samples to be analysed by a microplate reader | 58 |
| 3.23 | Calibration curve of ELISA for histone H3 | 58 |
| 3.24 | MS-PCR setting on a thermal cycler | 62 |
| 3.25 | Set-up for agarose gel electrophoresis | 62 |
| 4.1 | Selection of respondents | 68 |
| 4.2 | Distribution of respondents according to gender and location | 69 |
| 4.3 | Respondents' daily activities on (a) weekdays and (b) weekends | 76 |
| 4.4 | Mode of transportation to school among respondents | 77 |
| 4.5 | Number of respondents who reported (a) <100 vehicles per day around their residences and (b) ≥100 vehicles per day around their residences | 78 |
| 4.6 | Perception of traffic exposure in respondents' residences among (a) HT group and (b) LT group | 79 |
| 4.7 | The average count of passing vehicles per hour in the morning and afternoon | 82 |
| 4.8 | The average count of idling vehicles in the morning and afternoon | 83 |
| 4.9 | The average idling time of vehicles in the morning and afternoon | 84 |
| 4.10 | Daily variations of 24-h indoor and outdoor $PM_{2.5}$ and BC in (a) HT schools and (b) LT schools | 91 |

4.11 Daily variations of 6-h (a) indoor particulate matter in HT schools and (b) outdoor particulate matter in HT schools 93

4.12 Daily variations of 6-h (a) indoor particulate matter in LT schools and (b) outdoor particulate matter in LT schools 94

4.13 Hourly variations of 6-h indoor and outdoor $PM_{10}$ in (a) HT schools and (b) LT schools 96

4.14 Hourly variations of 6-h indoor and outdoor $PM_{2.5}$ in (a) HT schools and (b) LT schools 97

4.15 Hourly variations of 6-h indoor and outdoor $PM_1$ in (a) HT schools and (b) LT schools 98

4.16 Hourly variations of 6-h indoor and outdoor $NO_2$ in (a) HT schools and (b) LT schools 100

4.17 Hourly variations of 6-h indoor and outdoor $SO_2$ in (a) HT schools and (b) LT schools 102

4.18 Hourly variations of 6-h indoor and outdoor $O_3$ in (a) HT schools and (b) LT schools 104

4.19 Hourly variations of 6-h indoor and outdoor TVOC in (a) HT schools and (b) LT schools 106

4.20 Hourly variations of 6-h indoor and outdoor CO in (a) HT schools and (b) LT schools 108

4.21 Comparison of I/O ratio in (a) HT schools and (b) LT schools 110

4.22 Correlations between TRAP concentrations and TC in the morning 112

4.23 Correlations between TRAP concentrations and TC in the afternoon 112

4.24 Pollution rose of (a) $PM_{10}$ and (b) $PM_{2.5}$ in Batu Muda station in 2019 118

4.25 Pollution rose of (a) $NO_2$ and (b) $SO_2$ in Batu Muda station in 2019 119

4.26 Pollution rose of (a) $O_3$ and (b) CO in Batu Muda station in 2019 120

4.27 Pollution rose of (a) $PM_{10}$ and (b) $PM_{2.5}$ in Cheras station in 2019 121

4.28 Pollution rose of (a) $NO_2$ and (b) $SO_2$ in Cheras station in 2019 122

4.29 Pollution rose of (a) $O_3$ and (b) CO in Cheras station in 2019 123

4.30 Scatter plot diagram of standardised residuals and standard predicted value for (a) Batu Muda and (b) Cheras 128

4.31 Reported respiratory symptoms 130

4.32 Expression profile of histone H3 modification between two groups 134

4.33 Detected gel bands after MS-PCR on *TNFα* methylated (120 bp) and unmethylated (120 bp) primers among children from the (a) HT group and (b) LT group 136

4.34 Detected gel bands after MS-PCR on *CYP1A1* methylated (194 bp) and unmethylated (194 bp) primers among children from the (a) HT group and (b) LT group 137

4.35 Correlations between TRAP concentrations, lung function percentage and histone H3 level 144

5.1 The pick-up zone was also the location where the children waited for their parents or guardians after school 174

5.2 There were a few idling vehicles near the location where the children waited for their parents or guardians after school 174

5.3 The layout of a school near a highway that has already applied some of the mitigation strategies 175

5.4 A recommended layout for a new school and other land uses 176

5.5 Signage for road restriction during drop-off and pick-up hours 177

5.6 An example of a metal 'No Idling' signage for the school ground 177

5.7 Wall and vegetation barriers near (a) a residential area and (b) a school compound 178

5.8 A recommended design for roadside vegetation and solid barrier 179

# LIST OF ABBREVIATIONS

| | |
|---|---|
| < | Less than |
| > | More than |
| ≥ | At least |
| % | Per cent |
| °C | Degree Celsius |
| x g | Times gravity |
| µm | Micrometres |
| µg/$m^3$ | Microgram per metre cubic |
| ADT | Average Daily Traffic |
| AM | Traffic counts that passed by the schools from 7 to 8 a.m. |
| AT | Ambient Temperature |
| Alu | Short-interspersed nucleotide element |
| API | Air Pollutant Index |
| ATS | American Thoracic Society |
| BC | Black Carbon |
| bp | Base pair |
| CAQM | Continuous Air Quality Monitoring |
| CI | Confidence Interval |
| CO | Carbon Monoxide |
| $CO_2$ | Carbon Dioxide |
| *CYP1A1* | *Cytochrome P450 Family 1 Subfamily A Member 1* |
| DNA | Deoxyribonucleic Acid |
| DNAm | DNA Methylation |

| | |
|---|---|
| DOE | Department of Environment |
| DOS | Department of Statistics |
| DOSH | Department of Occupational Safety and Health |
| EH | Environmental Health |
| ELISA | Enzyme-Linked Immunosorbent Assay |
| EPA | Environmental Protection Agency |
| $FEV_1$ | Forced Expiratory Volume in 1 Second |
| FMHS | Faculty of Medicine and Health Sciences |
| FVC | Forced Vital Capacity |
| h | hours |
| HT | High Traffic |
| IAQ | Indoor Air Quality |
| I/O | Indoor/Outdoor |
| *IFNγ* | Interferon Gamma |
| IQR | Interquartile Range |
| ISAAC | International Study of Asthma and Allergies in Childhood |
| km | Kilometre |
| L/min | Litre per minute |
| LINE-1 | Long Interspersed Nuclear Element 1 |
| LOS | Level of Severity |
| LT | Low Traffic |
| m | Metre |
| m/s | Metre per second |
| MAAQS | Malaysia Ambient Air Quality Standard |
| MCE | Mixed Cellulose Esters |

| | |
|---|---|
| min | minutes |
| ml | Millilitre |
| MOE | Ministry of Education |
| MOH | Ministry of Health |
| MS-PCR | Methylation Specific Polymerase Chain Reaction |
| ng/µl | Nanogram per microlitre |
| ng/ml | Nanogram per millilitre |
| NIOSH | National Institute for Occupational Safety and Health |
| nm | Nanometre |
| NO | Nitric Oxide |
| $NO_2$ | Nitrogen Dioxide |
| $NO_x$ | Oxides of Nitrogen |
| NF-κB | Nuclear Factor Kappa B Cells |
| $O_2$ | Oxygen |
| $O_3$ | Ozone |
| OD | Optical Density |
| OD/ng | Optical Density/Nanogram |
| OR | Odds Ratio |
| PAH | Poly Aromatic Hydrocarbon |
| PCA | Principal Component Analysis |
| PCR | Polymerase Chain Reaction |
| pg/ml | Picogram per millilitre |
| PM | Traffic counts that passed by the schools from 12.30 to 1.30 p.m. |
| $PM_{10}$ | Particulate matter below 10 micrometres aerodynamic diameter |

| | |
|---|---|
| $PM_{2.5}$ | Particulate matter below 2.5 micrometres aerodynamic diameter |
| $PM_1$ | Particulate matter below 1 micrometre aerodynamic diameter |
| ppb | Parts per billion |
| ppm | Parts per million |
| PVC | Poly Vinyl Chloride |
| RH | Relative Humidity |
| RT | Room Temperature |
| ROS | Reactive Oxygen Species |
| rpm | Revolutions per minute |
| RTVM | Road Traffic Volume Malaysia |
| s | Seconds |
| SD | Standard Deviation |
| $SO_2$ | Sulphur Dioxide |
| SR | Solar Radiation |
| T | Temperature |
| TC | Traffic Counts |
| *TNFα* | *Tumour Necrosis Factor Alpha* |
| TRAP | Traffic-Related Air Pollution |
| TVOC | Total Volatile Organic Compounds |
| UKM | Universiti Kebangsaan Malaysia |
| UMT | Universiti Malaysia Terengganu |
| UPM | Universiti Putra Malaysia |
| URTI | Upper Respiratory Tract Illnesses |
| USA | United States of America |
| US EPA | United States Environmental Protection Agency |

| | |
|---|---|
| UV | Ultraviolet |
| V | Volume |
| Vel | Velocity |
| VIF | Variance Inflation Factor |
| WD | Wind Direction |
| WHO | World Health Organization |
| WS | Wind Speed |

# CHAPTER 1

# INTRODUCTION

## 1.1 Background

In a world where human activities are in full swing, both during the day and at night, air pollution is getting worse, and concerns about the effects of toxins on airways and their correspondence with lung diseases are also increasing. Traffic-generating particulate matter is now known to contribute substantially to ambient particulate matter, particularly in urban areas, and globally it creates a growing burden to us in the form of human disease (Awang, Jalaludin, Latif, & Mohamad Fandi, 2019; Haryanto, 2020; Mohamad Jamil et al., 2020). Apart from that, emissions from road vehicles are some of the most important sources of human exposure to air pollution, which are known to have adverse effects on health (Haryanto & Pratiwi, 2020) with the complex combination of many pollutants. This topic is of pivotal importance in the community. After being exposed to air pollutants, inhalation toxicity within the respiratory system may occur as the respiratory system is physically connected with air pollutants through breathing.

Many countries have taken the necessary steps to combat the adverse effects of particulate matter by implementing more stringent emission controls to reduce emissions from motor vehicles and improve air quality, as awareness of the related health issues has grown in recent years ( Lee, Lin, Yuan, Lin, & Chen, 2018; Sofwan & Latif, 2020; Winkler et al., 2018). Nevertheless, the populations residing and working close to busy roads and highways have increased throughout the years due to the expansion of urban areas and economic improvement. Banks have always provided accessible financing for car ownership, and land-use changes promote dependence on motor vehicles. As a result, a large proportion of the human population spends significant amounts of their time on or near roadways as part of their daily activities (Matz, Stieb, Egyed, Brion, & Johnson, 2018) include experiencing significantly long periods on the road during traffic congestion.

Work considering traffic-related air pollution (TRAP) has a rich background. Previous research have indicated that TRAP is linked to toxicity within the respiratory system in distinct types of studies – *in vitro*, *in vivo*, and epidemiology. TRAP triggers diverse respiratory health effects, generates reactive oxygen species (ROS), which then cause oxidative stress (Kim, Choi, Park, & Seo, 2017). Besides that, significant evidence has been found on the mechanisms which connect TRAP to epigenetic modifications triggered by damage to Deoxyribonucleic Acid (DNA) (Ding et al., 2017; Rider & Carlsten, 2019). Besides, there are studies documented the prevalence of respiratory symptoms in persons who live close to busy roads (Hegseth et al., 2019; Yi et al., 2017).

This study aimed to collect the baseline data on exposure levels of indoor and outdoor air pollutants among school children living in Klang Valley areas with high traffic. Also, to study the precise nature and sources of local air pollution components in those areas, which would be informative in developing tailored risk control strategies. By investigating the exposure to TRAP, risk factors can be recognised and taken into account for further actions to control the respiratory diseases associated with the exposure to air pollutants.

## 1.2 Problem Statement

Traffic congestion is a major problem in Klang Valley, which is a known concern with the community. The fast-growing population mainly causes the problem in Klang Valley in the past ten years (DOS Malaysia, 2019). Traffic and industrial air pollution have long been recognised as the crucial external causes of respiratory problems (Azhari, Latif, & Mohamed, 2018; Sopian, Jalaludin, Tengku Mayusi, & Latif, 2020). The problem of TRAP may be further compounded by the growing vehicle fleet, urban society's dependence and preference for private motorised travel. The growth in the number of private vehicles has resulted in increased emissions.

Malaysia is a tropical country where the weather is humid and warm, with low temperature and humidity variation all year round. The particular apprehension over electricity and operational expenditure has resulted in natural ventilation for all national schools in Malaysia. Moreover, natural ventilation through window openings provides a practical solution to enhance the classrooms' indoor environment. Nevertheless, high concentrations of outdoor air pollutants can also infiltrate the schools' indoor environment via open windows and doors and cracks in the building (Mohammadyan et al., 2017), air exchange rate, and micro-environment (Lv, Wang, Wei, Zhang, & Zhao, 2017). The location of classrooms near the main roads and highways in Malaysia have also contributed to poor air quality in the classrooms. Figure 1.1 shows a typical classroom in national schools in Malaysia. A few local studies pointed that traffic and industrial activity influence the indoor air quality (IAQ) in the classrooms by releasing air pollutants into ambient air, which could penetrate the indoor environment (Kamaruddin, Jalaludin, Hamedon, & Hisamuddin, 2019; Mohd Isa, Hashim, Jalaludin, Lung Than, & Hashim, 2020).


**Figure 1.1: A classroom in a national school in Malaysia**

One of the adverse environmental issues is air pollution generated by road-side exposures in the vicinity of urban localities. Children are vulnerable to air pollutants due to schools and residential complexes located in the urban and sub-urban areas. By 2030, urban areas are expected to accommodate 60% of the world's population, which means that one in every three people will live in cities with at least half a million residents (United Nations, 2016). There is a large crowd of human in cities because government hubs, offices, business parks, education centres and main crossroads of transportations are situated here. Increasing high-rise buildings and population around the area lead to build up of traffic flow, notably during peak hours, which are in the early morning when most people go to work, and in the late evening when most people come back home. According to the recent list of schools under the Ministry of Education Malaysia management, there are 5,895 public schools (57.7%) located in the urban areas of Malaysia out of a total of 10,218 national primary and secondary schools in Malaysia (Ministry of Education Malaysia, 2021). Out of these, 851 schools (90.5%) out of 940 schools are located in the urban areas in Selangor, and 295 schools (100.0%) are located in Kuala Lumpur. By referring to these figures on the schools located in the urban areas, extra attention should be paid to the IAQ of the school buildings, primarily national schools located near heavily-travelled roads.

Air pollutants released by urban air pollution threaten children's respiratory health (Zainudin, Jalaludin, & Sopian, 2019). Although it is a known issue, it has to be highlighted because children inhale a higher volume of air per unit of body weight than adults. Moreover, their body systems and organs are still growing, which means they are less able to detoxify dangerous pollutants. Diseases of the respiratory system have been reported to be the number 2 cause out of 10 leading sources of hospitalisation in both government and private hospitals after pregnancy, childbirth and the puerperium, accounting for 14.8% of cases (MOH Malaysia, 2020). Since specific environmental factors induce respiratory problems, attention, and early intervention to these environmental conditions could greatly reduce school children’s respiratory health effects.

Even though most of the aberrant changes in gene expression linked to the health effects of environmental agents exposure have been associated with genotoxic mechanisms, non-genotoxic mechanisms may also play a part (Ren, Atyah, Chen, & Zhou, 2017). Previous studies conducted on the epigenetic effects induced by environmental agents have revealed global and gene-specific changes of DNA methylation (DNAm) and histone modification level; these changes are similar or equal to the observed epigenetic changes found in patients whose conditions are induced by that particular environmental agent (Sharavanan et al., 2020; Zheng et al., 2017). Epigenetic research is emerging as a new option to decipher the possible consequences of air pollution on DNA because certain epigenetic mechanisms have been associated to diseases. Children’s detoxification enzymes are less efficient, which leads to epigenetic modifications after alterations in DNA or chromatin structure (Alvarado-Cruz, Alegría-Torres, Montes-Castro, Jiménez-Garza, & Quintanilla-Vega, 2018); hence, children are more susceptible to TRAP than adults.

## 1.3 Study Justifications

Environmental health impacts in Malaysia have achieved the state requiring a paradigm shift and should be granted a high priority. Klang Valley is a highly populated area in Malaysia. The population is expected to multiply faster due to the rapid development of various industries; thus, these activities are partly responsible for the high concentrations of TRAP in the vicinity. Although TRAP exposure may cause health impacts, not everyone would experience those effects immediately because the effects could have implications later in life due to human organs’ development process. Primary school children were chosen as the study subjects because they are more susceptible to air pollution, mainly TRAP in this study; hence, they are more remarkably to develop health effects. This research was focused on the exposure to TRAP in Klang Valley among school children by using selected epigenetic mechanisms, which are histone H3 modification and DNAm. Air pollution can affect epigenetics in every life cycle, but only children were focused on this study because TRAP can hinder lung growth in children. Along with these epigenetic mechanisms, respiratory symptoms and lung function status were also investigated in this study.

The school children in Malaysian public primary schools spend about 6 to 7 hours per day in their schools and mostly in their classrooms. These children are exposed to the indoor and outdoor environment in the classrooms most of their time on weekdays. Therefore, there is a need to assess air quality on the school buildings, particularly those near heavily-travelled roads. Despite this issue, insufficient local studies have examined indoor and outdoor air quality at the primary schools for devising the situation. There are also limited local studies performed in school settings and has complemented actual measurements of TRAP with children’s daily diary activities. Furthermore, it is noteworthy that children require different protection levels for environmental health strategies intended to safeguard adults. This study incorporated actual TRAP measurements at schools and residences, which were concurrently collected with respondents' biological samples. This study focused on children's exposure to TRAP in schools and residences. Actual measurements were carried out in schools and residences. Previous similar studies did not include black carbon (BC), carbon monoxide (CO) and ozone ($O_3$) although these are also pollutants produced by vehicle emissions. Besides, modelling of air pollutants using Principal Component Analysis (PCA) and trend of air quality at the nearby monitoring stations using Pollution Rose were included to validate the actual findings at schools. PCA had also identified the specific sources of air pollution at schools.

Epigenetics is a part of exposome, which is a theory in environmental health that clarifies the relation between health and all the exposures of a human in a lifetime from pre-conception onwards (Sarigiannis, 2019). The degree of environmental exposure at individual level that might be mediated through epigenetic mechanisms is still obscure although these mechanisms are excellent intermediates of environmental effects at molecular level (Ferrari, Carugno, & Bollati, 2019). Previously published epidemiological studies in epigenetic mechanisms and interaction with exposure to air pollution among children as the study population was scarce, even though this is a crucial life phase. Besides, the previous research findings for histone modification are still understudied compared to DNAm (Lu et al., 2016; Reddy, Khade, Pandya, & Gupta, 2017). There are also limited studies which have utilised saliva for monitoring of respiratory diseases although it has a direct anatomic relationship with the lower airway. Besides, there are complex associations between air pollutants and the genetic factors in the course of life. An additional aspect of this study is to associate epigenetic mechanisms with related health effects, mainly respiratory, as children underlined as the target study population in this work are considered the susceptible group. These epigenetic changes are also linked to respiratory health impacts such as respiratory symptoms and reduced lung function. The proposed mechanisms are portrayed in Figure 1.2.

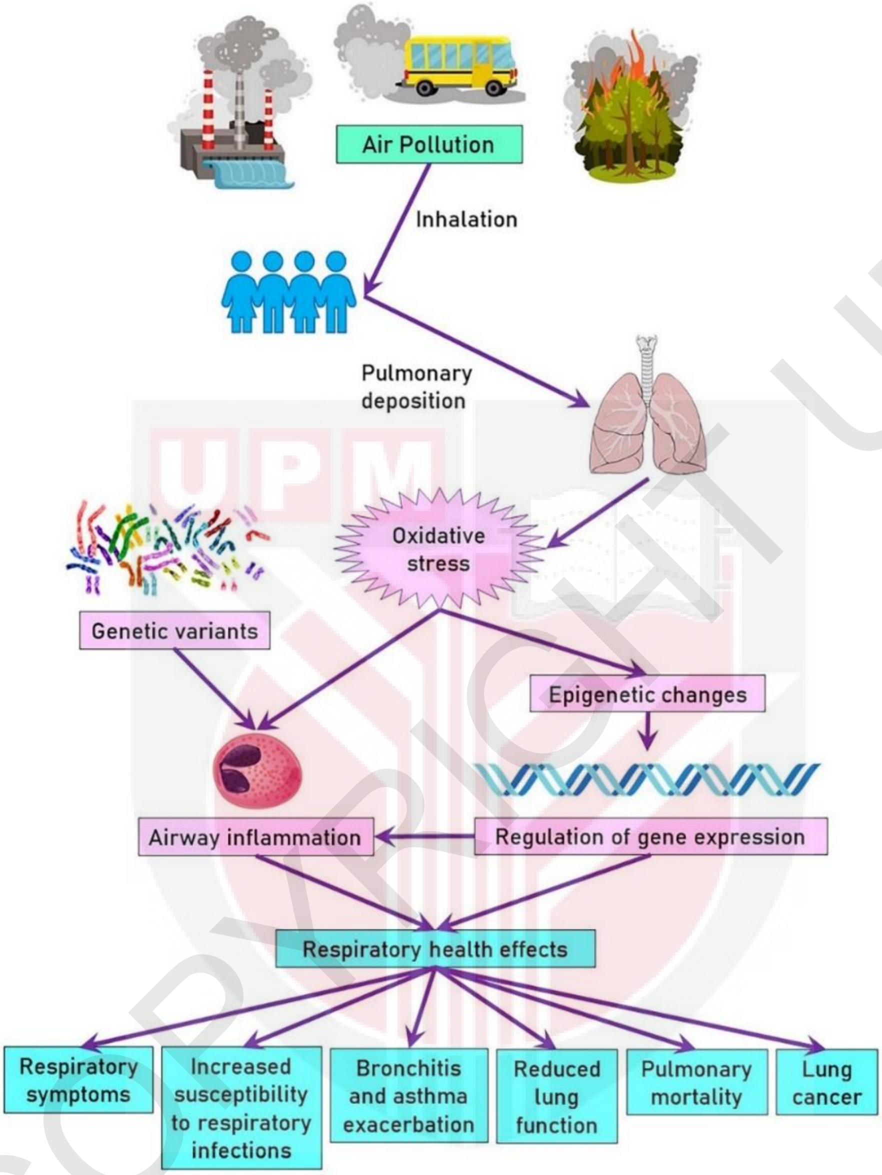


**Figure 1.2: A network of a few mechanisms connecting respiratory health effects and exposure to air pollution**

This study is also in line with the third goal of the Sustainable Development Goals (SDGs) 2030 by the United Nations Member States of which Malaysia is a signatory; the third goal is to ensure healthy lives and uphold well-being for all ages (United Nations Development Programme, 2021). Moreover, this research covers the issue of children's environmental health, which has been identified as an environmental health threat with the highest priority in Malaysia that call for immediate intervention, according to the Thematic Working Group 10 who are a team of Environmental Health experts under the National Environmental Health Action Plan (NEHAP) by Ministry of Health Malaysia (Ministry of Health Malaysia, 2021). This study provides data on the formulation of mitigation strategies for managing children's environmental health issues, particularly from the exposure to air pollution at schools and homes by emphasising on multi-pollutant emission reductions and overall air pollution-related risk. This step is a beneficial chance for Malaysia to establish a framework to tackle the emerging health impacts from environmental threats.

In general, this study is applicable to evaluate the potential risks from exposure to air pollutants with the incorporation of epigenetic data into human health risk assessments. This study contributes to the body of knowledge with a specific goal to fill in a gap within the works on epigenetic mechanisms as the mediator in connecting respiratory health effects and air pollution during the childhood phase. Research and data analysis performed in this study have solicited important scientific information, which would allow the related bodies to make strategic, scientific, and evidence-based decision-making. Therefore, this research complements the previous studies by linking epigenetic modification and exposure to air pollution, focusing on children.

## 1.4 Conceptual Framework

Figure 1.3 shows a diagram that represents the relationship that exists between the variables in the study. Generally, the framework explains the connection between the risk factors that contribute to epigenetic modifications and respiratory health effects among school children in Klang Valley. Both anthropogenic and natural sources could contribute to air pollution. This study focused on air pollution from transportation, which is one of the anthropogenic sources. By selecting transportation as the source of air pollution in the study, respondents' primary schools and residences were chosen for the data collection on TRAP exposure. Those residing, working or studying near the areas with high traffic congestion are the population who might be more affected by the TRAP exposure. The studied respondents were primary school children who were divided into the high-traffic and low-traffic groups. The respondents' exposure to TRAP was investigated by collecting data on respiratory symptoms and biological samples connected to the route of exposure via inhalation. Besides, confounders that may compete with the study's dependent variables were also included in the study.

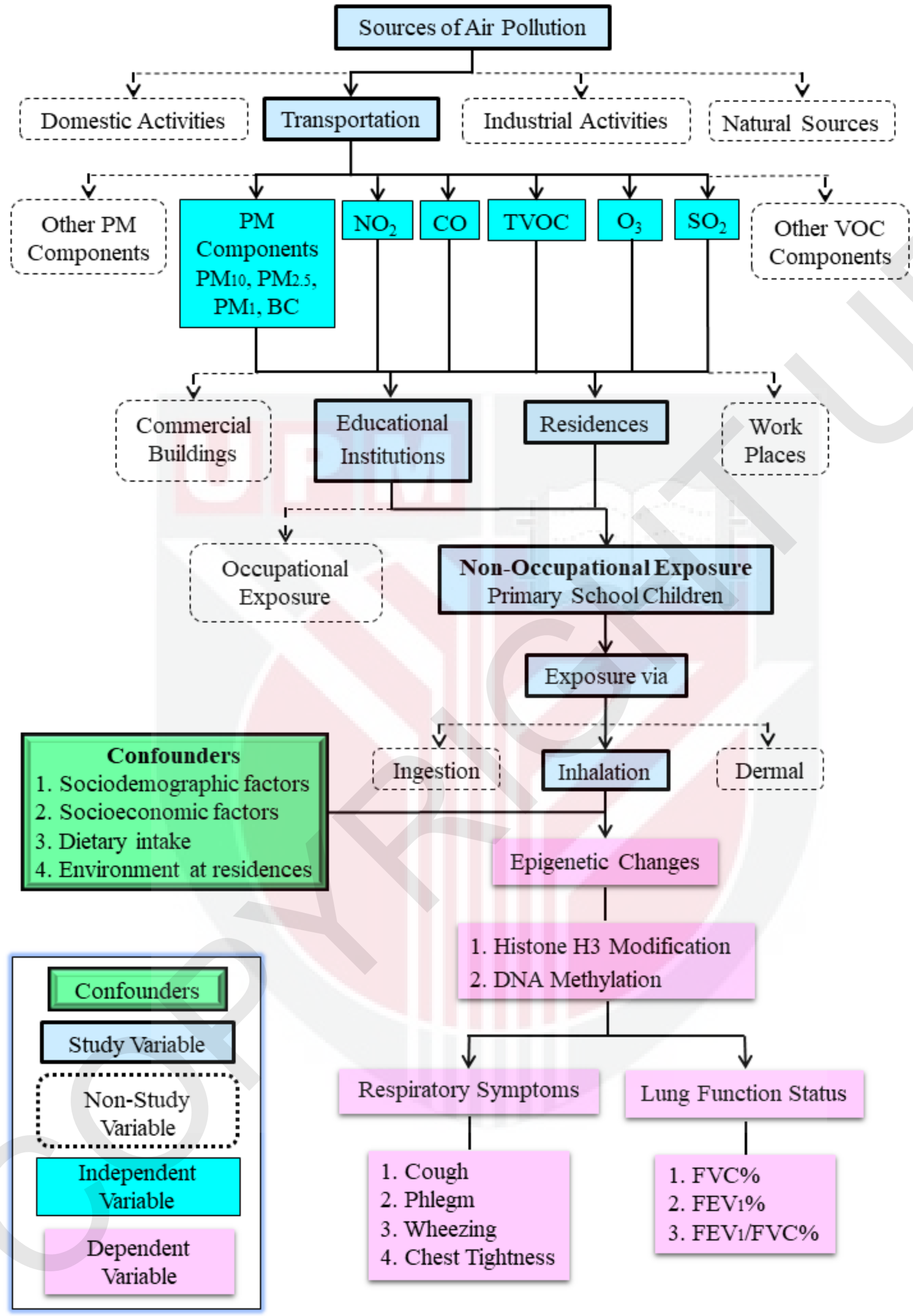


**Figure 1.3: Conceptual framework**

## 1.5 Study Objectives

### 1.5.1 General Objective

To assess the relationship between the magnitude of exposure to TRAP with respiratory health and epigenetic modifications among school children living near major roadways in Klang Valley.

### 1.5.2 Specific Objectives

1. To determine sociodemographic and socioeconomic information, house condition and location, family background and dietary intake between the respondents in high and low traffic areas.
2. To evaluate the concentrations of TRAP and IAQ parameters inside respondents' classrooms and residences in high and low traffic areas.
3. To compare the reported respiratory symptoms, lung function status, histone H3 level and DNAm status between the respondents in high and low traffic areas.
4. To assess the associations between TRAP exposure with respiratory symptoms, lung function status and epigenetic modifications assessed in the study.
5. To identify the factors that are significantly associated with the respiratory symptoms, lung function status, histone H3 level and DNAm status in response to TRAP-induced systemic inflammation after controlling the confounders.

## 1.6 Hypotheses

1. There are significant differences in sociodemographic and socioeconomic information, house condition and location, family background and dietary intake between the respondents in high and low traffic areas.
2. There are significant differences in the concentrations of air pollutants inside respondents' classrooms and residences between high and low traffic areas.
3. There are significant differences in reported respiratory symptoms, lung function status, histone H3 level and DNAm status among the respondents between high and low traffic areas.
4. There are significant associations between TRAP exposure with respiratory symptoms, lung function status and epigenetic modifications assessed in the study.
5. TRAP exposure could be the main factor influencing respiratory health and epigenetic modifications among children in response to TRAP-induced systemic inflammation after controlling the confounders.

## 1.7 Definition of Variables

### 1.7.1 Conceptual Definitions

#### 1.7.1.1 Traffic-Related Air Pollution (TRAP) Zone

The TRAP zone is described as 500 m on either side of highways with Average Daily Traffic (ADT) of ≥18,000 vehicles, or 100 m on either side of major urban roads with ADT of ≥15,000 vehicles, at least two lanes covering several km, a speed limit of more than 50 km/h (Brauer, Reynolds, & Hystad, 2013). Traffic pollutants travel, but exposures to TRAP are the highest near highways and busy roads.

#### 1.7.1.2 $PM_{10}$

$PM_{10}$ is a coarse particle with an aerodynamic diameter of 10 µm or less (0.0004 inches or one-seventh the width of a human hair) (United States EPA, 2021). $PM_{10}$ is primarily accumulated on the trachea (United States EPA, 2021).

#### 1.7.1.3 $PM_{2.5}$

$PM_{2.5}$ is a fine particle with an aerodynamic diameter of 2.5 µm or less (approximately one-thirtieth the average width of a human hair) (United States EPA, 2021). $PM_{2.5}$ can penetrate the bronchioles and alveoli (United States EPA, 2021).

#### 1.7.1.4 $PM_1$

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

#### 1.7.1.5 Black Carbon (BC)

BC is the primary light-absorbing element of particulate matter and is generated by the incomplete burning of biofuels, fossil fuels, and biomass (Liu et al., 2016). BC is emitted directly into the atmosphere in the form of fine particles. Its concentrations are usually higher at adjacent sources of emissions and heterogenous because BC has a short lifetime of about one week (Kholod & Evans, 2016).

#### 1.7.1.6 Nitrogen Dioxide ($NO_2$)

$NO_2$ is a molecule in the nitrogen oxides ($NO_X$) group (United States EPA, 2016b). The gas signifies much $NO_X$ that gets into the atmosphere from the fuel-burning of power plants and off-road machinery.

#### 1.7.1.7 Sulphur Dioxide ($SO_2$)

$SO_2$ is formed from the combustion of fossil fuels containing sulphur and is one of the significant polluting agents in the atmosphere (United States EPA, 2019). This colourless gas is easily soluble in water and is the determinant for the larger gaseous sulphur oxides ($SO_X$) group. $SO_2$ oxidation, primarily at the particulate surface, allows sulphurous and sulphuric acids to form in the presence of metallic catalysts.

#### 1.7.1.8 Carbon Monoxide (CO)

CO is a colourless and odourless gas that can be damaging if inhaled in large quantities (United States EPA, 2016a). It is the product of the incomplete combustion of organic compounds such as petrol and diesel from engines or equipment that burn fossil fuels.

#### 1.7.1.9 Ozone ($O_3$)

$O_3$ is a toxic light blue gas with an ordinary smell detected in environments where strong ultraviolet lights are present, and oxygen ($O_2$) is converted to $O_3$ (National Center for Biotechnology Information, 2019). As sunlight and air pollution create conditions suitable for reactions that create $O_3$, the community in polluted areas has more $O_3$ exposure during windless and dry afternoons.

#### 1.7.1.10 Total Volatile Organic Compounds (TVOC)

TVOCs are a wide variety of organic chemical compounds present in the atmosphere (United States EPA, 2017). They are of great concern due to their adverse effects on human health, as some chemicals can induce cancer directly and are associated with increased long-term health risks due to their carcinogenic and toxic properties.

#### 1.7.1.11 Carbon Dioxide ($CO_2$)

$CO_2$ levels determine the amount of ventilation inside buildings. The maximum limit for $CO_2$ indoors is 1000 ppm, which should not be surpassed at any time (DOSH Malaysia, 2020). Any reading that exceeds the ceiling limit reflects poor ventilation.

#### 1.7.1.12 Air Temperature

Air temperature is one of the IAQ physical parameters. The acceptable range for indoor air temperature is between 23 – 26ºC (DOSH Malaysia, 2020).

#### 1.7.1.13 Relative Humidity (RH)

RH is one of the IAQ physical parameters. The acceptable range for indoor RH is between 40 – 70% (DOSH Malaysia, 2020).

#### 1.7.1.14 Air Velocity

Air velocity is an indicator of ventilation indoors. It involves providing or removing air from space to control air pollutant levels, humidity, or temperature within the space. The acceptable range for indoor air velocity is between 0.15 – 0.50 m/s (DOSH Malaysia, 2020).

#### 1.7.1.15 Respiratory Health Symptoms

Respiratory health symptom is a broad term that can refer to a series of conditions that affect the human body's respiratory system (Zimmermann, 2019). Several respiratory diseases can affect humans at different severity levels (Kim, Chen, Zhou, & Huang, 2018). Some of the symptoms last only for a few days, with no medical treatment needed. Meanwhile, some of the symptoms may prolong without appropriate medical treatment.

#### 1.7.1.16 Lung Function Test

A lung function test is applied to assess how well the lungs work and how efficient the lungs can carry oxygen to the rest of the body (Graham et al., 2019). Forced vital capacity (FVC) measurement shows the amount of air a person can forcefully and quickly exhale after taking a deep breath (American Thoracic Society, 2019). Meanwhile, $FEV_1$ measurement shows the amount of air a person can forcefully exhale within one second of the FVC test (American Thoracic Society, 2019). $FEV_1$/FVC measurement is vital to figure out obstructive airways lung diseases.

#### 1.7.1.17 Histone H3 Modification

Histone modifications such as histone H3 modification have been known as epigenetic modifiers. Histone proteins, around which DNA is wrapped, can be chemically modified and alter chromatin structure by recruiting histone modifiers (Ohguchi, Hideshima, & Anderson, 2018). The modifiers are attached to the N-terminal tails of histones.

#### 1.7.1.18 DNA Methylation (DNAm)

DNAm usually governs gene expression via DNA transcription inhibition and silencing DNA, repetitive sequences and transposons (Lin et al., 2016). Decreased DNAm of repetitive elements, associated inflammation and cellular stress have been implicated in health conditions such as respiratory diseases (Ferrari et al., 2019).

### 1.7.2 Operational Definitions

#### 1.7.2.1 Primary Schools near a TRAP Zone

Primary schools located within TRAP Zone were chosen as high traffic (HT) group, whereas primary schools in low traffic (LT) group were decided from the location at a distance of more than 5 km away from nearby highways, major roadways and industrial sites in Selangor.

#### 1.7.2.2 Particulate Matter

$PM_{10}$, $PM_{2.5}$ and $PM_1$ in schools were measured using DustTrak DRX Aerosol Monitor in the unit of µg/m$^3$ for 6 h, based on the concept of light scattering. This instrument can recognise aerosol concentration ranges from 0.001 to 150 mg/m$^3$. As a result, it can concurrently measure both size fraction and mass concentration of $PM_{10}$, $PM_{2.5}$ and $PM_1$. The cut-point in bivariate analyses was 97.5 µg/m$^3$, 74.0 µg/m$^3$ and 63.0 µg/m$^3$ for $PM_{10}$, $PM_{2.5}$ and $PM_1$, respectively. Meanwhile, $PM_{10}$ and $PM_{2.5}$ in residences were measured gravimetrically in the unit of µg/m$^3$ by using an Escort Personal Sampling Pump for 24 h, with samples on a mixed cellulose ester membrane (MCE) filter paper. The cut-point in bivariate analyses was 81.7 µg/m$^3$ and 65.4 µg/m$^3$ for residential $PM_{10}$ and $PM_{2.5}$, respectively.

#### 1.7.2.3 Black Carbon (BC)

BC in $PM_{2.5}$ was measured gravimetrically by using a low volume sampler in the unit of $\mu g/m^3$ for 24 h, with samples on a quartz microfiber filter paper. Then, these samples were evaluated by using a smoke stain reflectometer. The blackness of a sample correlates to BC composition after calculating absorbed light spots all over the filter paper. The cut-point in bivariate analyses was 28.0 $\mu g/m^3$.

#### 1.7.2.4 $NO_2$, $SO_2$, CO and $O_3$

$NO_2$, $SO_2$, CO and $O_3$ were determined in the unit of parts per billion (ppb) using a portable gas sensor, Aeroqual S500, which quantifies air pollutants in real-time precisely. Various gases can be measured interchangeably using the same body because the sensor head could be easily removed and replaced. Interchangeable sensors were affixed to the monitor base. Each sensor head was set up with active sampling fan that reinforces the measurement accuracy and assures a representative sample. The cut-point in bivariate analyses was 74.7 ppb, 64.5 ppb, 300 ppb and 43.5 ppb for $NO_2$, $SO_2$, CO and $O_3$, respectively.

#### 1.7.2.5 TVOC

TVOC concentrations were measured using a handheld gas monitor, which is specially designed for VOC. It has a Photoionisation Detector (PID) that yields immediate detection and readings for gases, varing from 1 ppb up to 10,000 ppb. The cut-point in bivariate analyses was 210 ppb.

#### 1.7.2.6 $CO_2$

$CO_2$ was determined in the unit of parts per million (ppm) using Q-Trak IAQ Monitor. The detection range was from 0 – 5,000 ppm, with an accuracy of ±3% of reading or ±50 ppm $CO_2$. This equipment used a non-dispersive infrared sensor to detect the concentration of $CO_2$.

#### 1.7.2.7 Air Temperature

The air temperature was measured in the degree of Celsius ($^oC$) using Q-Trak IAQ Monitor. The range of detection was from -10 – 60 $^oC$, with an accuracy of ±0.5 °C. This equipment used a thermistor sensor to measure the air temperature.

#### 1.7.2.8 RH

RH was measured in percentage (% RH) using the Q-Trak IAQ Monitor. The detection range was from 5 – 95% RH, with an accuracy of ±3% RH. This equipment used a thin-film capacitive sensor to detect the humidity.

#### 1.7.2.9 Air Velocity

The type of ventilation system in selected primary schools was identified and observed through a site visit. The air velocity was measured in metre per second (m/s) using the VelociCalc Multifunction Ventilation Meter. The detection range was from 0 – 50 m/s, with an accuracy of ±3% of reading or ±0.015 m/s. This equipment used a thermal sensor of a pitot tube.

#### 1.7.2.10 Respiratory Symptoms

Respiratory symptoms were detected from questionnaires adapted from the International Study of Asthma and Allergies in Childhood (ISAAC) and the American Thoracic Society (ATS). These questionnaires assessed the distinctions within the prevalence of respiratory symptoms at the population level and their causes by questioning parents or legal guardians. In this study, the respiratory symptoms of interest were cough, phlegm, wheezing and chest tightness.

#### 1.7.2.11 Lung Function Test

Lung function tests, specifically spirometry tests, were done using a spirometer. Respondents breathed multiple times, with regular and maximal effort, through a tube that was connected to a spirometer. A computerised sensor calculates and graphs the results. $FEV_1$% was determined by dividing $FEV_1$ of the respondent from the spirometer with the predicted $FEV_1$. In contrast, the FVC% was determined by dividing the FVC of the respondent with the predicted FVC. $FEV_1$/FVC ratio was determined by dividing $FEV_1$ with FVC. All measurements were expressed in litres. In this study, the predicted values applied the reference values reported by Azizi & Henry (1994) for the spirometry test among Malay children in Malaysia.

#### 1.7.2.12 Histone H3 Modification

The level of histone H3 modification in the saliva samples was measured using an Enzyme-Linked Immunosorbent Assay (ELISA) kit for circulating total histone H3 modification after extraction. This assay showed whether a population of cells had changed its histone-modification profile in response to some exposure. The ELISA kit had high sensitivity with a detection limit as low as 2 ng/well in a dynamic range from 5 - 200 ng/well of the saliva. Moreover, the kit had high specificity for detecting total histone H3 modification whereby each histone H3 modified at specific sites was captured by an antibody coated on the strip wells and specifically targeted the appropriate histone modification pattern. The level of histone H3 modification in the saliva samples was determined by comparing the optical density (OD) of the samples against the standard curve.

#### 1.7.2.13 DNAm

The level of DNAm in the saliva samples was analysed by Methylation-Specific Polymerase Chain Reaction (MS-PCR) on bisulphite-treated DNA after extraction. Two independent primer sets were used for Polymerase Chain Reaction (PCR) amplification; one pair was designed to recognise the methylated sample and the other pair for the unmethylated versions of the bisulphite-modified sequence. The amplicons were visualised using novel juice staining following agarose gel electrophoresis. Amplicons of the expected size produced from either primer pair were indicative of the presence of DNA in the original sample with its respective methylation status. Because MS-PCR, as described here, was nonquantitative, these results provide a “present-or-absent” insight into methylation

## REFERENCES


Ab Jamil, N., Jalaludin, J., Kamaruddin, A. S., & Ibrahim, M. H. (2015). Exposure to Air Pollutants (PM10, NO2, SO2 and VOCs) on the Lung Functions among School Children Living Nearby the Petrochemical Industry Area in Kemaman, Terengganu. *Advances in Environmental Biology*, *9*(26), 55–63.

Abdul Hamid, H., Ho, G., & Ismail, S. (2019). *Demarcating Households: An Integrated Income and Consumption Analysis*. Retrieved from http://www.krinstitute.org/assets/contentMS/img/template/editor/Presentation Slides_Demarcating Households_Discussion Paper.pdf

Abdul Manan, M. M., Várhelyi, A., Çelik, A. K., & Hashim, H. H. (2018). Road Characteristics and Environment Factors Associated with Motorcycle Fatal Crashes in Malaysia. *IATSS Research*, *42*(4), 207–220. https://doi.org/10.1016/j.iatssr.2017.11.001

Abdul, Q. A., Yu, B. P., Chung, H. Y., Jung, H. A., & Choi, J. S. (2017). Epigenetic Modifications of Gene Expression by Lifestyle and Environment. *Archives of Pharmacal Research*, *40*(11), 1219–1237. https://doi.org/10.1007/s12272-017-0973-3

Abdul Rahman, Shamsiah, Hamzah, M. S., Elias, S., Ashifa, N., Salim, A., Hashim, A., … Wood, A. K. (2015). A Long Term Study on Characterization and Source Apportionment of Particulate Pollution in Klang Valley, Kuala Lumpur. *Aerosol and Air Quality Research*, *15*, 2291–2304. https://doi.org/10.4209/aaqr.2015.03.0188

Abdul Rahman, Shamsiah, Hamzah, M. S., Wood, A. K., Elias, M. S., Salim, N. A. A., & Sanuri, E. (2011). Sources Apportionment of Fine and Coarse Aerosol in Klang Valley, Kuala Lumpur using Positive Matrix Factorization. *Atmospheric Pollution Research*, *2*(2), 197–206. https://doi.org/10.5094/APR.2011.025

Abdul Rahman, SR, Ismail, S. N. S., Sahani, M., Firuz, Rm., & Latif, M. (2017). A Case Crossover Analysis of Primary Air Pollutants Association on Acute Respiratory Infection (ARI) among Children in Urban Region of Klang Valley, Malaysia. *Annals of Tropical Medicine and Public Health*, *10*(1), 44. https://doi.org/10.4103/ATMPH.ATMPH_75_17

Abdul Wahab, M. I., Razak, W. M. A. A., Sahani, M., & Khan, M. F. (2020). Characteristics and Health Effect of Heavy Metals on Non-Exhaust Road Dusts in Kuala Lumpur. *Science of the Total Environment*, *703*, 135535. https://doi.org/10.1016/j.scitotenv.2019.135535

Abdullah, R. (2020). Malaysia: Country Report on Children's Environmental Health. *Reviews on Environmental Health*. De Gruyter. https://doi.org/10.1515/reveh-2019-0077

Abdullah, S., Mansor, A. A., Napi, N. N. L. M., Mansor, W. N. W., Ahmed, A. N., Ismail, M., & Ramly, Z. T. A. (2020). Air Quality Status during 2020 Malaysia Movement Control Order (MCO) Due To 2019 Novel Coronavirus (2019-nCoV) Pandemic. *Science of the Total Environment*, *729*, 139022. https://doi.org/10.1016/j.scitotenv.2020.139022

Abhijith, K. V., Kumar, P., Gallagher, J., McNabola, A., Baldauf, R., Pilla, F., … Pulvirenti, B. (2017). Air Pollution Abatement Performances of Green Infrastructure in Open Road and Built-Up Street Canyon Environments – A Review. *Atmospheric Environment*, *162*, 71–86. https://doi.org/10.1016/j.atmosenv.2017.05.014

Abrams, S. T., Zhang, N., Manson, J., Liu, T., Dart, C., Baluwa, F., … Toh, C. H. (2013). Circulating Histones are Mediators of Trauma-Associated Lung Injury. *American Journal of Respiratory and Critical Care Medicine*, *187*, 160–169. https://doi.org/10.1164/rccm.201206-1037OC

Ahamad, F., Latif, M. T., Tang, R., Juneng, L., Dominick, D., & Juahir, H. (2014). Variation of Surface Ozone Exceedance around Klang Valley, Malaysia. *Atmospheric Research*, *139*, 116–127. https://doi.org/10.1016/j.atmosres.2014.01.003

Al-Qerem, W., & Ling, J. (2018). Pulmonary Function Tests in Egyptian Schoolchildren in Rural and Urban Areas. *Eastern Mediterranean Health Journal*, *24*(4), 325–332. https://doi.org/10.26719/2018.24.4.325

Alfano, R., Herceg, Z., Nawrot, T. S., Chadeau-Hyam, M., Ghantous, A., & Plusquin, M. (2018). The Impact of Air Pollution on Our Epigenome: How Far Is the Evidence? (A Systematic Review). *Current Environmental Health Reports*, *5*(4), 544–578. https://doi.org/https://doi.org/10.1007/s40572-018-0218-8

Alhamdi, Y., Abrams, S. T., Cheng, Z., Jing, S., Su, D., Liu, Z., … Toh, C.-H. (2015). Circulating Histones Are Major Mediators of Cardiac Injury in Patients With Sepsis. *Critical Care Medicine*, *43*(10), 2094–2103. https://doi.org/10.1097/CCM.0000000000001162

Alvarado-Cruz, I., Alegría-Torres, J. A., Montes-Castro, N., Jiménez-Garza, O., & Quintanilla-Vega, B. (2018). Environmental Epigenetic Changes, As Risk Factors for The Development of Diseases in Children: A Systematic Review. *Annals of Global Health*, *84*(2), 212–224. https://doi.org/https://doi.org/10.29024/aogh.909

Alvarado-Cruz, I., Sánchez-Guerra, M., Hernández-Cadena, L., De Vizcaya-Ruiz, A., Mugica, V., Pelallo-Martínez, N. 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/https://doi.org/10.1016/j.mrgentox.2016.11.007

American Lung Association. (2020). Living Near Highways and Air Pollution. Retrieved April 24, 2020, from https://www.lung.org/clean-air/outdoors/who-is-at-risk/highways

American Thoracic Society. (2019). Pulmonary Function Testing in Children.

Amil, N., Latif, M. T., Khan, M. F., & Mohamad, M. (2016). Seasonal Variability of PM2.5 Composition and Sources in the Klang Valley Urban-Industrial Environment. *Atmospheric Chemistry and Physics*, *16*(8), 5357–5381. https://doi.org/10.5194/acp-16-5357-2016

Amin, M. S. R., Tamima, U., & Amador Jimenez, L. (2017). Understanding Air Pollution from Induced Traffic During and After The Construction of A New Highway: Case Study of Highway 25 in Montreal. *Journal of Advanced Transportation*. https://doi.org/10.1155/2017/5161308

Ang, K. H. (2018). Applied Chemometric Approach in Identification Sources of Air Quality Pattern in Selangor, Malaysia. *Sains Malaysiana*, *47*(3), 471–479. https://doi.org/10.17576/jsm-2018-4703-06

Arif, M., & Parveen, S. (2020). Carcinogenic Effects of Indoor Black Carbon and Particulate Matters (PM2.5 and PM10) in Rural Households of India. *Environmental Science and Pollution Research*. https://doi.org/10.1007/s11356-020-10668-5

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/https://doi.org/10.5572/ajae.2019.13.1.021

Arphorn, Ishimaru, Hara, & Mahasandana. (2018). Considering the Effects of Ambient Particulate Matter on The Lung Function of Motorcycle Taxi Drivers in Bangkok, Thailand. *Journal of the Air & Waste Management Association*, *68*(2), 139–145. https://doi.org/10.1080/10962247.2017.1359217

Asrul, S., & Juliana, J. (2017). Indoor Air Quality and Its Association with Respiratory Health among Preschool Children in Urban and Suburban Area. *Malaysian Journal of Public Health Medicine*, *1*, 78–88. Retrieved from https://www.mjphm.org.my/mjphm/journals/2017 - Special Volume (1)/INDOOR AIR QUALITY AND ITS ASSOCIATION WITH RESPIRATORY HEALTH AMONG PRESCHOOL CHILDREN IN URBAN AND SUBURBAN AREA.pdf

Attorney General Chamber of Malaysia. (2013). *Births and Deaths Registration Act 1957*.

Awang, M. F., Jalaludin, J., Abu Bakar, S., Latif, M. T., Mohamad Fandi, N. F., & Abdul Hamid, H. H. (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), 73–82. https://doi.org/10.11113/jt.v82.14493

Awang, M. F., Jalaludin, J., Latif, M. T., & Mohamad Fandi, N. F. (2019). Exposure to PM2.5 in Urban Area and Respiratory Health Symptoms among Urban Workers in Klang Valley. *IOP Conference Series: Earth and Environmental Science*, *228*, 1–5. https://doi.org/10.1088/1755-1315/228/1/012015

Azeez, O. S., Pradhan, B., & Shafri, H. Z. M. (2018). Vehicular CO Emission Prediction using Support Vector Regression Model and GIS. *Sustainability*, *10*(10). https://doi.org/10.3390/su10103434

Azhari, A., Latif, M. T., & Mohamed, A. F. (2018). Road Traffic as An Air Pollutant Contributor within An Industrial Park Environment. *Atmospheric Pollution Research*, *9*, 680–687. https://doi.org/10.1016/j.apr.2018.01.007

Azid, A., Juahir, H., Ezani, E., Toriman, M. E., Endut, A., Rahman, M. N. A., … Umar, R. (2015). Identification Source of Variation on Regional Impact of Air Quality Pattern Using Chemometric. *Aerosol and Air Quality Research*, *15*(4), 1545–1558. https://doi.org/10.4209/aaqr.2014.04.0073

Azizi, B. H. O., & Henry, R. L. (1994). Ethnic Differences in Normal Spirometric Lung Function of Malaysian Children. *Respiratory Medicine*, *88*(5), 349–356. https://doi.org/10.1016/0954-6111(94)90040-X

Baccarelli, A., & Bollati, V. (2009). Epigenetics and Environmental Chemicals. *Current Opinion in Pediatrics*, *21*(2), 243–251. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3035853/

Baldauf, R. (2017). Roadside Vegetation Design Characteristics That Can Improve Local, Near-Road Air Quality. *Transportation Research Part D: Transport and Environment*, *52*, 354–361. https://doi.org/10.1016/j.trd.2017.03.013

Banerjee, T., & Christian, R. (2017). On-Field and Laboratory Measurement of Nanoparticle Emission in The Wake of Gasoline Vehicle. *Atmospheric Pollution Research*, *8*(6), 1179–1192. https://doi.org/10.1016/j.apr.2017.05.007

Barnes, N. M., Ng, T., 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), 611. https://doi.org/10.3390/ijerph15040611

Barwise, Y., & Kumar, P. (2020). Designing Vegetation Barriers for Urban Air Pollution Abatement: A Practical Review for Appropriate Plant Species Selection. *Npj Climate and Atmospheric Science 2020 3:1*, *3*(1), 1–19. https://doi.org/10.1038/s41612-020-0115-3

Bernama. (2019). Pengumuman Dasar Automotif Nasional Baharu Suku Kedua. Retrieved November 13, 2019, from https://www.sinarharian.com.my/article/22441/BISNES/Pengumuman-Dasar-Automotif-Nasional-baharu-suku-kedua

Bhargava, A., Bunkar, N., Aglawe, A., Pandey, K. C., Tiwari, R., Chaudhury, K., … Mishra, P. K. (2018). Epigenetic Biomarkers for Risk Assessment of Particulate Matter Associated Lung Cancer. *Current Drug Targets*, *19*(10), 1127–1147. https://doi.org/10.2174/1389450118666170911114342

Bhatti, U., Laghari, Z. A., & Syed, B. M. (2019). Effect of Body Mass Index on Respiratory Parameters: A Cross-Sectional Analytical Study. *Pakistan Journal of Medical Sciences*, *35*(6), 1724–1729. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6861468/pdf/PJMS-35-1724.pdf

Bintu, L., Yong, J., Antebi, Y. E., McCue, K., Kazuki, Y., Uno, N., … Elowitz, M. B. (2016). Dynamics of Epigenetic Regulation at The Single-Cell Level. *Science*, *351*(6274), 720–724. https://doi.org/10.1126/science.aab2956

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

Bourganis, V., Kammona, O., Alexopoulos, A., & Kiparissides, C. (2018). Recent Advances in Carrier Mediated Nose-to-Brain Delivery of Pharmaceutics. *European Journal of Pharmaceutics and Biopharmaceutics*, *128*, 337–362. https://doi.org/10.1016/j.ejpb.2018.05.009

Brauer, M., Reynolds, C., & Hystad, P. (2013). Traffic-Related Air Pollution and Health in Canada. *CMAJ: Canadian Medical Association Journal = Journal de l'Association Medicale Canadienne*, *185*(18), 1557–1558. https://doi.org/10.1503/cmaj.121568

Brown, J. S. (2015). Deposition of Particles. In *Comparative Biology of the Normal Lung: Second Edition* (pp. 513–536). Elsevier Inc. https://doi.org/10.1016/B978-0-12-404577-4.00027-8

Brunst, K. J., Leung, Y. K., Ryan, P. H., Khurana Hershey, G. K., Levin, L., Ji, H., … Ho, S. M. (2013). Forkhead Box Protein 3 (FOXP3) Hypermethylation is Associated with Diesel Exhaust Exposure and Risk for Childhood Asthma. *Journal of Allergy and Clinical Immunology*, *131*(2), 592-594.e3. https://doi.org/10.1016/j.jaci.2012.10.042

Carrion-Matta, A., Kang, C. M., Gaffin, J. M., Hauptman, M., Phipatanakul, W., Koutrakis, P., & Gold, D. R. (2019). Classroom Indoor PM2.5 Sources and Exposures in Inner-City Schools. *Environment International*, *131*, 104968. https://doi.org/10.1016/j.envint.2019.104968

Centre for Agriculture and Bioscience International. (2021). Grevillea robusta (Silky Oak). Retrieved July 29, 2021, from https://www.cabi.org/isc/datasheet/25866

Checkley, W., Robertson, N. M., Kayongo, A., Siddharthan, T., Pollard, S. L., Gomez Villalobos, J., … Kirenga, B. (2019). The Role of Epigenetics in Respiratory Health in Urban Populations in Low and Middle-Income Countries. *Global Health, Epidemiology and Genomics*, *4*(e8), 1–7. https://doi.org/10.1017/gheg.2019.7

Chin, Y. S. J., De Pretto, L., Thuppil, V., & Ashfold, M. J. (2019). Public Awareness and Support for Environmental Protection—A Focus on Air Pollution in Peninsular Malaysia. *PLOS ONE*, *14*(3), e0212206. https://doi.org/10.1371/journal.pone.0212206

Chong, H. S., Park, Y., Kwon, S., & Hong, Y. (2018). Analysis of Real Driving Gaseous Emissions from Light-Duty Diesel Vehicles. *Transportation Research Part D: Transport and Environment*, *65*(October), 485–499. https://doi.org/10.1016/j.trd.2018.09.015

Chong, T. L., Ahearn, E. L., & Cimmino, L. (2019). Reprogramming the Epigenome With Vitamin C. *Frontiers in Cell and Developmental Biology*, *7*, 128. https://doi.org/10.3389/fcell.2019.00128

Chowdhury, B., Cho, I.-H., & Irudayaraj, J. (2017). Technical Advances in Global DNA Methylation Analysis in Human Cancers. *Journal of Biological Engineering*, *11*(1), 10. https://doi.org/https://doi.org/10.1186/s13036-017-0052-9

Chu, M. Y., Law, T. H., Hamid, H., Law, S. H., & Lee, J. C. (2019). The Motorcycle to Car Ownership Ratio: Inflation and Its Indirect Effects. *IOP Conference Series: Materials Science and Engineering*, *512*, 012015. https://doi.org/10.1088/1757-899X/512/1/012015

Cordero, P., Campion, J., Milagro, F. I., Goyenechea, E., Steemburgo, T., Javierre, B. M., & Martinez, J. A. (2011). Leptin and TNF-Alpha Promoter Methylation Levels Measured by MSP Could Predict The Response to A Low-Calorie Diet. *Journal of Physiology and Biochemistry*, *67*(3), 463–470. https://doi.org/10.1007/s13105-011-0084-4

Das, N., Verstraete, K., Topalovic, M., Aerts, J.-M., & Janssens, W. (2019). Estimating Airway Resistance from Forced Expiration in Spirometry. *Applied Sciences*, *9*(14), 2842. https://doi.org/10.3390/app9142842

Deng, Q., Deng, L., Miao, Y., Guo, X., & Li, Y. (2019). Particle Deposition in The Human Lung: Health Implications of Particulate Matter from Different Sources. *Environmental Research*, *169*, 237–245. https://doi.org/10.1016/j.envres.2018.11.014

Department of Statistics Malaysia. (2020). Household Income & Basic Amenities Survey Report 2019. Retrieved October 23, 2020, from https://www.dosm.gov.my/v1/index.php?r=column/cthemeByCat&cat=120&bul_id=TU00TmRhQ1N5TUxHVWN0T2VjbXJYZz09&menu_id=amVoWU54UTl0a21NWmdhMjFMMWcyZz09

Deshmukh, P., Isakov, V., Venkatram, A., Yang, B., Zhang, K. M., Logan, R., & Baldauf, R. (2019). The Effects of Roadside Vegetation Characteristics on Local, Near-Road Air Quality. *Air Quality, Atmosphere and Health*, *12*, 259–270. https://doi.org/10.1007/s11869-018-0651-8

Ding, R., Jin, Y., Liu, X., Ye, H., Zhu, Z., Zhang, Y., … Xu, Y. (2017). Dose- and Time- Effect Responses of DNA Methylation and Histone H3K9 Acetylation Changes Induced by Traffic-Related Air Pollution. *Scientific Reports*, *7*, 43737. https://doi.org/10.1038/srep43737

Ding, R., Jin, Y., Liu, X., Zhu, Z., Zhang, Y., Wang, T., & Xu, Y. (2016). H3K9 Acetylation Change Patterns in Rats After Exposure to Traffic-Related Air Pollution. *Environmental Toxicology and Pharmacology*, *42*, 170–175. https://doi.org/10.1016/j.etap.2016.01.016

DOE Malaysia. (2020). New Malaysia Ambient Air Quality Standard. Retrieved May 9, 2020, from https://www.doe.gov.my/portalv1/en/category/info-umum/info-kualiti-udara

Dominick, D., Juahir, H., Latif, M. T., Zain, S. M., & Aris, A. Z. (2012). Spatial Assessment of Air Quality Patterns in Malaysia using Multivariate Analysis. *Atmospheric Environment*, *60*, 172–181. https://doi.org/10.1016/j.atmosenv.2012.06.021

DOS Malaysia. (2018a). *Children Statistics Malaysia 2018*. *Department of Statistics Malaysia*. Putrajaya: Department of Statistics Malaysia.

DOS Malaysia. (2018b). *Compendium of Environment Statistics*. *Department of Statistics Malaysia*. Putrajaya. https://doi.org/10.5860/choice.29-3644

DOS Malaysia. (2019). *Current Population Estimates Malaysia 2019*. *Department of Statistics Malaysia*. Putrajaya: Department of Statistics Malaysia. Retrieved from www.dosm.gov.my

DOS Malaysia. (2021). *Current Population Estimates Malaysia 2021*.

DOSH Malaysia. (2020). *Official Website Department of Occupational Safety and Health - Indoor Air Quality*. Retrieved from http://www.dosh.gov.my/index.php/chemical-management-v/indoor-air-quality

Erath, A., Fourie, P., Van Eggermond, M., & Ordoñez Medina, S. (2018). *Potential of Motorcycles As Urban Means of Transport*. Future Cities Laboratory (FCL). https://doi.org/10.3929/ethz-b-000306547

Ezani, E., Abdul Hisham, N. A., Syed Ismail, S. N., & Abdul Wahab, M. I. (2018). Air Pollution and Traffic Measurements within University Areas in Serdang, Malaysia. *Asia Pacific Environmental and Occupational Health Journal*, *4*(3), 58–65.

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. Retrieved from https://www.researchgate.net/publication/304109295_Indoor_Particulate_Matter_25_PM25_and_lung_function_among_children_living_near_busy_road_in_Cheras_Kuala_Lumpur

Ferrari, L., Carugno, M., & Bollati, V. (2019). Particulate Matter Exposure Shapes DNA Methylation Through the Lifespan. *Clinical Epigenetics*, *11*(129). https://doi.org/https://doi.org/10.1186/s13148-019-0726-x

Gaffin, J. M., Hauptman, M., Lai, P., Petty, C. R., Wolfson, J. M., Kang, C.-M., … Phipatanakul, W. (2017). Nitrogen Dioxide Exposure in School Classrooms Is Associated with Airflow Obstruction in Students with Asthma. *Journal of Allergy and Clinical Immunology*, *139*(2), AB174. https://doi.org/10.1016/j.jaci.2016.12.570

Galvez, M. C., Tipan, D. P., Valera, A. A., Vallar, E., & Nacua, A. (2020). Ozone, Nitrogen Dioxide, and PM2.5 Measurement at Three Urban Parks in Manila, Philippines using Portable Sensors. *Advances in Science, Technology and Engineering Systems Journal*, *5*(6), 1027–1032. https://doi.org/10.25046/aj0506124

Gauderman, W. J., Avol, E., Gilliland, F., Vora, H., Thomas, D., Berhane, K., … Peters, J. (2004). The Effect of Air Pollution on Lung Development from 10 to 18 Years of Age. *New England Journal of Medicine*, *351*(11), 1057–1067. https://doi.org/10.1056/nejmoa040610

Gawda, A., Majka, G., Nowak, B., & Marcinkiewicz, J. (2017). Air Pollution, Oxidative Stress, and Exacerbation of Autoimmune Diseases. *Central European Journal of Immunology*, *42*(3), 305–312. https://doi.org/10.5114/ceji.2017.70975

Ghasemian, M., Amini, S., & Princevac, M. (2017). The Influence of Roadside Solid and Vegetation Barriers on Near-Road Air Quality. *Atmospheric Environment*, *170*, 108–117. https://doi.org/10.1016/j.atmosenv.2017.09.028

Gowher, H., & Jeltsch, A. (2018). Mammalian DNA Methyltransferases: New Discoveries and Open Questions. *Biochemical Society Transactions*, *46*(5), 1191–1202. https://doi.org/10.1042/BST20170574

Graham, B. L., Steenbruggen, I., Miller, M. R., Barjaktarevic, I. Z., Cooper, B. G., Hall, G. L., … Thompson, B. R. (2019). Standardization of Spirometry 2019 Update: An Official American Thoracic Society and European Respiratory Society Technical Statement. *American Journal of Respiratory and Critical Care Medicine*, *200*(8), e70–e88. https://doi.org/10.1164/rccm.201908-1590ST

Gsell, C., Richly, H., Coin, F., & Naegeli, H. (2020). A Chromatin Scaffold for DNA Damage Recognition: How Histone Methyltransferases Prime Nucleosomes for Repair of Ultraviolet Light-Induced Lesions. *Nucleic Acids Research*, *48*(4), 1652–1668. https://doi.org/10.1093/nar/gkz1229

Gupta, A., Bush, A., & Nagakumar, P. (2020). Asthma in Children During The COVID-19 Pandemic: Lessons from Lockdown and Future Directions for Management. *The Lancet Respiratory Medicine*, *8*(11), 1070–1071. https://doi.org/10.1016/S2213-2600(20)30278-2

Hamid, H. H. A., Latif, M. T., Uning, R., Nadzir, M. S. M., Khan, M. F., Ta, G. C., & Kannan, N. (2020). Observations of BTEX in The Ambient Air of Kuala Lumpur by Passive Sampling. *Environmental Monitoring and Assessment*, *192*(6), 342. https://doi.org/10.1007/s10661-020-08311-4

Haque, M. S., & Singh, R. B. (2017). Air Pollution and Human Health in Kolkata, India: A Case Study. *Climate*, *5*(4), 77. https://doi.org/10.3390/cli5040077

Haryanto, B. (2018). Climate Change and Urban Air Pollution Health Impacts in Indonesia. In *Springer Climate* (pp. 215–239). Springer. https://doi.org/10.1007/978-3-319-61346-8_14

Haryanto, B. (2020). Indonesia: Country Report on Children's Environmental Health. *Reviews on Environmental Health*, *35*(1), 41–48. https://doi.org/10.1515/reveh-2019-0088

Haryanto, B., & Pratiwi, D. A. (2020). Effect of Particulate Matter 2.5 Exposure to Urinary Malondialdehyde Levels of Public Transport Drivers in Jakarta. *Reviews on Environmental Health*, *35*(3), 295–300. https://doi.org/10.1515/reveh-2020-0017

Hazenkamp-Von Arx, M. E., Schindler, C., Ragettli, M. S., Künzli, N., Braun-Fahrländer, C., & Liu, L. J. S. (2011). Impacts of Highway Traffic Exhaust in Alpine Valleys on The Respiratory Health in Adults: A Cross-Sectional Study. *Environmental Health: A Global Access Science Source*, *10*(1), 1–9. https://doi.org/10.1186/1476-069X-10-13

He, L., Gao, L., Shi, Z., Li, Y., Zhu, L., Li, S., … Feng, F. (2015). Involvement of Cytochrome P450 1A1 and Glutathione S-transferase P1 Polymorphisms and Promoter Hypermethylation in The Progression of Anti-Tuberculosis Drug-Induced Liver Injury: A Case-Control Study. *PLoS ONE*, *10*(3), 1–11. https://doi.org/10.1371/journal.pone.0119481

Hegseth, M. N., Oftedal, B. M., Höper, A. C., Aminoff, A. L., Thomassen, M. R., Svendsen, M. V., & Fell, A. K. M. (2019). Self-Reported Traffic-Related Air Pollution and Respiratory Symptoms among Adults in An Area with Modest Levels of Traffic. *PLOS ONE*, *14*(12), e0226221. https://doi.org/10.1371/journal.pone.0226221

Hind, C. R. K. (2013). Neurogenic respiratory failure. In *Handbook of Clinical Neurology* (Vol. 110, pp. 295–302). Elsevier B.V. https://doi.org/10.1016/B978-0-444-52901-5.00024-1

Hirota, K., & Kashima, S. (2020). How are Automobile Fuel Quality Standards Guaranteed? Evidence from Indonesia, Malaysia and Vietnam. *Transportation Research Interdisciplinary Perspectives*, *4*, 100089. https://doi.org/10.1016/j.trip.2019.100089

Hosaini, P. N., Khan, M. F., Mustaffa, N. I. H., Amil, N., Mohamad, N., Jaafar, S. A., … Latif, M. T. (2017). Concentration and Source Apportionment of Volatile Organic Compounds (VOCs) in The Ambient Air of Kuala Lumpur, Malaysia. *Natural Hazards*, *85*(1), 437–452. https://doi.org/10.1007/s11069-016-2575-7

Hou, D., Ge, Y., Chen, C., Tan, Q., Chen, R., Yang, Y., … Song, Y. (2020). Associations of Long-Term Exposure to Ambient Fine Particulate Matter and Nitrogen Dioxide with Lung Function: A Cross-Sectional Study in China. *Environment International*, *144*, 105977. https://doi.org/10.1016/j.envint.2020.105977

Hussin, F. S., & Jalaludin, J. (2016). Association of PM10 and PM2.5 Exposure with Respiratory Health of the Children Living Near Palm Oil Mill, Dengkil. *Malaysian Journal of Public Health Medicine*, *16*, 20–26.

Ichikawa, Y., Connelly, C. F., Appleboim, A., Miller, T. C. R., Jacobi, H., Abshiru, N. A., … Kaufman, P. D. (2017). A Synthetic Biology Approach To Probing Nucleosome Symmetry. *ELife*, *6*. https://doi.org/10.7554/eLife.28836

Jalaludin, J., Hashim, Z., Taib, N. M., Lubis, S., & Hashim, J. H. (2002). Comparison on the Influence of Residential Environment to Asthma Attacks among Children in Kuala Lumpur and Terengganu, Malaysia. *Malaysian Journal of Community Health*, *8*, 51–62.

Jalaludin, J., & Jasme, N. J. M. (2015). Exposure to Indoor Partculate Matter 2.5 (PM2.5) and Volatile Organic Compounds (VOC) among Preschool Children at an Industrial Area in Petaling Jaya, Selangor. *International Journal of Applied and Natural Sciences*, *4*(6), 41–50. Retrieved from www.iaset.us

Jalaludin, J., Syed Noh, S. N., Suhaimi, N. F., & Md Akim, A. (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

Janssen, B. G., Gyselaers, W., Byun, H. M., Roels, H. A., Cuypers, A., Baccarelli, A. A., & Nawrot, T. S. (2017). Placental Mitochondrial DNA and CYP1A1 Gene Methylation As Molecular Signatures for Tobacco Smoke Exposure in Pregnant Women and The Relevance for Birth Weight. *Journal of Translational Medicine*, *15*(1), 1–10. https://doi.org/10.1186/s12967-016-1113-4

Jasim, H., Olausson, P., Hedenberg-Magnusson, B., Ernberg, M., & Ghafouri, B. (2016). The Proteomic Profile of Whole and Glandular Saliva in Healthy Pain-Free Subjects. *Scientific Reports*, *6*. https://doi.org/10.1038/srep39073

Jeong, H., & Park, D. (2017). Characteristics of Elementary School Children's Daily Exposure to Black Carbon (BC) in Korea. *Atmospheric Environment*, *154*, 179–188. https://doi.org/10.1016/j.atmosenv.2017.01.045

Ji, H., Biagini Myers, J. M., Brandt, E. B., Brokamp, C., Ryan, P. H., & Khurana Hershey, G. K. (2016). Air Pollution, Epigenetics, and Asthma. *Allergy, Asthma and Clinical Immunology*, *12*(1), 1–14. https://doi.org/https://doi.org/10.1186/s13223-016-0159-4

Jiang, R., Jones, M. J., Sava, F., Kobor, M. S., & Carlsten, C. (2014). Short-Term Diesel Exhaust Inhalation in A Controlled Human Crossover Study is Associated with Changes in DNA Methylation of Circulating Mononuclear Cells in Asthmatics. *Particle and Fibre Toxicology*, *11*, 71. https://doi.org/10.1186/s12989-014-0071-3

Jirtle, R. L., & Skinner, M. K. (2007). Environmental Epigenomics and Disease Susceptibility. *Nature Reviews Genetics*, *8*, 253–262. https://doi.org/10.1038/nrg2045

Jo, E.-J., & Song, W.-J. (2019). Environmental Triggers for Chronic Cough. *Asia Pacific Allergy*, *9*(2). https://doi.org/10.5415/apallergy.2019.9.e16

Jun, K. E., Hamzah, N. A., & Anua, S. M. (2017). Indoor Air Quality and Symptoms of Sick Building Syndrome in Two Selected Building (New Versus Old). *Journal of Occupational Safety and Health*, *14*(2), 7–14.

Jung, K. H., Lovinsky-Desir, S., Yan, B., Torrone, D., Lawrence, J., Jezioro, J. R., … Miller, R. L. (2017). Effect of Personal Exposure to Black Carbon on Changes in Allergic Asthma Gene Methylation Measured 5 Days Later in Urban Children: Importance of Allergic Sensitization. *Clinical Epigenetics*, *9*, 61. https://doi.org/https://doi.org/10.1186/s13148-017-0361-3

Kadambari, S., Abo, Y.-N., Phuong, L. K., Osowicki, J., & Bryant, P. A. (2020). Decrease in Infection-Related Hospital Admissions During COVID-19: Why Are Parents Avoiding the Doctor? *Pediatric Infectious Disease Journal*, *39*(11), e385–e386. https://doi.org/10.1097/INF.0000000000002870

Kamaruddin, A. S., Jalaludin, J., & Choo, C. P. (2015). Indoor Air Quality and Its Association with Respiratory Health among Malay Preschool Children in Shah Alam and Hulu Langat. *Advances in Environmental Biology*, *9*(9), 17–26. Retrieved from http://www.aensiweb.net/AENSIWEB/aeb/aeb/2015/Special IPN BANDUNG/17-26.pdf

Kamaruddin, A. S., Jalaludin, J., & Hamedon, T. R. (2016). Exposure to Industrial Air Pollutants and Respiratory Health School and Home Exposure among Primary School Children in Kemaman, Terengganu. *International Journal of Applied Chemistry*, *12*(1), 45–50. Retrieved from https://www.ripublication.com/ijacspl/ijacv12n1spl_09.pdf

Kamaruddin, A. S., Jalaludin, J., Hamedon, T. R., & Hisamuddin, N. H. (2019). FeNO as a Biomarker for Airway Inflammation Due to Exposure to Air Pollutants among School Children Nearby Industrial Areas in Terengganu. *Pertanika Journal of Science & Technology*, *27*(2), 589–600. Retrieved from http://www.pertanika.upm.edu.my/Pertanika PAPERS/JST Vol. 27 (2) Apr. 2019/03 JST(S)-0477-2019.pdf

Kanchanasuta, S., Sooktawee, S., Patpai, A., & Vatanasomboon, P. (2020). Temporal Variations and Potential Source Areas of Fine Particulate Matter in Bangkok, Thailand. *Air, Soil and Water Research*, *13*, 117862212097820. https://doi.org/10.1177/1178622120978203

Keen, C. L., Holt, R. R., Oteiza, P. I., Fraga, C. G., & Schmitz, H. H. (2005). Cocoa Antioxidants and Cardiovascular Health. *The American Journal of Clinical Nutrition*, *81*(1), 298S-303S. https://doi.org/10.1093/ajcn/81.1.298S

Kelkar, H., Sharma, A. K., & Chaturvedi, S. (2019). Association of Air Pollution and Lung Function of Young Adult Females in New Delhi. *Journal of Health and Pollution*, *9*(22), 190611. https://doi.org/10.5696/2156-9614-9.22.190611

Kenyon, C. C., Hill, D. A., Henrickson, S. E., Bryant-Stephens, T. C., & Zorc, J. J. (2020). Initial Effects of The COVID-19 Pandemic on Pediatric Asthma Emergency Department Utilization. *Journal of Allergy and Clinical Immunology: In Practice*, *8*(8), 2774-2776.e1. https://doi.org/10.1016/j.jaip.2020.05.045

Khan, M. F., Hamid, A. H., Bari, M. A., Tajudin, A. B. A., Latif, M. T., Nadzir, M. S. M., … Kumar, P. (2019). Airborne Particles in The City Center of Kuala Lumpur: Origin, Potential Driving Factors, and Deposition Flux in Human Respiratory Airways. *Science of the Total Environment*, *650*, 1195–1206. https://doi.org/10.1016/j.scitotenv.2018.09.072

Kheirbek, I., Haney, J., Douglas, S., Ito, K., & Matte, T. (2016). The Contribution of Motor Vehicle Emissions to Ambient Fine Particulate Matter Public Health Impacts in New York City: A Health Burden Assessment. *Environmental Health: A Global Access Science Source*, *15*(1), 89. https://doi.org/10.1186/s12940-016-0172-6

Kholod, N., & Evans, M. (2016). Reducing Black Carbon Emissions from Diesel Vehicles in Russia: An Assessment and Policy Recommendations. *Environmental Science & Policy*, *56*, 1–8. https://doi.org/https://doi.org/10.1016/j.envsci.2015.10.017

Kietzmann, T., Petry, A., Shvetsova, A., Gerhold, J. M., & Görlach, A. (2017). The Epigenetic Landscape Related to Reactive Oxygen Species Formation in The Cardiovascular System. *British Journal of Pharmacology*, *174*(12), 1533–1554. https://doi.org/10.1111/bph.13792

Kim, D., Chen, Z., Zhou, L.-F., & Huang, S.-X. (2018). Air Pollutants and Early Origins of Respiratory Diseases. *Chronic Diseases and Translational Medicine*, *4*(2), 75–94. https://doi.org/10.1016/j.cdtm.2018.03.003

Kim, H. J., Choi, M. G., Park, M. K., & Seo, Y. R. (2017). Predictive and Prognostic Biomarkers of Respiratory Diseases due to Particulate Matter Exposure. *Journal of Cancer Prevention*, *22*(1), 6–15. https://doi.org/10.15430/JCP.2017.22.1.6

Kim, J. J., Huen, K., Adams, S., Smorodinsky, S., Hoats, A., Malig, B., … Ostro, B. (2008). Residential Traffic and Children's Respiratory Health. *Environmental Health Perspectives*, *116*(9), 1274–1279. https://doi.org/10.1289/ehp.10735

Krishnaswamy, J., Koon, S. S., & Annamalai, N. (2019). The Shadow Education System: Students' Responses to Private Tutorial Learning. *Malaysian Journal of Learning and Instruction*, *16*(2), 201–225.

Kumar, S., Joos, G., Boon, L., Tournoy, K., Provoost, S., & Maes, T. (2017). Role of Tumor Necrosis Factor-α and Its Receptors in Diesel Exhaust Particle-Induced Pulmonary Inflammation. *Scientific Reports*, *7*, 11508. https://doi.org/10.1038/s41598-017-11991-7

Kusumaningtyas, S. D. A., Aldrian, E., Wati, T., Atmoko, D., & Sunaryo, S. (2018). The Recent State of Ambient Air Quality in Jakarta. *Aerosol and Air Quality Research*, *18*(9), 2343–2354. https://doi.org/10.4209/aaqr.2017.10.0391

Langie, S. A. S., Moisse, M., Szarc vel Szic, K., Van Der Plas, E., Koppen, G., De Prins, S., … De Boever, P. (2018). GLI2 Promoter Hypermethylation in Saliva of Children with a Respiratory Allergy. *Clinical Epigenetics*, *10*(1), 1–13. https://doi.org/10.1186/s13148-018-0484-1

Latif, M. T., Abd Hamid, H. H., Ahamad, F., Khan, M. F., Mohd Nadzir, M. S., Othman, M., … Tahir, N. M. (2019). BTEX Compositions and Its Potential Health Impacts in Malaysia. *Chemosphere*, *237*, 124451. https://doi.org/10.1016/j.chemosphere.2019.124451

Lee, W. J., & Zhu, B. T. (2006). Inhibition of DNA Methylation by Caffeic Acid and Chlorogenic Acid, Two Common Catechol-Containing Coffee Polyphenols. *Carcinogenesis*, *27*(2), 269–277. https://doi.org/10.1093/carcin/bgi206

Lee, Y.-Y., Lin, S.-L., Yuan, C.-S., Lin, M.-Y., & Chen, K.-S. (2018). Reduction of Atmospheric Fine Particle Level by Restricting The Idling Vehicles around A Sensitive Area. *Journal of the Air & Waste Management Association*, *68*(7), 656–670. https://doi.org/10.1080/10962247.2018.1438320

Lei, X., Chen, R., Wang, C., Shi, J., Zhao, Z., Li, W., … Kan, H. (2020). Necessity of Personal Sampling for Exposure Assessment on Specific Constituents of PM2.5: Results of A Panel Study in Shanghai, China. *Environment International*, *141*, 105786. https://doi.org/10.1016/j.envint.2020.105786

Lemeshow, S., Hosmer Jr, D. W., Klar, J., & Lwanga, S. K. (1990). *Adequacy of Sample Size in Health Studies*. Chichester: World Health Organization. Retrieved from http://apps.who.int/iris/bitstream/handle/10665/41607/0471925179_eng.pdf?sequence=1&isAllowed=y

Leung, T. H., Hoffmann, A., & Baltimore, D. (2004). One Nucleotide in A κB Site Can Determine Cofactor Specificity for NF-κB Dimers. *Cell*, *118*(4), 453–464. https://doi.org/10.1016/j.cell.2004.08.007

Li, Y., Mu, Z., Wang, H., Liu, J., & Jiang, F. (2018). The Role of Particulate Matters on Methylation of IFN-γ and IL-4 Promoter Genes in Pediatric Allergic Rhinitis. *Oncotarget*, *9*(25), 17406–17419. https://doi.org/10.18632/oncotarget.24227

Lin, C., Gillespie, J., Schuder, M. D., Duberstein, W., Beverland, I. J., & Heal, M. R. (2015). Evaluation and Calibration of Aeroqual Series 500 Portable Gas Sensors for Accurate Measurement of Ambient Ozone and Nitrogen Dioxide. *Atmospheric Environment*, *100*, 111–116. https://doi.org/10.1016/j.atmosenv.2014.11.002

Lin, V. W., Baccarelli, A. A., & Burris, H. H. (2016). Epigenetics - A Potential Mediator between Air Pollution and Preterm Birth. *Environmental Epigenetics*, *2*(1), dvv008. https://doi.org/10.1093/eep/dvv008

Lin, Y. C., Chi, W. J., & Lin, Y. Q. (2020). The Improvement of Spatial-Temporal Resolution of PM2.5 Estimation Based on Micro-Air Quality Sensors By Using Data Fusion Technique. *Environment International*, *134*, 105305. https://doi.org/10.1016/j.envint.2019.105305

Lippmann, M. (2011). Regional Deposition of Particles in the Human Respiratory Tract. In *Comprehensive Physiology* (pp. 213–232). Hoboken, NJ, USA: John Wiley & Sons, Inc. https://doi.org/10.1002/cphy.cp090114

Liu, Q., Ma, T., Olson, M. R., Liu, Y., Zhang, T., Wu, Y., & Schauer, J. J. (2016). Temporal Variations of Black Carbon During Haze and Non-Haze Days in Beijing. *Scientific Reports*, *6*(1), 1–10. https://doi.org/10.1038/srep33331

Liu, S. K., Cai, S., Chen, Y., Xiao, B., Chen, P., & Xiang, X. D. (2016). The Effect of Pollutional Haze on Pulmonary Function. *Journal of Thoracic Disease*, *8*(1), E41–E56. https://doi.org/10.3978/j.issn.2072-1439.2016.01.18

Liu, T., Zhang, L., Joo, D., & Sun, S. C. (2017). NF-κB Signaling in Inflammation. *Signal Transduction and Targeted Therapy*, *2*(1), 1–9. https://doi.org/10.1038/sigtrans.2017.23

Liu, Y., Zhang, B., Zhang, T., Wang, H., Peng, L., & Zhou, L. (2020). Effect of NF-κB Signal Pathway on Mucus Secretion Induced by Atmospheric PM2.5 in Asthmatic Rats. *Ecotoxicology and Environmental Safety*, *190*, 110094. https://doi.org/10.1016/j.ecoenv.2019.110094

Long, M., Park, S. G., Strickland, I., Hayden, M. S., & Ghosh, S. (2009). Nuclear Factor-κB Modulates Regulatory T Cell Development by Directly Regulating Expression of Foxp3 Transcription Factor. *Immunity*, *31*(6), 921–931. https://doi.org/10.1016/j.immuni.2009.09.022

Lovinsky-Desir, S., Jung, K. H., Jezioro, J. R., Torrone, D. Z., de Planell-Saguer, M., Yan, B., … Miller, R. L. (2017). Physical Activity, Black Carbon Exposure, and DNA Methylation in the FOXP3 Promoter. *Clinical Epigenetics*, *9*(1), 65. https://doi.org/https://doi.org/10.1186/s13148-017-0364-0

Lu, C., Jain, S. U., Hoelper, D., Bechet, D., Rosalynn, C., Ran, L., … Bruce, R. (2016). Histone H3K36 Mutations Promote Sarcomagenesis through Altered Histone Methylation Landscape. *Science*, *352*(6287), 844–849. https://doi.org/10.1126/science.aac7272.Histone

Lutfi, M. F. (2017). The Physiological Basis and Clinical Significance of Lung Volume Measurements. *Multidisciplinary Respiratory Medicine*, *12*(1), 3. https://doi.org/10.1186/s40248-017-0084-5

Lv, Y., Wang, H., Wei, S., Zhang, L., & Zhao, Q. (2017). The Correlation between Indoor and Outdoor Particulate Matter of Different Building Types in Daqing, China. *Procedia Engineering*, *205*, 360–367. https://doi.org/10.1016/j.proeng.2017.10.002

Ma, D., Jiang, C., Hu, X., Liu, H., Li, Q., Li, T., … Li, O. (2014). Methylation Patterns of the IFN-γ Gene in Cervical Cancer Tissues. *Scientific Reports*, *4*, 1–6. https://doi.org/10.1038/srep06331

Mafort, T. T., Rufino, R., Costa, C. H., & Lopes, A. J. (2016). Obesity: Systemic and Pulmonary Complications, Biochemical Abnormalities, and Impairment of Lung Function. *Multidisciplinary Respiratory Medicine*, *11*. https://doi.org/10.1186/s40248-016-0066-z

Matz, C. J., Stieb, D. M., Egyed, M., Brion, O., & Johnson, M. (2018). Evaluation of Daily Time Spent in Transportation and Traffic-Influenced Microenvironments by Urban Canadians. *Air Quality, Atmosphere and Health*, *11*(2), 209–220. https://doi.org/10.1007/s11869-017-0532-6

McCarthy, K. (2018). Pulmonary Function Testing. Retrieved November 13, 2019, from https://emedicine.medscape.com/article/303239-overview

McConnell, R., Berhane, K., Yao, L., Jerrett, M., Lurmann, F., Gilliland, F., … Peters, J. (2006). Traffic, Susceptibility, and Childhood Asthma. *Environmental Health Perspectives*, *114*(5), 766–772. https://doi.org/10.1289/ehp.8594

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*(3), 316–323. https://doi.org/10.4209/aaqr.2010.08.0072

Mei, M., Song, H., Chen, L., Hu, B., Bai, R., Xu, D., … Chen, C. (2018). Early-life Exposure to Three Size-Fractionated Ultrafine and Fine Atmospheric Particulates in Beijing Exacerbates Asthma Development in Mature Mice. *Particle and Fibre Toxicology*, *15*(1), 13. https://doi.org/10.1186/s12989-018-0249-1

Meldrum, K., Guo, C., Marczylo, E. L., Gant, T. W., Smith, R., & Leonard, M. O. (2017). Mechanistic Insight into The Impact of Nanomaterials on Asthma and Allergic Airway Disease. *Particle and Fibre Toxicology*, *14*(1), 1–35. https://doi.org/10.1186/s12989-017-0228-y

Ministry of Education Malaysia. (2021). Senarai Sekolah Kementerian Pendidikan Malaysia. Retrieved February 3, 2021, from https://www.moe.gov.my/en/muat-turun/laporan-dan-statistik/senarai-sekolah

Ministry of Health Malaysia. (2021). Priority List of Environmental Health Issues in Malaysia. Retrieved February 5, 2021, from http://nehapmalaysia.moh.gov.my/priority-list-of-environmental-health-issues-in-malaysia/?fbclid=IwAR0l5bFMeHR5hStF94p_c2gwJVoqn0O7yV8QjA_qNPjpfFhHVcqTkg803v0

Moen, E. L., Mariani, C. J., Zullow, H., Jeff-Eke, M., Litwin, E., Nikitas, J. N., & Godley, L. A. (2015). New Themes in The Biological Functions of 5-Methylcytosine and 5-Hydroxymethylcytosine. *Immunological Reviews*, *263*(1), 36–49. https://doi.org/10.1111/imr.12242

MOH Malaysia. (2020). *Health Facts 2020 (Reference Data for 2019)*. *Ministry of Health Malaysia*. Putrajaya. Retrieved from https://www.moh.gov.my/moh/resources/Penerbitan/Penerbitan Utama/HEALTH FACTS/Health Facts 2020.pdf

Mohamad Fandi, N. F., Jalaludin, J., Latif, M. T., Abd Hamid, H. H., & 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

Mohamad Fandi, N. F., Wan Mansor, W. A., & Jalaludin, J. (2018). Work Exposure to Traffic Air Pollutants (PM10, Benzene, Toluene, and Xylene) and Respiratory Health Implications among Urban Traffic Policemen in Klang Valley, Malaysia. *Malaysian Journal of Medicine and Health Sciences*, *14*(SP2), 2636–9346. Retrieved from http://www.medic.upm.edu.my/upload/dokumen/2018120408583509_MJMHS_SP_Nov_2018.pdf

Mohamad Jamil, P. A. S., Mohammad Yusof, N. A. D., Karuppiah, K., Rasdi, I., Jalaludin, J., Mohd Tamrin, S. B., … Hashim, N. M. (2020). Malaysian Traffic Police in Highly Populated Areas: Is It Safe Working Outdoors on A Daily Basis? *Aerosol and Air Quality Research*, *20*(9), 2003–2011. https://doi.org/10.4209/aaqr.2020.02.0080

Mohamad, ND, Ash’aari, Z., & Othman, M. (2015). Preliminary Assessment of Air Pollutant Sources Identification at Selected Monitoring Stations in Klang Valley, Malaysia. *Procedia Environmental Sciences*, *30*, 121–126. https://doi.org/10.1016/j.proenv.2015.10.021

Mohamad, Noorlin, Latif, M. T., & Khan, M. F. (2016). Source Apportionment and Health Risk Assessment of PM10 in A Naturally Ventilated School in A Tropical Environment. *Ecotoxicology and Environmental Safety*, *124*, 351–362. https://doi.org/10.1016/j.ecoenv.2015.11.002

Mohammadyan, M., Alizadeh-Larimi, A., Etemadinejad, S., Latif, M. T., Heibati, B., Yetilmezsoy, K., & Abdul-Wahab, A. (2017). Particulate Air Pollution at Schools: Indoor-Outdoor Relationship and Determinants of Indoor Concentrations. *Aerosol and Air Quality Research*, *17*, 857–864. https://doi.org/10.4209/aaqr.2016.03.0128

Mohd Isa, K. N., Hashim, Z., Jalaludin, J., Lung Than, L. T., & Hashim, J. H. (2020). The Effects of Indoor Pollutants Exposure on Allergy and Lung Inflammation: An Activation State of Neutrophils and Eosinophils in Sputum. *International Journal of Environmental Research and Public Health*, *17*(15), 5413. https://doi.org/10.3390/ijerph17155413

Mohd Nadzir, M. S., Ooi, M. C. G., Alhasa, K. M., Abu Bakar, M. A., Ahmad Mohtar, A. A., Mohd Nor, M. F. F., … Mohd Nor, M. Z. (2020). The Impact of Movement Control Order (MCO) during Pandemic COVID-19 on Local Air Quality in an Urban Area of Klang Valley, Malaysia. *Aerosol and Air Quality Research*, *20*, 1237–1248. https://doi.org/10.4209/aaqr.2020.04.0163

Mohd Nor Rawi, N. A., Jalaludin, J., & Chua, P. C. (2015). Indoor Air Quality and Respiratory Health among Malay Preschool Children in Selangor. *BioMed Research International*, 248178. https://doi.org/https://doi.org/10.1155/2015/248178

Mohd Shafie, S. H., & Mahmud, M. (2017). Public Perception on Traffic Pollution in Federal Territory of Kuala Lumpur, Malaysia. *Planning Malaysia*, *15*(4), 105–114. https://doi.org/10.21837/pmjournal.v15.i4.321

Montrose, L., Ward, T. J., Semmens, E. O., Cho, Y. H., Brown, B., & Noonan, C. W. (2017). Dietary Intake is Associated with Respiratory Health Outcomes and DNA Methylation in Children with Asthma. *Allergy, Asthma and Clinical Immunology*, *13*(1), 1–12. https://doi.org/10.1186/s13223-017-0187-8

Morawska, L., Thai, P. K., Liu, X., Asumadu-Sakyi, A., Ayoko, G., Bartonova, A., … Williams, R. (2018). Applications of Low-Cost Sensing Technologies for Air Quality Monitoring and Exposure Assessment: How Far Have They Gone? *Environment International*, *116*, 286–299. https://doi.org/10.1016/j.envint.2018.04.018

Morgenstern, V., Zutavern, A., Cyrys, J., Brockow, I., Koletzko, S., Krämer, U., … Schäfer, T. (2008). Atopic Diseases, Allergic Sensitization, and Exposure to Traffic-Related Air pollution in Children. *American Journal of Respiratory and Critical Care Medicine*, *177*(12), 1331–1337. https://doi.org/10.1164/rccm.200701-036OC

Muhamad Daud, S. A., Jalaludin, J., & Sopian, N. A. (2018). Air Pollutants Exposure and Frequency of Micronuclei (MN) among Primary School Children Nearby Industrial Area. *Malaysian Journal of Medicine and Health Sciences*, *14*(SP2), 2636–9346. Retrieved from http://www.medic.upm.edu.my/upload/dokumen/2018120408575208_MJMHS_SP_Nov_2018.pdf

Nakayama, T., Matsumi, Y., Kawahito, K., & Watabe, Y. (2018). Development and Evaluation of a Palm-Sized Optical PM2.5 Sensor. *Aerosol Science and Technology*, *52*(1), 2–12. https://doi.org/10.1080/02786826.2017.1375078

Nathan, C., & Cunningham-Bussel, A. (2013). Beyond Oxidative Stress: An Immunologist's Guide to Reactive Oxygen Species. *Nature Reviews Immunology*, *13*(5), 349–361. https://doi.org/10.1038/nri3423

National Center for Biotechnology Information. (2019). Ozone. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/Ozone

Nédélec, Y., Sanz, J., Baharian, G., Szpiech, Z. A., Pacis, A., Dumaine, A., … Barreiro, L. B. (2016). Genetic Ancestry and Natural Selection Drive Population Differences in Immune Responses to Pathogens. *Cell*, *167*(3), 657-669.e21. https://doi.org/10.1016/j.cell.2016.09.025

Neft, I., Scungio, M., Culver, N., & Singh, S. (2016). Simulations of Aerosol Filtration by Vegetation: Validation of Existing Models with Available Lab Data and Application to Near-Roadway Scenario. *Aerosol Science and Technology*, *50*(9), 937–946. https://doi.org/10.1080/02786826.2016.1206653

Neves, A., & Brand, C. (2019). Assessing The Potential for Carbon Emissions Savings from Replacing Short Car Trips with Walking and Cycling Using A Mixed GPS-Travel Diary Approach. *Transportation Research Part A: Policy and Practice*, *123*, 130–146. https://doi.org/10.1016/j.tra.2018.08.022

NIOSH. (1994). *NMAM 0500: Particulates Not Otherwise Regulated, Total*. Retrieved from https://www.cdc.gov/niosh/docs/2003-154/pdfs/0500.pdf

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

Niu, Y., Desmarais, T. L., Tong, Z., Yao, Y., & Costa, M. (2015). Oxidative Stress Alters Global Histone Modification and DNA Methylation. *Free Radical Biology and Medicine*, *82*, 22–28. https://doi.org/10.1016/j.freeradbiomed.2015.01.028

Nucleus Medical Media. (2016). Respiratory System of Child. Retrieved November 8, 2019, from https://ebsco-smartimagebase-com.ezadmin.upm.edu.my/respiratory-system-of-child/view-item?ItemID=13299

Ohguchi, H., Hideshima, T., & Anderson, K. C. (2018). The Biological Significance of Histone Modifiers in Multiple Myeloma: Clinical Applications. *Blood Cancer Journal*, *8*(9), 1–13. https://doi.org/10.1038/s41408-018-0119-y

Othman, M., & Latif, M. T. (2020). Pollution Characteristics, Sources, and Health Risk Assessments of Urban Road Dust in Kuala Lumpur City. *Environmental Science and Pollution Research*, *27*(10), 11227–11245. https://doi.org/10.1007/s11356-020-07633-7

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

Patel, M. M., Hoepner, L., Garfinkel, R., Chillrud, S., Reyes, A., Quinn, J. W., … Miller, R. L. (2009). Ambient Metals, Elemental Carbon, and Wheeze and Cough in New York City Children through 24 Months of Age. *American Journal of Respiratory and Critical Care Medicine*, *180*(11), 1107–1113. https://doi.org/10.1164/rccm.200901-0122OC

Paunescu, A. C., Casas, M., Ferrero, A., Pañella, P., Bougas, N., Beydon, N., … Momas, I. (2019). Associations of Black Carbon with Lung Function and Airway Inflammation in Schoolchildren. *Environment International*, *131*, 104984. https://doi.org/10.1016/j.envint.2019.104984

Pellegrino, R., Viegi, G., Brusasco, V., Crapo, R. O., Burgos, F., Casaburi, R., … Wanger, J. (2005). Interpretative Strategies for Lung Function Tests. *European Respiratory Journal*, *26*, 948–968. https://doi.org/10.1183/09031936.05.00035205

Peng, H., Zong, D., Zhou, Z., & Chen, P. (2016). Pulmonary Diseases and Epigenetics. In *Medical Epigenetics* (pp. 221–242). Elsevier Inc. https://doi.org/10.1016/B978-0-12-803239-8.00013-2

Petit, P. C., Fine, D. H., Vásquez, G. B., Gamero, L., Slaughter, M. S., & Dasse, K. A. (2017). The Pathophysiology of Nitrogen Dioxide During Inhaled Nitric Oxide Therapy. *ASAIO Journal*, *63*(1), 7–13. https://doi.org/10.1097/MAT.0000000000000425

Plusquin, M., Guida, F., Polidoro, S., Vermeulen, R., Raaschou-Nielsen, O., Campanella, G., … Chadeau-Hyam, M. (2017). DNA Methylation and Exposure to Ambient Air Pollution in Two Prospective Cohorts. *Environment International*, *108*(August), 127–136. https://doi.org/10.1016/j.envint.2017.08.006

Prunicki, M., Stell, L., Dinakarpandian, D., de Planell-Saguer, M., Lucas, R. W., Hammond, S. K., … Nadeau, K. C. (2018). Exposure to NO2, CO and PM2.5 is Linked to Regional DNA Methylation Differences in Asthma. *Clinical Epigenetics*, *10*, 2. https://doi.org/10.1186/s13148-017-0433-4

Public Works Department Malaysia. (2019). *Statistik Jalan Malaysia Edisi 2019*. (M. E. Abd Kasim, M. I. Ismail, N. S. Abdullah, H. F. Hamzah, F. Abdullah, V. Muniandy, … Z. Hashim, Eds.) (2019th ed.). Kuala Lumpur: Cawangan Senggara Fasiliti Jalan, Ibu Pejabat JKR Malaysia.

Quincey, P. (2007). A Relationship between Black Smoke Index and Black Carbon Concentration. *Atmospheric Environment*, *41*(36), 7964–7968. https://doi.org/10.1016/j.atmosenv.2007.09.033

Rani, N. L. A., Azid, A., Khalit, S. I., Juahir, H., & Samsudin, M. S. (2018). Air Pollution Index Trend Analysis in Malaysia, 2010-15. *Polish Journal of Environmental Studies*, *27*(2), 801–808. https://doi.org/10.15244/pjoes/75964

Reddy, D., Khade, B., Pandya, R., & Gupta, S. (2017). A Novel Method for Isolation of Histones from Serum and Its Implications in Therapeutics and Prognosis of Solid Tumours. *Clinical Epigenetics*, *9*(1), 1–11. https://doi.org/https://doi.org/10.1186/s13148-017-0330-x

Ren, N., Atyah, M., Chen, W. Y., & Zhou, C. H. (2017). The Various Aspects of Genetic and Epigenetic Toxicology: Testing Methods and Clinical Applications. *Journal of Translational Medicine*, *15*(1), 110. https://doi.org/10.1186/s12967-017-1218-4

Rice, M. B., Rifas-Shiman, S. L., Litonjua, A. A., Oken, E., Gillman, M. W., Kloog, I., … Gold, D. R. (2016). Lifetime Exposure to Ambient Pollution and Lung Function in Children. *American Journal of Respiratory and Critical Care Medicine*, *193*(8), 881–888. https://doi.org/10.1164/rccm.201506-1058OC

Rider, C. F., & Carlsten, C. (2019). Air Pollution and DNA Methylation: Effects of Exposure in Humans. *Clinical Epigenetics*, *11*(1). https://doi.org/https://doi.org/10.1186/s13148-019-0713-2

Roldán-Henao, N., Hoyos, C. D., Herrera-Mejía, L., & Isaza, A. (2020). An Investigation of The Precipitation Net Effect on The Particulate Matter Concentration in A Narrow Valley: Role of Lower-Troposphere Stability. *Journal of Applied Meteorology and Climatology*, *59*(3), 401–426. https://doi.org/10.1175/JAMC-D-18-0313.1

Saad, N. J., Patel, J., Minelli, C., & Burney, P. G. J. (2017). Explaining Ethnic Disparities in Lung Function among Young Adults: A Pilot Investigation. *PLOS ONE*, *12*(6), e0178962. https://doi.org/10.1371/journal.pone.0178962

Sadiq, S., Rizvi, N. A., Soleja, F. K., & Abbasi, M. (2019). Factors Affecting Spirometry Reference Range in Growing Children. *Pakistan Journal of Medical Sciences*, *35*(6), 1587–1591. https://doi.org/10.12669/pjms.35.6.1212

Sampson, S. (2017). Spirometry: What to Expect and How to Interpret Your Results. Retrieved November 13, 2019, from https://www.healthline.com/health/spirometry

Sarigiannis, D. A. (2019). The Exposome: A New Tool for Improved Health Risk Assessment. *Management of Emerging Public Health Issues and Risks: Multidisciplinary Approaches to the Changing Environment*, xxiii–xlv. https://doi.org/10.1016/B978-0-12-813290-6.02002-3

Schalch, T., & Steiner, F. A. (2017). Structure of Centromere Chromatin: From Nucleosome to Chromosomal Architecture. *Chromosoma*, *126*(4), 443–455. https://doi.org/10.1007/s00412-016-0620-7

Schultz, E. S., Litonjua, A. A., & Melén, E. (2017). Effects of Long-Term Exposure to Traffic-Related Air Pollution on Lung Function in Children. *Current Allergy and Asthma Reports*, *17*(6), 996–1006. https://doi.org/10.1007/s11882-017-0709-y

Schulze, F., Gao, X., Virzonis, D., Damiati, S., Schneider, M. R., & Kodzius, R. (2017). Air Quality Effects on Human Health and Approaches for Its Assessment through Microfluidic Chips. *Genes*, *8*(10). https://doi.org/https://doi.org/10.3390/genes8100244

Sharavanan, V. J., Sivaramakrishnan, M., Sivarajasekar, N., Senthilrani, N., Kothandan, R., Dhakal, N., … Naushad, M. (2020). Pollutants Inducing Epigenetic Changes and Diseases. *Environmental Chemistry Letters*, *18*(2), 325–343. https://doi.org/10.1007/s10311-019-00944-3

Shukla, A., Bunkar, N., Kumar, R., Bhargava, A., Tiwari, R., Chaudhury, K., … Mishra, P. K. (2019). Air Pollution Associated Epigenetic Modifications: Transgenerational Inheritance and Underlying Molecular Mechanisms. *Science of The Total Environment*, *656*, 760–777. https://doi.org/https://doi.org/10.1016/J.SCITOTENV.2018.11.381

Singh, H., Yadav, M., Kumar, N., Kumar, A., & Kumar, M. (2020). Assessing Adaptation and Mitigation Potential of Roadside Trees Under The Influence of Vehicular Emissions: A Case Study of Grevillea robusta and Mangifera indica Planted in An Urban City of India. *PLOS ONE*, *15*(1), e0227380. https://doi.org/10.1371/JOURNAL.PONE.0227380

Sofer, T., Baccarelli, A., Cantone, L., Coull, B., Maity, A., & Schwartz, J. (2013). Methylation Pattern in the Asthma Pathway. *Epigenomics*, *5*(2), 147–154. https://doi.org/10.2217/epi.13.16.Exposure

Sofwan, N. M., & Latif, M. T. (2021). Characteristics of The Real-Driving Emissions from Gasoline Passenger Vehicles in the Kuala Lumpur Urban Environment. *Atmospheric Pollution Research*, *12*(1), 306–315. https://doi.org/10.1016/j.apr.2020.09.004

Somineni, H. K., Zhang, X., Biagini Myers, J. M., Kovacic, M. B., Ulm, A., Jurcak, N., … Ji, H. (2016). Ten-Eleven Translocation 1 (TET1) Methylation Is Associated with Childhood Asthma and Traffic-Related Air Pollution. *The Journal of Allergy and Clinical Immunology*, *137*(3), 797-805.e5. https://doi.org/10.1016/j.jaci.2015.10.021

Sopian, N. A., Jalaludin, J., Tengku Mayusi, T. Z. A., & Latif, M. T. (2020). Increased Chromosomal Damage among Children in Proximity to Industrial Zone. *Aerosol and Air Quality Research*, *20*, 944–955. https://doi.org/10.4209/aaqr.2019.12.0653

Spinelle, L., Gerboles, M., Kok, G., Persijn, S., & Sauerwald, T. (2017). Review of Portable and Low-Cost Sensors for the Ambient Air Monitoring of Benzene and Other Volatile Organic Compounds. *Sensors*, *17*(7), 1520. https://doi.org/10.3390/s17071520

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

Stover, P. J., James, W. P. T., Krook, A., & Garza, C. (2018). Emerging Concepts on The Role of Epigenetics in The Relationships between Nutrition and Health. *Journal of Internal Medicine*, *284*, 37–49. https://doi.org/10.1111/joim.12768

Suhaimi, N., Jalaludin, J., & Abu Bakar, S. (2015). Association between School and Residential Air Pollutants with Respiratory Symptoms among School Children at an Industrial Area. *Advances in Environmental Biology*, *9*(26), 77–86. Retrieved from https://www.researchgate.net/publication/291833606_Association_between_School_and_Residential_Air_Pollutants_with_Respiratory_Symptoms_among_School_Children_at_an_Industrial_Area

Sulong, N. A., Latif, M. T., Khan, M. F., Amil, N., Ashfold, M. J., Abdul Wahab, M. I., … Sahani, M. (2017). Source Apportionment and Health Risk Assessment among Specific Age Groups During Haze and Non-Haze Episodes in Kuala Lumpur, Malaysia. *Science of the Total Environment*, *601–602*, 556–570. https://doi.org/10.1016/j.scitotenv.2017.05.153

Sulong, N. A., Latif, M. T., Sahani, M., Khan, M. F., Fadzil, M. F., Tahir, N. 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

Sultan, Z., Ngadiman, N., Dela, F., Kadir, A., Roslan, N., & Moeinaddini, M. (2016). *Factor Analysis of Motorcycle Crashes in Malaysia*. *Planning Malaysia* (Vol. 14). https://doi.org/10.21837/PM.V14I4.154

Sun, B., Shi, Y., Yang, X., Zhao, T., Duan, J., & Sun, Z. (2018). DNA Methylation: A Critical Epigenetic Mechanism Underlying the Detrimental Effects of Airborne Particulate Matter. *Ecotoxicology and Environmental Safety*, *161*(June), 173–183. https://doi.org/https://doi.org/10.1016/j.ecoenv.2018.05.083

Tajudin, M. A. B. A., Khan, M. F., Mahiyuddin, W. R. W., Hod, R., Latif, M. T., Hamid, A. H., … Sahani, M. (2019). Risk of Concentrations of Major Air Pollutants on The Prevalence of Cardiovascular and Respiratory Diseases in Urbanized Area of Kuala Lumpur, Malaysia. *Ecotoxicology and Environmental Safety*, *171*, 290–300. https://doi.org/10.1016/j.ecoenv.2018.12.057

Tan, S. Y., Praveena, S. M., Abidin, E. Z., & Cheema, M. S. (2018). Heavy Metal Quantification of Classroom Dust in School Environment and Its Impacts on Children Health from Rawang (Malaysia). *Environmental Science and Pollution Research*, *25*(34), 34623–34635. https://doi.org/10.1007/s11356-018-3396-x

Tang, C. S., Lung, S. C. C., Chang, T. Y., Tu, H. H., & Chang, L. Te. (2019). Investigation of Microenvironmental Exposures to Particle-Bound Polycyclic Aromatic Hydrocarbons for Elementary School Children. *International Journal of Environmental Research and Public Health*, *16*. https://doi.org/10.3390/ijerph16224390

Taylor-Clark, T. E., & Undem, B. J. (2010). Ozone Activates Airway Nerves via The Selective Stimulation of TRPA1 Ion Channels. *The Journal of Physiology*, *588*(3), 423–433. https://doi.org/10.1113/jphysiol.2009.183301

Teleszewski, T. J., & Gładyszewska-Fiedoruk, K. (2020). Characteristics of Humidity in Classrooms with Stack Ventilation and Development of Calculation Models of Humidity Based on The Experiment. *Journal of Building Engineering*, *31*, 101381. https://doi.org/10.1016/j.jobe.2020.101381

Tirado-Magallanes, R., Rebbani, K., Lim, R., Pradhan, S., & Benoukraf, T. (2017). Whole Genome DNA Methylation: Beyond Genes Silencing. *Oncotarget*, *8*(3), 5629–5637. https://doi.org/10.18632/oncotarget.13562

Tran, P. T. M., Ngoh, J. R., & Balasubramanian, R. (2020). Assessment of the Integrated Personal Exposure to Particulate Emissions in Urban Micro-environments: A Pilot Study. *Aerosol and Air Quality Research*, *20*(2), 341–357. https://doi.org/10.4209/aaqr.2019.04.0201

Tuck, N. W., Zaki, S. A., Hagishima, A., Rijal, H. B., Zakaria, M. A., & Yakub, F. (2019). Effectiveness of Free Running Passive Cooling Strategies for Indoor Thermal Environments: Example From A Two-Storey Corner Terrace House in Malaysia. *Building and Environment*, *160*, 106214. https://doi.org/10.1016/j.buildenv.2019.106214

UniProt. (2020). H3C1 Histone H3.1 - Homo sapiens (Human). Retrieved November 13, 2020, from https://www.uniprot.org/uniprot/P68431

United Nations. (2016). *The World's Cities in 2016 Data Booklet* ((ST/ESA/ S). Department of Economic and Social Affairs, Population Division, United Nations. Retrieved from http://www.un.org/en/development/desa/population/publications/pdf/urbanization/the_worlds_cities_in_2016_data_booklet.pdf

United Nations Development Programme. (2021). Sustainable Development Goals. Retrieved February 5, 2021, from https://www.my.undp.org/content/malaysia/en/home/sustainable-development-goals.html

United States EPA. (2015). *Best Practices for Reducing Near-Road Pollution Exposure at Schools*. *US EPA*. Retrieved from https://www.epa.gov/schools/basic-information-about-best-practices-reducing-near-road-pollution-exposure-schools

United States EPA. (2016a). Basic Information about Carbon Monoxide (CO) Outdoor Air Pollution | Carbon Monoxide (CO) Pollution in Outdoor Air. Retrieved November 5, 2019, from https://www.epa.gov/co-pollution/basic-information-about-carbon-monoxide-co-outdoor-air-pollution

United States EPA. (2016b). Basic Information about NO2 | Nitrogen Dioxide (NO2) Pollution. Retrieved from https://www.epa.gov/no2-pollution/basic-information-about-no2

United States EPA. (2017). Technical Overview of Volatile Organic Compounds | Indoor Air Quality (IAQ). Retrieved November 5, 2019, from https://www.epa.gov/indoor-air-quality-iaq/technical-overview-volatile-organic-compounds

United States EPA. (2019). Sulfur Dioxide Basics | Sulfur Dioxide (SO2) Pollution. Retrieved November 5, 2019, from https://www.epa.gov/so2-pollution/sulfur-dioxide-basics#what is so2

United States EPA. (2021). Particulate Matter (PM) Basics. Retrieved February 1, 2021, from https://www.epa.gov/pm-pollution/particulate-matter-pm-basics

Urman, R., Eckel, S., Deng, H., Berhane, K., Avol, E., Lurmann, F., … Gilliland, F. (2018). Risk Effects of Near-Roadway Pollutants and Asthma Status on Bronchitic Symptoms in Children. *Environmental Epidemiology*, *2*(2), e012. https://doi.org/10.1097/ee9.0000000000000012

Urman, R., Mcconnell, R., Islam, T., Avol, E. L., Lurmann, F. W., Vora, H., … Gauderman, W. J. (2014). Associations of Children's Lung Function with Ambient Air Pollution: Joint Effects of Regional and Near-Roadway Pollutants. *Thorax*, *69*, 540–547. https://doi.org/10.1136/thoraxjnl-2012-203159

van der Zee, S. C., Strak, M., Dijkema, M. B. A., Brunekreef, B., & Janssen, N. A. H. (2017). The Impact of Particle Filtration on Indoor Air Quality in A Classroom Near A Highway. *Indoor Air*, *27*(2), 291–302. https://doi.org/10.1111/ina.12308

Van Vliet, E. D. S., Kinney, P. L., Owusu-Agyei, S., Schluger, N. W., Ae-Ngibise, K. A., Whyatt, R. M., … Asante, K. P. (2019). Current Respiratory Symptoms and Risk Factors in Pregnant Women Cooking with Biomass Fuels in Rural Ghana. *Environment International*, *124*, 533–540. https://doi.org/10.1016/j.envint.2019.01.046

Vrijens, K., Trippas, A. J., Lefebvre, W., Vanpoucke, C., Penders, J., Janssen, B. G., & Nawrot, T. S. (2020). Association of Prenatal Exposure to Ambient Air Pollution With Circulating Histone Levels in Maternal Cord Blood. *JAMA Network Open*, *3*(5), e205156. https://doi.org/10.1001/jamanetworkopen.2020.5156

Wang, M., Liu, F., & Zheng, M. (2020). Air Quality Improvement from COVID-19 Lockdown: Evidence from China. *Air Quality, Atmosphere and Health*, 1–14. https://doi.org/10.1007/s11869-020-00963-y

Wang, Z., Calderón, L., Patton, A. P., Sorensen Allacci, M., Senick, J., Wener, R., … Mainelis, G. (2016). Comparison of Real-Time Instruments and Gravimetric Method When Measuring Particulate Matter in A Residential Building. *Journal of the Air & Waste Management Association*, *66*(11), 1109–1120. https://doi.org/10.1080/10962247.2016.1201022

Wargocki, P., Porras-Salazar, J. A., Contreras-Espinoza, S., & Bahnfleth, W. (2020). The Relationships between Classroom Air Quality and Children's Performance in School. *Building and Environment*, *173*, 106749. https://doi.org/10.1016/j.buildenv.2020.106749

Wendt Hess, J., Bachler, G., Momin, F., & Sexton, K. (2019). Assessing Agreement in Exposure Classification between Proximity-Based Metrics and Air Monitoring Data in Epidemiology Studies of Unconventional Resource Development. *International Journal of Environmental Research and Public Health*, *16*(17), 3055. https://doi.org/10.3390/ijerph16173055

WHO. (2013). Definition of Key Terms. Retrieved from https://www.who.int/hiv/pub/guidelines/arv2013/intro/keyterms/en/

Winck, F. V., Ribeiro, A. C. P., Domingues, R. R., Ling, L. Y., Riaño-Pachón, D. M., Rivera, C., … Leme, A. F. P. (2015). Insights into Immune Responses in Oral Cancer Through Proteomic Analysis of Saliva and Salivary Extracellular Vesicles. *Scientific Reports*, *5*. https://doi.org/10.1038/srep16305

Winkler, S., Anderson, J., Garza, L., Ruona, W., Vogt, R., & Wallington, T. (2018). Vehicle Criteria Pollutant (PM, NOx, CO, HCs) Emissions: How Low Should We Go? *Npj Climate and Atmospheric Science*, *1*, 26. https://doi.org/10.1038/s41612-018-0037-5

Wright, R. J., & Brunst, K. J. (2013). Programming of Respiratory Health in Childhood: Influence of Outdoor Air Pollution. *Current Opinion in Pediatrics*, *25*(2), 232–239. https://doi.org/https://doi.org/10.1097/MOP.0b013e32835e78cc

Yang, J., Chang, Y., & Yan, P. (2015). Ranking The Suitability of Common Urban Tree Species for Controlling PM2.5 Pollution. *Atmospheric Pollution Research*, *6*(2), 267–277. https://doi.org/10.5094/APR.2015.031

Yang, M., Guo, Y. M., Bloom, M. S., Dharmagee, S. C., Morawska, L., Heinrich, J., … Dong, G. H. (2020). Is PM1 Similar to PM2.5? A New Insight into The Association of PM1 and PM2.5 with Children's Lung Function. *Environment International*, *145*, 106092. https://doi.org/10.1016/j.envint.2020.106092

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 in Malaysia. *Building and Environment*, *87*, 108–116. https://doi.org/10.1016/j.buildenv.2015.01.015

Yarza, S., Hassan, L., Shtein, A., Lesser, D., Novack, L., Katra, I., … Novack, V. (2020). Novel Approaches to Air Pollution Exposure and Clinical Outcomes Assessment in Environmental Health Studies. *Atmosphere*, *11*(2), 122. https://doi.org/10.3390/atmos11020122

Yen, Y., Yang, C., Mena, K., Cheng, Y., & Chen, P. (2019). Cooking/Window Opening and Associated Increases of Indoor PM2.5 and NO2 Concentrations of Children's Houses in Kaohsiung, Taiwan. *Applied Sciences*, *9*(20), 4306. https://doi.org/10.3390/app9204306

Yi, S.-J., Shon, C., Min, K.-D., Kim, H.-C., Leem, J.-H., Kwon, H.-J., … Kim, S.-Y. (2017). Association between Exposure to Traffic-Related Air Pollution and Prevalence of Allergic Diseases in Children, Seoul, Korea. *BioMed Research International*. https://doi.org/10.1155/2017/4216107

Yoda, Y., Takagi, H., Wakamatsu, J., Ito, T., Nakatsubo, R., Horie, Y., … Shima, M. (2017). Acute Effects of Air Pollutants on Pulmonary Function among Students: A Panel Study in An Isolated Island. *Environmental Health and Preventive Medicine*, *22*(1), 33. https://doi.org/10.1186/s12199-017-0646-3

Zainudin, M. A., Jalaludin, J., & Sopian, N. A. (2019). Indoor Air Quality (IAQ) in Preschools and Its Association with Respiratory Inflammation among Pre-schoolers. *Malaysian Journal of Medicine and Health Sciences*, *15*(SP4), 2636–9346.

Zakaria, M., Ezani, E., Hassan, N., Ramli, N., & Wahab, M. (2019). Traffic-Related Air Pollution (TRAP), Air Quality Perception and Respiratory Health Symptoms of Active Commuters in a University Outdoor Environment. *IOP Conf. Series: Earth and Environmental Science*, *228*, 012017. https://doi.org/10.1088/1755-1315/228/1/012017

Zaki, S. A., Azid, N. S., Shahidan, M. F., Hassan, M. Z., Md Daud, M. Y., Abu Bakar, N. A., … 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*, *12*(18). https://doi.org/10.3390/SU12187301

Zamri, M., Ismail, M., & Kim, Y. (2012). Mapping the Spatial Distribution of Criteria Air Pollutants in Peninsular Malaysia Using Geographical Information System (GIS). In *Air Pollution - Monitoring, Modelling and Health*. InTech. https://doi.org/10.5772/32902

Zhang, Y., & Kutateladze, T. G. (2018). Diet and The Epigenome. *Nature Communications*, *9*, 3375. https://doi.org/10.1038/s41467-018-05778-1

Zhang, Z., Chen, L., Xing, X., Li, D., Gao, C., He, Z., … Chen, W. (2016). Specific Histone Modifications Were Associated with the PAH-Induced DNA Damage Response in Coke Oven Workers. *Toxicology Research*, *5*(4), 1193–1201. https://doi.org/10.1039/c6tx00112b

Zheng, Y., Sanchez-Guerra, M., Zhang, Z., Joyce, B. T., Zhong, J., Kresovich, J. K., … Hou, L. (2017). Traffic-Derived Particulate Matter Exposure and Histone H3 Modification: A Repeated Measures Study. *Environmental Research*, *153*(December 2016), 112–119. https://doi.org/10.1016/j.envres.2016.11.015

Zimmermann, K. A. (2019). Respiratory System: Facts, Function and Diseases. Retrieved November 12, 2019, from https://www.livescience.com/22616-respiratory-system.html

Zordoky, B., & El-Kadi, A. (2009). Role of NF-kappaB in the Regulation of Cytochrome P450 Enzymes. *Current Drug Metabolism*, *10*(2), 164–178. https://doi.org/10.2174/138920009787522151

Zou, B., Zheng, Z., Wan, N., Qiu, Y., & Wilson, J. G. (2016). An Optimized Spatial Proximity Model for Fine Particulate Matter Air Pollution Exposure Assessment in Areas of Sparse Monitoring. *International Journal of Geographical Information Science*, *30*(4), 727–747. https://doi.org/10.1080/13658816.2015.1095921

# BIODATA OF STUDENT

Nur Faseeha Binti Suhaimi was born on 1st August 1991 in Kuala Lumpur Hospital. She received her primary education at Sekolah Kebangsaan Serdang, Selangor from 1998 to 2002. She passed Level One Evaluation (PTS) in 2000, so she was offered to skip Standard 4 and went straight to Standard 5. In 2002, she obtained 5A in Primary School Evaluation Test (UPSR) but continued her lower secondary education in a co-ed daily school of Sekolah Menengah Kebangsaan Seri Serdang, Selangor. Later in 2005, she obtained 9A in Lower Secondary Evaluation (PMR) and was offered to further her upper secondary education in an all-girls boarding school of Tunku Kurshiah College, Negeri Sembilan, from 2006 to 2007. In 2008, she passed the Malaysian Certificate of Education (SPM) with 8A1 and 2A2 and was offered a full government scholarship by Public Service Department (JPA) to further her first degree in the United States of America under the American Degree Foundation Programme. She obtained her Bachelor of Science in Molecular Bioscience and Biotechnology from Rochester Institute of Technology, USA, in 2013. In 2014, she received scholarships from the Ministry of Higher Education (MOHE) Malaysia and the UPM Graduate Research Fund (GRF) to pursue her master's degree. She was conferred a Master of Science degree in Environmental Health from Universiti Putra Malaysia in 2016.

Faseeha is married and is blessed with a daughter and a son. She is currently furthering her study in Doctor of Philosophy in Environmental Health from Universiti Putra Malaysia. She is fully sponsored by Ministry of Higher Education (MOHE) Malaysia under *Skim Latihan Akademik Bumiputera* (SLAB) and UPM under *Tenaga Akademik Muda* (TAM).

# LIST OF PUBLICATIONS

## Journals

Nur Faseeha Suhaimi, Juliana Jalaludin and Suhaili Abu Bakar (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. IF 3.390

Nur Faseeha Suhaimi, Juliana Jalaludin and Suhaili Abu Bakar (2021). Deoxyribonucleic Acid (DNA) Methylation in Children Exposed to Air Pollution: A Possible Mechanism Underlying Respiratory Health Effects Development. Reviews on Environmental Health, 36(1): 77-93. https://doi.org/10.1515/reveh-2020-0065. IF 3.458

Nur Faseeha Suhaimi, Juliana Jalaludin and Muhammad Afif Mohd Juhari (2020). The Impact of Traffic-Related Air Pollution on Lung Function Status and Respiratory Symptoms among Children in Klang Valley, Malaysia. International Journal of Environmental Health Research. (Published ahead of print) https://doi.org/10.1080/09603123.2020.1784397. IF 3.411

Nur Faseeha Suhaimi, Juliana Jalaludin and Mohd Talib Latif (2020). Demystifying A Possible Relationship between COVID-19, Air Quality and Meteorological Factors: Evidence from Kuala Lumpur, Malaysia. Aerosol and Air Quality Research, 20: 1520-1529. https://doi.org/10.4209/aaqr.2020.05.0218. IF 3.063

Ili Nabila Ismail, Juliana Jalaludin, Suhaili Abu Bakar, Nur Hazirah Hisamuddin, Nur Faseeha Suhaimi (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): 106-116. https://doi.org/10.5572/ajae.2019.13.2.106

## Conferences

Nur Faseeha Suhaimi, Juliana Jalaludin and Muhammad Afif Mohd Juhari. Children's Respiratory Health and Indoor Air Pollutants (IAP) in Selected Malaysian Primary Schools. The 16th Conference of the International Society of Indoor Air Quality & Climate on 1 November 2020 held online and organised by International Society of Indoor Air Quality (ISIAQ)

Nur Faseeha Suhaimi, Juliana Jalaludin, Ili Nabila Ismail and Suhaili Abu Bakar. Association of Traffic-Related Air Pollution (TRAP) with DNA Damage and Respiratory Symptoms among Primary School Children in Selangor. The 10th Better Air Quality Conference on 14-16 November 2018 at Borneo Convention Centre Kuching, Sarawak. – Best Poster Presenter (5th Place)

UNIVERSITI PUTRA MALAYSIA

STATUS CONFIRMATION FOR THESIS / PROJECT REPORT AND COPYRIGHT

ACADEMIC SESSION : FIRST SEMESTER 2021/2022

TITLE OF THESIS / PROJECT REPORT :
INFLUENCE OF TRAFFIC-RELATED AIR POLLUTION EXPOSURE ON RESPIRATORY HEALTH, TNFα AND CYP1A1 GENE AND HISTONE MODIFICATIONS AMONG SCHOOL CHILDREN IN THE KLANG VALLEY, MALAYSIA

NAME OF STUDENT : NUR FASEEHA BINTI SUHAIMI

I acknowledge that the copyright and other intellectual property in the thesis/project report belonged to Universiti Putra Malaysia and I agree to allow this thesis/project report to be placed at the library under the following terms:

1. This thesis/project report is the property of Universiti Putra Malaysia.
2. The library of Universiti Putra Malaysia has the right to make copies for educational purposes only.
3. The library of Universiti Putra Malaysia is allowed to make copies of this thesis for academic exchange.

I declare that this thesis is classified as :

*Please tick (√ )

| | | |
|---|---|---|
| ☐ | CONFIDENTIAL | (Contain confidential information under Official Secret Act 1972). |
| ☐ | RESTRICTED | (Contains restricted information as specified by the organization/institution where research was done). |
| ☑ | OPEN ACCESS | I agree that my thesis/project report to be published as hard copy or online open access. |

This thesis is submitted for :

| | | |
|---|---|---|
| ☐ | PATENT | Embargo from_____________ until _____________ (date) (date) |

**Approved by:**

(Signature of Student)
New IC No/ Passport No.:

Date :

(Signature of Chairman of Supervisory Committee)
Name: PROF. DR JULIANA JALALUDIN

Date :

**[Note : If the thesis is CONFIDENTIAL or RESTRICTED, please attach with the letter from the organization/institution with period and reasons for confidentially or restricted. ]**