Biomarkers of Air Pollution in Respiratory Disease

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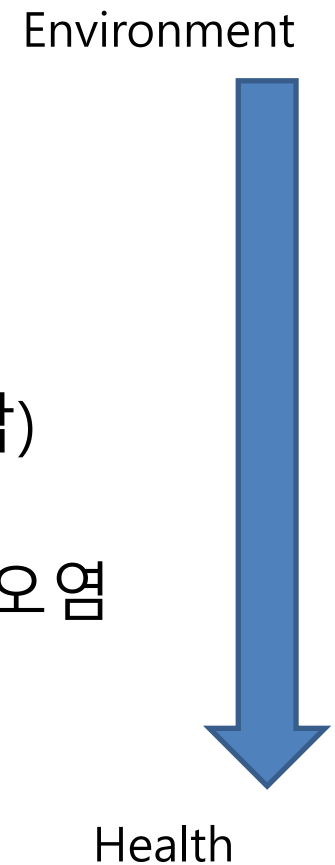
Environmental Health

- 환경공학 - 노출, 성분, 배출원, 저감
- 환경역학(예방의학, 보건통계) - 모델링, GBD
- 직업환경의학 - 직업성질환, 환경성질환(공장 밖)
- 호흡기내과 - 석면, 가습기살균제, 시멘트, 대기오염
  - 환자 코호트, 동물/세포 질환 모델(독성학)



Environmental exposure

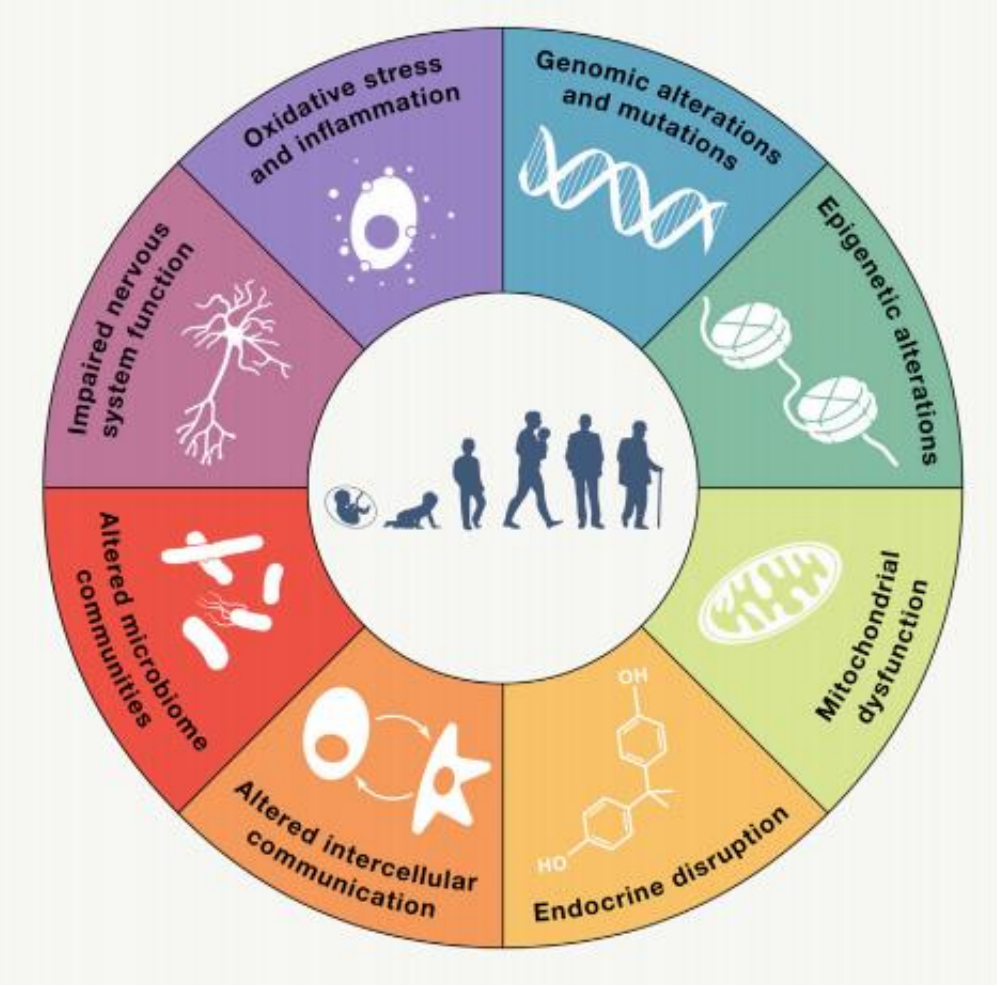
- PM, ozone, heavy metal, chemicals
- Contribute to modifiable risk factors
  - Jointly with lifestyle-related risk factors
    - Diet, physical activity, cigarette smoking, alcohol
  - Environmental diseases
    - Cancer, respiratory, cardiovascular, nervous and metabolic diseases

Cell
Leading Edge

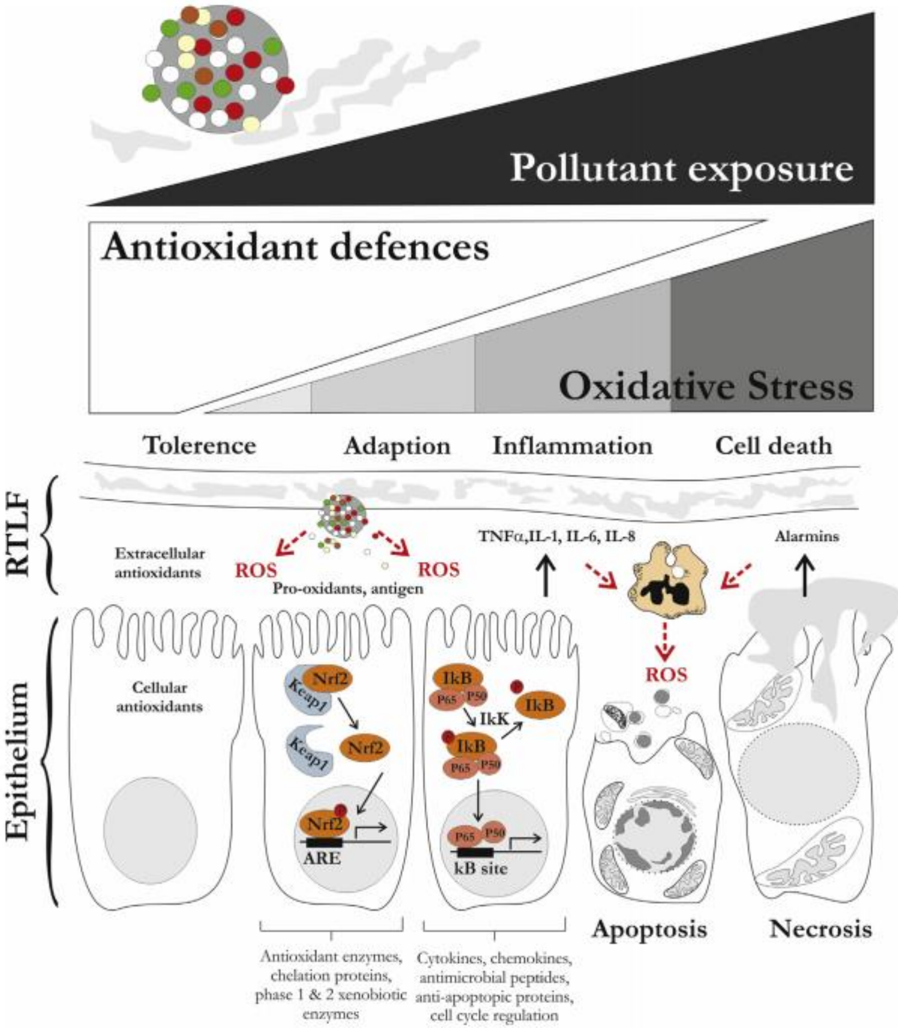
Review

Hallmarks of environmental insults

Annette Peters,[1,2,3,*] Tim S. Nawrot,[4,5] and Andrea A. Baccarelli[6]



- Biomarker of Exposure
- Biomarker of Environmental Disease
- Biomarker of Exacerbation



Pollutant exposure
Antioxidant defences
Oxidative Stress
Tolerence
Adaption
Inflammation
Cell death
RTLF
Extracellular antioxidants
ROS
ROS
Pro-oxidants, antigen
TNFα,IL-1, IL-6, IL-8
Alarmins
Epithelium
Cellular antioxidants
Nrf2
Keap1
Keap1
Nrf2
Nrf2
ARE
IkB
P65
P50
IkK
IkB
IkB
P65
P50
P65
P50
kB site
ROS
Apoptosis
Necrosis
Antioxidant enzymes, chelation proteins, phase 1 & 2 xenobiotic enzymes
Cytokines, chemokines, antimicrobial peptides, anti-apoptopic proteins, cell cycle regulation

Author, year	Study design	Location	Follow-up	Age, year*	Number	Pollutant	Biomarker	Sample	Outcome	Effect estimate
Grady ST, et al., 2018 (22)	Repeated measure (prospectively)	USA	2012.11-2014.12	72.7 ± 8.4	82	$PM_{2.5}$, NO_2	8-OHdG, MDA	urine	biomarkers	↑8-OHdG ↑MDA
Huang Q, et al., 2018 (37)	Cross-sectional study	China	2016.3-2016.5	71.0 ± 7.8	41	$PM_{2.5}$	Uric acid, GABP, Dopamine 4-sulfate	urine	COPD-related metabolic biomarkers (vs healthy control)	↓Uric acid ↓GABP ↓Dopamine 4-sulfate
Huang S, et al., 2021 (23)	Repeated measure (prospectively)	USA	2012.11-2014.12	72.7 ± 8.4	81	PM-gamma activities	8-OHdG, MDA	urine	biomarkers	↑8-OHdG ↑MDA
Lee KY et al., 2016 (38)	Repeated measure (from retrospective cohort)	Taipei	2013.01-2014.12	70.3 ± 9.0	43	PM_{10}	Ubiquitin, Beclin 1	blood	biomarkers, lung function	↑Ubiquitin ↑Beclin 1
Tang L, et al., 2021 (39)	Cross-sectional analysis (from retrospective cohort)	China	2017.03-2019.09	<65 28.7% >65 71.3%	317	$PM_{2.5}$	Prothrombin Time (PT)	blood	markers, acute exacerbation of COPD (hospitalization)	↓PT
Manney S, et al., 2012 (24)	Repeated measure (prospectively)	Finland Greece Netheralands UK	2002.10-2004.03	62.3 ± 10.6	111	$PM_{2.5}$, PM_{10}, coarse particle, PNC	NOx	EBC	Biomarker	No association

Kim J et al., JTD under revision

Tang et al. BMC Pulm Med (2021) 21:296
https://doi.org/10.1186/s12890-021-01650-z

BMC Pulmonary Medicine

RESEARCH **Open Access**

Effect of urban air pollution on CRP and coagulation: a study on inpatients with acute exacerbation of chronic obstructive pulmonary disease

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Table 1 Patients' demographic and clinical characteristics

Variable	Description
Age years	
<65	91 (28.71%)
≥ 65	226 (71.29%)
Sex	
Female	64 (20.19%)
Male	253 (79.81%)
BMI (kg/m^2)	
< 18.5	31 (9.78%)
≥ 18.5	286 (90.22%)
GOLD classes	
Moderate	31 (9.78%)
Severe	196 (61.83%)
Very severe	90 (28.39%)
Current smoker	
Yes	42 (13.25%)
No	275 (86.75%)

Table 5 Estimated changes in coagulation function and CRP in AECOPD patients associated with $PM_{2.5}$

Variable	$PM_{2.5}$											
	The day of hospitalization				The day before hospitalization				Two day before hospitalization			
	< 25 mg/L n = 228	≥ 25 mg/L n = 89	*t*	*p*	< 25 mg/L n = 228	≥ 25 mg/L n = 89	*t*	*p*	< 25 mg/L n = 220	≥ 25 mg/L n = 97	*t*	*p*
D dimer	0.75 ± 1.06	0.70 ± 1.01	0.384	0.702	0.68 ± 1.01	0.73 ± 1.03	0.690	0.399	0.69 ± 0.89	0.72 ± 1.08	0.249	0.804
TT	16.39 ± 3.47	16.13 ± 2.49	0.763	0.446	16.39 ± 2.39	16.13 ± 2.94	0.731	0.465	16.31 ± 2.24	16.16 ± 3.02	0.433	0.665
PT	12.41 ± 2.29	12.29 ± 2.07	0.450	0.653	12.61 ± 2.76	12.03 ± 1.89	2.052	0.041	12.42 ± 2.59	12.28 ± 1.90	0.550	0.583
FIB	4.33 ± 3.20	4.39 ± 4.45	0.110	0.912	4.55 ± 4.85	4.31 ± 3.83	0.466	0.642	4.29 ± 4.60	4.41 ± 3.93	0.246	0.806
APTT	27.97 ± 4.44	28.40 ± 4.35	0.770	0.442	28.13 ± 4.27	28.34 ± 4.42	0.703	0.382	28.36 ± 4.48	28.24 ± 4.32	0.229	0.819
CRP	10.52 ± 11.94	10.42 ± 12.19	0.066	0.947	8.27 ± 11.84	11.30 ± 12.13	2.008	0.046	9.33 ± 12.21	10.89 ± 12.02	1.060	0.290

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Respiratory Research

RESEARCH Open Access

Black carbon content in airway macrophages is associated with increased severe exacerbations and worse COPD morbidity in SPIROMICS

- SPIROMICS AIR cohort

Table 1 Participant Characteristics, N = 324

	Mean ± SD or n (%)
Age, yrs	63.58 ± 8.78
Sex, n (% female)	134 (41.4%)
Race, n (% white)	260 (80.7%)
Education, n (% > HS grad)	223 (69.0%)
Annual Household Income	
<$35,000	116 (35.8%)
$35,000 - $74,999	101 (31.2%)
≥$75,000	62 (19.1%)
Decline to answer	45 (13.9%)
Body Mass Index, kg/m^2	28.50 ± 5.07
Medication LABA/LAMA, n (%)	87 (27.1%)
Smoking (pack-years)	47.76 ± 22.46
FEV_1, percent predicted	84.30 ± 18.96
Current Smoker, n (%)	143 (44.4%)

BMJ Open Respiratory Research

Design of the Subpopulations and Intermediate Outcome Measures in COPD (SPIROMICS) AIR Study

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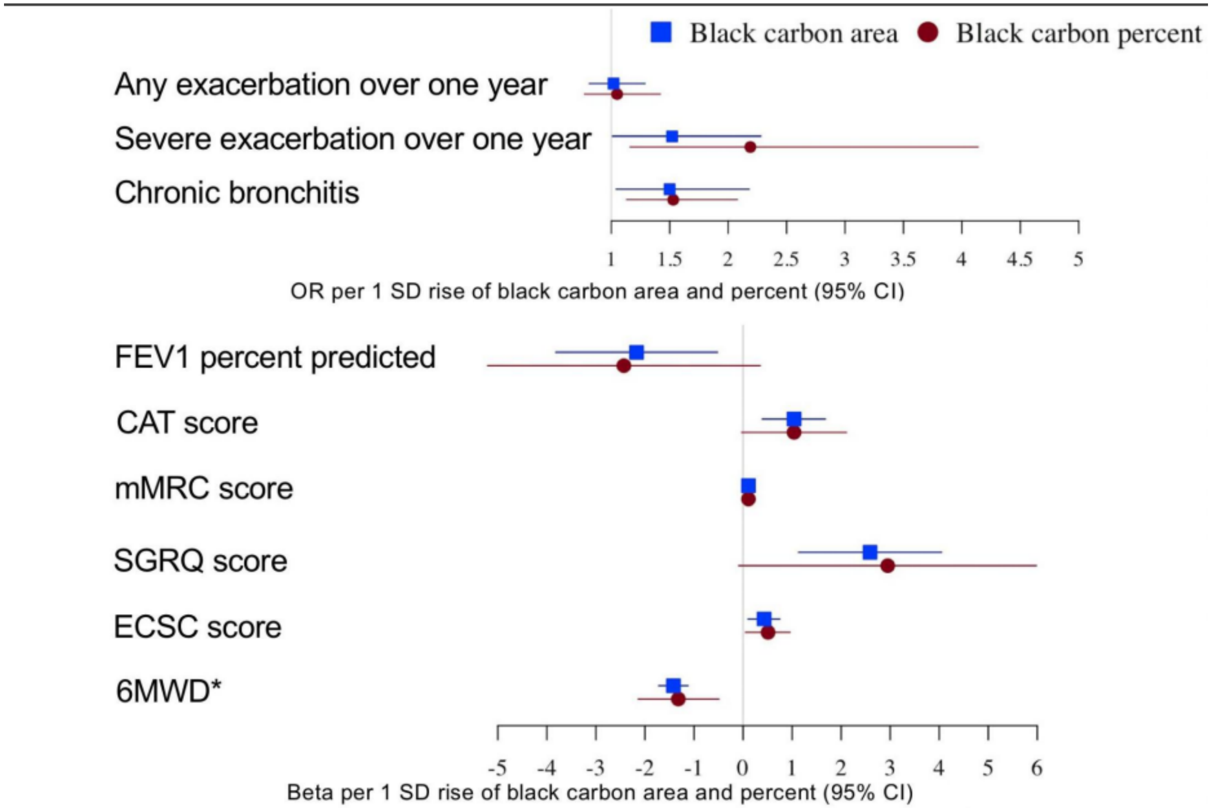
Roger D Peng,[3] Neil Alexis,[4] Vincent S Fan,[2,5] Eugene Bleecker,[6] Russell Bowler,[7]
Alejandro P Comellas,[8] Mark Dransfield,[9] MeiLan K Han,[10] Victor Kim,[11]
Jerry A Krishnan,[12] Cheryl Pirozzi,[13] Christopher B Cooper,[14] Fernando Martinez,[15]
Prescott G Woodruff,[16] Patrick J Breysse,[17] R Graham Barr,[18] Joel D Kaufman[2]

Table 1 Timeline for environmental monitoring of the SPIROMICS Air Study from 2013 to 2016

2013				2014				2015				2016			
Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Clinical data and questionnaires															
SPIROMICS enrolment (n=2982)															
				Visit 2 (n=2350)											
								Visit 3 (n=1492)							
										Visit 4 (n=894)					
						HIQ administered (n=1938)*									
Environmental monitoring															
						Baltimore									
							LA								
								SLC		SLC					
									SF		SF				
									NYC						
												AA		AA	
													W-S		

Association of black carbon area and percent to COPD outcomes



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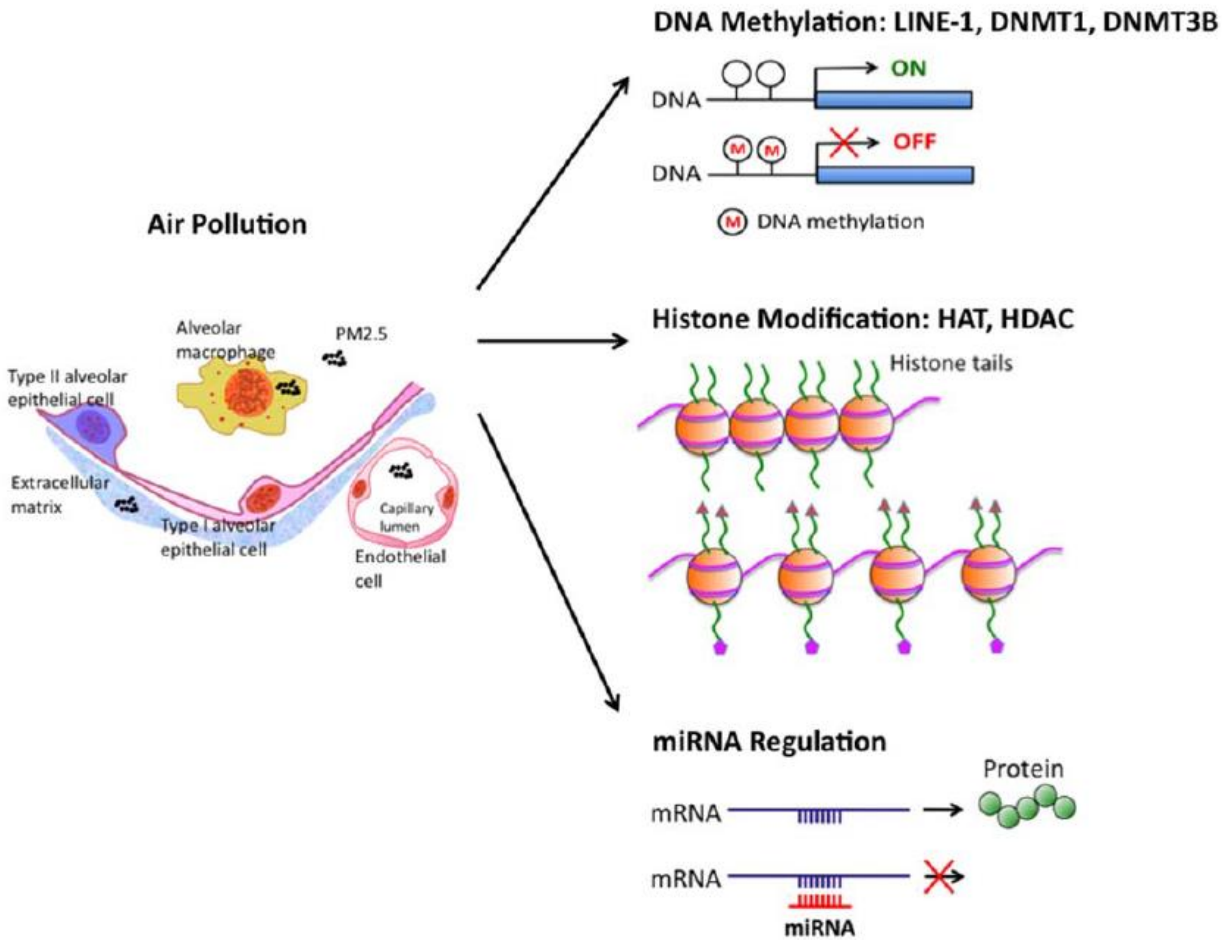
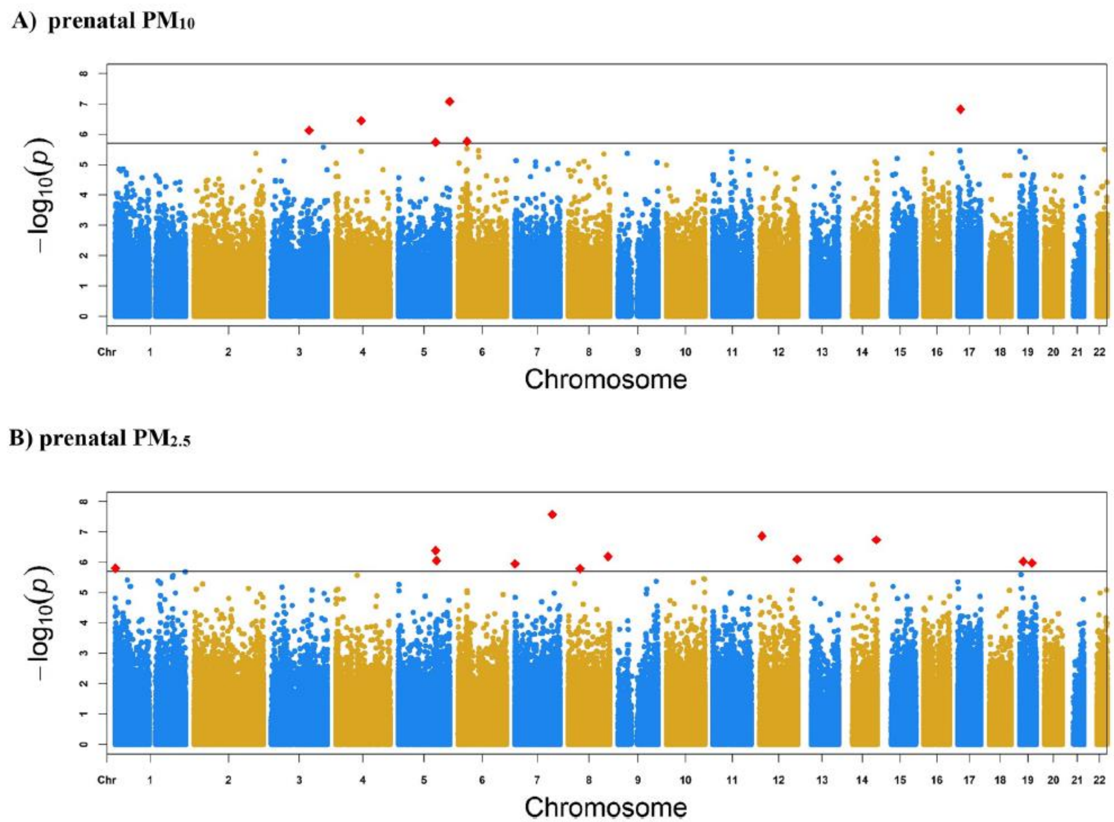

Air Pollution
Alveolar macrophage
PM2.5
Type II alveolar epithelial cell
Extracellular matrix
Type I alveolar epithelial cell
Capillary lumen
Endothelial cell
DNA Methylation: LINE-1, DNMT1, DNMT3B
DNA
ON
DNA
OFF
DNA methylation
Histone Modification: HAT, HDAC
Histone tails
miRNA Regulation
Protein
mRNA
mRNA
miRNA

Prenatal Particulate Air Pollution and DNA Methylation in Newborns: An Epigenome-Wide Meta-Analysis

Olena Gruzieva,[1,2] Cheng-Jian Xu,[3,4,5] Paul Yousefi,[6,7] Caroline Relton,[6,7] Simon Kebede Merid,[1] Carrie V. Breton,[8] Lu Gao,[8] Heather E. Volk,[9,10] Jason I. Feinberg,[9] Christine Ladd-Acosta,[11] Kelly Bakulski,[11] Charles Auffray,[12] Nathanaël Lemonnier,[12,13] Michelle Plusquin,[14,15] Akram Ghantous,[16] Zdenko Herceg,[16] Tim S. Nawrot,[14,17] Costanza Pizzi,[18] Lorenzo Richiardi,[18] Franca Rusconi,[19] Paolo Vineis,[15] Manolis Kogevinas,[20-22] Janine F. Felix,[23-25] Liesbeth Duijts,[23,26] Herman T. den Dekker,[23-25] Vincent W. V. Jaddoe,[23-25] José L. Ruiz,[27,28] Mariona Bustamante,[20-22,27] Josep Maria Antó,[20-22,29] Jordi Sunyer,[20-22,29] Martine Vrijheid,[20-22] Kristine B. Gutzkow,[30] Regina Grazuleviciene,[31] Carles Hernandez-Ferrer,[20,32] Isabella Annesi-Maesano,[33] Johanna Lepeule,[34] Jean Bousquet,[35,36] Anna Bergström,[1,2] Inger Kull,[1,37,38] Cilla Söderhäll,[39,40] Juha Kere,[40-42] the Biobank-based Integrative Omics Studies (BIOS) Consortium,[43] Ulrike Gehring,[44] Bert Brunekreef,[44,45] Allan C. Just,[46] Rosalind J. Wright,[47] Cheng Peng,[48] Diane R. Gold,[48,49] Itai Kloog,[50] Dawn L. DeMeo,[48] Göran Pershagen,[1,2] Gerard H. Koppelman,[3,4] Stephanie J. London,[51] Andrea A. Baccarelli,[52] and Erik Melén[1,38*]*

Table 1. Basic characteristics of cohorts included in the discovery EWAS meta-analysis.

STUDY	Country	Enrollment period	Total *N* enrolled	Selection criteria for EWAS	Air pollution exposure assessment	DNA methylation measurement
INMA	Spain	1997–2008	3768	available DNA from one of the subcohorts (Sabadell)	LUR	Illumina 450K
Generation R	Netherlands	2002–2006	9901	European, complete follow-up	LUR	Illumina 450K
CHS	USA	1995–1997	5341	non-Hispanic white/Hispanic white	Outdoor air pollution monitoring stations in each of the study communities	Illumina 450K
EARLI	USA	2009–2012	232	NA	used inverse distance-squared weighting	Illumina 450K
PRISM	USA	2012–2014	592	Random sample	hybrid land use regression and satellite-based model	Illumina 450K
Project Viva	USA	1999–2003	2128	Available cord blood or early/mid-childhood blood sample	hybrid land use regression and satellite-based model	Illumina 450K
ENVIR*ON*AGE	Belgium	2010–2016	1210	Random sample	spatial-temporal interpolation method	Illumina 450K
Piccolipiù	Italy	2011–2015	3338	Participants resident in the municipality of Turin with enough stored biological material and with 24-month follow-up data	LUR	Illumina 450K
Rhea	Greece	2007–2008	1500	Random sample	LUR	Illumina 450K



				Discovery: newborns[a]		Replication: newborns	Replication: age 7–9 years			Replication: age 15–16 years	
				($n=1,949$)		ALSPAC ($n=688$)	BAMSE EpiGene + MeDALL ($n=692$)	HELIX ($n=525$)	ALSPAC ($n=901$)	BAMSE 16 years ($n=198$)	ALSPAC 15 years (n = 903)
Chr	Position[b]	CpG	Gene[c]	β (*p*-value)	Direction[d]	β (*p*-value)	β (*p*-value)	β (*p*-value)	β (*p*-value)	β (*p*-value)	β (*P*-value)
5	180670110	cg15082635	*GNB2L1; SNORD96A*	0.001 (8.29E-08)	↓↑↓↑↑↑↑	−0.0004 (0.17)	<0.0001 (1.00)	0.0001 (0.75)	0.0006 (0.02)	−0.0001 (0.63)	0.00006 (0.05)
17	9559558	cg20340716	*USP43*	−0.002 (1.50E-07)	↓↑↓↓↓↓↓	0.0011 (0.50)	<0.0001 (0.73)	−0.0013 (0.39)	0.0002 (0.89)	0.0003 (0.19)	0.0004 (0.15)
4	89744363	cg00905156	*FAM13A*	0.001 (3.55E-07)	↓↑X↑↑↑↑	−0.0003 (0.33)	0.0017 (0.03)	−0.0001 (0.84)	0.0004 (0.15)	0.0001 (0.72)	0.00001 (0.90)
3	133524572	cg24127244	*SRPRB*	0.001 (7.33E-07)	↓↑↑↑↑↑↑	−0.00001 (0.97)	<0.0001 (0.77)	0.0002 (0.61)	−0.0003 (0.28)	−0.0002 (0.12)	0.00004 (0.42)
6	32165893	cg06849931	*NOTCH4*	−0.001 (1.72E-06)	↓↓↓↑↑↓↓	0.0003 (0.81)	0.0022 (0.03)	−0.0023 (0.002)	0.0010 (0.33)	0.00002 (0.95)	−0.0002 (0.30)
5	131563610	cg18640183	*P4HA2*	0.001 (1.80E-06)	↑↑↑↑↑↑↑	0.0003 (0.44)	0.0006 (0.61)	0.0009 (0.03)	−0.0001 (0.82)	0.0001 (0.53)	0.00001 (0.86)

Genome-wide DNA methylation and long-term ambient air pollution exposure in Korean adults

Mi Kyeong Lee[1], Cheng-Jian Xu[2,3,4], Megan U. Carnes[5], Cody E. Nichols[1], James M. Ward[1], The BIOS consortium, Sung Ok Kwon[6], Sun-Young Kim[7*†], Woo Jin Kim[6*†] and Stephanie J. London[1*†]

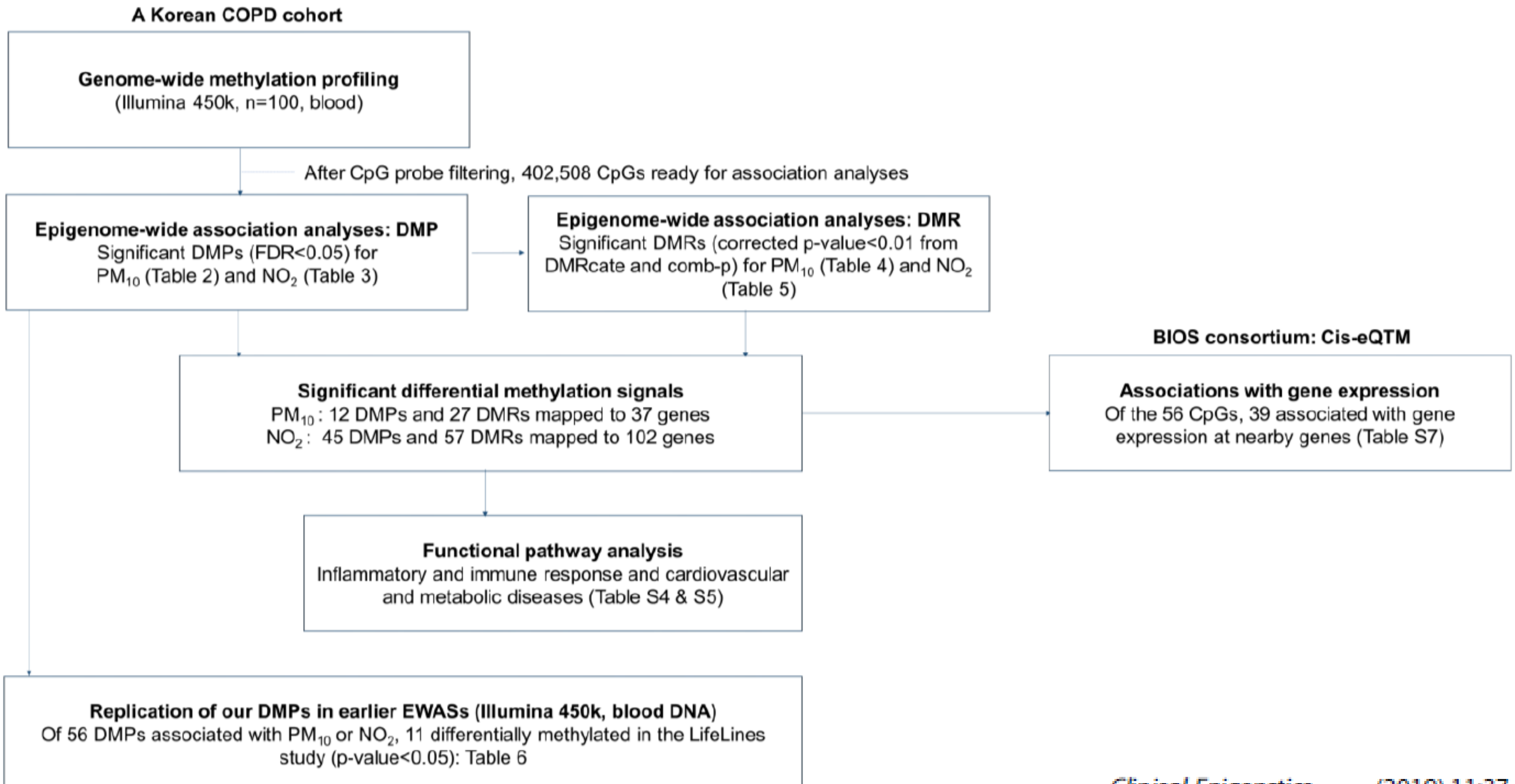


Table 1 Descriptive characteristics of the study population

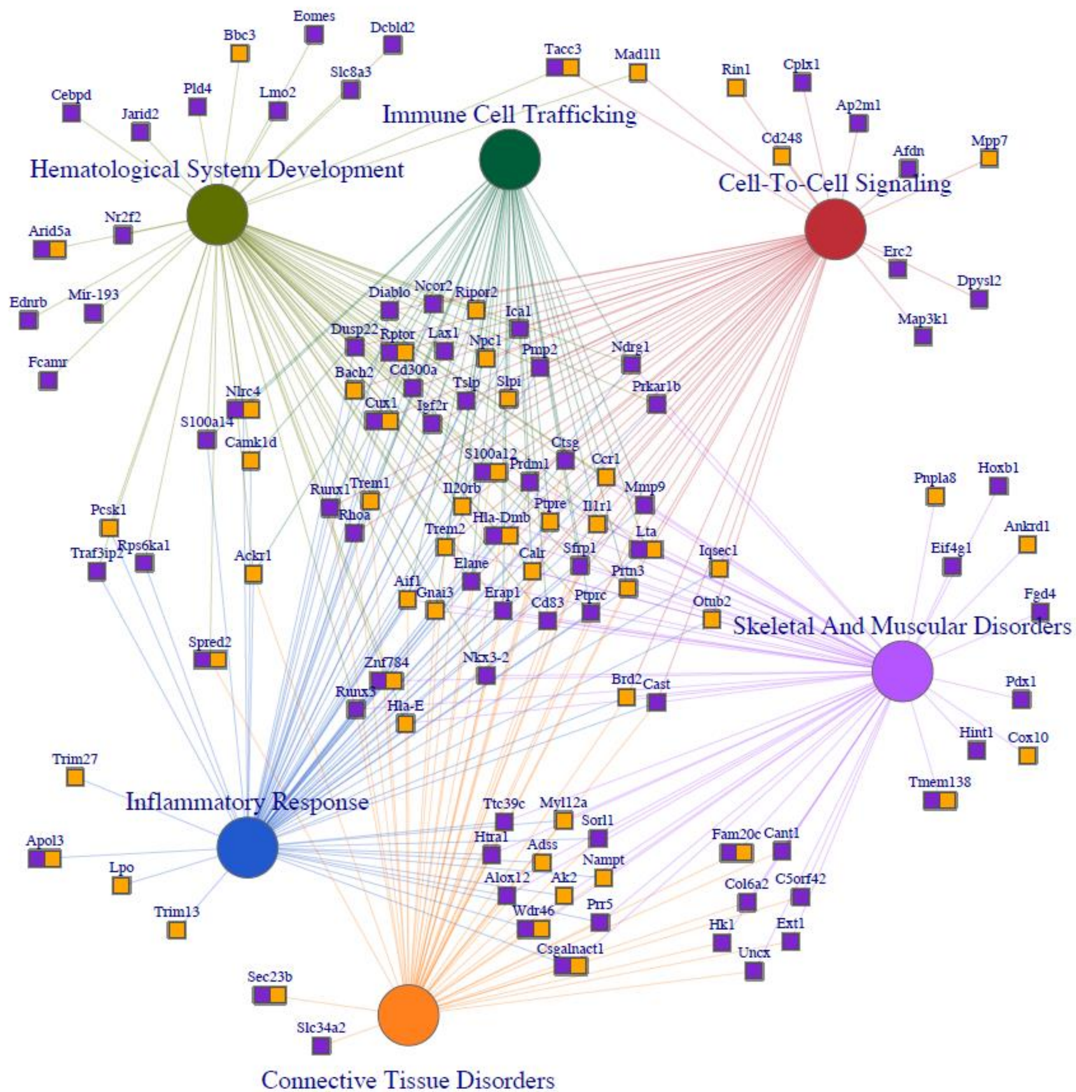
Characteristics	The Korean COPD[a] cohort ($N = 100$)
Age, years	72.8 ± 6.3
Male	66 (66%)
Body mass index, kg/m^2	22.9 ± 2.9
COPD, case	60 (60%)
Cigarette smoking	
Never	39 (39%)
Former	30 (30%)
Current	31 (31%)
Pack-years	
Former smoker	28.9 ± 19.6
Current smoker	35.7 ± 19.1
Annual average air pollution concentration at residential addresses	
PM_{10}, μg/m^3	45.1 ± 2.0
NO_2, ppb	13.1 ± 1.4

Table 2 Differentially methylated CpGs in blood DNA in relation to PM_{10} exposure (FDR < 0.05), ordered by chromosomal location

Chr[a]	Gene (distance to gene[b])	Probe	Position[c]	Coef[d]	SE[e]	P[f]
1	*NEGR1*	cg07721244	72749275	0.004	0.001	1.6E-07
2	*ARID5A*	cg04722215	97205147	−0.006	0.001	1.4E-07
3	*FOXL2* (− 81,364)	cg21742790	138581702	0.005	0.001	8.6E-07
3	*XXYLT1* (−92,147)	cg04252203	194696866	0.005	0.001	6.7E-07
6	*WDR46*	cg05454562[g]	33254447	0.006	0.001	4.3E-09
7	*FAM20C* (− 5283)	cg16998831	187686	0.008	0.002	3.0E-07
8	*KIF13B*	cg07023317	28961315	0.008	0.002	1.4E-06
9	*AKNA*	cg13999433[g]	117156883	0.007	0.001	3.9E-08
11	*SYTL2*	cg11691844[g]	85460604	0.006	0.001	1.1E-07
14	*OTUB2*	cg06992688	94491958	0.008	0.002	1.0E-06
16	*MIR5093* (11,6079)	cg26964426	85455911	0.025	0.005	8.3E-07
18	*NPC1*	cg12709880	21163172	0.007	0.001	3.8E-07

Table 6 Look-up analysis of CpGs associated with NO_2 exposure in the Korean COPD Cohort (FDR < 0.05) in a previous publication from the LifeLines Cohort from the Netherlands

Chr[a]	Gene (distance to gene[b])	Probe	The Korean COPD study		The LifeLines cohort study [7]	
			Coef[c] (per 1 ppb NO_2) ± SE[d]	*P*[e]	Coef (per 10 μg/m^3 NO_2) ± SE	*P*
1	*MAN1C1* (− 7282)	cg16396978	0.008 ± 0.002	3.9E-06	0.013 ± 0.004	5.4E-04
1	*S100A12*	cg02901136	0.012 ± 0.002	2.7E-06	0.027 ± 0.006	3.1E-05
2	*PLEKHM3*	cg09950920	0.013 ± 0.003	2.7E-07	0.024 ± 0.007	3.4E-04
3	*AP2M1*	cg17343451	0.009 ± 0.002	3.3E-06	0.020 ± 0.005	1.4E-05
5	*ZNF366*	cg21770462	0.008 ± 0.002	4.7E-06	0.015 ± 0.004	4.1E-05
10	*ZNF438*	cg10575075	0.014 ± 0.003	2.0E-06	0.026 ± 0.007	2.7E-04
11	*TMEM138*	cg03370752	0.010 ± 0.002	5.5E-06	0.028 ± 0.008	2.4E-04
11	*SORL1*	cg17510957	0.011 ± 0.002	5.1E-06	0.023 ± 0.007	4.7E-04
12	*STK38L*	cg05171937	0.010 ± 0.002	1.1E-08	0.036 ± 0.009	4.0E-05
14	*OTUB2*	cg06992688	0.013 ± 0.003	3.3E-06	0.026 ± 0.007	1.4E-04
21	*MORC3*	cg01261013	0.010 ± 0.002	4.1E-06	0.023 ± 0.006	3.3E-04


Hematological System Development
Immune Cell Trafficking
Cell-To-Cell Signaling
Skeletal And Muscular Disorders
Inflammatory Response
Connective Tissue Disorders
Bbc3
Eomes
Dcbld2
Tacc3
Mad1l1
Rin1
Cplx1
Slc8a3
Cebpd
Pld4
Lmo2
Ap2m1
Jarid2
Cd248
Afdn
Mpp7
Arid5a
Nr2f2
Erc2
Dpysl2
Ednrb
Mir-193
Diablo
Ncor2
Ripor2
Ical
Map3k1
Fcamr
Dusp22
Rptor
Lax1
Npc1
Pmp2
Ndrg1
Bach2
Cd300a
Tslp
Slpi
Prkar1b
Nlrc4
Cux1
Igf2r
S100a14
Camk1d
Ctsg
S100a12
Prdm1
Ccr1
Pnpla8
Hoxb1
Runx1
Trem1
Il20rb
Mmp9
Pcsk1
Rhoa
Ptpre
Il1r1
Hla-Dmb
Ankrd1
Trem2
Lta
Traf3ip2
Rps6ka1
Ackr1
Sfrp1
Iqsec1
Eif4g1
Calr
Elane
Prtn3
Fgd4
Aif1
Gnai3
Erap1
Cd83
Ptprc
Otub2
Spred2
Nkx3-2
Znf784
Brd2
Cast
Pdx1
Runx3
Hla-E
Hint1
Cox10
Trim27
Tmem138
Ttc39c
Myl12a
Sorl1
Htra1
Adss
Cant1
Fam20c
Apol3
Nampt
Lpo
Alox12
Ak2
Col6a2
C5orf42
Trim13
Wdr46
Prr5
Hk1
Ext1
Csgalnact1
Uncx
Sec23b
Slc34a2

Integration of gene expression and DNA methylation identifies epigenetically controlled modules related to $PM_{2.5}$ exposure

Simon Kebede Merid [a], Mariona Bustamante [b,c,d], Marie Standl [e], Jordi Sunyer [b,c,d,f], Joachim Heinrich [g,h], Nathanaël Lemonnier [i], Daniel Aguilar [j], Josep Maria Antó [b,c,d,f], Jean Bousquet [k,l,m], Loreto Santa-Marina [n,o,p], Aitana Lertxundi [n,o,q], Anna Bergström [r,s], Inger Kull [a,t], Åsa M. Wheelock [u], Gerard H. Koppelman [v,w], Erik Melén [a,t,1], Olena Gruzieva [r,s,*,1]

Table 2
FDR-significant DEGs from the meta-analysis of the association between $PM_{2.5}$ exposure at birth and gene expression in children and adolescents (n = 656 from the BAMSE, GINIplus, and INMA cohorts).

Probe.Set.ID	Gene	Log2FC	SE	P-value	FDR	Direction*	Het. P-value
TC10001332.hg.1	*MIR1296*	−0.19	0.04	1.74E-07	0.01	—	0.196
TC14001976.hg.1		0.42	0.09	1.02E-06	0.03	+++	0.844

Exposure to $PM_{2.5}$	Seed	Size (number of genes)	Modularity	FDR*
Birth	*NR1I2*	11	2.12	0.001
	SH3GL2	26	2.00	0.005
	TENT5A	24	1.94	0.006
	MAPK6	64	1.95	0.010
	UBE2W	61	1.35	0.012
	KCTD15	10	1.86	0.014
	MLST8	10	2.11	0.018
	RPP40	12	1.61	0.024
	GGA1	14	1.59	0.025
Current	*TAF8*	20	2.17	<0.0001
	TAF5	20	2.17	0.001
	GNAI3	31	2.07	0.002
	ISLR	22	2.05	0.024
	TRIM69	10	1.84	0.032
	SCARA3	19	1.84	0.040

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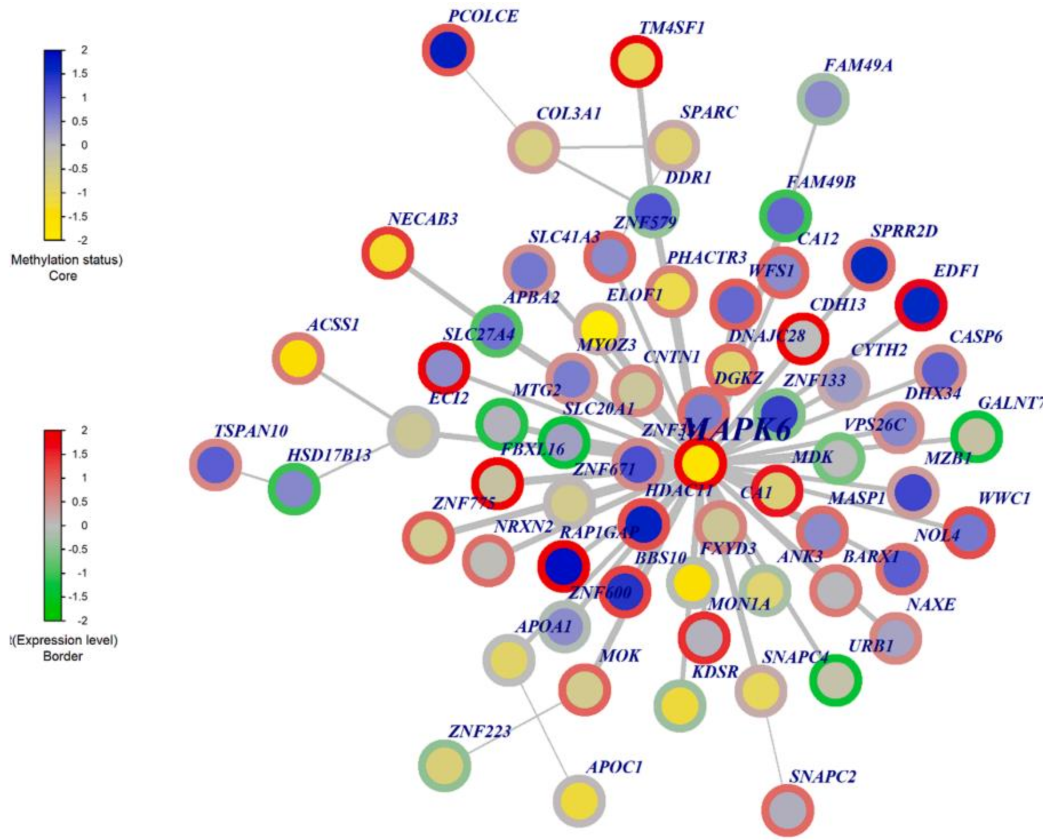
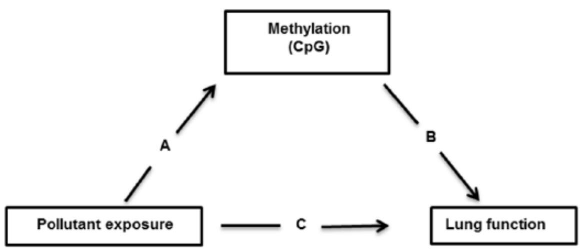
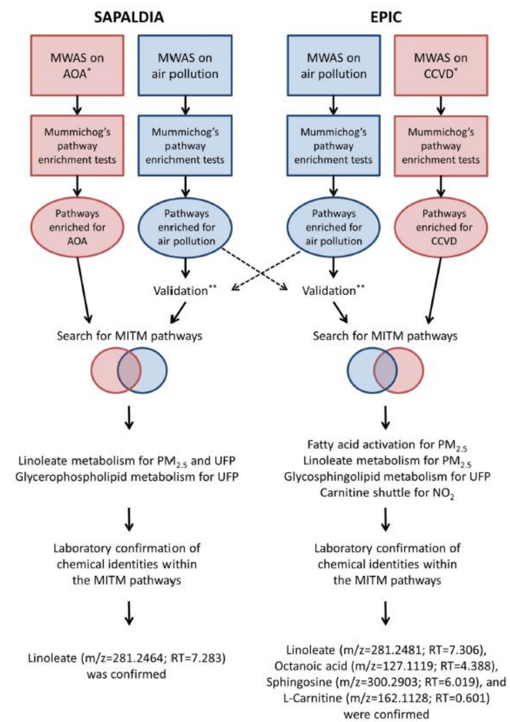


Methylation status)
Core
(Expression level)
Border
MAPK6
PCOLCE
TM4SF1
FAM49A
COL3A1
SPARC
DDR1
FAM49B
NECAB3
ZNF579
SLC41A3
CA12
SPRR2D
PHACTR3
WFS1
EDF1
APBA2
ELOF1
CDH13
ACSS1
SLC27A4
DNAJC28
CYTH2
CASP6
MYOZ3
CNTN1
DGKZ
ZNF133
DHX34
GALNT7
EC12
MTG2
SLC20A1
TSPAN10
VPS26C
HSD17B13
FBXL16
MDK
MZB1
ZNF671
HDAC11
CA1
MASP1
WWC1
ZNF775
NRXN2
RAP1GAP
NOL4
BBS10
FXYD3
ANK3
BARX1
ZNF600
MON1A
NAXE
APOA1
MOK
SNAPC4
URB1
KDSR
ZNF223
APOC1
SNAPC2

노출 마커와 질환 마커의 연결



Mediation analysis



Environment International 119 (2018) 334–345

Maternal serum metabolome and traffic-related air pollution exposure in pregnancy

Qi Yan[a], Zeyan Liew[b,c], Karan Uppal[d], Xin Cui[e,f], Chenxiao Ling[a], Julia E. Heck[a], Ondine S. von Ehrenstein[a], Jun Wu[g], Douglas I. Walker[h], Dean P. Jones[d,i], Beate Ritz[a,j,*]

Table 1
Demographic characteristics of mothers and children.

	High exposure n = 98		Low exposure n = 62	
	n	%	n	%
Maternal age at time of pregnancy (years)				
≤18	18	18.4	5	8.1
19–25	42	42.9	17	27.4
26–30	24	24.5	20	32.3
> 30	14	14.3	20	32.3
Maternal race/ethnicity				
Non-Hispanic White	11	11.2	21	33.9
Hispanic	70	71.4	30	48.5
Others (African American/ Black, Asian)	17	17.4	11	17.7
Maternal education				
Less than 12th grade	47	48.0	11	17.7
High school graduate or equivalent	24	24.5	22	35.5
Some college	20	20.4	12	19.4
College or more	7	7.1	17	27.4
Mother born in the US				
Yes	61	62.2	46	74.2
No	37	37.8	15	24.2
Missing	0	0.0	1	1.6
Preterm birth				
Yes	12	12.2	7	11.3
No	86	87.8	55	88.7
Child sex				
Male	79	80.8	46	74.2
Female	19	19.2	16	25.8

Table 3
Enriched metabolic pathways associated with traffic-related air pollution.

Column	Pathway	Overlap size	Pathway size	P-value[a]
HILIC	Urea cycle/amino group metabolism	7	40	0.0015
	Glycosphingolipid metabolism	5	22	0.0015
	Histidine metabolism	4	17	0.0020
	Glycerophospholipid metabolism	4	30	0.0081
	Linoleate metabolism	3	19	0.0100
	Glycine, serine, alanine and threonine metabolism	4	36	0.0162
	Pyrimidine metabolism	3	30	0.0435
C18	Fatty acid activation	10	16	0.0002
	De novo fatty acid biosynthesis	7	15	0.0002
	Glycosphingolipid metabolism	7	24	0.0003
	Keratan sulfate degradation	3	6	0.0006
	Fatty Acid Metabolism	4	13	0.0008
	TCA cycle	3	14	0.0049
	Prostaglandin formation from arachidonate	8	54	0.0061
	Lysine metabolism	4	24	0.0074
	Glycerophospholipid metabolism	6	40	0.0074
	Xenobiotics metabolism	8	59	0.0110
	Glycolysis and Gluconeogenesis	4	27	0.0123
	Methionine and cysteine metabolism	6	44	0.0127
	Fructose and mannose metabolism	3	19	0.0141
	Vitamin E metabolism	4	29	0.0167
	Butanoate metabolism	3	20	0.0168
	Linoleate metabolism	3	20	0.0168
	Phosphatidylinositol phosphate metabolism	3	22	0.0231
	Purine metabolism	5	42	0.0276
	Leukotriene metabolism	5	43	0.0307
	Sialic acid metabolism	3	28	0.0491

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Metabolomics Reveals Dysregulated Sphingolipid and Amino Acid Metabolism Associated with Chronic Obstructive Pulmonary Disease

Jeeyoung Kim[1], Bharathi Suresh[2], Myoung Nam Lim[1], Seok-Ho Hong[3], Kye-Seong Kim[2,4],
Ha Eun Song[5], Hyo Yeong Lee[5], Hyun Ju Yoo[5], Woo Jin Kim[1]

Table 1 Demographics Data for Participants Included in the Current Study

	All (n=200)	Non-COPD (n=80)	COPD (n=120)	*p-value
		*Mean ± SD or N (%)		
Age, mean (SD)	72.14±6.66	70.71±7.41	73.09±5.96	**0.0176**
50–59	11(5.5)	7(8.8)	4(3.3)	
60–69	45(22.5)	26(32.5)	19(15.8)	
70–79	127(63.5)	40(50.0)	87(72.5)	
80–89	17(8.5)	7(8.8)	10(8.3)	
Gender				0.4360
Male	132(66.0)	48(60.0)	84(70.0)	
Female	68(34.0)	32(40.0)	36(30.0)	
Smoking				**0.0471**
Current	57(28.5)	17(21.3)	40(33.3)	
Former	63(31.5)	23(28.7)	40(33.3)	
Never	80(40.0)	40(50.0)	40(33.3)	

Table 2 Statistical Correlations Between Plasma Metabolites and COPD

	Non-COPD (n=80)		COPD (n=120)		*p-value of t-test
	LSmean	SD	LSmean	SD	
Ceramides (nM)					
C14	2.70	0.05	2.78	0.05	0.3411
C16	5.61	0.04	5.61	0.03	0.8987
C18	4.80	0.07	4.76	0.05	0.7525
C18_1	3.03	0.06	3.00	0.05	0.7956
C20	4.91	0.07	4.94	0.05	0.7681
C24	7.92	0.06	7.96	0.05	0.6808
C24_1	7.09	0.06	7.05	0.05	0.6547
SM18_0	9.46	0.05	9.53	0.04	0.3057
SM18_1	8.70	0.05	8.76	0.04	0.4468
SM16_0	11.10	0.04	11.18	0.03	0.1743
SM24_0	9.72	0.06	9.90	0.04	**0.0357**
SM24_1	10.51	0.05	10.60	0.04	**0.0265**

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코호트 자료를 활용한 바이오마커 발굴 및 검증

- 노출에 대한 정확한 평가
  - 모델링
  - Personal level
- 통계적 power
  - 적절한 샘플수
- False positive
  - Multiple testing
  - 다른 요인들 보정
  - Replication

Korea Exposome Study

International Journal of *Environmental Research and Public Health*

Article

Prenatal Exposure to Traffic-Related Air Pollution and the DNA Methylation in Cord Blood Cells: MOCEH Study

Jaehyun Park [1,†], Woo Jin Kim [2,†], Jeeyoung Kim [2], Chan-Yeong Jeong [2], Hyesook Park [3,4], Yun-Chul Hong [5], Mina Ha [6], Yangho Kim [7], Sungho Won [1,8,9,10,*] and Eunhee Ha [4,11,12,*]

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Prenatal lead exposure and cord blood DNA methylation in the Korean Exposome Study

Jaehyun Park [a], Jeeyoung Kim [b], Esther Kim [b], Woo Jin Kim [b,*], Sungho Won [a,c,**]

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DNA methylation changes associated with prenatal mercury exposure: A meta-analysis of prospective cohort studies from PACE consortium

Manuel Lozano [a,b,*,1], Paul Yousefi [c,d,1], Karin Broberg [e,f], Raquel Soler-Blasco [b], Chihiro Miyashita [g], Giancarlo Pesce [h], Woo Jin Kim [i], Mohammad Rahman [j], Kelly M. Bakulski [k], Line S. Haug [l], Atsuko Ikeda-Araki [g,m], Guy Huel [h], Jaehyun Park [n], Caroline Relton [c,d], Martine Vrijheid [o,p,q], Sheryl Rifas-Shiman [j], Emily Oken [j], John F. Dou [k], Reiko Kishi [g], Kristine B. Gutzkow [l], Isabella Annesi-Maesano [r], Sungho Won [n,s], Marie-France Hivert [j,t], M. Daniele Fallin [u], Marina Vafeiadi [v], Ferran Ballester [b,o,w], Mariona Bustamante [o,p,q,2], Sabrina Llop [b,o,2]

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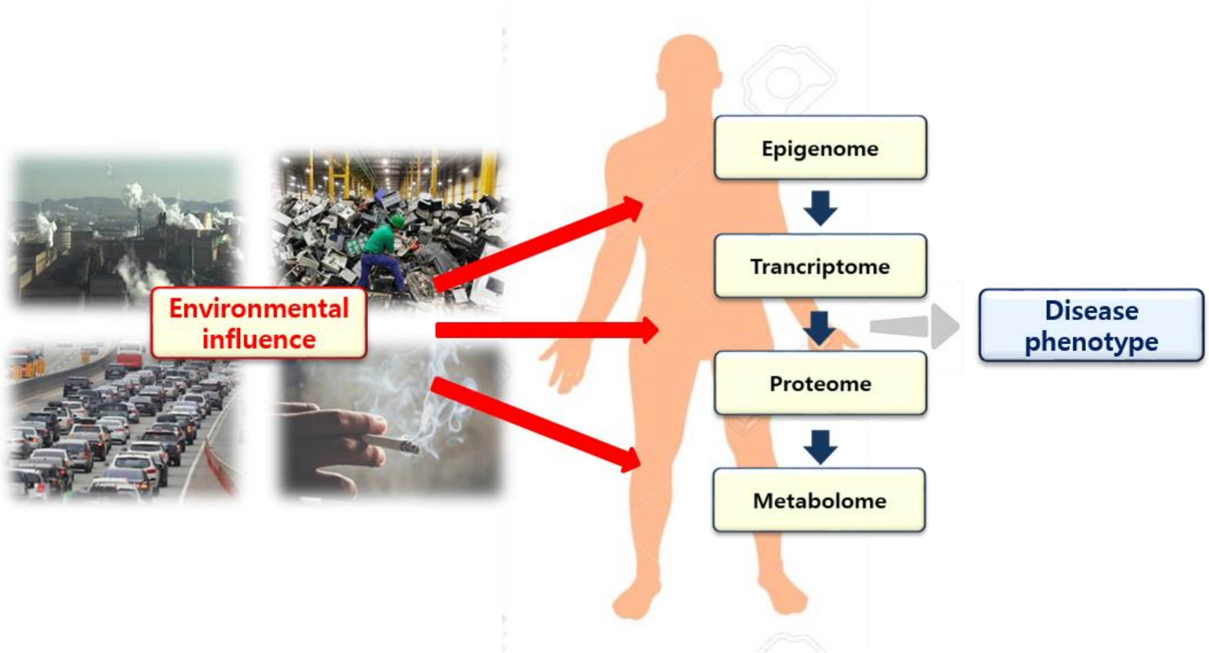
Association between prenatal cadmium exposure and cord blood DNA methylation

Jaehyun Park [a,1], Jeeyoung Kim [b,1], Esther Kim [b,1], Sungho Won [a,c,d,e,*], Woo Jin Kim [b,**]

FROM study group

Forensic Research via Omics Markers

in environmental health vulnerable areas



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- 환경성질환(환경산업기술원)
  - 오믹스분석을 통한 취약지역 환경성질환 원인물질 추적기술개발(2021-2025)
  - 미세먼지 노출에 의한 호흡계질환 상관성 규명(2022-2026)