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Supplemental Material

Sex-Specific Associations between Particulate Matter Exposure and Gene Expression in Independent Discovery and Validation Cohorts of Middle-Aged Men and Women

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- **Supplemental Code and Data ZIP File**
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Excel File Table S4. The top 50 genes associated with a 5-μg/m^3 increase in $PM_{2.5}$ in women, and p-values, q-values, and fold changes (with 95% CI) for each gene.

Table S1. Associations of the selected candidate biomarker genes with long term $PM_{2.5}$ exposure in the discovery and validation cohort

	Gene description	Gene function	Link to disease	Discovery cohort FC (95% CI)	p-value	Validation cohort FC (95% CI)	p-value	q-value
Men								
DNAJB5	DnaJ (Hsp40) homolog, subfamily B, member 5	Heat shock protein 40	CVD[40]	1.62 (1.20, 2,18)	0.003	2.16 (1.00, 4.73)	0.06	0.16
RAC3	ras-related C3 botulinum toxin substrate 3 (rho family, small GTP binding protein Rac3)	Regulation of cellular responses (cell growth)	Lung cancer [50]	1.62 (1.21, 2.18)	0.003	1.26 (0.94, 1.69)	0.32	0.62
EAPP	E2F associated phosphoprotein	Cell cycle/Apoptosis	Lung cancer [51]	1.31 (1.14, 1.50)	0.009	1.55 (1.08, 2.22)	0.02	0.16
HDLBP	high density lipoprotein binding protein (vigilin)	Sterol metabolism	CVD [52]	1.20 (1.06, 1.37)	0.0004	1.00 (0.69, 1.44)	0.77	0.77
PRG2	Proteoglycan 2	Eosinophil major basic protein	CVD [53], asthma [54]	1.57 (1.15, 2.13)	0.0069	1.30 (0.63, 2.71)	0.48	0.62
PER1	period homolog 1 (Drosophila)	Circadian rhythm	CVD [55]	1.37 (1.11, 1.69)	0.0061	0.52 (0.29, 0.96)	0.04	0.16
PIK3R1	phosphoinositide-3-kinase, regulatory subunit 1 (p85 alpha)	Insulin metabolism	Lung cancer [56]	1.45 (1.12, 1.89)	0.0079	1.25 (0.74, 2.10)	0.41	0.62
SLA2	Src-like adaptor 2	SLAP adapter protein	CVD [57]	1.44 (1.10, 1.90)	0.01	1.16 (0.73, 1.85)	0.54	0.62
Women								
AKAP6	A kinase (PRKA) anchor protein 6	Regulatory subunit of protein kinase A	CVD [58]	1.39 (1.26, 1.67)	0.002	0.44 (0.23, 0.81)	0.01	0.03
LIMK1	LIM domain kinase 1	Regulation of actin filament dynamics	Lung cancer [59] Alzheimer's [60]	1.51 (1.29, 2.04)	0.01	0.64 (0.41, 0.99)	0.05	0.07
SIRT7	sirtuin (silent mating type information regulation 2 homolog) 7 (S. cerevisiae)	Transcription repressor	CVD [61]	0.85 (0.80, 0.97)	0.02	0.44 (0.22, 0.86)	0.02	0.04
ARHGAP4	Rho GTPase Activating protein 4	regulation of small GTP-binding proteins from the	cognition [62]	0.82 (0.76, 0.93)	0.005	0.16 (0.05, 0.47)	0.002	0.008

		RAS superfamily						
ATG16L2	autophagy related 16-like 2 (S. cerevisiae)	Autophagy	CVD [63]	0.72 (0.66, 0.86)	0.0005	0.59 (0.37. 0.94)	0.03	0.05
TPM3	Tropomyosin 3	Actin-binding protein	Lung cancer [64]	0.44 (0.35, 0.70)	0.001	1.38 (0.85, 2.23)	0.20	0.20
5-HTR1B	5-hydroxytryptamine (serotonin) receptor 1B	Neurotransmitter/ vasoconstriction	CVD [65]	1.16 (1.38, 2.19)	0.004	5.35 (0.63, 45.5)	0.13	0.15
PYGO2	Pygophus homolog 2	Related to Wnt signaling	Lung cancer [66]	0.91 (0.85, 1.04)	0.17	0.48 (0.46, 0.51)	0.002	0.008

Models adjusted for age, BMI, SES, smoking (validation cohort), leukocyte and neutrophil count, daytime of blood sampling and season. FC= fold change calculated for an increase in $PM_{2.5}$ of 5 $\mu g/m^3$. Q-value= corrected p-value for multiple testing.

Table S2: Associations between long term PM_{10} and $PM_{2.5}$ exposure and log2- transformed gene expression for the complete validation cohort and the validation cohort excluding current smokers.

PM_{10}	Current smokers included		Current smokers excluded		**$PM_{2.5}$**	Current smokers included		Current smokers excluded	
Gene name	Estimated effect (95% CI)	p-value	Estimated effect (95% CI)	p-value		Estimated effect (95% CI)	p-value	Estimated effect (95% CI)	p-value
Men									
DNAJB5	1.64 (1.20, 2.23)	0.003	1.82 (1.30-2.56)	0.001		2.16 (1.00, 4.73)	0.06	2.96 (1.20, 7.29)	0.02
RAC3	1.26 (0.94, 1.96)	0.10	1.27 (0.92-1.76)	0.15		1.26 (0.94, 1.69)	0.32	1.50 (0.65, 3.43)	0.34
EAPP	1.18 (1.02, 1.38)	0.03	1.15 (0.98, 1.36)	0.09		1.55 (1.08, 2.22)	0.02	1.52 (1.02, 2.29)	0.05
HDLBP	1.02 (0.88, 1.19)	0.75	0.98 (0.84-1.15)	0.84		1.00 (0.69, 1.44)	0.77	0.94 (0.64, 1.39)	0.89
PRG2	1. 29 (0.98, 1.71)	0.07	1.09 (0.77-1.53)	0.64		1.30 (0.63, 2.71)	0.48	0.92 (0.32, 2.27)	0.85
PER1	0.95 (0.74, 1.23)	0.72	0.99 (0.74-1.33)	0.93		0.52 (0.29, 0.96)	0.04	1.94 (0.94, 4.05)	0.08
PIK3R1	1.01 (0.82, 1.26)	0.91	0.96 (0.75-1.22)	0.72		1.25 (0.74, 2.10)	0.41	1.19 (0.24, 2.62)	0.58
SLA2	1.16 (0.97, 1.39)	0.11	1.16 (0.95, 1.41)	0.16		1.16 (0.73, 1.85)	0.54	1.05 (0.61, 1.80)	0.87
Women									
AKAP6	0.72 (0.55-0.94)	0.017	0.74 (0.54-1.01)	0.06		0.44 (0.23, 0.81)	0.01	0.50 (0.26, 1.00)	0.05
LIMK1	0.75 (0.61-0.91)	0.0057	0.79 (0.61-1.02)	0.07		0.64 (0.41, 0.99)	0.05	0.77 (0.47, 1.27)	0.31
SIRT7	0.80 (0.6-1.07)	0.14	0.93 (0.66-1.32)	0.69		0.44 (0.22, 0.86)	0.02	0.61 (0.28, 1.33)	0.22
ARHGAP4	0.62 (0.38-1.00)	0.054	0.77 (0.43-1.37)	0.37		0.16 (0.05, 0.47)	0.002	0.25 (0.07, 0.85)	0.03
ATG16L2	0.81 (0.59-1.11)	0.19	0.89 (0.61-1.31)	0.70		0.59 (0.37. 0.94)	0.03	0.72 (0.43, 1.20)	0.21
TPM3	1.02 (0.83-1.26)	0.85	1.00 (0.78-1.30)	0.98		1.38 (0.85, 2.23)	0.20	1.37 (0.79, 2.39)	0.27
5-HTR1B	1.28 (0.49-3.34)	0.62	0.79 (0.25-2.53)	0.70		5.35 (0.63, 45.5)	0.13	2.54 (0.21, 30.4)	0.46

PYGO2	0.75 (0.61-0.92)	0.008	0.78 (0.60-1.01)	0.06	0.48 (0.46, 0.51)	0.002	0.58 (0.33, 1.01)	0.06