**SUPPLEMENTARY MATERIAL**

**Long-term Ambient Fine Particulate Matter and DNA Methylation in Inflammation Pathways: Results from the Sister Study**

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**Table S1.** Genes’ information, the locations of the amplified region and each CpG sites in our previous panel study [1].

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Genes | Chromosome | Amplicon | Length | promoter | CpGs (position) |
|  |  | *Start* | *End* |  | *pos 1* | *pos 2* | *pos 3* | *pos 4* | *pos 5* |
| *TNF-α* | 6 | -217 | -86 | 132 | no | -151 | **-123 a** |  |  |  |
| *ICAM-1* | 19 | -483 | -234 | 250 | no | -298 | -291 | -280 |  |  |
| *CD40L* | X | -66 | 12 | 79 | no | -37 | -29 |  |  |  |
| *IL-6* | 7 | 472 | 608 | 137 | yes | Intron 2 | Intron 2 |  |  |  |
| *TLR-2* | 4 | -289 | -109 | 182 | no | **-143 b** | -139 | -137 | **-129 c** | -125 |

**a** as cg21370522 in the Sister Study

**b** as cg16547110 in the Sister Study

**c** as cg 06405222 in the Sister Study

Abbreviations: *TNF-α, tumor necrosis factor-alpha; ICAM-1, Intercellular adhesion molecule-1; CD40L, CD40L ligand; IL-6, interleukin-6; TLR-2, Toll-like receptor-2;*

**Table S2.** The percentage changes (95% CI) in *LINE-1*, and methylation at locus-specific loci associated with an increase of 5 µg/m3 increase in PM2.5 in main analyses.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | *LINE-1* | *TNF- α* at *c*g21370522 | *TLR-2* atcg16547110 | *TLR-2* at cg06405222 |
| Linear regression | -0.13 (-0.51,0.25) | -6.5 (-13.34, 0.35) | -2.62 (-7.25, 2.00) | 0.91 (-3.46, 5.28) |
| Quantile regression |  |  |  |  |
|  10th  | -0.35 (-0.97, 0.28) | -15.99 (-31.54, -0.43) \* | -1.51 (-10.65, 7.62) | -2.79 (-9.26, 3.67) |
|  20th  | -0.32 (-0.81, 0.16) | -7.46 (-19.61, 4.69) | -3.12 (-9.66, 3.41) | -2.07 (-7.67, 3.53) |
|  30th  | -0.43 (-0.89, 0.04) | -6.43 (-15.82, 2.97) | -3.09 (-9.15, 2.97) | 0.66 (-4.90, 6.22) |
|  40th  | -0.34 (-0.70, 0.02) | -6.85 (-14.88, 1.18) | -2.95 (-8.48, 2.58) | 0.72 (-3.59, 5.03) |
|  50th  | -0.31 (-0.70, 0.07) | -5.01 (-11.80, 1.79) | -2.72 (-8.34, 2.91) | -1.07 (-5.26, 3.12) |
|  60th  | -0.05 (-0.52, 0.42) | -4.52 (-12.58, 3.54) | -2.05 (-9.13, 5.03) | -1.31 (-7.30, 4.67) |
|  70th  | 0.07 (-0.35, 0.50) | 0.73 (-6.49, 7.96) | -2.11 (-7.54, 3.33) | 2.09 (-3.64, 7.82) |
|  80th  | -0.20 (-0.67, 0.27) | -0.30 (-9.06, 8.47) | 0.05 (-6.36, 6.45) | 4.62 (-1.90, 11.13) |
|  90th  | -0.01 (-0.82, 0.80) | 0.49 (-8.60, 9.58) | 0.55 (-6.36, 7.46) | 8.82 (-1.67, 19.32) |

Abbreviations: *LINE-1*: *long interspersed nucleotide element*; *TNF-α*, *tumor necrosis factor-alpha*; *TLR-2,* *Toll-like receptor-2**;* PM2.5, particulate matter having an aerodynamic diameter less than or equal to 2.5 μm.

\*p<0.05

**Figure S1.** Distribution of *LINE-1,* and methylation at gene-specific locus.

Abbreviations: *LINE-1, long interspersed nucleotide element; TNF-α, tumor necrosis factor-alpha; TLR-2, Toll-like receptor-2.*

**Figure S2.** Distribution of mean annual PM2.5 in random sub-cohort 1 and 2.

Abbreviations:PM2.5, particulate matter having an aerodynamic diameter less than or equal to 2.5 μm.



**Figure S3A.** Percentage change in DNA methylation associated with a 5 µg/m3 increase in ambient PM2.5 at each decile of the methylation distribution, in subjects who spent more than 4 hours per week outdoors. The X-axis refers to different quantiles; the Y-axis refers to the corresponding changes (mean and 95% confidence interval). (Number of subjects in *LINE-1* analysis is 491; number of subjects in locus-specific analysis is 882.)

Abbreviations: *LINE-1, long interspersed nucleotide element; TNF-α, tumor necrosis factor*

*-alpha; TLR-2, Toll-like receptor-2;* PM2.5, particulate matter having an aerodynamic diameter

less than or equal to 2.5 μm.



**Figure S3B.** Percentage changes in DNA methylation (expressed in %5mC with 95% CI) associated with a 5 µg/m3 increase in ambient PM2.5 according to the deciles of the methylation distribution, in younger and older women. The X-axis refers to different quantiles; the Y-axis refers to the corresponding changes (mean and 95% confidence interval). (The median age in *LINE-1* analysis is 56.2, the median age in locus-specific analyses is 57.0)

Abbreviations: *LINE-1, long interspersed nucleotide element; TNF-α, tumor necrosis factor*

*-alpha; TLR-2, Toll-like receptor-2;* PM2.5, particulate matter having an aerodynamic diameter

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**Reference**

1. Wang C, Chen R, Shi M, et al. Possible Mediation by Methylation in Acute Inflammation Following Personal Exposure to Fine Particulate Air Pollution. [Am J Epidemiol](https://www-ncbi-nlm-nih-gov.ezp-prod1.hul.harvard.edu/pubmed/?term=Possible+Mediation+by+Methylation+in+Acute+Inflammation+Following+Personal+Exposure+to+Fine+Particulate+Air+Pollution) 2017; PubMed PMID: 29020142; PubMed Central PMCID: 5860518; http://dx.doi.org/[10.1093/aje/kwx277](https://doi-org.ezp-prod1.hul.harvard.edu/10.1093/aje/kwx277%22%20%5Ct%20%22_blank).