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Supplemental Material

Particulate Air Pollution Exposure and Expression of Viral and Human MicroRNAs in Blood: The Beijing Truck Driver Air Pollution Study

Lifang Hou, Jitendra Barupal, Wei Zhang, Yinan Zheng, Lei Liu, Xiao Zhang, Chang Dou, John P. McCracken, Anaité Díaz, Valeria Motta, Marco Sanchez-Guerra, Katherine Rose Wolf, Pier Alberto Bertazzi, Joel D. Schwartz, Sheng Wang, and Andrea A. Baccarelli

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Figure S8. Functional analysis using Gene Ontology (GO) biological process terms. GO analysis was performed using combined target genes of all miRNAs with significant changes in each analysis group. Gene sets containing a minimum of eight genes at $FDR < 1\%$ were considered significant. miRBase assigns P -values to individual miRNA-3'-UTR target binding site, so different set of genes can be predicated with a miRBase threshold. Two threshold cutoffs (i.e. 10^{-6} and 10^{-8}) in miRBase database are shown on X-axis. Color of a tile represents enrichment of a GO term; Green= YES, Red= NO. GO term classification which is based on title of a GO term were shown on the right side. In the pooled analysis of both groups, 3 out of 5 total biological processes were related to biological regulation. In office workers, more than 35% of biological processes were related to immune response, and in truck drivers, 50% of biological processes were related to cell proliferation and differentiation. Two biological processes were common in all analysis groups. Seven biological processes were common between office workers and truck drivers.

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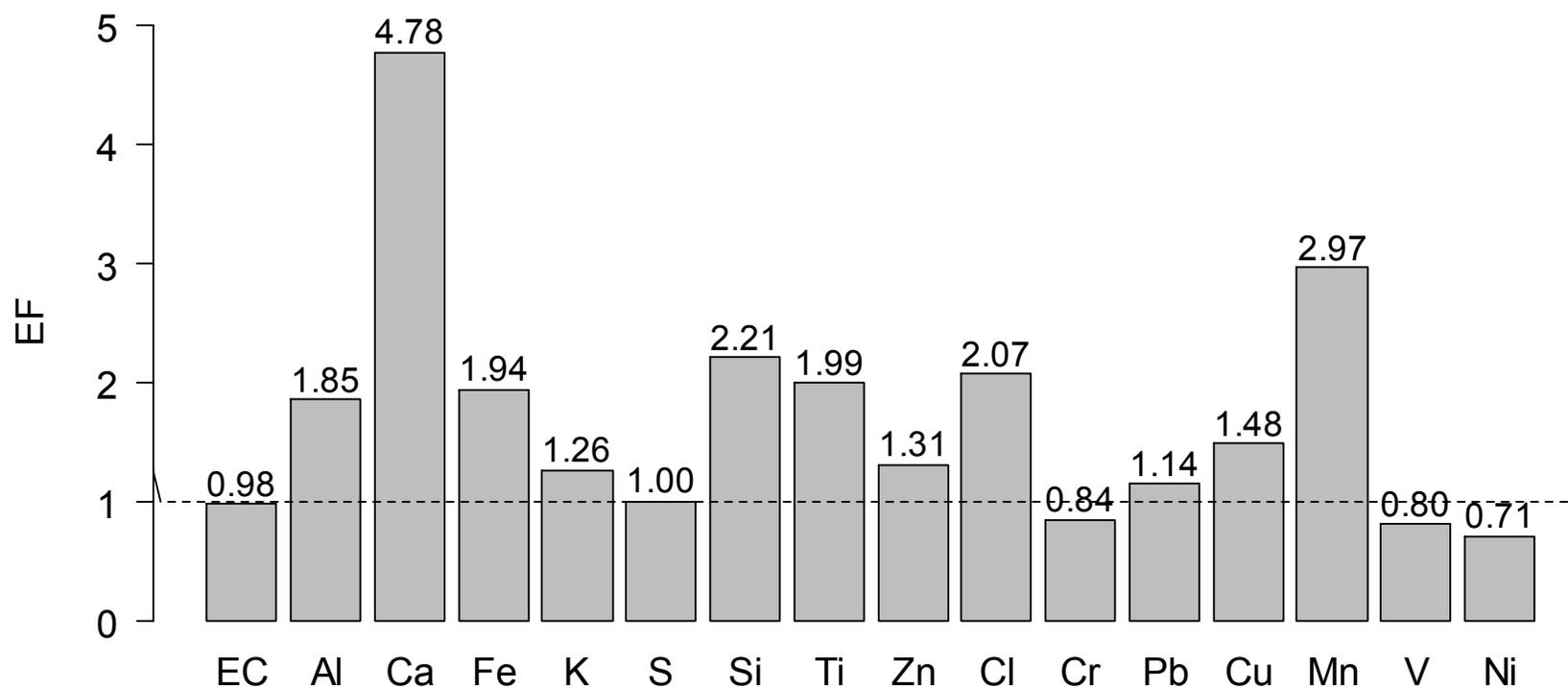


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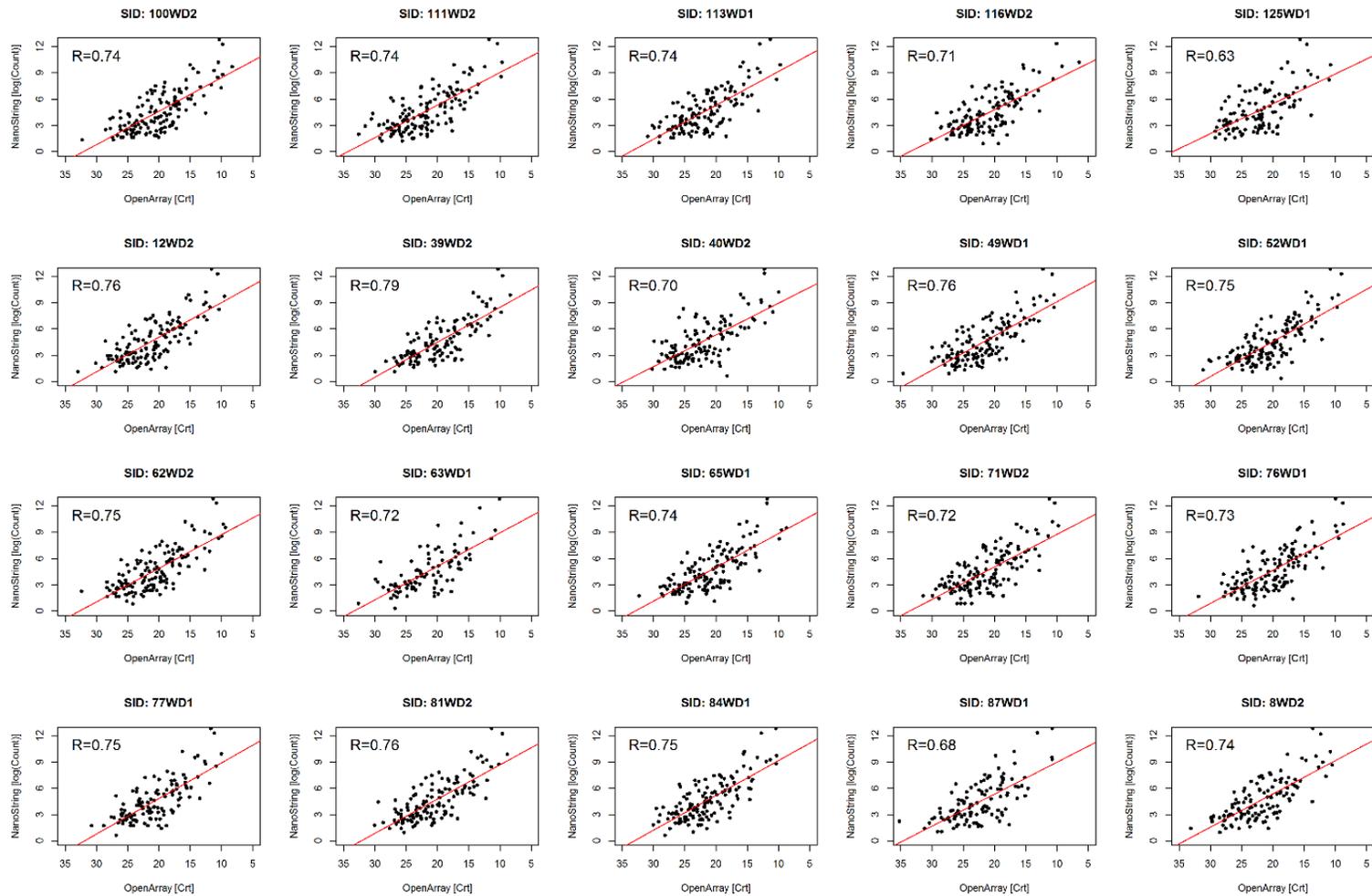


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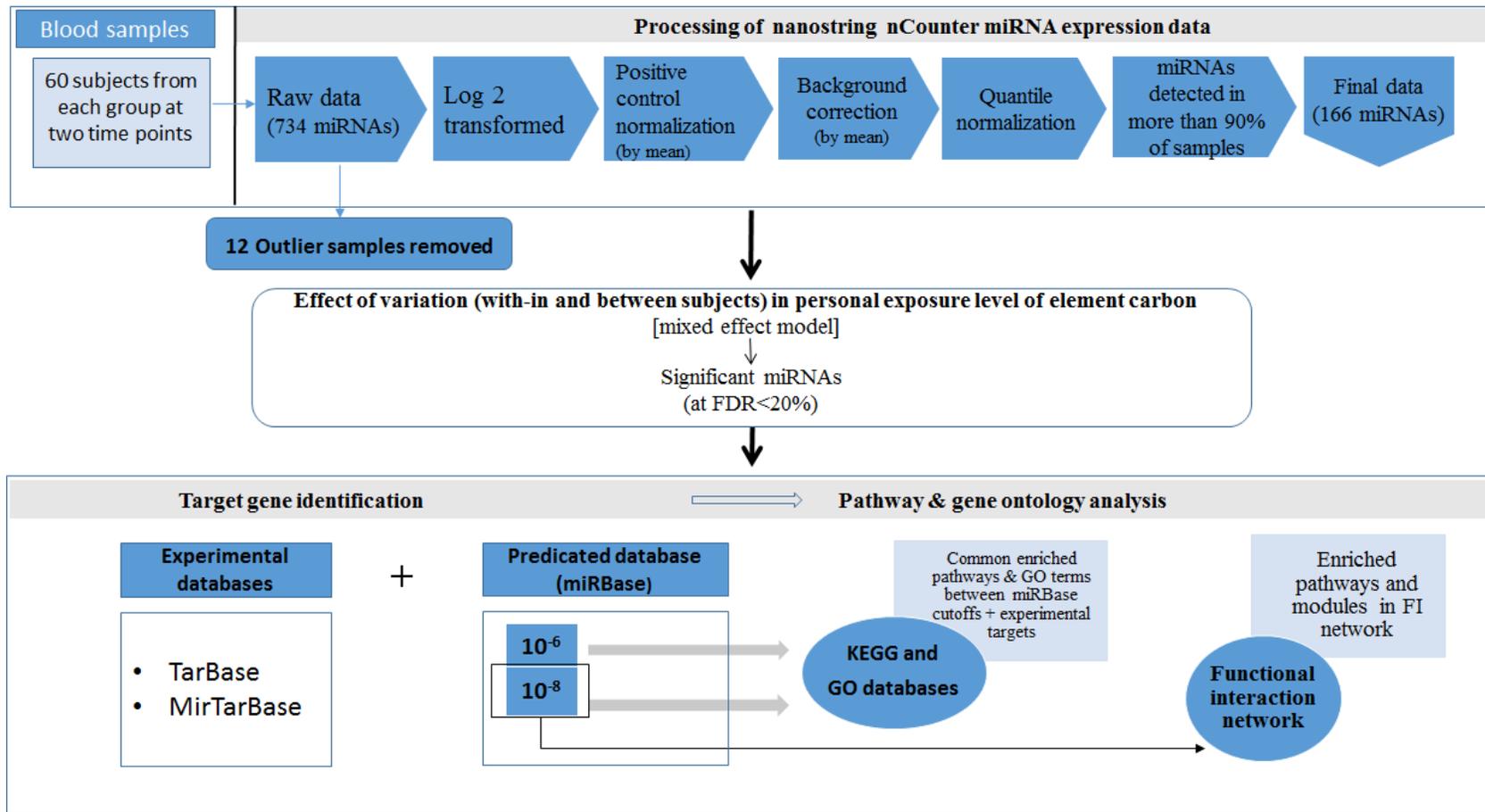


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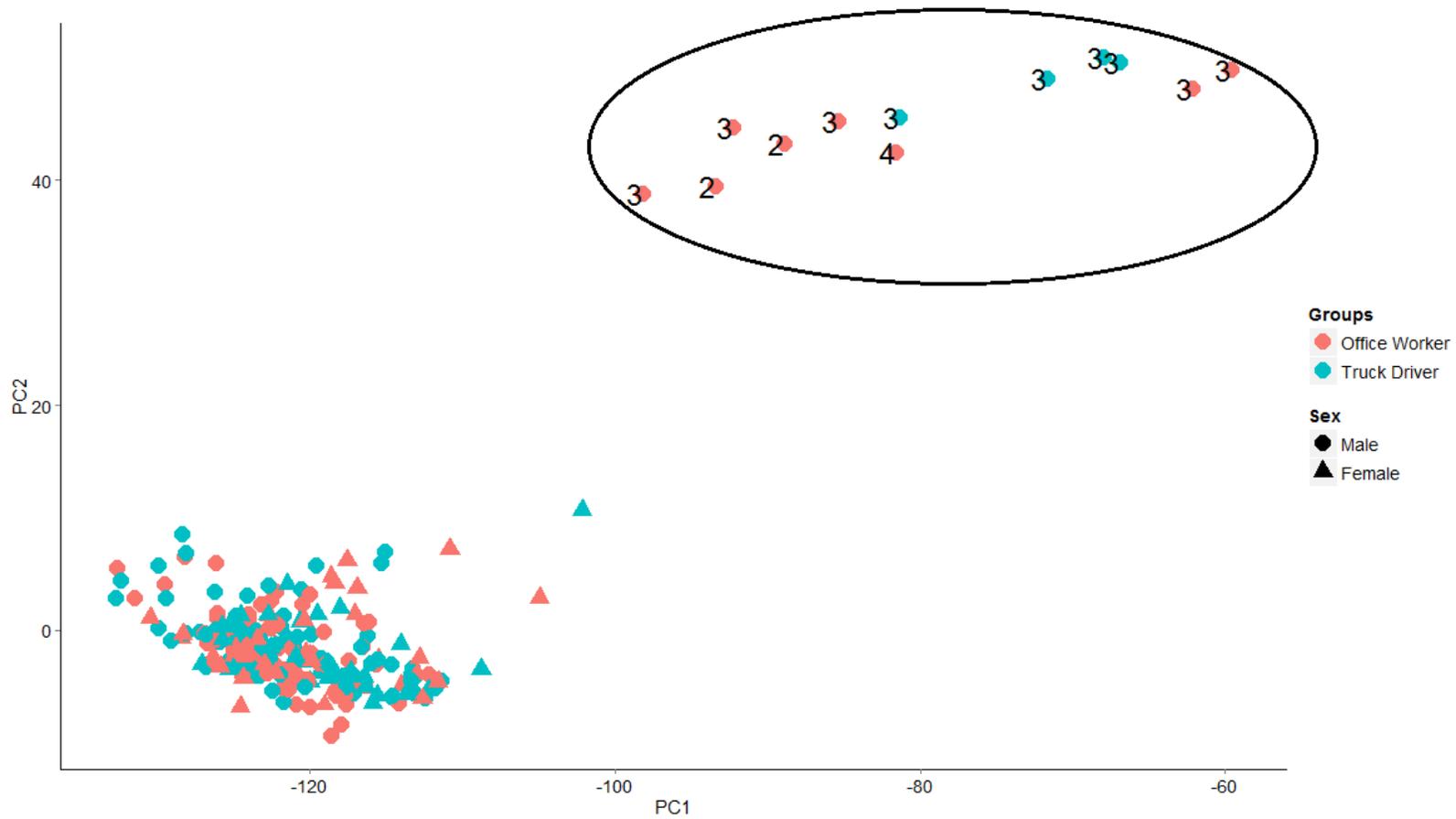


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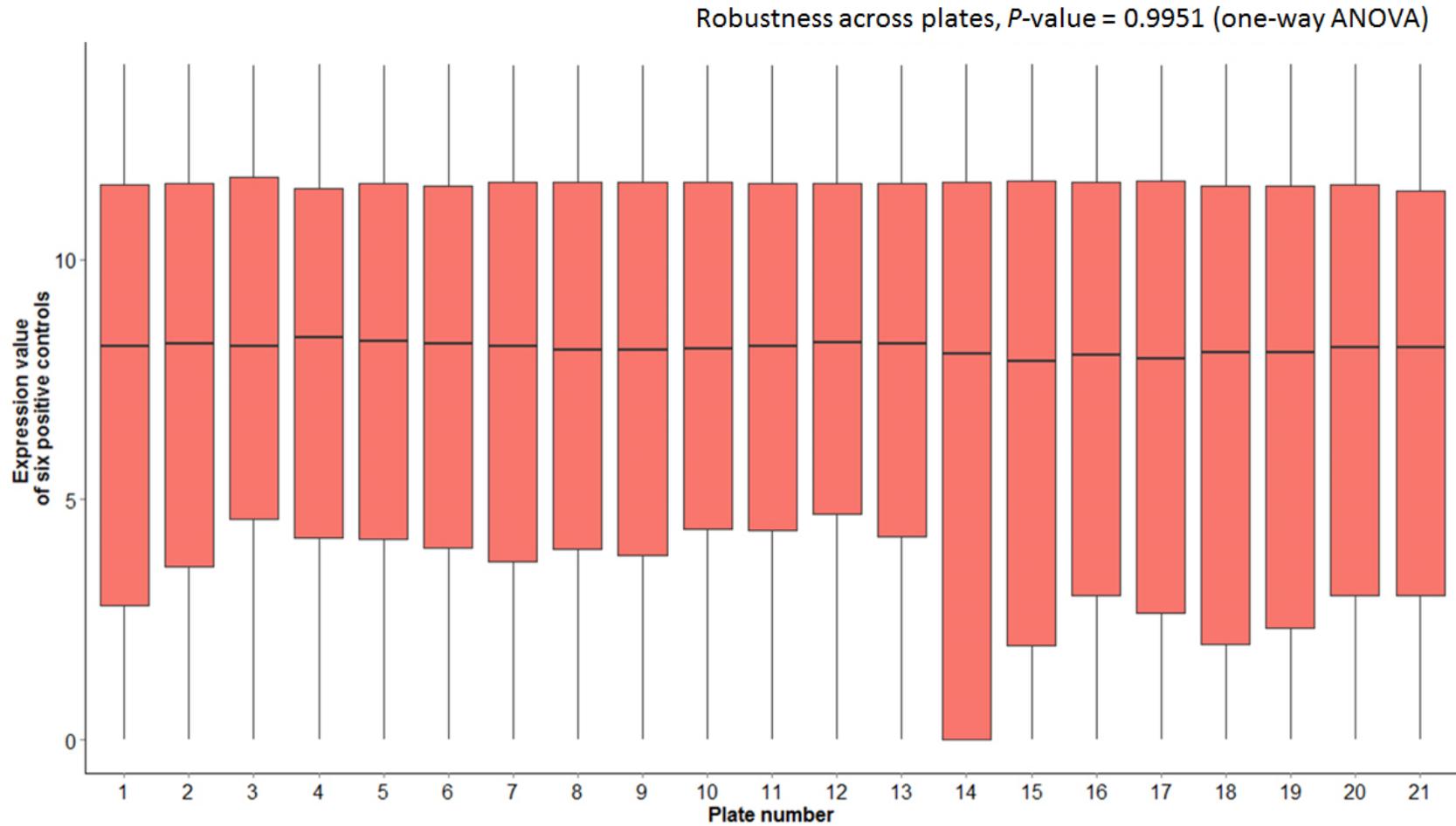


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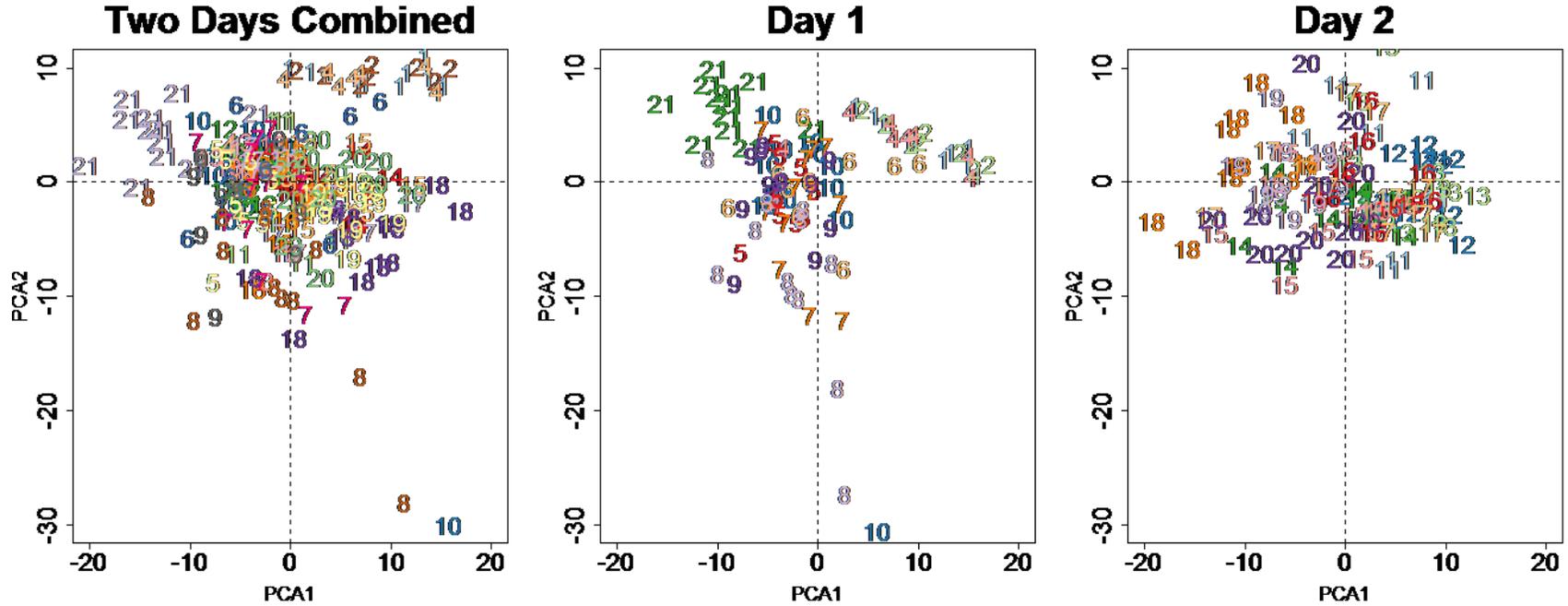


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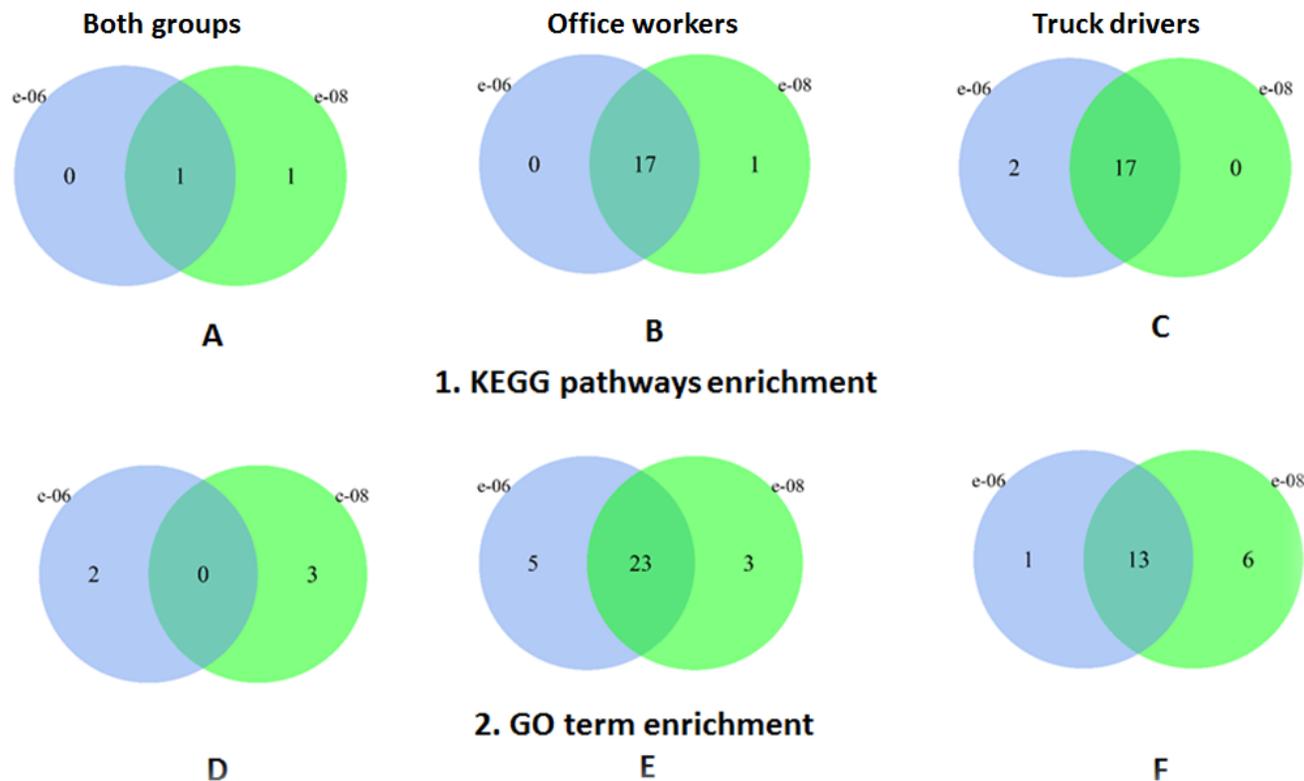


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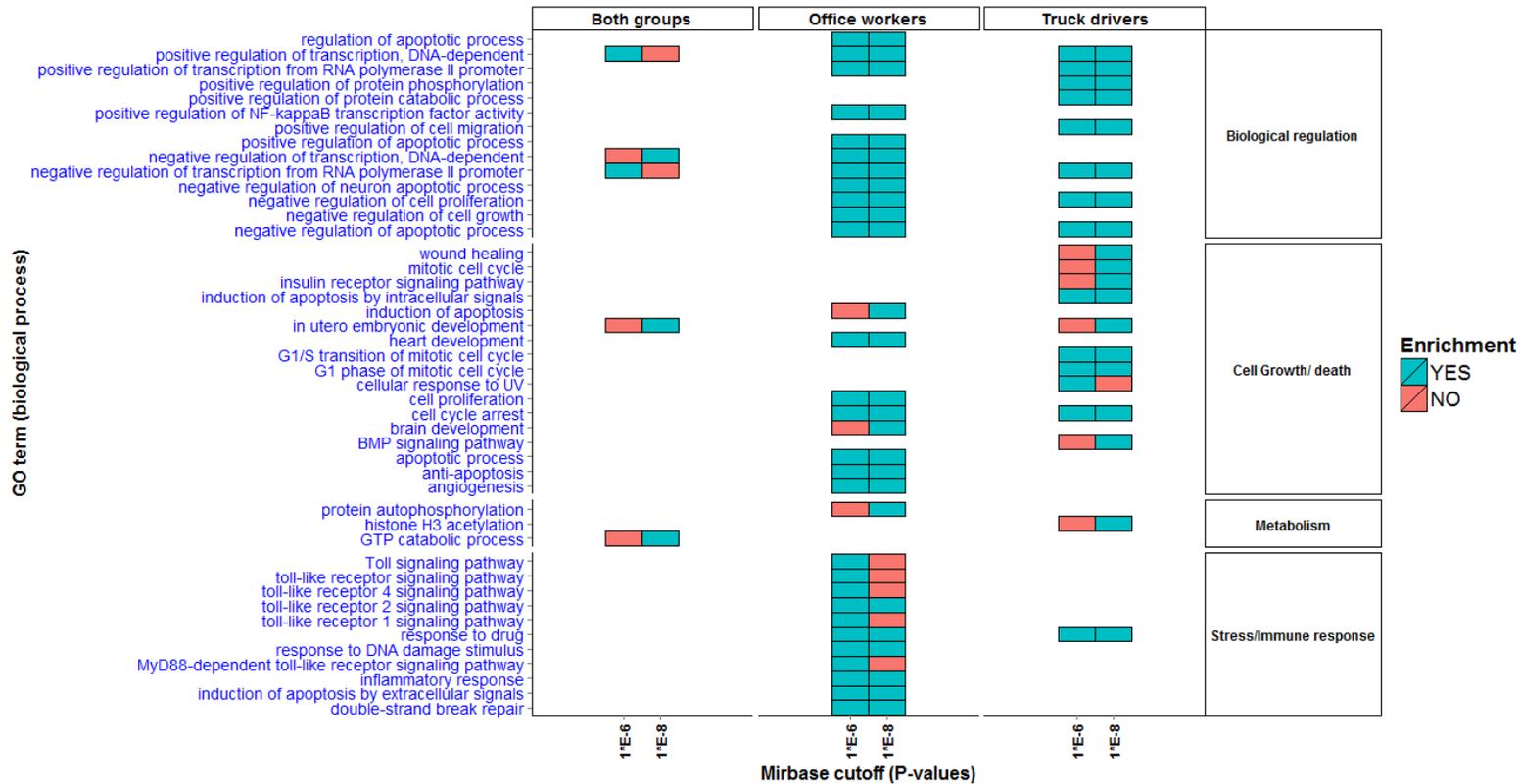


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Table S1. Percent change in miRNA expression level with one $\mu\text{g}/\text{m}^3$ increase in Elemental Carbon (EC) at FDR <20%.

| miRNA name | % change (95% CI) | P-value | FDR * |
|---|--------------------------|----------------|--------------|
| Pooled analysis ^a [within subject (short-term) effects] | | | |
| hsa-miR-1537 | 11.99 (5.07, 9.38) | 0.001 | 0.102 |
| hsa-miR-548h | 7.36 (2.69, 2.25) | 0.002 | 0.145 |
| hsa-miR-200a | 1.41 (0.43, 0.40) | 0.005 | 0.145 |
| hsa-miR-520a-3p | 11.13 (3.21, 9.66) | 0.006 | 0.145 |
| hsa-miR-155 | 4.79 (1.25, 0.46) | 0.008 | 0.145 |
| hsa-miR-501-3p | 8.43 (2.04, 5.21) | 0.010 | 0.145 |
| hsa-miR-647 | 7.33 (1.23, 3.70) | 0.019 | 0.193 |
| Office workers ^b [within subject (short-term) effects] | | | |
| ebv-miR-BART2-5p | 7.08 (3.04, 11.28) | 0.001 | 0.062 |
| hsa-miR-548h | 16.97 (6.86, 28.03) | 0.001 | 0.062 |
| hsa-miR-1243 | 13.67 (4.95, 23.13) | 0.002 | 0.062 |
| hsa-miR-181b/181d | 12.12 (4.29, 20.54) | 0.003 | 0.062 |
| hsa-miR-302f | 7.96 (2.65, 13.54) | 0.004 | 0.062 |
| hsa-miR-647 | 19.03 (6.10, 33.53) | 0.004 | 0.062 |
| hsa-miR-340 | 9.44 (3.17, 16.08) | 0.004 | 0.062 |
| hsa-miR-210 | -7.92 (-12.85, -2.71) | 0.004 | 0.062 |
| hsa-miR-532-3p | -1.55 (-2.58, -0.52) | 0.004 | 0.062 |
| hsa-miR-642 | 7.62 (2.43, 13.08) | 0.004 | 0.062 |
| ebv-miR-BART6-5p | -24.19 (-37.17, -8.53) | 0.005 | 0.062 |
| hsa-miR-423-3p | -2.32 (-3.88, -0.72) | 0.005 | 0.062 |
| hsa-miR-484 | -4.19 (-6.99, -1.31) | 0.006 | 0.062 |
| hsa-miR-937 | 2.14 (0.68, 3.62) | 0.006 | 0.062 |
| hsa-miR-125a-5p | -2.84 (-4.81, -0.82) | 0.008 | 0.084 |
| hsa-miR-21 | 4.46 (1.10, 7.94) | 0.011 | 0.108 |
| hsa-miR-154 | 2.63 (0.65, 4.66) | 0.012 | 0.108 |
| hsa-miR-10a | -17.23 (-28.65, -4.00) | 0.014 | 0.120 |
| hsa-miR-142-3p | 3.80 (0.78, 6.91) | 0.015 | 0.120 |
| hsa-miR-600 | -15.97 (-26.80, -3.55) | 0.015 | 0.120 |

| miRNA name | % change (95% CI) | P-value | FDR[*] |
|--|--------------------------|----------------|------------------------|
| hsa-miR-146a | 2.67 (0.52, 4.87) | 0.018 | 0.129 |
| hsa-miR-2114 | 19.60 (3.60, 38.07) | 0.018 | 0.129 |
| hsa-miR-150 | -4.04 (-7.27, -0.70) | 0.021 | 0.142 |
| hsa-miR-1283 | -13.65 (-23.94, -1.97) | 0.026 | 0.170 |
| hsa-miR-1274a | -8.39 (-15.20, -1.03) | 0.029 | 0.172 |
| hsa-miR-328 | -11.70 (-21.04, -1.25) | 0.032 | 0.172 |
| kshv-miR-K12-9 | 13.40 (1.25, 27.00) | 0.032 | 0.172 |
| hsa-miR-515-5p | 16.19 (1.13, 33.50) | 0.037 | 0.185 |
| Truck drivers^b [within subject (short-term) effects] | | | |
| hsa-miR-513a-3p | 1.49 (0.60, 2.39) | 0.002 | 0.064 |
| hsa-miR-1537 | 14.03 (5.17, 23.63) | 0.002 | 0.064 |
| hsa-miR-155 | 6.73 (2.51, 11.13) | 0.002 | 0.064 |
| ebv-miR-BHRF1-3 | 0.98 (0.38, 1.59) | 0.002 | 0.064 |
| ebv-miR-BHRF1-1 | 0.98 (0.36, 1.59) | 0.002 | 0.064 |
| hsa-miR-520a-3p | 14.64 (4.92, 25.26) | 0.003 | 0.064 |
| hsa-miR-125a-5p | 3.15 (1.08, 5.26) | 0.004 | 0.064 |
| ebv-miR-BART9 | 1.59 (0.54, 2.66) | 0.004 | 0.064 |
| hsa-miR-652 | 13.62 (4.30, 23.77) | 0.004 | 0.064 |
| hsa-miR-501-3p | 12.70 (3.96, 22.17) | 0.005 | 0.064 |
| hsa-let-7b | 1.76 (0.57, 2.97) | 0.005 | 0.064 |
| hsa-miR-320a | 1.55 (0.48, 2.63) | 0.005 | 0.064 |
| hiv1-miR-H1 | 1.30 (0.41, 2.20) | 0.006 | 0.066 |
| hsa-miR-518f | 6.73 (1.85, 11.83) | 0.008 | 0.068 |
| hsa-miR-208b | 7.10 (1.91, 12.54) | 0.009 | 0.070 |
| hsa-miR-192 | -11.69 (-19.82, -2.73) | 0.013 | 0.080 |
| hsa-miR-361-3p | 2.55 (0.55, 4.59) | 0.014 | 0.080 |
| hsa-miR-1308 | 7.26 (1.50, 13.34) | 0.014 | 0.080 |
| hsa-miR-125b | 2.42 (0.52, 4.36) | 0.016 | 0.083 |
| hsa-miR-1979 | 2.00 (0.39, 3.63) | 0.016 | 0.083 |
| hsa-miR-1274a | 6.15 (1.14, 11.41) | 0.017 | 0.083 |
| hsa-miR-96 | 2.38 (0.43, 4.38) | 0.018 | 0.083 |

| miRNA name | % change (95% CI) | P-value | FDR[*] |
|-------------------|--------------------------|----------------|------------------------|
| hsa-miR-195 | 6.25 (1.02, 11.76) | 0.021 | 0.090 |
| hsa-miR-10b | 9.39 (1.38, 18.04) | 0.023 | 0.097 |
| hsa-miR-206 | 4.20 (0.47, 8.06) | 0.030 | 0.110 |
| hsa-miR-600 | 10.13 (0.85, 20.26) | 0.034 | 0.118 |
| hsa-miR-1283 | 8.98 (0.75, 17.89) | 0.034 | 0.118 |
| hsa-miR-10a | 9.62 (0.76, 19.25) | 0.035 | 0.118 |
| hsa-miR-708 | 10.49 (0.78, 21.13) | 0.036 | 0.118 |

^aAdjusted for occupational group, age, sex, BMI, smoking status, number of cigarettes smoked, work hours, examination date, and humidity and temperature of the study days.

^bAdjusted for age, sex, BMI, smoking status, number of cigarettes smoked, work hours, examination date, and humidity and temperature of the study days.

* FDRs (Benjamini-Hochberg false discovery rates) <20% were considered significant. Non-significant results are not shown.

Table S2. Significance of interaction between the exposure (short term exposure to EC) and occupational groups for miRNAs associated with EC by group analysis at FDR<10%.

| miRNA | <i>P</i>-value * |
|---|-------------------------|
| Significant miRNAs in office workers | |
| ebv-miR-BART6-5p | <0.001 |
| hsa-miR-532-3p | <0.001 |
| hsa-miR-423-3p | 0.001 |
| hsa-miR-181b/181d | 0.002 |
| hsa-miR-125a-5p | 0.002 |
| hsa-miR-1243 | 0.002 |
| hsa-miR-484 | 0.005 |
| hsa-miR-647 | 0.006 |
| hsa-miR-302f | 0.022 |
| hsa-miR-548h | 0.024 |
| hsa-miR-340 | 0.027 |
| hsa-miR-642 | 0.033 |
| ebv-miR-BART2-5p | 0.034 |
| hsa-miR-937 | 0.036 |
| hsa-miR-210 | 0.247 |
| Significant miRNAs in truck drivers | |
| hsa-miR-1274a | 0.001 |
| hsa-miR-518f | 0.002 |
| hsa-miR-125a-5p | 0.002 |
| hsa-miR-320a | 0.002 |
| hsa-miR-652 | 0.003 |
| hsa-miR-192 | 0.003 |
| hsa-miR-96 | 0.004 |
| hsa-miR-520a-3p | 0.007 |
| hsa-miR-501-3p | 0.007 |
| hsa-miR-1979 | 0.009 |
| hsa-let-7b | 0.011 |

| miRNA | <i>P</i>-value[*] |
|-----------------|-----------------------------------|
| hsa-miR-1308 | 0.012 |
| hsa-miR-361-3p | 0.013 |
| ebv-miR-BHRF1-1 | 0.015 |
| ebv-miR-BHRF1-3 | 0.020 |
| hsa-miR-208b | 0.029 |
| hsa-miR-10b | 0.037 |
| hsa-miR-513a-3p | 0.039 |
| hiv1-miR-H1 | 0.048 |
| hsa-miR-195 | 0.084 |
| hsa-miR-155 | 0.106 |
| hsa-miR-125b | 0.174 |
| ebv-miR-BART9 | 0.175 |
| hsa-miR-1537 | 0.630 |

* *P*-value for interaction between change in EC level and occupational group (office worker or truck driver). The model adjusted for group, age, sex, BMI, smoking status, number of cigarettes smoked, work hours, examination date, and humidity and temperature of the study days.

Table S3. Percent change in miRNA expression level with one-unit increase in elemental carbon (EC) (non-smokers only). ^a

| miRNA name | % change (95% CI) | P-value | FDR [*] |
|-------------------------------|--------------------------|----------------|-------------------------|
| Office workers | | | |
| hsa-miR-451 | 1.67 (0.78, 2.57) | 0.001 | 0.123 |
| ebv-miR-BART2-5p ^b | 11.13 (4.22, 18.49) | 0.003 | 0.128 |
| hsa-miR-92a | -1.59 (-2.56, -0.61) | 0.003 | 0.128 |
| hsa-miR-642 ^b | 13.26 (4.40, 22.88) | 0.004 | 0.128 |
| hsa-miR-340 ^b | 16.75 (5.58, 29.10) | 0.005 | 0.128 |
| hsa-miR-548h ^{b,d} | 21.16 (6.68, 37.61) | 0.005 | 0.128 |
| hsa-miR-937 ^b | 3.48 (1.11, 5.89) | 0.006 | 0.128 |
| ebv-miR-BART6-5p ^b | -28.26 (-43.19, -9.40) | 0.007 | 0.128 |
| hsa-miR-21 ^b | 7.93 (2.37, 13.79) | 0.008 | 0.128 |
| hsa-miR-1243 ^b | 21.66 (5.96, 39.68) | 0.008 | 0.128 |
| hsa-miR-154 ^b | 4.52 (1.32, 7.82) | 0.009 | 0.128 |
| hsa-miR-302f ^b | 12.18 (3.31, 21.81) | 0.010 | 0.131 |
| Truck drivers | | | |
| hsa-miR-374b | -11.00 (-16.70, -4.91) | 0.001 | 0.180 |
| hsa-miR-15b | 4.59 (1.73, 7.53) | 0.003 | 0.180 |
| hsa-miR-183 | 3.15 (1.13, 5.22) | 0.004 | 0.180 |
| ebv-miR-BART9 ^c | 1.79 (0.59, 3.00) | 0.005 | 0.180 |
| ebv-miR-BHRF1-1 ^c | 1.32 (0.43, 2.22) | 0.005 | 0.180 |

^a Adjusted for age, sex, BMI, smoking status, number of cigarettes smoked, work hours, examination date, and humidity and temperature of the study days.

^b miRNA significantly associated with EC in analysis that included all participants of office workers.

^c miRNA significantly associated with EC in analysis that included all participants of truck drivers.

^d miRNA significantly associated with EC in analysis that included all participants.

* FDRs (Benjamini-Hochberg false discovery rates) <20% were considered significant results. Non-significant results are not shown.

Table S4. Change in miRNA expression level (log2) with one unit increase in PM₁₀.

| miRNA name | % change (95% CI) | P-value | FDR * |
|--|----------------------|---------|--------|
| Pooled analysis^a [Within Subject (short-term) effects] | | | |
| hsa-miR-515-5p | 0.99 (0.41, 1.57) | 0.001 | 0.133 |
| Office workers^b [Within subject (short-term) effects] | | | |
| hsa-miR-10b ^d | -1.47 (-2.02, -0.92) | <0.001 | <0.001 |
| hsa-miR-648 | -1.55 (-2.16, -0.94) | <0.001 | <0.001 |
| hsa-miR-137 | -1.68 (-2.44, -0.91) | <0.001 | 0.004 |
| hsa-miR-10a ^{c,d} | -2.02 (-2.95, -1.08) | <0.001 | 0.004 |
| hsa-miR-1183 | -1.08 (-1.61, -0.54) | <0.001 | 0.004 |
| hsa-miR-501-3p ^{d,e} | -1.21 (-1.81, -0.61) | <0.001 | 0.004 |
| ebv-miR-BART6-5p ^d | -2.05 (-3.27, -0.82) | 0.002 | 0.012 |
| hsa-miR-300 | -1.51 (-2.44, -0.56) | 0.002 | 0.014 |
| hsa-miR-559 | -1.49 (-2.43, -0.55) | 0.003 | 0.016 |
| hsa-miR-515-5p ^c | 1.39 (0.48, 2.31) | 0.004 | 0.017 |
| hsa-miR-651 ^c | -1.48 (-2.44, -0.52) | 0.004 | 0.019 |
| hsa-miR-520a-3p ^{d,e} | -1.39 (-2.36, -0.41) | 0.008 | 0.030 |

^a Adjusted for occupational group, age, sex, BMI, smoking status, number of cigarettes smoked, work hours, examination date, and humidity and temperature of the study days.

^b Adjusted for age, sex, BMI, smoking status, number of cigarettes smoked, work hours, examination date, and humidity and temperature of the study days.

^c miRNA significantly associated with EC in office workers.

^d miRNA significantly associated with EC in truck drivers.

^e miRNA significantly associated with EC in pooled analysis.

* FDRs (Benjamini-Hochberg false discovery rates) <20% were considered significant. Non-significant results are not shown.

Table S5. Percent change in miRNA expression level with one-unit increase in PM_{2.5}.

| miRNA name | % change (95% CI) | P-value * | FDR |
|---|--------------------------|------------------|------------|
| Pooled analysis ^a [Between-subjects effects] | | | |
| hsa-miR-1537 | 5.86 (1.51, 10.40) | 0.008 | 0.982 |
| Pooled analysis ^a [Within subject (short-term) effects] | | | |
| hsa-miR-1537 | 6.35 (1.87, 11.03) | 0.006 | 0.886 |
| hsa-miR-374b | -3.02 (-5.37, -0.61) | 0.015 | 0.886 |
| Office workers ^b [Between-subjects effects] | | | |
| hsa-miR-647 | 12.10 (4.58, 20.16) | 0.002 | 0.287 |
| hsa-miR-181b/181d | 6.25 (1.65, 11.06) | 0.009 | 0.468 |
| hsa-miR-302f | 4.00 (0.84, 7.26) | 0.014 | 0.468 |
| hsa-miR-601 | 9.58 (1.92, 17.82) | 0.015 | 0.468 |
| ebv-miR-BART6-5p | -12.78 (-22.11, -2.34) | 0.020 | 0.468 |
| hsa-miR-1243 | 5.93 (0.85, 11.27) | 0.024 | 0.492 |
| hsa-miR-1323 | 8.71 (0.67, 17.40) | 0.036 | 0.512 |
| hsa-miR-759 | 7.14 (0.55, 14.16) | 0.036 | 0.512 |
| Office workers ^b [Within subject (short-term) effects] | | | |
| hsa-miR-647 | 11.77 (4.12, 19.98) | 0.003 | 0.451 |
| hsa-miR-181b/181d | 6.33 (1.63, 11.25) | 0.009 | 0.589 |
| hsa-miR-302f | 4.03 (0.81, 7.36) | 0.016 | 0.589 |
| hsa-miR-601 | 9.72 (1.90, 18.15) | 0.016 | 0.589 |
| hsa-miR-1243 | 6.04 (0.85, 11.50) | 0.024 | 0.589 |
| hsa-miR-759 | 7.57 (0.83, 14.77) | 0.030 | 0.589 |
| ebv-miR-BART6-5p | -11.93 (-21.53, -1.15) | 0.033 | 0.589 |
| hsa-miR-647 | 11.77 (4.12, 19.98) | 0.003 | 0.451 |
| Truck drivers ^b [Between-subjects effects] | | | |
| hsa-miR-192 | -9.74 (-15.62, -3.44) | 0.004 | 0.598 |
| hsa-miR-1537 | 7.75 (1.75, 14.10) | 0.012 | 0.881 |
| hsa-miR-374b | -3.13 (-5.80, -0.39) | 0.028 | 0.881 |
| Truck drivers ^b [Within subject (short-term) effects] | | | |
| hsa-miR-192 | -10.13 (-16.14, -3.69) | 0.003 | 0.521 |
| hsa-miR-1537 | 7.56 (1.42, 14.08) | 0.017 | 0.831 |
| hsa-miR-877 | -5.54 (-10.02, -0.84) | 0.024 | 0.831 |

^a Adjusted for age, sex, BMI, smoking status, group, number of cigarettes smoked, work hours, examination date, and humidity and temperature of the study days.

^b Adjusted for age, sex, BMI, smoking status, number of cigarettes smoked, work hours, examination date, and humidity and temperature of the study days.

* *P*-values <0.05 are included.

Table S6. KEGG pathway enrichment analysis for targets of significant EC-associated miRNAs (for miRBase gene targets at P -value $<10^{-8}$).

| KEGG ID | Pathway | Gene list ^a | Total no. of genes ^b | P -value [*] | FDR ^{**} | Enrichment score | KEGG Higher Categories (Level-1) | KEGG Higher Categories (Level-2) |
|------------------------|---|------------------------|---------------------------------|-------------------------|-------------------|------------------|--------------------------------------|-------------------------------------|
| Pooled analysis | | | | | | | | |
| hsa05210 | Colorectal cancer | 8 | 62 | <0.001 | 0.001 | 9.92 | Human Disease | Cancer |
| hsa05200 | Pathways in cancer | 13 | 326 | 0.001 | 0.028 | 3.07 | Human Disease | Cancer |
| Office workers | | | | | | | | |
| hsa05200 | Pathways in cancer | 24 | 326 | <0.001 | <0.001 | 4.53 | Human Disease | Cancer |
| hsa05219 | Bladder cancer | 10 | 42 | <0.001 | <0.001 | 14.65 | Human Disease | Cancer |
| hsa05212 | Pancreatic cancer | 11 | 70 | <0.001 | <0.001 | 9.67 | Human Disease | Cancer |
| hsa05222 | Small cell lung cancer | 10 | 85 | <0.001 | <0.001 | 7.24 | Human Disease | Cancer |
| hsa05215 | Prostate cancer | 10 | 89 | <0.001 | <0.001 | 6.91 | Human Disease | Cancer |
| hsa04620 | Toll-like receptor signaling pathway | 10 | 102 | <0.001 | <0.001 | 6.03 | Organismal Systems | Immune system |
| hsa05142 | Chagas disease (American trypanosomiasis) | 10 | 104 | <0.001 | <0.001 | 5.91 | Human Disease | Infectious diseases: Parasitic |
| hsa05210 | Colorectal cancer | 8 | 62 | <0.001 | <0.001 | 7.94 | Human Disease | Cancer |
| hsa04210 | Apoptosis | 9 | 87 | <0.001 | <0.001 | 6.36 | Cellular Processes | Cell growth and death |
| hsa05218 | Melanoma | 8 | 71 | <0.001 | 0.001 | 6.93 | Human Disease | Cancer |
| hsa04520 | Adherens junction | 8 | 73 | <0.001 | 0.001 | 6.74 | Cellular Processes | Cell Communication |
| hsa05220 | Chronic myeloid leukemia | 8 | 73 | <0.001 | 0.001 | 6.74 | Human Disease | Cancer |
| hsa04060 | Cytokine-cytokine receptor interaction | 15 | 265 | <0.001 | 0.001 | 3.48 | Environmental Information Processing | Signaling molecules and interaction |
| hsa04010 | MAPK signaling pathway | 15 | 268 | <0.001 | 0.001 | 3.44 | Environmental Information Processing | Signal transduction |
| hsa04722 | Neurotrophin signaling pathway | 9 | 127 | <0.001 | 0.003 | 4.36 | Organismal Systems | Nervous system |

| KEGG ID | Pathway | Gene list ^a | Total no. of genes ^b | P-value [*] | FDR ^{**} | Enrichment score | KEGG Higher Categories (Level-1) | KEGG Higher Categories (Level-2) |
|----------------------|--------------------------------|------------------------|---------------------------------|----------------------|-------------------|------------------|----------------------------------|----------------------------------|
| hsa04110 | Cell cycle | 8 | 124 | 0.002 | 0.008 | 3.97 | Cellular Processes | Cell growth and death |
| hsa05145 | Toxoplasmosis | 8 | 132 | 0.002 | 0.011 | 3.73 | Human Diseases | Infectious diseases: Parasitic |
| hsa04062 | Chemokine signaling pathway | 9 | 189 | 0.006 | 0.024 | 2.93 | Organismal Systems | Immune system |
| Truck drivers | | | | | | | | |
| hsa05200 | Pathways in cancer | 35 | 326 | <0.001 | <0.001 | 2.99 | Human Disease | Cancer |
| hsa05210 | Colorectal cancer | 13 | 62 | <0.001 | <0.001 | 5.84 | Human Disease | Cancer |
| hsa05218 | Melanoma | 14 | 71 | <0.001 | <0.001 | 5.49 | Human Disease | Cancer |
| hsa05219 | Bladder cancer | 11 | 42 | <0.001 | <0.001 | 7.29 | Human Disease | Cancer |
| hsa05215 | Prostate cancer | 15 | 89 | <0.001 | <0.001 | 4.69 | Human Disease | Cancer |
| hsa04110 | Cell cycle | 17 | 124 | <0.001 | <0.001 | 3.82 | Cellular Processes | Cell growth and death |
| hsa05213 | Endometrial cancer | 11 | 52 | <0.001 | <0.001 | 5.89 | Human Disease | Cancer |
| hsa05223 | Non-small cell lung cancer | 11 | 54 | <0.001 | <0.001 | 5.67 | Human Disease | Cancer |
| hsa05212 | Pancreatic cancer | 12 | 70 | <0.001 | 0.001 | 4.77 | Human Disease | Cancer |
| hsa05214 | Glioma | 11 | 65 | <0.001 | 0.001 | 4.71 | Human Disease | Cancer |
| hsa05221 | Acute myeloid leukemia | 10 | 57 | <0.001 | 0.002 | 4.88 | Human Disease | Cancer |
| hsa05220 | Chronic myeloid leukemia | 11 | 73 | <0.001 | 0.002 | 4.19 | Human Disease | Cancer |
| hsa04115 | p53 signaling pathway | 10 | 68 | <0.001 | 0.005 | 4.09 | Cellular Processes | Cell growth and death |
| hsa00240 | Pyrimidine metabolism | 12 | 99 | 0.001 | 0.007 | 3.37 | Metabolism | Nucleotide metabolism |
| hsa00230 | Purine metabolism | 15 | 162 | 0.002 | 0.017 | 2.58 | Metabolism | Nucleotide metabolism |
| hsa04120 | Ubiquitin mediated proteolysis | 13 | 135 | 0.002 | 0.022 | 2.68 | Genetic Information Processing | Folding |
| hsa04910 | Insulin signaling pathway | 13 | 138 | 0.003 | 0.025 | 2.62 | Organismal Systems | Endocrine system |

^a No. of genes in a pathway (from 76 Entrez gene IDs in all participants combined, 95 Entrez gene IDs in office workers and 210 Entrez gene IDs in truck drivers, for genes selected at miRBase 10^{-8}).

^b Number of genes in the a pathway (from 5,844 total genes as background).

* *P*-values calculated using Fisher's exact test.

** FDRs (Benjamini-Hochberg false discovery rates) <5% were considered significant. Non-significant results are not shown.

Table S7. Gene Ontology (biological term) enrichment analysis (FDR< 1%) for significant EC-associated miRNAs (miRBase gene targets at P -value $<10^{-8}$).

| GO ID | Biological process term | Gene list ^a | Total no. of genes ^b | P -value [*] | FDR ^{**} | Enrichment score | GO term categories ^c |
|------------------------|--|------------------------|---------------------------------|-------------------------|-------------------|------------------|---------------------------------|
| Pooled analysis | | | | | | | |
| GO:0001701 | in utero embryonic development | 10 | 165 | <0.001 | 0.006 | 5.44 | Cell Growth/ death |
| GO:0006184 | GTP catabolic process | 10 | 178 | <0.001 | 0.008 | 5.04 | Metabolism |
| GO:0045892 | negative regulation of transcription, DNA-dependent | 16 | 440 | <0.001 | 0.009 | 3.26 | Biological regulation |
| Office workers | | | | | | | |
| GO:0006915 | apoptotic process | 36 | 702 | <0.001 | <0.001 | 4.60 | Cell Growth/ death |
| GO:0043066 | negative regulation of apoptotic process | 21 | 276 | <0.001 | <0.001 | 6.83 | Biological regulation |
| GO:0045893 | positive regulation of transcription, DNA dependent | 28 | 539 | <0.001 | <0.001 | 4.66 | Biological regulation |
| GO:0008285 | negative regulation of cell proliferation | 22 | 348 | <0.001 | <0.001 | 5.67 | Biological regulation |
| GO:0045944 | positive regulation of transcription from RNA polymerase II promoter | 29 | 650 | <0.001 | <0.001 | 4.00 | Biological regulation |
| GO:0051092 | positive regulation of NF-kappaB transcription factor activity | 12 | 106 | <0.001 | <0.001 | 10.16 | Biological regulation |
| GO:0045892 | negative regulation of transcription, DNA -dependent | 22 | 440 | <0.001 | <0.001 | 4.49 | Biological regulation |
| GO:0042493 | response to drug | 17 | 290 | <0.001 | <0.001 | 5.26 | Stress/Immune response |
| GO:0000122 | negative regulation of transcription from RNA polymerase II promoter | 21 | 454 | <0.001 | <0.001 | 4.15 | Biological regulation |
| GO:0007507 | heart development | 11 | 133 | <0.001 | <0.001 | 7.42 | Cell Growth/ Death |
| GO:0007050 | cell cycle arrest | 11 | 137 | <0.001 | <0.001 | 7.21 | Cell Growth/ Death |
| GO:0006302 | double-strand break repair | 8 | 62 | <0.001 | <0.001 | 11.58 | Stress/immune response |

| GO ID | Biological process term | Gene list ^a | Total no. of genes ^b | <i>P</i> -value [*] | FDR ^{**} | Enrichment score | GO term categories ^c |
|----------------------|--|------------------------|---------------------------------|------------------------------|-------------------|------------------|---------------------------------|
| GO:0034134 | toll-like receptor 2 signaling pathway | 8 | 72 | <0.001 | <0.001 | 9.97 | Stress/immune response |
| GO:0006974 | response to DNA damage stimulus | 10 | 130 | <0.001 | <0.001 | 6.90 | Stress/immune response |
| GO:0043524 | negative regulation of neuron apoptotic process | 8 | 78 | <0.001 | <0.001 | 9.21 | Biological regulation |
| GO:0008283 | cell proliferation | 15 | 326 | <0.001 | 0.001 | 4.13 | Cell growth/ death |
| GO:0006916 | anti-apoptosis | 12 | 215 | <0.001 | 0.001 | 5.01 | Cell growth/ death |
| GO:0001525 | angiogenesis | 11 | 189 | <0.001 | 0.001 | 5.22 | Cell growth/ death |
| GO:0006954 | inflammatory response | 13 | 273 | <0.001 | 0.001 | 4.27 | Stress/immune response |
| GO:0008624 | induction of apoptosis by extracellular signals | 8 | 110 | <0.001 | 0.002 | 6.53 | Stress/immune response |
| GO:0043065 | positive regulation of apoptotic process | 10 | 181 | <0.001 | 0.002 | 4.96 | Biological regulation |
| GO:0030308 | negative regulation of cell growth | 8 | 118 | <0.001 | 0.003 | 6.09 | Biological regulation |
| GO:0046777 | protein autophosphorylation | 9 | 158 | <0.001 | 0.003 | 5.11 | Metabolism |
| GO:0042981 | regulation of apoptotic process | 9 | 176 | <0.001 | 0.006 | 4.59 | Biological regulation |
| GO:0006917 | induction of apoptosis | 9 | 195 | 0.001 | 0.009 | 4.14 | Cell growth/ death |
| GO:0007420 | brain development | 8 | 156 | 0.001 | 0.009 | 4.60 | Cell growth/ death |
| Truck drivers | | | | | | | |
| GO:0008285 | negative regulation of cell proliferation | 34 | 348 | <0.001 | <0.001 | 3.38 | Biological regulation |
| GO:0000082 | G1/S transition of mitotic cell cycle | 21 | 149 | <0.001 | <0.001 | 4.87 | Cell growth/ death |
| GO:0043066 | negative regulation of apoptotic process | 28 | 276 | <0.001 | <0.001 | 3.51 | Biological regulation |
| GO:0045944 | positive regulation of transcription from RNA polymerase II promoter | 48 | 650 | <0.001 | <0.001 | 2.55 | Biological regulation |
| GO:0045732 | positive regulation of protein catabolic process | 10 | 31 | <0.001 | <0.001 | 11.15 | Metabolism |
| GO:0045893 | positive regulation of transcription | 41 | 539 | <0.001 | <0.001 | 2.63 | Biological regulation |

| GO ID | Biological process term | Gene list ^a | Total no. of genes ^b | <i>P</i> -value [*] | FDR ^{**} | Enrichment score | GO term categories ^c |
|------------|--|------------------------|---------------------------------|------------------------------|-------------------|------------------|---------------------------------|
| GO:0008629 | induction of apoptosis by intracellular signals | 11 | 46 | <0.001 | <0.001 | 8.27 | Cell growth/ death |
| GO:0000122 | negative regulation of transcription from RNA polymerase II promoter | 35 | 454 | <0.001 | <0.001 | 2.67 | Biological regulation |
| GO:0007050 | cell cycle arrest | 17 | 137 | <0.001 | 0.001 | 4.29 | Cell growth/death |
| GO:0042493 | response to drug | 26 | 290 | <0.001 | 0.001 | 3.10 | Stress/immune response |
| GO:0001934 | positive regulation of protein phosphorylation | 12 | 75 | <0.001 | 0.001 | 5.53 | Metabolism |
| GO:0030335 | positive regulation of cell migration | 14 | 103 | <0.001 | 0.001 | 4.70 | Cell growth/ death |
| GO:0000080 | G1 phase of mitotic cell cycle | 9 | 40 | <0.001 | 0.001 | 7.78 | Cell growth/death |
| GO:0030509 | BMP signaling pathway | 11 | 70 | <0.001 | 0.003 | 5.43 | Cell growth/death |
| GO:0000278 | mitotic cell cycle | 25 | 324 | <0.001 | 0.004 | 2.67 | Cell growth/death |
| GO:0042060 | wound healing | 10 | 62 | <0.001 | 0.004 | 5.58 | Cell growth/ death |
| GO:0043966 | histone H3 acetylation | 8 | 39 | <0.001 | 0.005 | 7.09 | Metabolism |
| GO:0001701 | in utero embryonic development | 16 | 165 | <0.001 | 0.007 | 3.35 | Cell growth/death |
| GO:0008286 | insulin receptor signaling pathway | 15 | 154 | <0.001 | 0.010 | 3.37 | Cell growth/death |

^a No. of genes in a pathway (from 161 Entrez gene IDs in all participants combined, 161 Entrez gene IDs in office workers, and 418 Entrez gene IDs in truck drivers, for genes selected at miRBase 10⁻⁸).

^b Number of genes in the a pathway (from 14,451 total genes as background).

^c Based on title of GO term four type of categories were considered; 1. Stress/ immune responses, 2. Biological Regulation, 3. Metabolism 4. Cell growth/death.

* *P*-values calculated using Fisher's exact test.

** FDRs (Benjamini-Hochberg false discovery rates) <1% were considered significant. Non-significant results are not shown.