Supplemental Material

Ambient PM$_{2.5}$-Exposure Up-regulates the Expression of Co-Stimulatory Receptors on Circulating Monocytes in Diabetic Individuals

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Online Supplement Figure 3. Subject-specific associations (random slopes) with a 10µg/m³ increment in PM$_{2.5}$ (lag of 4 days) for CD23 monocytes (MFI). Individuals 2 and 7 had to be excluded from the analysis as one declined venipuncture and for one the withdrawn blood amount was not enough for flow-cytometry analysis.

Online Supplement Figure 4. Effect estimates for IL-6 and TNFα with 95%-confidence intervals for immediate and delayed associations with PM$_{2.5}$ (Schneider et al. 2010).
<table>
<thead>
<tr>
<th>CD (cluster of differentiation) Marker</th>
<th>Major Cell Type Expressed</th>
<th>Receptor and Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD23</td>
<td>Mature B cells; activated Macrophages; Eosinophils</td>
<td>Low affinity IgE receptor; mediates IgE allergic responses</td>
</tr>
<tr>
<td>FceR1</td>
<td>Mast cells; Basophils; Monocytes; Eosinophils</td>
<td>High affinity IgE receptor; mediates IgE allergic responses</td>
</tr>
<tr>
<td>CD80</td>
<td>APCs: Dendritic cells; Macrophages</td>
<td>Co-stimulatory receptor; antigen presentation to T cells</td>
</tr>
<tr>
<td>CD86</td>
<td>APCs: Dendritic cells; Macrophages</td>
<td>Co-stimulatory receptor; antigen presentation to T cells</td>
</tr>
<tr>
<td>CD40</td>
<td>APCs: Dendritic cells; B cells; Macrophages</td>
<td>Co-stimulatory receptor; activation of APCs; antibody production</td>
</tr>
<tr>
<td>HLA-DR</td>
<td>Macrophages; Dendritic cells; Monocytes</td>
<td>Major histocompatibility (MHC) class II receptor; antigen presentation</td>
</tr>
<tr>
<td>CD1a</td>
<td>APCs</td>
<td>Transmembrane glycoprotein receptor; presentation of lipid antigens to T cells</td>
</tr>
<tr>
<td>CD11b</td>
<td>Neutrophils; Macrophages; Monocytes</td>
<td>Complement receptor 3 for opsonised immune complexes; mediates complement mediated immune responses; phagocytosis; neutrophil migration</td>
</tr>
<tr>
<td>CD54/ICAM-1</td>
<td>Leukocytes; endothelial cells</td>
<td>Intercellular adhesion molecule; binds to leukocyte integrins/ligands and induces cell transmigration into tissue</td>
</tr>
<tr>
<td>mCD14</td>
<td>Monocytes; Macrophages</td>
<td>LPS receptor; mediates LPS-induced innate immune responses</td>
</tr>
<tr>
<td>CD16</td>
<td>Neutrophils; NK cells;</td>
<td>Fc gamma Receptor for IgG opsonized innate immune complexes; mediates innate immune responses</td>
</tr>
<tr>
<td>CD64</td>
<td>Macrophages; Monocytes</td>
<td>Fc gamma Receptor for IgG opsonised immune complexes; mediates innate immune responses; phagocytosis</td>
</tr>
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</table>

APC = antigen presenting cells; ICAM-1 = intercellular adhesion molecule-1
Online Supplement Table 2. Description of the study population clinical characteristics: current non-smoking subjects with type 2 diabetes mellitus.

<table>
<thead>
<tr>
<th>Clinical Characteristics</th>
<th>N=20 individuals</th>
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<tbody>
<tr>
<td><strong>Disease history</strong></td>
<td>Total number or mean</td>
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<tr>
<td>Type 2 diabetes mellitus</td>
<td>20</td>
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<tr>
<td>Time since diabetes diagnosis [yrs]</td>
<td>6.1</td>
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<tr>
<td>Hyperlipidemia</td>
<td>18</td>
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<tr>
<td>Hypertension</td>
<td>18</td>
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<tr>
<td>Past myocardial infarction</td>
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<tr>
<td>Coronary artery disease</td>
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<tr>
<td>Peripheral vascular disease</td>
<td>3</td>
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<tr>
<td>Cerebrovascular disease</td>
<td>1</td>
</tr>
<tr>
<td>Diabetic retinopathy</td>
<td>1</td>
</tr>
<tr>
<td>Diabetic nephropathy*</td>
<td>8</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Medication intake</th>
<th>Total number</th>
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<tr>
<td>Sulfonylureas</td>
<td>9</td>
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<tr>
<td>Thiazolidinediones</td>
<td>6</td>
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<tr>
<td>Metformin</td>
<td>13</td>
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<td>Statins</td>
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<tr>
<td>Aspirin</td>
<td>13</td>
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<tr>
<td>Beta-blockers</td>
<td>9</td>
</tr>
<tr>
<td>Angiotensin converting enzyme-inhibitors</td>
<td>11</td>
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<tr>
<td>Calcium-blockers</td>
<td>1</td>
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<tr>
<td>Diuretics</td>
<td>8</td>
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<tr>
<td>Angiotension II-receptor blocker</td>
<td>3</td>
</tr>
<tr>
<td>Estrogen</td>
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\*Based on the screening urine (>30 µg albumin/mg creatinine) on spot collection.
Online Supplement Table 3. Description of PM$_{2.5}$ and of meteorology parameters throughout the study period (19 Nov 2004 to 09 December 2005).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N</th>
<th>Mean</th>
<th>SD$^a$</th>
<th>Min.</th>
<th>Max.</th>
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<tr>
<td><strong>Environmental Public Health Division Rooftop PM$_{2.5}^{b}$</strong></td>
<td></td>
<td></td>
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<tr>
<td>PM$_{2.5}^{c}$ [$\mu$g/m$^3$], imputed</td>
<td>383</td>
<td>14.2</td>
<td>7.2</td>
<td>1.5</td>
<td>42.8</td>
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<tr>
<td>PM$_{2.5}^{c}$ [$\mu$g/m$^3$]</td>
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<td>14.3</td>
<td>7.5</td>
<td>1.5</td>
<td>42.8</td>
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<tr>
<td><strong>Environmental Public Health Division Rooftop Meteorology</strong></td>
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<tr>
<td>Air temperature [°C]</td>
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<td>15.9</td>
<td>8.5</td>
<td>-6.5</td>
<td>31.5</td>
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<tr>
<td>Relative humidity [%]</td>
<td>385</td>
<td>62.5</td>
<td>16.6</td>
<td>25.1</td>
<td>97.7</td>
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<tr>
<td>Barometric pressure [hPa]</td>
<td>386</td>
<td>1001.2</td>
<td>6.5</td>
<td>981.4</td>
<td>1021.9</td>
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</table>

$^a$SD: standard deviation  
$^b$PM$_{2.5}$: particulate matter with a diameter <2.5μm (study period: 386 days)
Online Supplement Table 4. Description of inflammation and cell surface markers (descriptive statistics were calculated from patient means).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N*</th>
<th>Mean</th>
<th>SD^a</th>
<th>Min.</th>
<th>Max.</th>
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</thead>
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<td><strong>Inflammation Parameters</strong></td>
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<tr>
<td>Interleukin (IL)-6 [pg/ml]</td>
<td>79</td>
<td>3.5</td>
<td>2.2</td>
<td>1.3</td>
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<tr>
<td>Tumor necrosis factor (TNF) α [pg/ml]</td>
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<td>1.7</td>
<td>0.9</td>
<td>0.8</td>
<td>4.7</td>
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<td><strong>Monocytes (%)</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>CD23</td>
<td>75</td>
<td>6.0</td>
<td>6.6</td>
<td>0.7</td>
<td>27.5</td>
</tr>
<tr>
<td>FceR1</td>
<td>75</td>
<td>18.8</td>
<td>12.6</td>
<td>2.7</td>
<td>50.9</td>
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<td>6.2</td>
<td>0.4</td>
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<td>6.2</td>
<td>12.6</td>
<td>37.4</td>
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<td><strong>Neutrophils (%)</strong></td>
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<td>CD23</td>
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<td>2.1</td>
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</table>

Neutrophils (MFI)

<table>
<thead>
<tr>
<th></th>
<th>CD11b</th>
<th>CD14</th>
<th>CD16</th>
<th>CD64</th>
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<td>340.4</td>
<td>28.5</td>
<td>7774.63</td>
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</table>

*20 patients with a maximum of 4 measurements each; *SD: standard deviation
### Online Supplement Table 5. Absolute changes of analyzed cell surface markers with 95%-confidence intervals based on a 1 µg/m³ increase in PM$_{2.5}$.

<table>
<thead>
<tr>
<th>Monocytes (%)</th>
<th>Lag 0</th>
<th>Lag 1</th>
<th>Lag 2</th>
<th>Lag 3</th>
<th>Lag 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD23</td>
<td>-0.21</td>
<td>-0.11</td>
<td>-0.22</td>
<td>-0.19</td>
<td>-0.05</td>
</tr>
<tr>
<td></td>
<td>[-0.49;0.06]</td>
<td>[-0.41;0.20]</td>
<td>[-0.59;0.16]</td>
<td>[-0.61;0.23]</td>
<td>[-0.40;0.30]</td>
</tr>
<tr>
<td>CD86</td>
<td>0.07</td>
<td>0.39</td>
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<td>-1.04</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td>[-0.51;0.65]</td>
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<td>[-0.85;0.69]</td>
<td>[-1.83;0.25]</td>
<td>[-0.61;0.75]</td>
</tr>
<tr>
<td>CD40</td>
<td>0.53</td>
<td>0.35</td>
<td>-0.36</td>
<td>-0.32</td>
<td>0.23</td>
</tr>
<tr>
<td></td>
<td>[-0.16;1.21]</td>
<td>[-0.36;1.05]</td>
<td>[-1.25;0.54]</td>
<td>[-1.27;0.63]</td>
<td>[-0.60;1.06]</td>
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<tr>
<td>HLA-DR</td>
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<td>0.05</td>
<td>-0.45</td>
<td>-0.57</td>
<td>0.38</td>
</tr>
<tr>
<td></td>
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<td>[-1.41;0.27]</td>
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<td>0.02</td>
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<td>-0.07</td>
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<td>[-0.51;0.61]</td>
<td>[-0.47;0.33]</td>
</tr>
<tr>
<td>CD11b</td>
<td>-0.19</td>
<td>-0.15</td>
<td>-0.35</td>
<td>-0.31</td>
<td>-0.14</td>
</tr>
<tr>
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<td>[-0.43;0.05]</td>
<td>[-0.40;0.11]</td>
<td>[-0.65;0.04]</td>
<td>[-0.64;0.03]</td>
<td>[-0.45;0.18]</td>
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<td>-0.55</td>
<td>-0.19</td>
<td>-1.06</td>
<td>-1.44</td>
<td>0.11</td>
</tr>
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<td>[-1.26;0.16]</td>
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<td>[-2.04;0.08]</td>
<td>[-2.50;0.37]</td>
<td>[-0.83;1.04]</td>
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<td>FcεRI</td>
<td>0.58</td>
<td>0.37</td>
<td>-0.19</td>
<td>-0.51</td>
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### Monocytes (MFI)

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Online Supplement Table 6. Pearson correlation coefficients between cell surface markers on monocytes (%-data) and inflammatory markers IL-6 and TNFα.

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Online Supplement Table 7. Pearson correlation coefficients between cell surface markers on monocytes (MFI-data) and inflammatory markers IL-6 and TNFα.

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Online Supplement Table 8. Pearson correlation coefficients between cell surface markers on neutrophils (%-data) and inflammatory markers IL-6 and TNFα.

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<tr>
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<td>-0.03</td>
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<tr>
<td>TNFα</td>
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Online Supplement Table 9. Pearson correlation coefficients between cell surface markers on neutrophils (MFI-data) and inflammatory markers IL-6 and TNFα.

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<th>Cell surface marker</th>
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<th>CD16</th>
<th>CD11b</th>
<th>CD14</th>
<th>IL-6</th>
<th>TNFα</th>
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<tr>
<td>TNFα</td>
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Online Supplement Figure 1. Subject-specific associations (random slopes) with a 10µg/m³ increment in PM$_{2.5}$ (lag of 2 and 3 days) for CD40 monocytes (MFI). Subjects 2 and 7 had to be excluded from the analysis as one declined venipuncture and for one the withdrawn blood amount was not enough for flow-cytometry analysis.
Online Supplement Figure 2. Subject-specific associations (random slopes) with a 10µg/m³ increment in PM$_{2.5}$ (lag of 2 and 3 days) for CD80 monocytes (MFI). Individuals 2 and 7 had to be excluded from the analysis as one declined venipuncture and for one the withdrawn blood amount was not enough for flow-cytometry analysis.
Online Supplement Figure 3. Subject-specific associations (random slopes) with a 10µg/m³ increment in PM$_{2.5}$ (lag of 4 days) for CD23 monocytes (MFI). Individuals 2 and 7 had to be excluded from the analysis as one declined venipuncture and for one the withdrawn blood amount was not enough for flow-cytometry analysis.
Online Supplement Figure 4. Effect estimates for IL-6 and TNFα with 95%-confidence intervals for immediate and delayed associations with PM$_{2.5}$ (Schneider et al. 2010).

Reference: