DNA methylation differences in exposed workers and nearby residents of the Ma Ta Phut industrial estate, Rayong, Thailand

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Background Adverse biological effects from airborne pollutants are a primary environmental concern in highly industrialized areas. Recent studies linked air pollution exposures with altered blood Deoxyribonucleic acid (DNA) methylation, but effects from industrial sources and underlying biological mechanisms are still largely unexplored.

Methods The Ma Ta Phut industrial estate (MIE) in Rayong, Thailand hosts one of the largest steel, oil refinery and petrochemical complexes in south-eastern Asia. We measured a panel of blood DNA methylation markers previously associated with air pollution exposures, including repeated elements [long interspersed nuclear element-1 (LINE-1) and Alu] and genes [p53, hypermethylated-in-cancer-1 (HIC1), p16 and interleukin-6 (IL-6)], in 67 MIE workers, 65 Ma Ta Phut residents and 45 rural controls. To evaluate the role of DNA damage and oxidation, we correlated DNA methylation measures with bulky DNA adducts and 3-(2-deoxy-D-erythro-pentofuranosyl)pyrimido[1,2-α]purin-10(3H)-one deoxyguanosine (M1dG) adducts.

Results In covariate-adjusted models, MIE workers, compared with rural residents, showed lower LINE-1 (74.8% vs 78.0%; P < 0.001), p53 (8.0% vs 15.7%; P < 0.001) and IL-6 methylation (39.2% vs 45.0%; P = 0.027) and higher HIC1 methylation (22.2% vs 15.3%, P < 0.001). For all four markers, Ma Ta Phut residents exhibited methylation levels intermediate between MIE workers and rural controls (LINE-1, 75.7%, P < 0.001; p53, 9.0%, P < 0.001; IL-6, 39.8%, P = 0.041; HIC1, 17.8%, P = 0.05; all P-values vs rural controls). Bulky DNA adducts showed negative correlation with p53 methylation (P = 0.01). M1dG showed negative correlations with LINE-1 (P = 0.003) and IL-6 methylation (P = 0.05).
Conclusions Our findings indicate that industrial exposures may induce alterations of DNA methylation patterns detectable in blood leucocyte DNA. Correlation of DNA adducts with DNA hypomethylation suggests potential mediation by DNA damage.

Keywords Air pollution, Ma Ta Phut, blood leucocytes, DNA methylation, DNA damage

Introduction
Air quality is a primary environmental concern in highly industrialized areas, owing to potential exposures of both industrial workers and nearby residents. The Ma Ta Phut industrial estate (MIE) in Amphur Muang district, Rayong, Thailand hosts the largest steel, oil refinery and petrochemical complexes in south-eastern Asia. Coal and oil power generation plants are also located in the industrial complexes. The potential health effects on MIE workers and nearby Ma Ta Phut residents have been a source of intense concern. We recently conducted a cross-sectional study to evaluate the macromolecular damage induced by polycyclic aromatic hydrocarbons (PAHs) and reactive oxygen species, as reflected in aromatic/hydrophobic bulky Deoxyribo-nucleic acid (DNA) adducts and 3-(2-deoxy-β-D-erythropentafuranosyl)pyrimido[1,2-α]purin-10(3H)-one deoxyguanosine (M1dG) adducts, respectively. We found increased DNA damage in MIE workers compared with rural controls. Ma Ta Phut residents living near the MIE complexes also showed increased DNA damage relative to rural controls. Recent studies have linked air pollution exposures with alterations of repeated element and gene-specific methylation in peripheral blood leucocytes (PBLs). DNA methylation is an epigenetic mechanism that contributes to suppress gene expression and maintain genome stability. Lower methylation of long interspersed nuclear element-1 (LINE-1) and Alu repeated elements has been found in individuals exposed to traffic or industrial pollutants. Differences in blood DNA methylation patterns of the promoters of tumour suppressor genes, including p53, cyclin-dependent kinase inhibitor 2A (p16), hypermethylated-in-cancer-1 (HIC1) and the inflammatory cytokine interleukin-6 (IL-6), have been associated with occupational and environmental air pollution exposures. Abnormal DNA methylation patterns are a frequent characteristic of a wide variety of cancers. For instance, p53 hypomethylation has been suggested to participate in lung cancer development. Conversely, several tumour suppressor genes, including p16 and HIC1, are hypermethylated in cancer tissues. Repeated element and gene-specific hypomethylation occurs early in animal models of carcinogenesis and may even induce methyltransferase activity and subsequent focal DNA hypermethylation. Repeated element hypomethylation can lead to genome instability and inappropriate activation of oncogenes. Blood LINE-1 hypomethylation has been recently associated with increased cancer risk in a prospective analysis of the Normative Aging Study.

In the present study, we examined whether exposure to MIE emissions was associated with differences of repeated element and gene-specific methylation in PBL DNA from 67 MIE workers, 65 Ma Ta Phut residents and 45 rural residents living in a control district in Rayong province. We measured methylation levels of LINE-1 and Alu repeated elements, as well as of candidate genes, including p53, HIC1, p16 and IL-6. The selection of methylation markers was based on previous work that showed associations of DNA methylation in blood DNA with environmental exposures. In particular, LINE-1 and Alu have been shown to have lower methylation in association with particulate matter exposures. Methylation of p53, HIC1 and IL-6 was previously associated with exposure to PAHs in a study of Polish coke oven workers. Methylation of p16 has been associated with exposure to indoor air pollution from unventilated stove coal use in Guizhou, China. The marker selection has the advantage of covering different pathways that could be activated by exposure to airborne industrial pollutants, including apoptosis, cell cycle and growth control and inflammation.

Methods
Study participants
Blood leucocyte DNA methylation analysis was conducted on 67 MIE workers, 65 Ma Ta Phut residents and 45 rural controls (Tables 1 and 2) recruited between July 2000 and April 2001. Rural controls lived in a district from the same province of Rayong, with no proximity to major air pollution sources. Both local residents and rural controls had no work history of exposure to known or suspected carcinogens and were similar to MIE workers in lifestyle and socio-economic status. Participation rates were ~95% in each study group. Approval by the institutional review boards of the participating institutions and written informed consent were obtained before initiation of this study. Blood leucocyte levels of aromatic/hydrophobic bulky DNA adducts, as well

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as of M1dG adducts, were available from previous analyses on this population.2,3

Bisulphite Polymerase Chain Reaction and pyrosequencing
DNA was purified from buffy coat samples using phenol extraction.2 DNA methylation was quantified using bisulphite PCR and pyrosequencing, as described in previous work.9–10 DNA methylation analysis was performed in a single batch in 2009. Under standard freezing conditions, 5-methylcytosine is stable, and DNA methylation analysis can be successfully and reliably performed several years after the initial sample collection.17 DNA samples from different exposure groups were interspersed across plates to avoid any possible bias from plate effects. Briefly, the samples were bisulphite treated using the EZ-96 DNA Methylation-Gold KitTM (Zymo Research, Orange, CA, USA). The degree of methylation was expressed as the mean for each gene of the percent 5-methylcytosine (% 5mC), which represents the proportion of methylated cytosines divided by the sum of methylated and unmethylated cytosines. Details on assay set-up, validation and analytical procedures are described in the supplementary materials (available as Supplementary data at IJE online).

Statistical analysis
Standard descriptive analyses were used to evaluate DNA methylation by gender, smoking, residence/employment and job types. Multivariate analyses were performed by fitting linear regression models adjusted by age, gender and smoking (never, former and current). In addition, we adjusted for percent neutrophils in differential blood counts to account for possible differences in the proportion of leucocyte subtypes. The regression parameters estimated from multiple regression models are presented as adjusted marginal means. The adjusted means were computed at the average values of all the other variables in the models. As some studies report a relationship of folic acid and certain B vitamins with DNA methylation,18,19 we also conducted sensitivity analyses by adding as a covariate in the models the weekly intake of fruit and vegetables. A log-normal multiple regression model adjusting for age, gender and percent neutrophils in differential blood counts was used to evaluate the relationship of bulky DNA and M1dG adducts with DNA methylation. Data were analysed using SPSS 13.0 (IBM SPSS Statistics, New York, NY, USA).

Results
Subjects characteristics
Table 1 shows the distribution of the demographic and lifestyle characteristics of the study participants across the exposure categories. The mean age of MIE workers, Ma Ta Phut residents and rural controls was 31.2 years ± 6.4, 36.2 years ± 8.5 and 34.6 years ± 6.7, respectively. Although all the study population was fairly young (mean age = 33.9 years ± 7.0), the group of MIE workers was younger than the Ma Ta Phut residents.
Smoking was more common among MIE workers compared with the Ma Ta Phut residents and rural controls (P = 0.06 and P < 0.001, respectively). Conversely, the dietary weekly intake of fruit and vegetables, a source of one-carbon nutrients, did not show major differences by residence/employment (P = 0.92 for MIE workers vs controls and P = 0.11 for Ma Ta Phut residents vs controls). MIE workers, and to a lesser degree Ma Ta Phut residents, showed higher blood DNA levels of aromatic/hydrophobic bulky DNA and M1dG adducts compared with rural controls (P < 0.001 and P = 0.011 for bulky DNA adducts and P < 0.001 and P = 0.005 for M1dG adducts, respectively, for MIE workers and Ma Ta Phut residents).

Differences in DNA methylation in MIE workers, Ma Ta Phut residents and rural controls

Several of the methylation markers showed differences between MIE workers and rural controls, with intermediate levels in the Ma Ta Phut residents (Table 2). LINE-1 methylation was 78.0% in rural controls, 75.7% in Ma Ta Phut residents (P < 0.001 vs rural controls) and 74.8% in MIE workers (P = 0.11 vs Ma Ta Phut residents; P < 0.001 vs rural controls). A decrease in LINE-1 methylation was found in tin-plating workers compared with Ma Ta Phut residents, but not in oil refinery or steel factory workers (P = 0.01, P = 0.28 and P = 0.69 vs Ma Ta Phut residents, P = 0.06 vs oil refinery workers and P = 0.82 vs steel factory workers, respectively). Higher Alu methylation was found in steel factory workers (P = 0.01 vs Ma Ta Phut residents; P = 0.002 vs rural controls), but not in the other two groups. MIE workers included three different kinds of industrial exposures, i.e. steel factory, oil refinery and tin-plating workers. A decrease in LINE-1 methylation was found in tin-plating workers, but not in oil refinery or steel factory workers (P < 0.001 vs rural controls). An increase in HIC1 methylation was found in Ma Ta Phut residents (P = 0.05 vs rural controls) and 22.2% in MIE workers (P = 0.0002 vs rural controls). Alu methylation did not show differences across the exposure groups (Table 3). All the associations reported did not show major differences after adjusting for the average weekly intake of fruit and vegetables (data not shown).

Differences in DNA methylation by job type

Table 2 Adjusted marginal means of blood DNA methylation levels in MIE workers, Ma Ta Phut residents and rural controls

<table>
<thead>
<tr>
<th>Residence and employment</th>
<th>LINE-1</th>
<th>Alu</th>
<th>p53</th>
<th>HIC1</th>
<th>IL-6</th>
<th>p16</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean&lt;sup&gt;a&lt;/sup&gt;</td>
<td>P&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Mean&lt;sup&gt;a&lt;/sup&gt;</td>
<td>P&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Mean&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Rural controls</td>
<td>45</td>
<td>78.0</td>
<td>Ref.</td>
<td>24.7</td>
<td>Ref.</td>
<td>15.7</td>
</tr>
<tr>
<td>Ma Ta Phut residents</td>
<td>63</td>
<td>75.7</td>
<td>&lt;0.001</td>
<td>24.9</td>
<td>0.47</td>
<td>Ref.</td>
</tr>
<tr>
<td>MIE workers</td>
<td>65</td>
<td>74.8</td>
<td>&lt;0.001</td>
<td>25.2</td>
<td>0.13</td>
<td>0.36</td>
</tr>
</tbody>
</table>

<sup>a</sup>Estimated from multiple regression models as independent variables age, gender, smoking, percent neutrophils in differential blood counts and residence/employment. The adjusted means were computed at the average values of the other covariates.

<sup>b</sup>For each of the covariates, the P-value refers to comparison with its reference level.

<sup>c</sup>P-value for difference between Ma Ta Phut residents and MIE workers.
p53 methylation was lower \((P < 0.001)\) in all three MIE worker job types compared with rural controls. However, only oil refinery workers showed p53 methylation lower than Ma Ta Phut residents \((P = 0.01)\). HIC1 methylation was higher \((P \leq 0.01)\) in all three job types than in rural controls, but this difference was higher than in Ma Ta Phut residents only in tin plating \((P = 0.02)\) and steel foundry workers \((P = 0.003)\). None of the job types individually showed differences in IL-6 methylation compared with rural controls or Ma Ta Phut residents. p16 methylation in oil refinery workers was lower than in rural controls \((P = 0.03)\) and Ma Ta Phut residents \((P = 0.002)\). p16 methylation in steel foundry workers was lower than in Ma Ta Phut residents \((P = 0.004)\), but only marginally lower than in rural residents \((P = 0.08)\).

**Correlations of DNA methylation with DNA damage markers**

In the analysis of all participants, increasing levels of aromatic/hydrophobic bulky DNA adducts were correlated with marginally lower methylation in LINE-1 \((\beta = -0.036; P = 0.06)\) and lower methylation in p53 \((\beta = -0.022; P = 0.01)\). Also, M1dG showed negative correlations with LINE-1 \((\beta = -0.073; P = 0.003)\) and IL-6 methylation \((\beta = -0.016; P = 0.05)\).

**Discussion**

In the present study, MIE workers and Ma Ta Phut residents exhibited lower LINE-1, p53 and IL-6 methylation and higher methylation of the HIC1 tumour suppressor gene compared with rural controls. Our findings suggest that exposures to MIE emissions can induce alteration in blood DNA methylation of repeated elements and genes with tumour suppressor and/or apoptotic, inflammatory, cell cycle and growth control functions. We also demonstrated inverse correlations of the amounts of aromatic/hydrophobic bulky DNA or M1dG adducts with LINE-1, p53 and IL-6 methylation levels.

Several of our findings are consistent with previous investigations conducted in different settings of exposure to air pollutants. For instance, MIE workers and Ma Ta Phut residents showed lower LINE-1 methylation, consistent with previous reports showing PBL DNA hypomethylation in repeated elements in individuals exposed to air pollution.\(^7,6,10,11\) Cancer tissues commonly show profound LINE-1 hypomethylation, which may determine widespread alterations in gene expression and chromatin packaging control, as well as higher genomic instability.\(^9,0\) More moderate decreases in LINE-1 methylation have been associated with air pollution exposure in blood DNA samples from individuals working in a steel production plant in Brescia, Italy,\(^10\) the participants of the Normative

<table>
<thead>
<tr>
<th>Residence and Factory Type</th>
<th>LINE-1</th>
<th>p53</th>
<th>HIC1</th>
<th>IL-6</th>
<th>p16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rural controls</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Ma Ta Phut residents</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Tin plating</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Oil refinery</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Steel foundry</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residence and Factory Type</td>
<td>Mean(^b)</td>
<td>P(^c)</td>
<td>Mean(^b)</td>
<td>P(^d)</td>
<td>Mean(^b)</td>
</tr>
<tr>
<td>Rural controls</td>
<td>45</td>
<td>Ref.</td>
<td>78.0</td>
<td>Ref.</td>
<td>24.7</td>
</tr>
<tr>
<td>Ma Ta Phut residents</td>
<td>63</td>
<td>Ref.</td>
<td>75.7</td>
<td>Ref.</td>
<td>24.9</td>
</tr>
<tr>
<td>Tin plating</td>
<td>12</td>
<td>&lt;0.001</td>
<td>73.3</td>
<td>&lt;0.001</td>
<td>24.9</td>
</tr>
<tr>
<td>Oil refinery</td>
<td>21</td>
<td>&lt;0.001</td>
<td>74.8</td>
<td>&lt;0.001</td>
<td>24.7</td>
</tr>
<tr>
<td>Steel foundry</td>
<td>32</td>
<td>&lt;0.001</td>
<td>75.4</td>
<td>&lt;0.001</td>
<td>25.5</td>
</tr>
</tbody>
</table>

\(^a\)Some figures do not add up to the total because of missing values.

\(^b\)Means adjusted for age, gender, smoking and percent neutrophils in differential blood counts.

\(^c\)P-values for comparison of types of MIE workers (tin plating, oil refinery or steel foundry) vs rural controls.

\(^d\)P-values for comparison of types of MIE workers (tin plating, oil refinery or steel foundry) vs Ma Ta Phut residents.
Aging Study, Boston, MA, USA \cite{8,11} and gas station attendants and police officers from Milan, Italy.\cite{9}

Gene-specific methylation analyses showed hypermethylation of the promoter region of \textit{p53} and of the inflammatory cytokine \textit{IL-6} in MIE workers and Ma Ta Phut residents. Pavanello \textit{et al.}\cite{9} also found \textit{p53} hypomethylation in Polish coke oven workers with high PAH exposure. In the MIE complexes, coal and oil power generation and fully integrated steel plants also contribute to high emissions of PAHs. For instance, one MIE factory in Ma Ta Phut is equipped with an electric arc furnace, which melts \(\sim 500,000\) tonnes of metal/year, with an average emission of 2.6 mg PAHs/kW/h.\cite{2} \textit{IL-6} has been proposed as a central mediator of inflammatory responses in individuals exposed to inhalable pollutants.\cite{21} Our results indicate \textit{IL-6} hypomethylation as an epigenetic mechanism that might promote \textit{IL-6} expression in exposed individuals. We observed \textit{HIC1} hypermethylation in MIE workers and a borderline hypermethylation in Ma Ta Phut residents. \textit{HIC1} is a tumour suppressor gene that is inactivated by DNA methylation in cancer tissues, including in lung cancer.\cite{22} Our finding indicates epigenetic effects of inhalable carcinogens that can be detected in peripheral blood DNA, consistent with results on other tumour suppressor genes in individuals exposed to airborne pollutants.\cite{21,26}

Some of our findings are at variance with the previous DNA methylation study of Polish coke oven workers exposed to high levels of airborne PAHs, which showed hypermethylation of LINE-1 and \textit{IL-6} and hypomethylation of \textit{HIC1}.\cite{9} The apparent discrepancies between our present study and some of the findings in the Polish study might be attributed to difference in the types of exposures. In fact, the MIE group represents three different kinds of industrial exposures, i.e. steel factory, oil refinery and tin-plating workers, which produce complex mixtures of nitrogen dioxide, ozone, propylene, ethylene, heavy metals, benzene and PAHs.\cite{23,24} Different sources of pollution result in different complex mixtures of airborne agents, which in turn might have different biological effects. Indeed, different patterns of DNA methylation differences were observed among the three job types. Steel foundry workers showed Alu and \textit{HIC1} hypermethylation and \textit{p16} hypomethylation; oil refinery workers showed \textit{p53} and \textit{p16} hypomethylation; tin-plating workers showed \textit{HIC1} hypermethylation and LINE-1 hypomethylation. We note that some of the differences we have observed might have derived from the relatively small sample size of the groups investigated in each of the job types, as well as from the multiple statistical tests performed.

Aromatic/hydrophobic bulky DNA adducts are considered reliable biomarkers of exposure to environmental/occupational carcinogens, including PAHs.\cite{21,25} When unrepaired, bulky DNA adducts can cause mutations, including mutational hot spots in the \textit{p53} tumour suppressor gene.\cite{26} The M$_1$dG adduct is derived from the interaction with the DNA of malondialdehyde, which is produced in individuals exposed to air pollution as a result of oxidative damage.\cite{27} In our study, most of the methylation markers that showed alterations in MIE workers and/or Ma Ta Phut residents—i.e. LINE-1, \textit{p53} and \textit{IL-6}—were also negatively correlated with the aromatic/hydrophobic DNA and/or the M$_1$dG adducts. Anti-benz[a]pyrene diolepoxide adducts have been found to inhibit the interactions of DNA methyltransferases with DNA.\cite{28} Bulky DNA and M$_1$dG adducts could interact with the DNA-binding domain of methyltransferases and, by changing the stereo structure of guanines and the chemical surrounding at such nucleotide sequences, interfere with the methyl groups’ transfer to the cytosine at CpG sites. Also, repair of DNA adducts causes the substitution of methylated cytosines with native non-methylated cytosines, thus effectively determining DNA methylation loss.\cite{29} Taken together, these findings suggest that cytosine hypomethylation at CpG sites of LINE-1, \textit{p53} and \textit{IL-6} might be mediated by the formation of DNA adducts.

In our study, we analysed DNA methylation in blood leukocyte DNA. PBLs are one of the most accessible sources of DNA, are largely used as surrogate tissues in molecular epidemiology and human epigenetic studies and provide the highest potential to develop biomarkers amenable to preventive use.\cite{29} However, our findings cannot be extended to other relevant tissues, such as the bronchial mucosa, which is directly exposed to airborne environmental carcinogens. We surmise that the exposure-related differences in DNA methylation observed in our study might reflect the induction of biological functions specific to blood leukocytes rather than a systemic effect associated with respiratory effects. The differences we observed might represent markers of exposure or biological effects limited to leukocytes and not necessarily correlated with aberrant DNA methylation in the lungs.

We used pyrosequencing analysis that yields accurate quantification of DNA methylation and can detect relatively small average differences across exposure groups. The absolute differences in DNA methylation we observed between MIE workers and rural controls ranged between 2.3 and 7.7 % 5mC, consistent with the size of effects reported in previous blood DNA methylation studies on individuals exposed to environmental toxicants. For instance, Pavanello \textit{et al.}\cite{9} found a mean difference of \(-4.6\) % 5mC of LINE-1 methylation and \(-6.8\) % 5mC of \textit{p53} methylation among PAH-exposed coke oven workers relative to controls, which is remarkably similar to the differences of \(-3.2\) % 5mC and \(-7.7\) % 5mC that we observed between MIE workers and rural controls for LINE-1 and \textit{p53}, respectively. Bollati \textit{et al.}\cite{7} reported a \(-3.4\) % 5mC difference of blood LINE-1 methylation in gas station attendants exposed to
benzene compared with indoor control workers. Other studies have reported even smaller size effects on blood DNA methylation of smaller size in response to environmental exposures. The interpretation of the functional significance of the effect size that we observed is uncertain and may just represent non-causal biomarkers. Blood leucocytes are a heterogeneous mixed-cell population, and each of the individual subtypes might carry different DNA methylation patterns. Exposure to industrial pollutants might have specific effects limited to one of the leucocyte subtypes that may be diluted when analysing unfractionated blood leucocytes. Precisely because we used unfractionated leucocytes, we cannot determine which of the leucocyte subtypes is sensitive to the effects of the exposure on DNA methylation. It is worth noting, however, that small differences in blood methylation have been associated in longitudinal studies with increased risk of cancer and cardiovascular disease, thus suggesting that the effect sizes we observed might be within the range associated with prediction of chronic disease risk. Previous investigations in the area showed increased risks of occupational lung and respiratory diseases, cancers and outpatient visits in Ma Ta Phut residents. Our present work, however, was cross-sectional and, therefore, could not provide information on the value of the observed differences in DNA methylation in predicting future risk of disease.

In summary, the present study showed DNA methylation differences in relation to occupational and residential groups with different levels of exposures to industrial emissions. The presence of negative correlations of DNA methylation of LINE-1, p53 and IL-6 with DNA adducts, a primary type of biomarker of exposure or biological dose, suggests that DNA methylation loss might be mediated by DNA damage. Larger studies are warranted to characterize the epigenetic effects of mixtures of exposures, such as those present in the MIE complexes and Ma Ta Phut area, as well as to investigate the links of exposure-related methylation patterns with disease risks.

Supplementary Data
Supplementary data are available at IJE online.

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Conflict of interest
None declared.

KEY MESSAGES
- Air quality is a primary environmental concern in highly industrialized areas, owing to potential exposures of both industrial workers and nearby residents.
- Analysis of DNA methylation, an epigenetic mechanism that can be readily used in human populations, may provide biomarkers of biological effects of industrial pollutants.
- The present study in the MIE in Amphur Muang district, Rayong, Thailand, which houses the largest steel, oil refinery and petrochemical complexes in south-eastern Asia, shows differences in blood DNA methylation—both lower and higher methylation depending on the gene—in industrial workers and nearby residents compared with rural controls.
- Correlations of hypomethylation of LINE-1, p53 and IL-6 methylation with DNA adduct levels suggest that environmentally induced DNA methylation loss may be mediated by DNA damage.

References