Epigenetic effects of Polycyclic Aromatic Hydrocarbons (PAHs) Exposure

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Education

1996.09-2001.07  SUMS  Preventive Medicine
2001.09-2004.07  SYSU  Toxicology
2005.09-2008.07  SYSU  Nutrition
Preventive Medicine

Public Health

Life course dimension

Health risk and impact assessment

Internal environment

Specific external environment

General external environment

Diet

Tobacco

Physical activity

Water

Transcriptomics

Proteomics

Metabolomics

Climate

Green spaces

Urban environment

Traffic

Social capital

Consumer products

Thorax 2014;69:876-878
Our research

cross-sectional study

◆ Sixty-nine occupational PAH-exposed workers (coke-oven workers) and 59 subjects without occupational PAHs exposure

◆ Internal exposure:
  urinary 1-hydroxypyrene (1-OHP)

◆ Outcomes:
  frequency of cytokinesis block micronucleus (CBMN)

◆ Biomarker:
  methylation status of p16 promoter in peripheral blood lymphocytes (PBL)
Table 1. Distribution of select variables and biomarkers in PAH-exposed workers

<table>
<thead>
<tr>
<th>Variables</th>
<th>Controls</th>
<th>PAH-exposed workers</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Number</td>
<td>59</td>
<td>69</td>
<td></td>
</tr>
<tr>
<td>Age (mean ± SD), y</td>
<td>41.95 ± 4.75</td>
<td>42.18 ± 6.51</td>
<td>0.82&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Current smokers (yes/no), %</td>
<td>46/16 (74.2)</td>
<td>56/11 (83.6)</td>
<td>0.19&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Alcohol user (yes/no), %</td>
<td>38/24 (61.3)</td>
<td>52/15 (77.6)</td>
<td>0.044&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Urinary 1-OHP levels [GM (95% CI)], μg/L</td>
<td>2.52 (2.28–2.77)</td>
<td>10.62 (8.13–13.87)</td>
<td>&lt;0.001&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>CBMN frequencies (mean ± SD), %</td>
<td>2.92 ± 3.04</td>
<td>7.28 ± 4.16</td>
<td>&lt;0.001&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Coking history (mean ± SD), y</td>
<td>—</td>
<td>21.29 ± 7.55</td>
<td>—</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; GM, geometric mean.

<sup>a</sup>Two-sided 2-sample t test.

<sup>b</sup>Two-tailed χ² test.

<sup>c</sup>Two-sided 2-sample t test.
Figure 2. Level of p16 methylation in CpG sites
Cancer Epidemiology, Biomarkers & Prevention

CpG Site–Specific Hypermethylation of $p16^{INK4a}$ in Peripheral Blood Lymphocytes of PAH-Exposed Workers

Ping Yang, Junxiang Ma, Bo Zhang, et al.

Environment effects are gradually decreasing in the progress of life course.
Prenatal exposure to environmental polycyclic aromatic hydrocarbons (PAHs), low birth weight and epigenetic mechanisms
World Trade Center (WTC) Cohort

Frederica P. Perera
Professor of Environmental Health Sciences
Mailman School of Public Health
Columbia University
Director of the Columbia Center for Children's Environmental Health
Results: 82

The Effects of the World Trade Center Event on Birth Outcomes among Term Deliveries at Three Lower Manhattan Hospitals

Relationships among Polycyclic Aromatic Hydrocarbon–DNA Adducts, Proximity to the World Trade Center, and Effects on Fetal Growth

Relationship between Polycyclic Aromatic Hydrocarbon–DNA Adducts, Environmental Tobacco Smoke, and Child Development in the World Trade Center Cohort

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1 EXPOSURE
Pregnant woman inhales polycyclic aromatic hydrocarbons (PAHs).

PAH-DNA adduct

2 EFFECT ON DNA
PAHs bind with DNA to form adducts.
### PAHs exposure in China

<table>
<thead>
<tr>
<th></th>
<th>检测指标 measures</th>
<th>浓度（ng/m³） concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>纽约的队列研究 NY Cohort study</strong></td>
<td>$\sum 8 \text{PAH}_{\text{BaPeq}}$</td>
<td>1.48</td>
</tr>
<tr>
<td><strong>北京奥运会期间 During Olympic Games</strong></td>
<td>$\sum 17 \text{PAH}_{\text{BaPeq}}$</td>
<td>4.33</td>
</tr>
<tr>
<td>（Beijing 8.8-8.24）</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>北京奥运后前后 After Olympic Games</strong></td>
<td>$\sum 17 \text{PAH}_{\text{BaPeq}}$</td>
<td>11.7</td>
</tr>
<tr>
<td>（Beijing7.28-8.7 and 8.25-10.7）</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>中国全国平均 Average level in China</strong></td>
<td>$\sum 16 \text{PAH}_{\text{BaPeq}}$</td>
<td>2.40</td>
</tr>
</tbody>
</table>
Epigenetics

Classic genetics do not explain how, despite their identical DNA sequences, monozygotic twins or cloned animals can have different phenotypes and different susceptibilities to a disease.

The concept of epigenetics
1939: “the causal interactions between genes and their products, which bring the phenotype into being”

Now: “heritable changes in gene expression that are not due to any alteration in the DNA sequence”
An epigenetic system should be
heritable,
self-perpetuating,
reversible
The best-known epigenetic marker is DNA methylation.
**Distribution of methylation and its effect on gene expression.**

Open boxes indicate exons; open circles indicate unmethylated CpG sites; and closed circles indicate methylated CpG sites.

- a Most CpG islands (CGIs) in normal tissue samples taken from young individuals are unmethylated, resulting in gene expression.

- b Methylation of a non-promoter CGI regions, does not block transcription.

- c Non-core regions within a promoter CGI, does not block transcription.

- d ‘Seeding of methylation’ is proposed to be important for induction of dense methylation (e).

- e Methylation of the core regions represses transcription.

- f Methylation of the core regions represses transcription, but methylation limited to the core region is in fact only rarely observed.
DNA Methylation and Health

1. DNA methylation is required to complete embryonic development and has been directly implicated in genomic imprinting and X-chromosome inactivation.

2. Alterations in DNA methylation are associated with many human diseases and are a hallmark of cancer.
Epigenetic Alternations in Tumor Progression
Figure. Epigenetics in cancer management  (N Engl J Med 2008;358:1148-1159)
Hypothesis

Nutrition and lifestyle
Chemicals
Stress
Disease

Aberrant DNA methylation
LBW
Study design: cohort study (birth cohort)

Questionnaire
• Information on the pregnancy, delivery, and birth outcomes
• Demographics; reproductive history; background environmental exposures including ETS (number of smoking household members and regular visitors to the home), dietary PAH exposure via grilled, smoked, and barbecued foods; and so on.
Biological specimen
  maternal peripheral blood and urine
  umbilical cord blood
  placenta tissue

Lab test and analysis
  internal exposure
  biomarkers

Outcomes
  gestational age
  birth size
  respiratory health
  neuro-cognitive development
• Joint effects (interactions)
• Developing an Environmental Exposure Matrix (EEM)
• Mechanism research
• More on intervention evaluation (targeting at epigenetic biomarkers)
THANKS