Biomonitoring of Air Pollution Exposure and Pathological Changes in Individuals

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Highlights

➢ Exposure Biomarker for diesel nitro-PAHs
  Urine (CEF published work)
  Urine (HEART study)
  Hb-adducts of BaP and nitro-PAHs

➢ Biomarkers of physiological response/pathway
  MDA
  8-OHdG
  nitrite
Exposure Biomarker for diesel nitro-PAHs

Urine

- Diesel exhaust (DE) is a significant source of air pollution that has been linked to respiratory and cardiovascular morbidity and mortality.

- Nitro-PAHs have been detected from diesel exhaust particles, and appear to be a more specific marker of DE exposure.

- Nitro-PAHs, once inhaled, can be partially metabolized to the corresponding amino-PAHs and excreted in urine.
Nitroreductase

\[ \text{Nitroreductase} \]

\[ \text{cytochrome P-450} \]

\[ \text{Hydrolysis} \]

\[ \text{Hydrolysis} \]

\[ \text{Hemoglobin adducts} \]

\[ \text{DNA adducts} \]

1-Nitro-Pyrene

1-Amino-Pyrene

1-Nitroso-Pyrene

Hemoglobin adducts

DNA adducts
Quantification of 1-aminopyrene in human urine after a controlled exposure to diesel exhaust

Robert Laumbach, Jian Tong, Lin Zhang, Pamela Ohman-Strickland, Alan Stern, Nancy Fiedler, Howard Kipen, Kathie Kelly-McNeil, Paul Lioy and Junfeng Zhang

- An **HPLC-fluorescence** system was used to analyze **1-aminopyrene** in human urine samples collected prior to and during 24 h following the start of 1 h controlled exposure to DE (target concentration 300 µg/m³ as PM₁₀) and clean air control.
Urinary polycyclic aromatic hydrocarbon metabolites as biomarkers of exposure to traffic-emitted pollutants

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1&2-amino-naphthalene

[Graph showing percent changes in 1&2-AN per IQR increases in pollutants]
1-amino-pyrene
1-OH-pyrene

Percent changes in 1-OHP per IQR increases in pollutants

Pollutant * Lag

CO  NO₂  O₃  PM₂.₅  PN  EC  pyrene  B[a]P  Total PAHs

Pollutant * Lag

-20  0  20  40  60

Percent changes in 1-OHP per IQR increases in pollutants

Pollutant * Lag

CO  NO₂  O₃  PM₂.₅  PN  EC  pyrene  B[a]P  Total PAHs

Exposure Biomarker for diesel nitro-PAHs
Hemoglobin adducts

- The formation of DNA and protein adducts from benzo[a]pyrene
Biomarkers of physiological response / pathway

Particulate Matter

Epithelial cells
- Mitochondria
- NADPH oxidase

Fenton reactions
- Transit metals: Fe, Cu, V, Cr, etc

Inflammation
- Macrophage cells
- iNOS (NO synthase)

ROS
- $H_2O_2 \rightarrow OH^-$
- $O_2^-$
- $ONOO^-$

DNA oxidation
- DNA repair
- 8-OHdG

Lipid peroxidation
- $\omega$-6-polyunsaturated acids
- MDA

Oxidation of NO
- RS-NO$\leftrightarrow$RS-H
- $NO_2^-$
### Biomarkers of physiological response / pathway malondialdehyde (MDA)

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<th>Method</th>
<th>Rapid</th>
<th>Easy</th>
<th>Economical</th>
<th>Less specific</th>
<th>Less sensitive</th>
<th>Less reproducible</th>
<th>Specific</th>
<th>Reproducible</th>
<th>Easily available</th>
<th>Sensitive</th>
<th>Pre-treatment required</th>
<th>On-fibre derivatization</th>
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Biomarkers of physiological response / pathway malondialdehyde (MDA)

- **Free MDA** VS **Total MDA**
  - Broncho-alveolar lavage fluid (BALF)
  - Urine
  - Serum
Free and total MDA
Urine

\[ y = 0.2053x - 2.2772 \]
\[ R^2 = 0.7868 \]
Free and total MDA Serum

**Asthmatic** vs **non-Asthmatic**
Biomarkers of physiological response / pathway

Animal Inhalation Chambers

Flow rate = 35 L/min
Velocity = 0.0004 m/s
Temp = 24 ± 1 °C
Lighting = natural day/night cycle
Biomarkers of physiological response / pathway

**MDA: Animal Inhalation Chambers**

**Mean(SD) of MDA**

- **Pregnant rats after 14 day exposure**
  - (n=6)
  - P=0.01

**Pups at 3 or 8 wks old (male + female)**

- **Filtered**
- **Unfiltered**
- Mother Rats

- **Mean(SD) of MDA**
  - (n=10)
  - P=0.001
Biomarkers of physiological response / pathway

MDA: Beijing Olympic study

% changes in EBC MDA associated with IQR increases in ambient SO2 and PM2.5
Biomarkers of physiological response / pathway
MDA: Beijing Olympic study

% changes in Urine MDA associated with IQR increases in
ambient SO$_2$ and PM$_{2.5}$
Biomarkers of physiological response / pathway 8-hydroxy-2’-deoxyguanosine (8-OHdG)

• Analyzing methods

ELISA
• Easy to perform
• Non-specific
• Lower reproducibility

HPLC-ECD
• Specific
• Sensitive
• Possible interferences from the biological matrix

LC-MSMS
• Specific
• More sensitive

Biomarkers of physiological response / pathway
Urinary 8-OHdG: Beijing Olympic study

% changes in urine 8-OHdG associated with IQR increases in ambient SO₂ and PM₂.₅
Biomarkers of physiological response / pathway

Nitrite

- HPLC-UV
  - Sensitive
  - Reproducible
  - Easy to perform (no pretreatment required for exhaled breath condensate and BALF samples)
Biomarkers of physiological response / pathway
Nitrite: Beijing Olympic study

% changes in EBC Nitrite associated with IQR increases in ambient SO2 and PM2.5
Thank you

Jake Chung

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Mingquan Li

Drew Day

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Jicheng Gong

Linchen He