



EMORY

ROLLINS  
SCHOOL OF  
PUBLIC  
HEALTH

Health Effect Institute

Annual Meeting

May 1, 2023

Donghai Liang, PhD



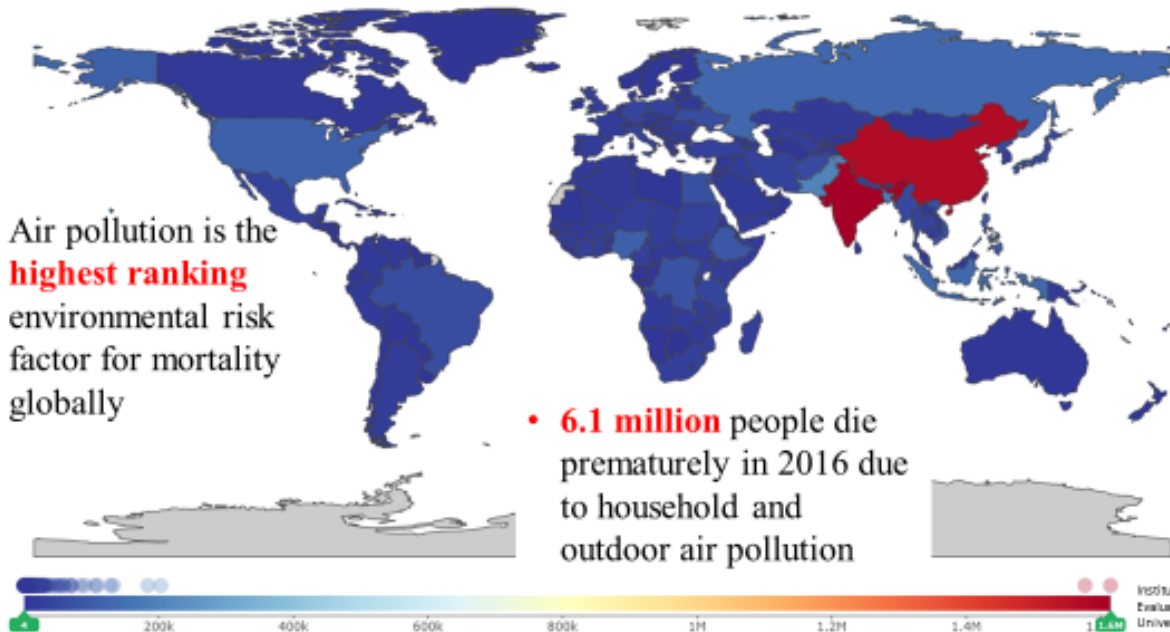
# Use of High-Resolution Metabolomics in Assessing Potential Biomarkers to Measure Community and Cumulative Exposures to Air Pollution

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<https://scholarblogs.emory.edu/environmentalmetabolomics>

# BACKGROUND

All causes attributable to Air pollution  
Both sexes, All ages, 2016, Deaths



## Complex Health Responses

### Respiratory

Coughing, wheezing, ↓ lung function

Exacerbation of asthma, COPD

Lung cancer

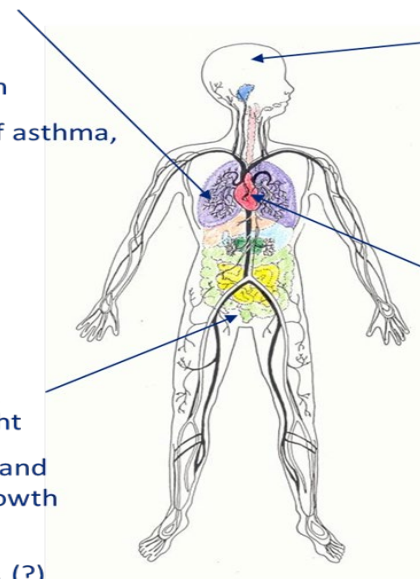
Mortality

### Reproductive

Low birth weight

Preterm births and intrauterine growth retardation (?)

↑ Birth defects (?)



### Central Nervous

Cerebrovascular impairment

Parkinson's (?)

↑ Stroke (?)

### Cardiovascular

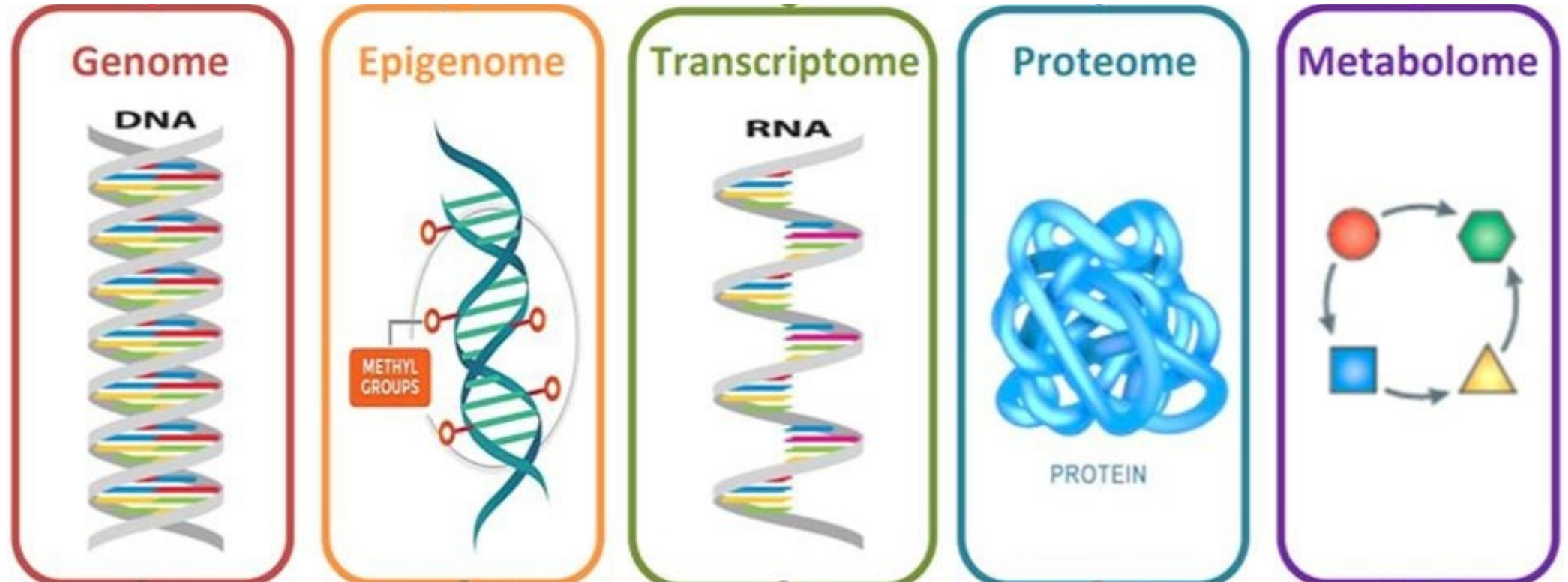
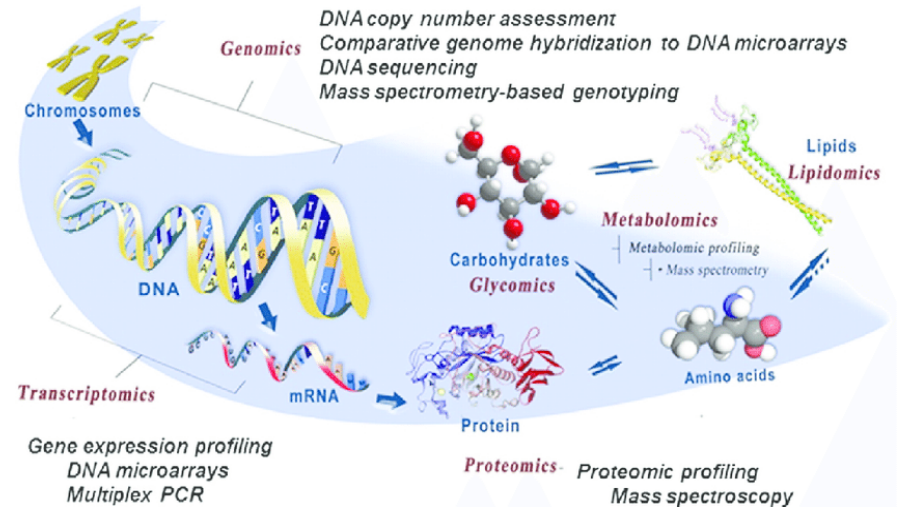
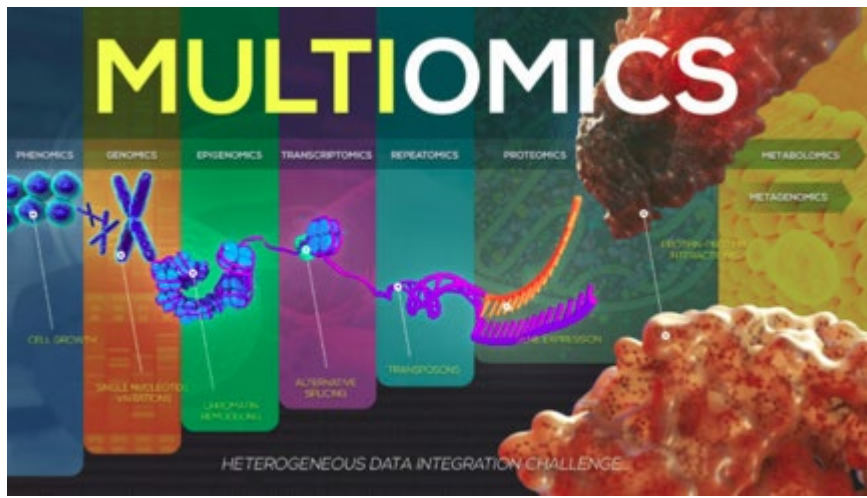
↑ Systemic inflammation

Autonomic system disorder (HRV reduction, HR increase dysrhythmias)

↑ Atherosclerosis

↑ Myocardial infarctions

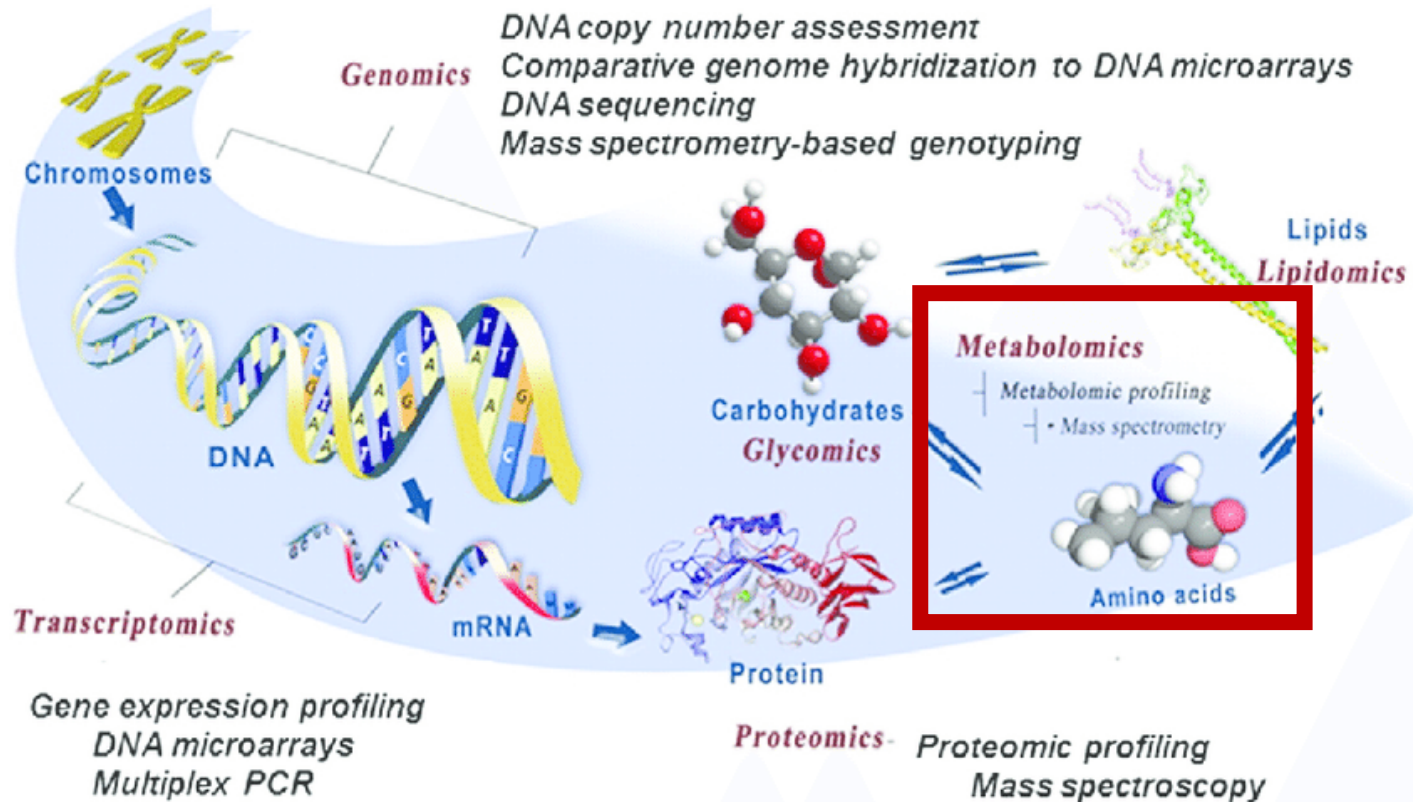
Mortality



# Metabolomics

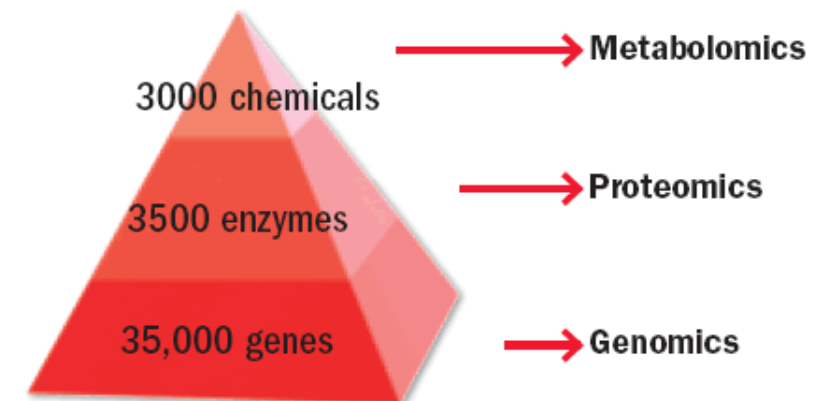
- Measurement of small molecules
- Chemical fingerprint of cellular activity
  - Transient, snapshot
- Analytical platforms:
  - Mass spectrometry
  - NMR spectroscopy

Emory Clinical Biomarkers Laboratory (Dr. Dean Jones) High Resolution Mass Spectrometry coupled with Liquid/Gas Chromatography



Metabolomics: the most direct functional readout of cellular activity and physiological status

## The pyramid of life



# Metabolomic Workflow: Wet-lab pipeline

## Biospecimen

- Saliva
- Exhaled breath Condensate
- Plasma
- Serum
- Urine
- Dried blood spots
- Fecal samples
- Tissue samples

Sample

LC Separation  
(Ionization)

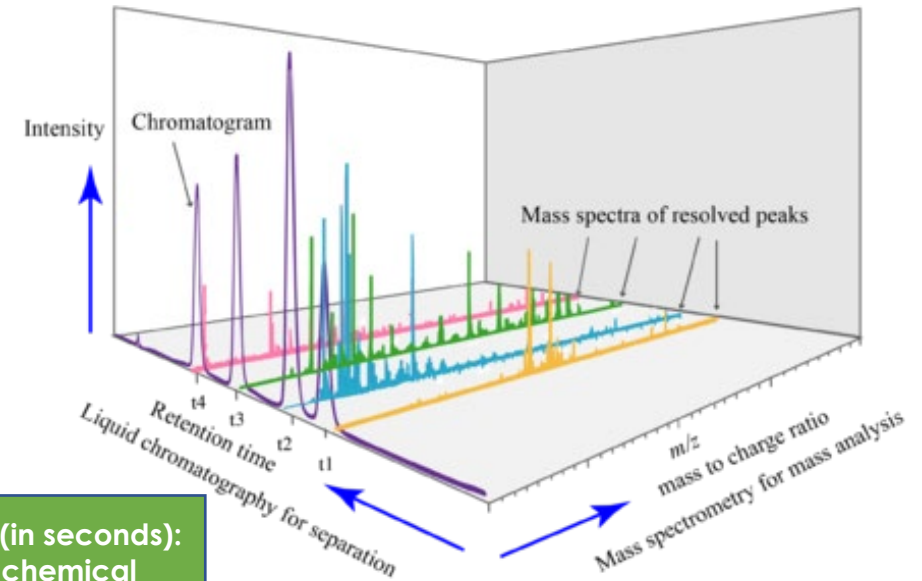
MS  
Detection



LC-MS

Retention Time (in seconds):  
Total time a chemical  
passing through a  
chromatography column

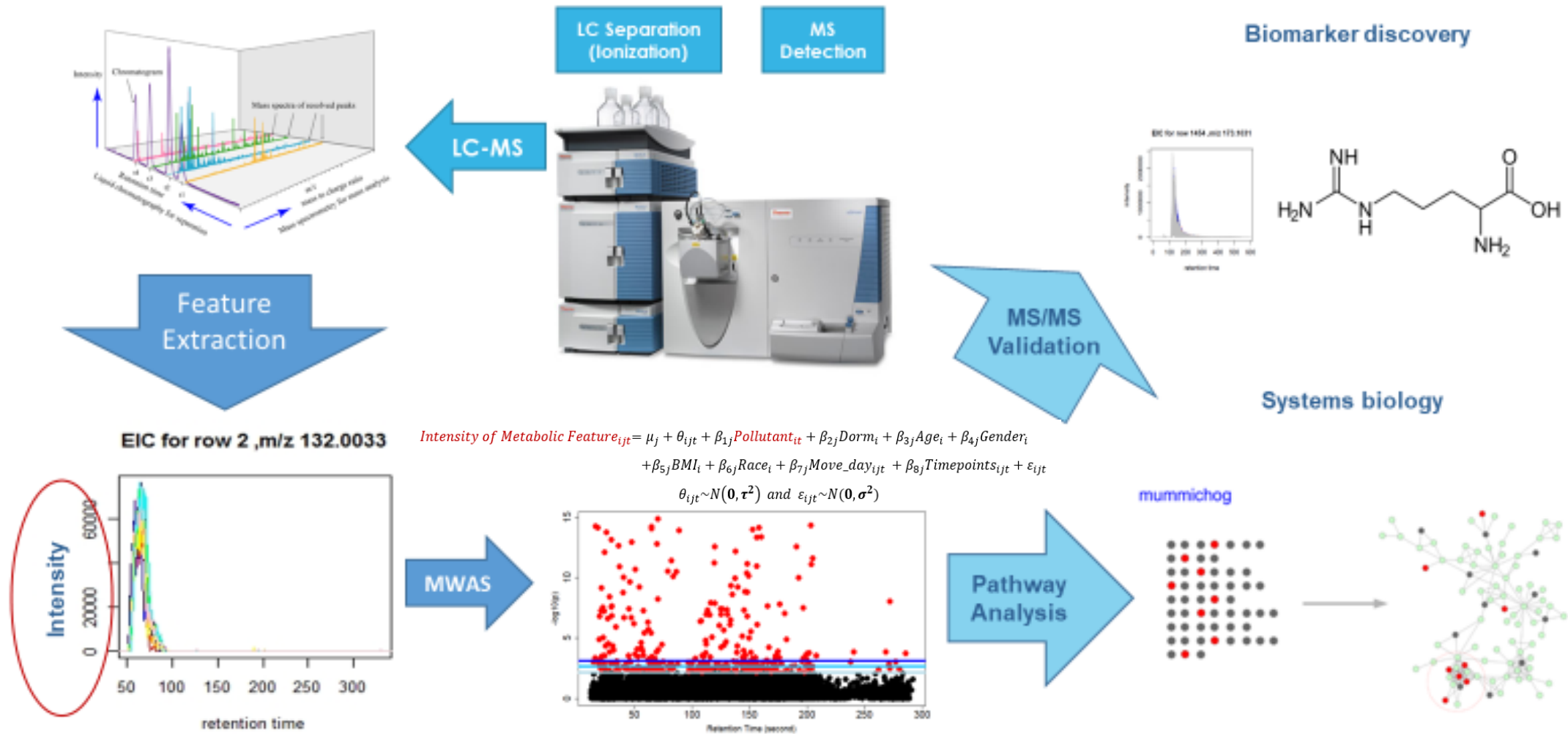
Intensity:  
Signal intensity of the ions—  
indicator of relative concentration



Mass to Charge Ratio ( $m/z$ ):  
the mass of the cation (positively  
charged ion) divided by its charge

$m/z$  spectral features

# Metabolomic Workflow: Data analysis pipeline



Contents lists available at ScienceDirect

**Environment International**

journal homepage: [www.elsevier.com/locate/envint](http://www.elsevier.com/locate/envint)

Use of high-resolution metabolomics for the identification of metabolic signals associated with traffic-related air pollution

Donghai Liang<sup>a,\*</sup>, Jennifer L. Moutinho<sup>b</sup>, Rachel Golan<sup>c</sup>, Tianwei Yu<sup>d</sup>, Chandresh N. Ladva<sup>a</sup>, Megan Niedzwiecki<sup>f</sup>, Douglas I. Walker<sup>e</sup>, Stefanie Ebel Sarnat<sup>a</sup>, Howard H. Chang<sup>g</sup>, Roby Greenwald<sup>f</sup>, Dean P. Jones<sup>h</sup>, Armistead G. Russell<sup>i</sup>, Jeremy A. Sarnat<sup>a</sup>

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Periconception air pollution, metabolomic biomarkers, and fertility among women undergoing assisted reproduction

Andrew J. Gaskins<sup>a,\*</sup>, Ziyin Tang<sup>b</sup>, Robert B. Hood<sup>c</sup>, Jennifer Ford<sup>d</sup>, Joel D. Schwartz<sup>e,f,g</sup>, Dean P. Jones<sup>h</sup>, Francine Laden<sup>i,j,k</sup>, Donghai Liang<sup>l</sup>, for the EAL

Contents lists available at ScienceDirect

**Environment International**

journal homepage: [www.elsevier.com/locate/envint](http://www.elsevier.com/locate/envint)

Per- and polyfluoroalkyl substance (PFAS) exposure, maternal metabolomic perturbation, and fetal growth in African American women: A meet-in-the-middle approach

Che-Jung Chang<sup>a</sup>, Dana Boyd Barr<sup>b</sup>, P. Barry Ryan<sup>c</sup>, Parinya Panuwet<sup>d</sup>, Melissa M. Smarr<sup>e</sup>, Ken Liu<sup>f</sup>, Kurumachalam Kannan<sup>g</sup>, Volha Yakimavets<sup>h</sup>, Younan Tan<sup>i</sup>, ViLinh Ly<sup>j</sup>, Carmen J. Marsit<sup>k</sup>, Dean P. Jones<sup>l</sup>, Elizabeth J. Corwin<sup>m</sup>, Anne L. Dunlop<sup>n</sup>, Donghai Liang<sup>o,\*</sup>

Contents lists available at ScienceDirect

**Environment International**

journal homepage: [www.elsevier.com/locate/envint](http://www.elsevier.com/locate/envint)

Pesticide residue intake from fruits and vegetables and alterations in the serum metabolome of women undergoing infertility treatment

Robert B. Hood<sup>a,\*</sup>, Donghai Liang<sup>b</sup>, Yu-Han Chiu<sup>c</sup>, Helena Sandoval-Insauti<sup>d</sup>, Jorge E. Chavarro<sup>e,f,g</sup>, Dean Jones<sup>h</sup>, Russ Hauser<sup>i,j</sup>, Audrey J. Gaskins<sup>k</sup>

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**Environment International**

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Using follicular fluid metabolomics to investigate the association between air pollution and oocyte quality

Sueyoun Hwang<sup>a</sup>, Robert B. Hood<sup>b</sup>, Russ Hauser<sup>b,c</sup>, Joel Schwartz<sup>b,c,d</sup>, Francine Laden<sup>b,c,d</sup>, Dean Jones<sup>e</sup>, Donghai Liang<sup>f</sup>, Audrey J. Gaskins<sup>b</sup>

**ENVIRONMENTAL Science & Technology**

pubs.acs.org/est

Evaluation of the Use of Saliva Metabolome as a Surrogate of Blood Metabolome in Assessing Internal Exposures to Traffic-Related Air Pollution

Zhenjiang Li, Jeremy A. Sarnat, Ken H. Liu, Robert B. Hood, Che-Jung Chang, Xin Hu, ViLinh Tran, Roby Greenwald, Howard H. Chang, Armistead Russell, Tianwei Yu, Dean P. Jones, and Donghai Liang<sup>\*</sup>

**ENVIRONMENTAL Science & Technology**

pubs.acs.org/est

The Oxidative Potential of Fine Particulate Matter and Biological Perturbations in Human Plasma and Saliva Metabolome

Ziyin Tang, Jeremy A. Sarnat, Rodney J. Weber, Armistead G. Russell, Xiaoyue Zhang, Zhenjiang Li, Tianwei Yu, Dean P. Jones, and Donghai Liang<sup>\*</sup>

Contents lists available at ScienceDirect

**Environment International**

journal homepage: [www.elsevier.com/locate/envint](http://www.elsevier.com/locate/envint)

Full length article

Use of high-resolution metabolomics to assess the biological perturbations associated with maternal exposure to Bisphenol A and Bisphenol F among pregnant African American women

Rachel Tehen<sup>a,b</sup>, Younan Tan<sup>a,b</sup>, Dana Boyd Barr<sup>c</sup>, P. Barry Ryan<sup>d</sup>, ViLinh Tran<sup>b</sup>, Zhenjiang Li<sup>a</sup>, Yi-Juan Hu<sup>e</sup>, Alicia K. Smith<sup>e</sup>, Dean P. Jones<sup>d</sup>, Anne L. Dunlop<sup>e</sup>, Donghai Liang<sup>a,\*</sup>

Contents lists available at ScienceDirect

**Environmental Pollution**

journal homepage: [www.elsevier.com/locate/envpol](http://www.elsevier.com/locate/envpol)

High-resolution metabolomics of exposure to tobacco smoke during pregnancy and adverse birth outcomes in the Atlanta African American maternal-child cohort<sup>†</sup>

Younan Tan<sup>a</sup>, Dana Boyd Barr<sup>b</sup>, P. Barry Ryan<sup>b</sup>, Veronika Fedirko<sup>b</sup>, Jeremy A. Sarnat<sup>a</sup>, Audrey J. Gaskins<sup>c</sup>, Che-Jung Chang<sup>d</sup>, Ziyin Tang<sup>e</sup>, Carmen J. Marsit<sup>f</sup>, Elizabeth J. Corwin<sup>g</sup>, Dean P. Jones<sup>h</sup>, Anne L. Dunlop<sup>i</sup>, Donghai Liang<sup>a,\*</sup>

Contents lists available at ScienceDirect

**Environmental Research**

journal homepage: [www.elsevier.com/locate/envres](http://www.elsevier.com/locate/envres)

Application of high-resolution metabolomics to identify biological pathways perturbed by traffic-related air pollution

Zhenjiang Li<sup>a</sup>, Donghai Liang<sup>b</sup>, Dongni Ye<sup>c</sup>, Howard H. Chang<sup>b</sup>, Thomas R. Ziegler<sup>d</sup>, Dean P. Jones<sup>e</sup>, Stefania A. Ebel<sup>b,\*</sup>

Original Research Article

**ENVIRONMENTAL EPIDEMIOLOGY**

OPEN

Length of PM<sub>2.5</sub> exposure and alterations in the serum metabolome among women undergoing infertility treatment

Robert B. Hood<sup>a</sup>, Donghai Liang<sup>b</sup>, Ziyin Tang<sup>c</sup>, Itai Kloog<sup>d</sup>, Joel Schwartz<sup>d,e,f</sup>, Francine Laden<sup>d,e,f</sup>, Dean Jones<sup>g</sup>, Russ Hauser<sup>h</sup>, Stefania A. Ebel<sup>b,\*</sup>

**metabolites**

MDPI

Maternal Plasma Metabolic Profile Demarcates a Role for Neuroinflammation in Non-Typical Development of Children

Rebecca J. Schmidt<sup>1,2</sup>, Donghai Liang<sup>3</sup>, Stefanie A. Busgang<sup>4,5</sup>, Paul Curtin<sup>4</sup> and Cecilia Giulivi<sup>2,5,\*</sup>

Bioinformatics, 38(14), 2022, 3662–3664  
<https://doi.org/10.1093/bioinformatics/btac364>  
 Advance Access Publication Date: 27 May 2022  
 Applications Note

**OXFORD**

Data and text mining

**Metapone: a Biiconductor package for joint pathway testing for untargeted metabolomics data**

Leqi Tian<sup>1,2</sup>, Zhenjiang Li<sup>3</sup>, Guoxuan Ma<sup>2,4</sup>, Xiaoyue Zhang<sup>3</sup>, Ziyin Tang<sup>3</sup>, Siheng Wang<sup>2</sup>, Jian Kang<sup>4</sup>, Donghai Liang<sup>3,\*</sup> and Tianwei Yu<sup>1,2,5,\*</sup>

scientific reports

OPEN

**Longitudinal profiles of the fecal metabolome during the first 2 years of life**

Elizabeth A. Holzhausen<sup>1</sup>, Natalie Shen<sup>1</sup>, Bridget Chalifour<sup>1</sup>, ViLinh Tran<sup>1</sup>, Zhenjiang Li<sup>2</sup>, Jeremy A. Sarnat<sup>2</sup>, Howard H. Chang<sup>2</sup>, Dean P. Jones<sup>2</sup>, Michael I. Goran<sup>3</sup>, Donghai Liang<sup>2</sup> & Tanya L. Alderete<sup>1,2</sup>

RESEARCH ARTICLE

Particulate metal exposures induce plasma metabolome changes in a commuter panel study

Chandresh Nanji Ladva<sup>a</sup>, Rachel Golan, Donghai Liang, Roby Greenwald, Douglas I. Walker, Karan Uppal, Amit U. Raysoni, ViLinh Tran, Tianwei Yu, W. Dana Flanders, Gary W. Miller, Dean P. Jones, Jeremy A. Sarnat

Contents lists available at ScienceDirect

**Science of the Total Environment**

journal homepage: [www.elsevier.com/locate/scitotenv](http://www.elsevier.com/locate/scitotenv)

Assessment of metabolic perturbations associated with exposure to phthalates among pregnant African American women

Xiaoyue Zhang<sup>a</sup>, Dana Boyd Barr<sup>b</sup>, Anne L. Dunlop<sup>b</sup>, Parinya Panuwet<sup>a</sup>, Jeremy A. Sarnat<sup>a</sup>, Grace E. Lee<sup>a</sup>, Younan Tan<sup>a</sup>, Elizabeth J. Corwin<sup>c</sup>, Dean P. Jones<sup>d</sup>, P. Barry Ryan<sup>a</sup>, Donghai Liang<sup>a,\*</sup>

Contents lists available at ScienceDirect

**Environmental Research**

journal homepage: [www.elsevier.com/locate/envres](http://www.elsevier.com/locate/envres)

Metabolome-wide association study of the relationship between chlorpyrifos exposure and first trimester serum metabolite levels in pregnant Thai farmworkers

Donghai Liang<sup>a,b,c,d</sup>, Jonathan Batross<sup>a,b</sup>, Nancy Fiedler<sup>b</sup>, Tippawan Prapanontol<sup>e</sup>, Panitapee Suttivan<sup>a</sup>, Parinya Panuwet<sup>a</sup>, Warangkana Nakson<sup>f</sup>, Brittney O. Baumert<sup>a,g</sup>, Volha Yakimavets<sup>h</sup>, Younan Tan<sup>i</sup>, Priya D'Souza<sup>j</sup>, Ampica Mangklabruks<sup>k</sup>, Supattra Sittiwang<sup>l</sup>, Kristiansachai Kaewthit<sup>m</sup>, Kanyapak Kohsuwan<sup>n</sup>, Nattawadee Promkam<sup>o</sup>, Sureewan Pingwong<sup>p</sup>, P. Barry Ryan<sup>a</sup>, Dana Boyd Barr<sup>a,\*</sup>, for the SAWADEE birth cohort

Journal of Breath Research

PAPER

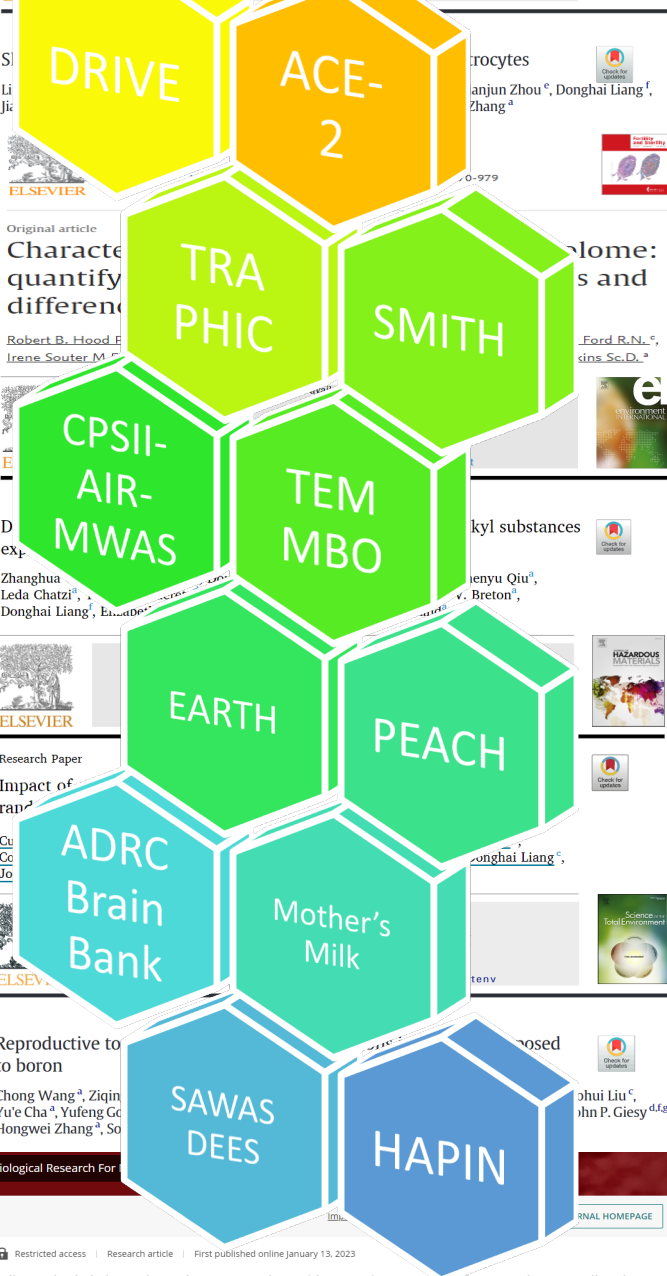
Metabolomic profiles of plasma, exhaled breath condensate, and saliva are correlated with potential for air toxics detection

Chandresh Nanji Ladva<sup>a</sup>, Rachel Golan<sup>a</sup>, Roby Greenwald<sup>a</sup>, Tianwei Yu<sup>a</sup>, Stefanie Ebel Sarnat<sup>a</sup>, W. Dana Flanders<sup>a,b</sup>, Karan Uppal<sup>c</sup>, Douglas I. Walker<sup>d</sup>, ViLinh Tran<sup>e</sup>, Donghai Liang<sup>f</sup>, Dean P. Jones<sup>g</sup> and Jeremy A. Sarnat<sup>h</sup>

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**Science of the Total Environment**

journal homepage: [www.elsevier.com/locate/scitotenv](http://www.elsevier.com/locate/scitotenv)



Reproductive to boron

Chong Wang<sup>a</sup>, Ziqin Yu'e Cha<sup>a</sup>, Yufeng Ge<sup>b</sup>, Hongwei Zhang<sup>a</sup>, So

Biological Research For

Restricted access | Research article | First published online January 13, 2023

Saliva and Exhaled Breath Condensate Correlate With Serum in 4-12-Year-Olds Exposed to Secondhand Electronic Cigarette Vapors: A Pilot Study

Jeanine Rodriguez, PhD, RN, APRN, Donghai Liang, PhD, MPH, Irene Yang, PhD, RN

View all authors and affiliations

# Application of Untargeted High-Resolution Metabolomics in Assessing Internal Exposures to Air Pollution and the Corresponding Health Responses

**Dorm Room Inhalation to Vehicle Emission Study  
DRIVE Study (N=60)  
Panel Study on Healthy Young Adults  
Repeated Measurements**

**Atlanta Commuter Study  
ACE-2 Study (N=45)  
Panel Study on Commuters with/without Asthma  
Repeated Measurements**

**Environment and Reproductive Health  
EARTH Study (N=200)  
Cross-sectional Study on Women  
Undergoing Assisted Reproduction**

**Emory Center for Health Discovery  
and Well-Being cohort (N=180)  
Cross-sectional Study on Adult  
without Chronic Disease**



Use of high-resolution metabolomics for the identification of metabolic signals associated with traffic-related air pollution

Perturbations of the arginine metabolome following exposures to traffic-related air pollution in a panel of commuters with and without asthma

Periconception air pollution, metabolomic biomarkers, and fertility among women undergoing assisted reproduction

Application of high-resolution metabolomics to identify biological pathways perturbed by traffic-related air pollution

Donghai Liang<sup>a,\*</sup>, Jennifer L. Moutinho<sup>b</sup>, Rachel Golan<sup>c</sup>, Tianwei Yu<sup>d</sup>, Chandresh N. Ladva<sup>a</sup>, Megan Niedzwiecki<sup>e</sup>, Douglas I. Walker<sup>f</sup>, Stefanie Ebelt Sarnat<sup>g</sup>, Howard H. Chang<sup>h</sup>, Roby Greenwald<sup>i</sup>, Dean P. Jones<sup>j</sup>, Armistead G. Russell<sup>k</sup>, Jeremy A. Sarnat<sup>l</sup>

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Audrey J. Gaskins<sup>a,\*</sup>, Ziyin Tang<sup>b</sup>, Robert B. Hood<sup>c</sup>, Jennifer Ford<sup>d</sup>, Joel D. Schwartz<sup>e,f,g</sup>, Dean P. Jones<sup>h</sup>, Francine Laden<sup>i,j,k</sup>, Donghai Liang<sup>l</sup>, for the EARTH Study Team

Zhenjiang Li<sup>a</sup>, Donghai Liang<sup>b</sup>, Dongni Ye<sup>c</sup>, Howard H. Chang<sup>d</sup>, Thomas R. Ziegler<sup>e</sup>, Dean P. Jones<sup>f</sup>, Stefanie T. Ebelt<sup>g</sup>



OPEN ACCESS PEER-REVIEWED  
RESEARCH ARTICLE



**Fudan University Study  
Randomized, Double-blind,  
Crossover Trial (N=22)  
on Healthy Young Adults**

**Evaluation of the Use of Saliva Metabolome as a Surrogate of Blood Metabolome in Assessing Internal Exposures to Traffic-Related Air Pollution**

**Particulate metal exposures induce plasma metabolome changes in a commuter panel study**

Using follicular fluid metabolomics to investigate the association between air pollution and oocyte quality

Journal of Hazardous Materials

Zhenjiang Li, Jeremy A. Sarnat, Ken H. Liu, Robert B. Hood, Che-Jung Chang, Xin Hu, ViLinh Tran, Roby Greenwald, Howard H. Chang, Armistead Russell, Tianwei Yu, Dean P. Jones, and Donghai Liang<sup>\*</sup>

Chandresh Nanji Ladva<sup>a</sup>, Rachel Golan, Donghai Liang, Roby Greenwald, Douglas I. Walker, Karan Uppal, Amit U. Raysoni, ViLinh Tran, Tianwei Yu, W. Dana Flanders, Gary W. Miller, Dean P. Jones, Jeremy A. Sarnat

Sueyong Hwang<sup>a</sup>, Robert B. Hood<sup>b</sup>, Russ Hauser<sup>c,d</sup>, Joel Schwartz<sup>b,c,d</sup>, Francine Laden<sup>b,c,d</sup>, Dean Jones<sup>e</sup>, Donghai Liang<sup>f</sup>, Audrey J. Gaskins<sup>g</sup>

Research Paper



Journal of Breath Research

Original Research Article

Impact of ozone exposure on heart rate variability and stress hormones: A randomized-crossover study

Ziyin Tang, Jeremy A. Sarnat, Rodney J. Weber, Armistead G. Russell, Xiaoyue Zhang, Zhenjiang Li, Tianwei Yu, Dean P. Jones, and Donghai Liang<sup>\*</sup>

**Metabolomic profiles of plasma, exhaled breath condensate, and saliva are correlated with potential for air toxics detection**

**Length of PM<sub>2.5</sub> exposure and alterations in the serum metabolome among women undergoing infertility treatment**

Cuiqing Wang<sup>a,b</sup>, Jingyu Lin<sup>b,c</sup>, Yue Niu<sup>b,c</sup>, Weidong Wang<sup>b</sup>, Jianfen Wen<sup>b</sup>, Lili Lv<sup>b</sup>, Cong Liu<sup>b</sup>, Xihao Du<sup>b</sup>, Qingli Zhang<sup>b</sup>, Bo Chen<sup>b</sup>, Jing Cai<sup>b</sup>, Zhuohui Zhao<sup>b</sup>, Donghai Liang<sup>d</sup>, John S. Ji<sup>e</sup>, Honglei Chen<sup>f</sup>, Renjie Chen<sup>g</sup>, Haidong Kan<sup>h,i</sup>

Robert B. Hood<sup>a</sup>, Donghai Liang<sup>b</sup>, Ziyin Tang<sup>c</sup>, Itai Kloog<sup>d</sup>, Joel Schwartz<sup>d,e,f</sup>, Francine Laden<sup>d,e,f</sup>, Dean Jones<sup>g</sup>, Audrey J. Gaskins<sup>h</sup>

**The Oxidative Potential of Fine Particulate Matter and Biological Perturbations in Human Plasma and Saliva Metabolome**

**Traffic Exposure, Maternal Metabolome, And Birth Outcome (TEMMBO Study) Repeated Measurements on Pregnant African American People (N=313)**

**Southern California Mother's Milk Study (N=124) Repeated Measurements on Pregnant Hispanic Mothers and Infants**

**MWAS on Air Pollution and Lung Cancer (N=1,462) Cross-Sectional Study on Adult Participants Enrolled in the Cancer Prevention Studies**

Ziyin Tang, Jeremy A. Sarnat, Rodney J. Weber, Armistead G. Russell, Xiaoyue Zhang, Zhenjiang Li, Tianwei Yu, Dean P. Jones, and Donghai Liang<sup>\*</sup>

Jeremy A. Sarnat, Armistead (Ted) Russell, Donghai Liang, Jennifer L. Moutinho, Rachel Golan, Rodney J. Weber, Dong Gao, Stefanie Ebelt Sarnat, Howard H. Chang, Roby Greenwald, and Tianwei Yu

**Longitudinal profiles of the fecal metabolome during the first 2 years of life**

Using High-Resolution Metabolomics for Identifying Metabolic Profiles Associated with Ambient Air Pollution in the Cancer Prevention Study-II Nutrition Cohort

**HEALTH EFFECTS INSTITUTE**  
Number 196  
April 2018

**RESEARCH REPORT**

**Developing Multipollutant Exposure Indicators of Traffic Pollution: The Dorm Room Inhalation to Vehicle Emissions (DRIVE) Study**

Jeremy A. Sarnat, Armistead (Ted) Russell, Donghai Liang, Jennifer L. Moutinho, Rachel Golan, Rodney J. Weber, Dong Gao, Stefanie Ebelt Sarnat, Howard H. Chang, Roby Greenwald, and Tianwei Yu

**ehp Environmental Health Perspectives**

HOME ISSUE IN PROGRESS ARCHIVES COLLECTIONS AUTHORS REVIEWERS ABOUT INTRODUCING JHP

**ISEE**

Metabolome-wide association study of prenatal exposure to air pollution and adverse birth outcomes in the Atlanta African American Maternal-Child cohort

Zhenjiang Li, Anne L. Dunlop, Jeremy A. Sarnat, Haoran Cheng, Youran Tan, Dana Boyd Barr, Anke Huels, Alicia Smith, Carmen Marsit, Dean P. Jones, and Donghai Liang

**scientific reports**

OPEN

Elizabeth A. Holzhausen<sup>a</sup>, Natalie Shen<sup>b</sup>, Bridget Chalfour<sup>c</sup>, ViLinh Tran<sup>d</sup>, Zhenjiang Li<sup>e</sup>, Jeremy A. Sarnat<sup>f</sup>, Howard H. Chang<sup>g</sup>, Dean P. Jones<sup>h</sup>, Michael I. Goran<sup>i</sup>, Donghai Liang<sup>j</sup> & Tanya L. Alderete<sup>k</sup>

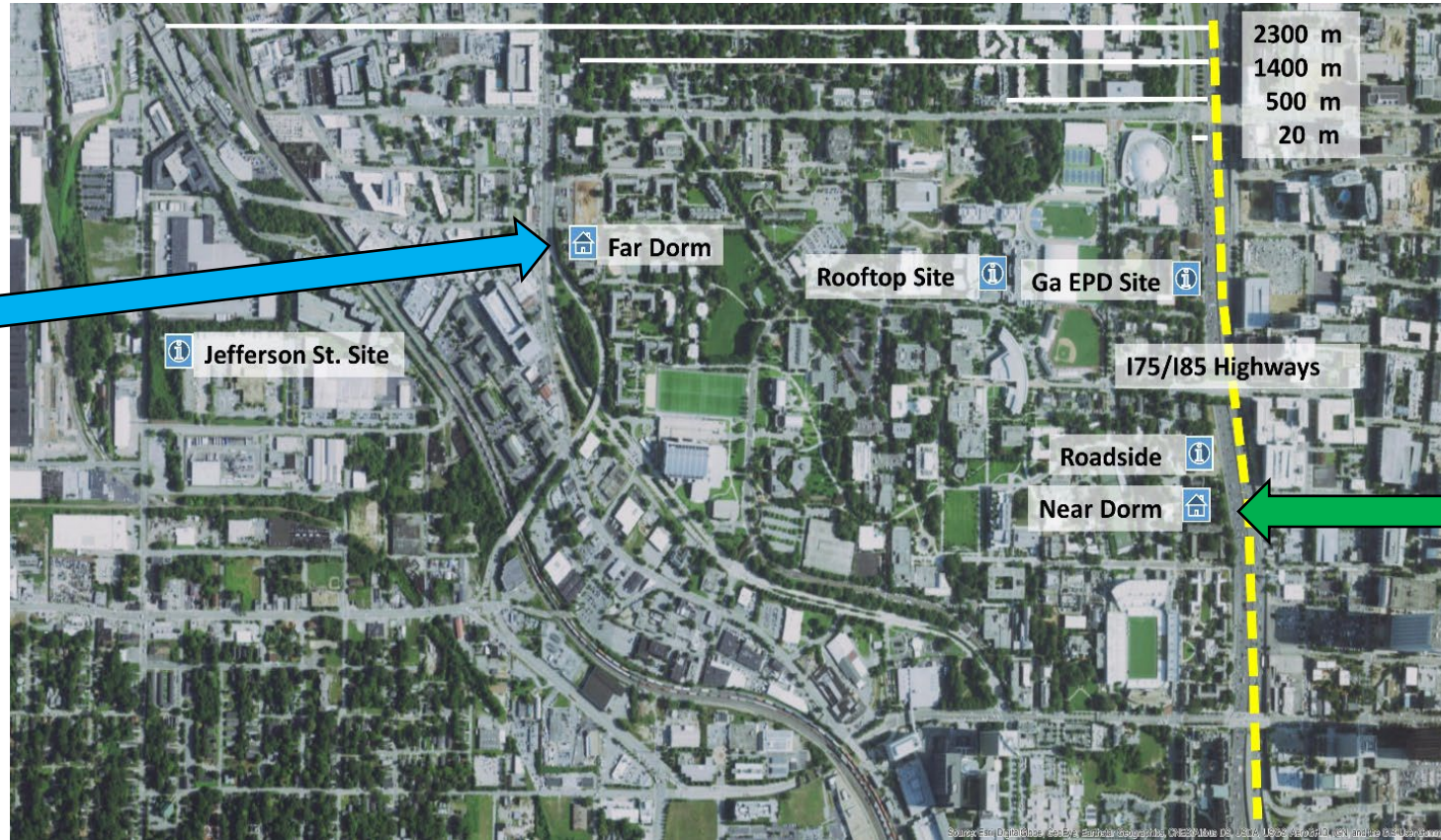


# Dorm Room Inhalation to Vehicle Emissions (DRIVE) study

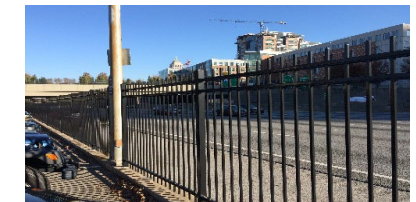


DRIVE Study PI  
Dr. Jeremy Sarnat

Far Dorm  
(1.4 km)



Near Dorm  
(20 m)



Continuous  
Sampling



Integrated  
Sampling



Low-Cost  
Sensors

September, 2014 to December, 2014



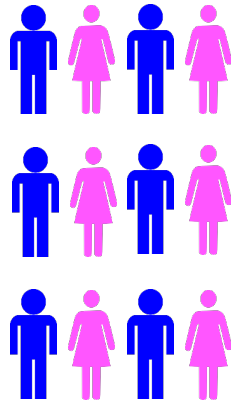
Black Carbon (BC), Nitrogen Oxides (NO, NO<sub>2</sub>, NO<sub>x</sub>),  
Carbon Monoxide (CO) and Fine Particle Mass (PM<sub>2.5</sub>)



Near Dorm(20 Meters)



Far Dorm(1.4 KM)



54 college students



GPS monitor



Questionnaire on daily activity, dietary pattern and health status

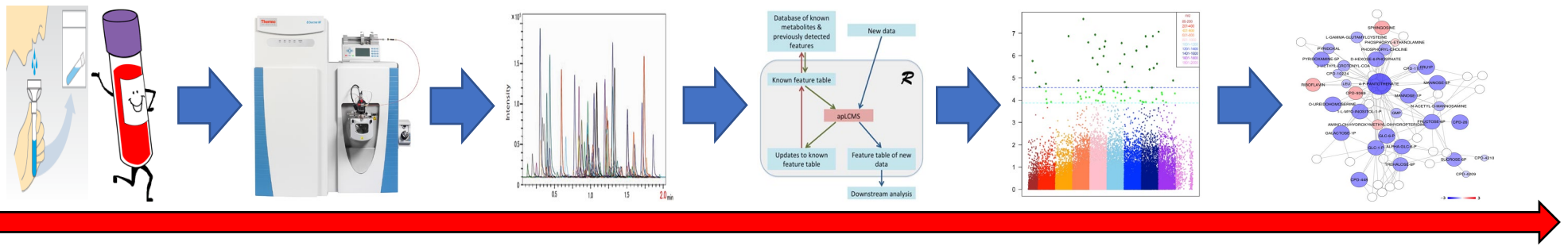


Biomonitoring of weekly saliva sample and monthly blood sample



### Untargeted Metabolome-Wide Association (MWAS) Work Flow

### Metabolomics Analysis



#### Section B. HEALTH STATUS

The following questions ask about your health status.

B1. Would you say that in general your health is excellent, very good, good, fair, or poor?  
 Excellent  Very good  Good  Fair  Poor  
 Don't know  Refused

	Yes	No	Don't know	Refused
Has a doctor, nurse, or other health professional EVER told you that you had any of the following:				

#### Section C. FAMILY HISTORY

The next section of questions asks about your family history of disease. We are interested in your close blood relatives, including your father, mother, sisters, and brothers.

	Yes	No	Don't know	Refused
Were any of your close blood relatives, including both living and deceased, EVER told by a doctor, nurse, or other health professional that they had any of the following?				

#### Section D. MEDICATION

Please provide a list of the medications (including both prescription and over the counter) you have used in the past 3 months and how often you use each medication.

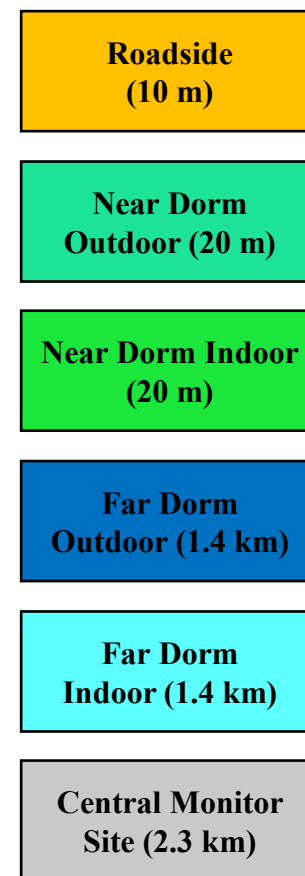
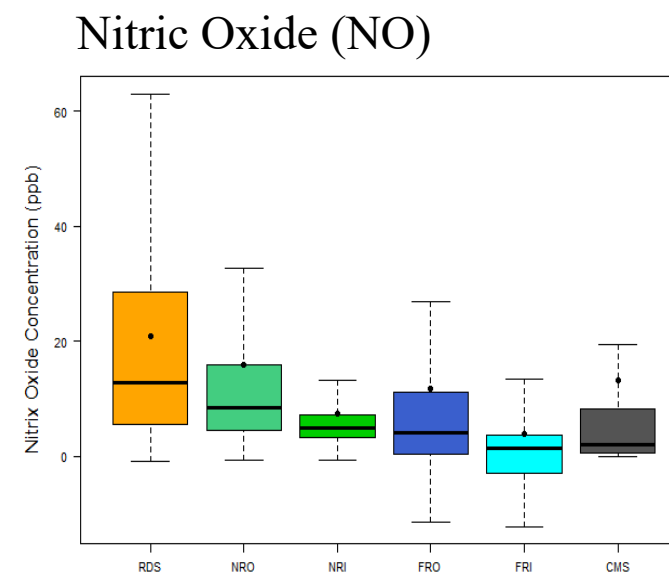
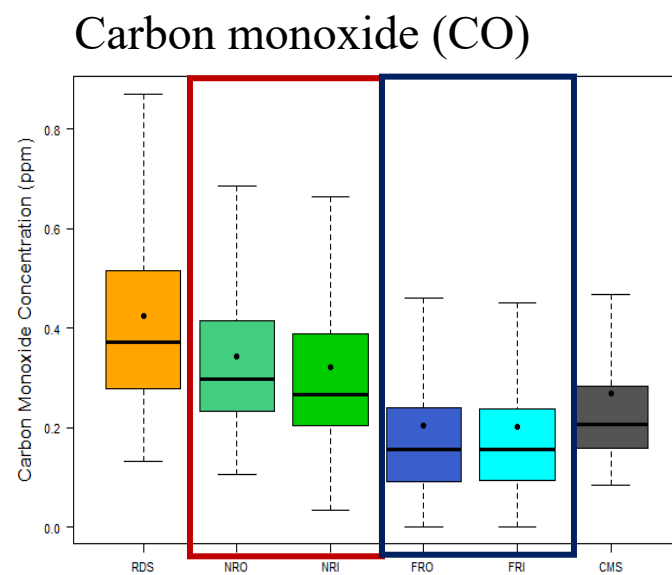
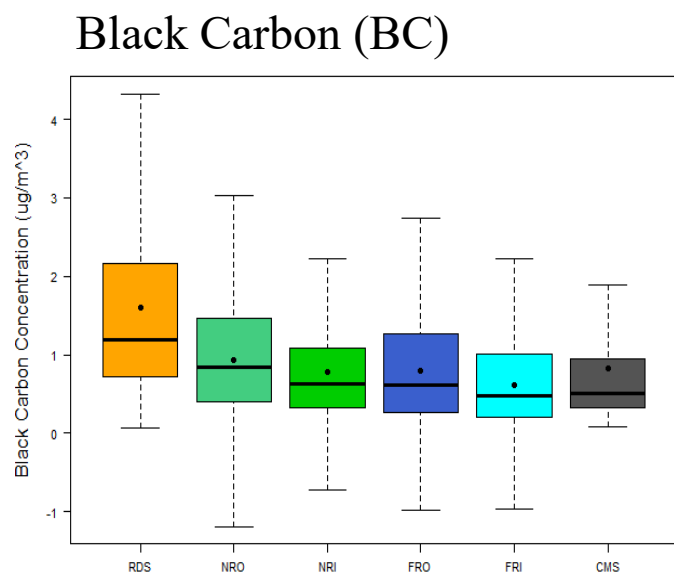
D0. Have you used any medications (either prescription or over the counter) in the past 3 months?  
 Yes, move to D1  No, move to section E

#### Section F. LIFESTYLE

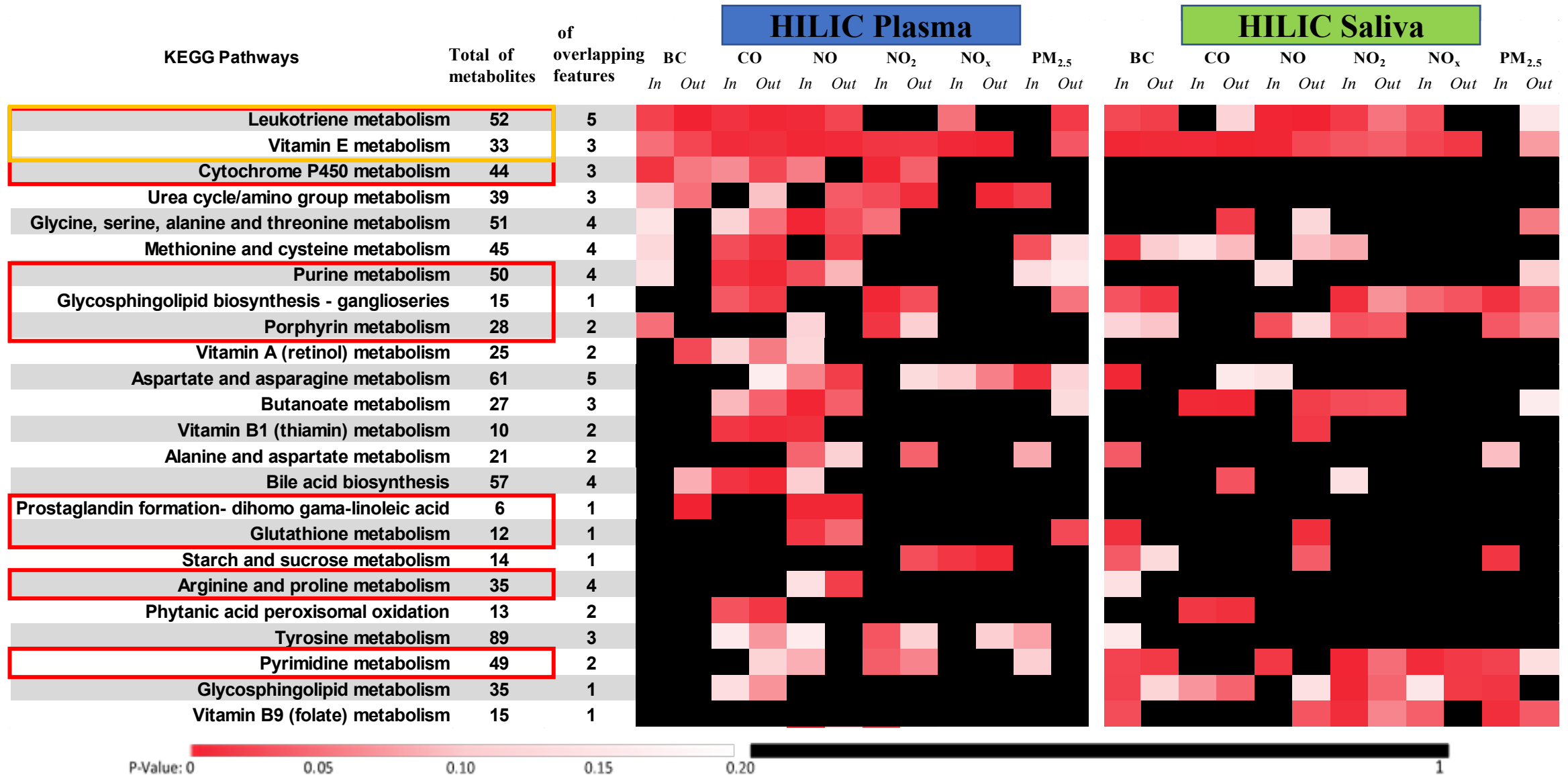
The following questions ask about lifestyle.

F1. How many days in a typical week do you perform some type of moderate exercise for at least 30 minutes at a time? (Brisk walking, bicycling, jogging, or anything else that causes some increase in breathing or heart rate?)  
 \_\_\_ Days per week  Don't know  Refused

# DRIVE Study Results- Traffic Exposure Assessment



# DRIVE Study Results- Pathway associated with TRAPs

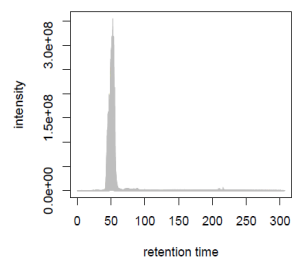


# DRIVE Study Results- Chemical Identification

## Nucleic Acid Damage & Repair

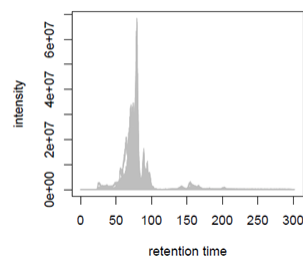
### HYPOXANTHINE

EIC for row 1126 ,m/z 137.046



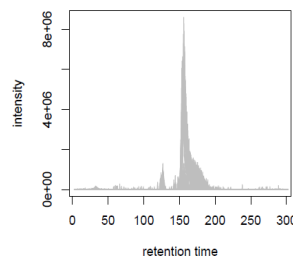
### CYTOSINE

EIC for row 272 ,m/z 112.0507



### ADENOSINE 5'-MONOPHOSPHATE

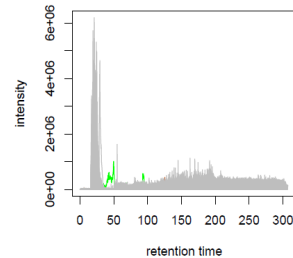
EIC for row 4118 ,m/z 348.0708



## Oxidative Stress and Inflammation

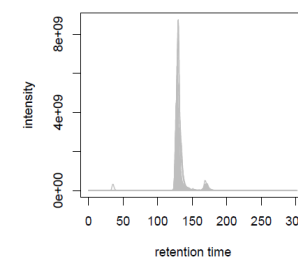
### GAMMA-LINOLENIC ACID

EIC for row 4307 ,m/z 279.2328



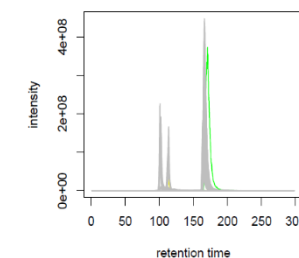
### PROLINE

EIC for row 357 ,m/z 116.0707



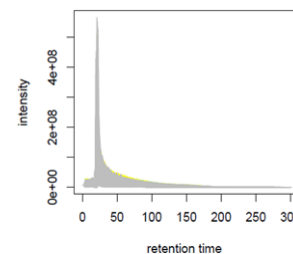
### HISTIDINE

EIC for row 1813 ,m/z 156.077



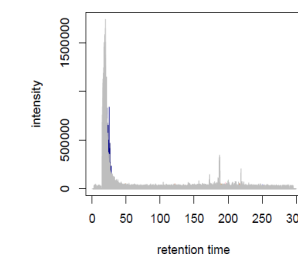
### (S)-LACTATE GLYCERALDEHYDE

EIC for row 31 ,m/z 89.0246



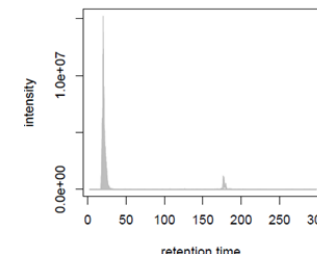
### ARGININE

EIC for row 724 ,m/z 173.105



### 3-HYDROXY KYNURENINE

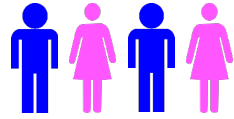
EIC for row 1197 ,m/z 223.0723



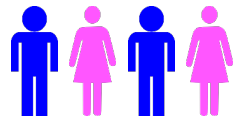
# Atlanta Commuter Exposures (ACE-2) Study



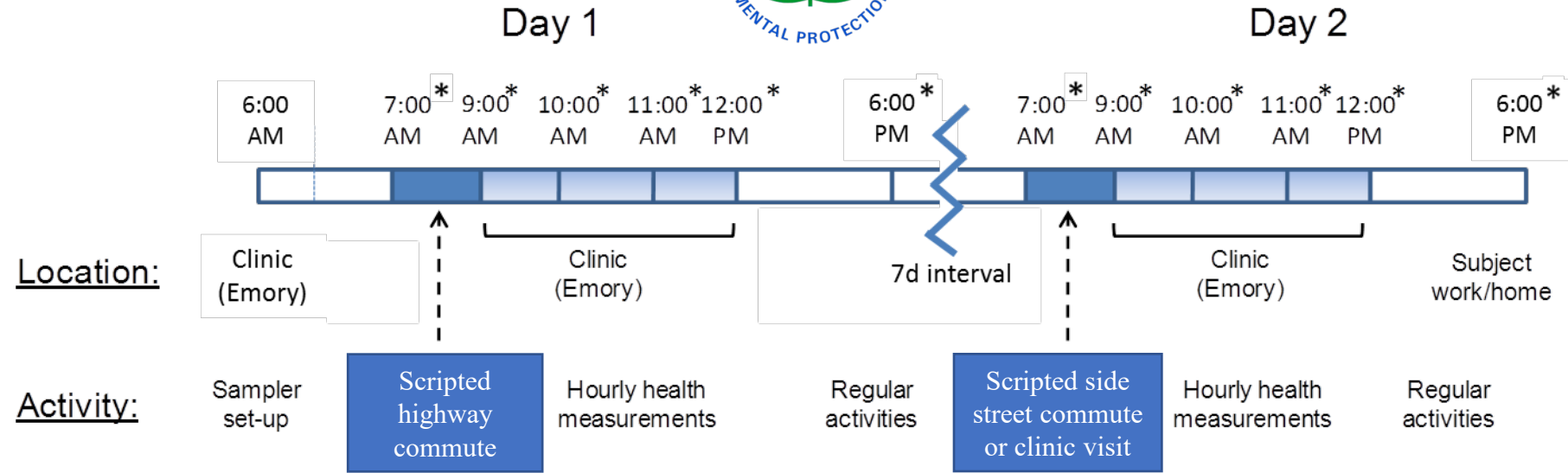
ACE-2 Study PI  
Dr. Jeremy Sarnat



**24 participants  
with asthma**

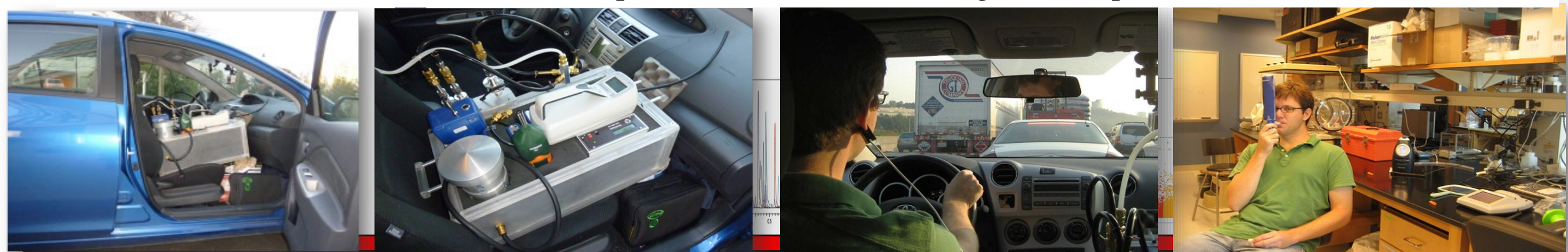


**21 participants  
without asthma**

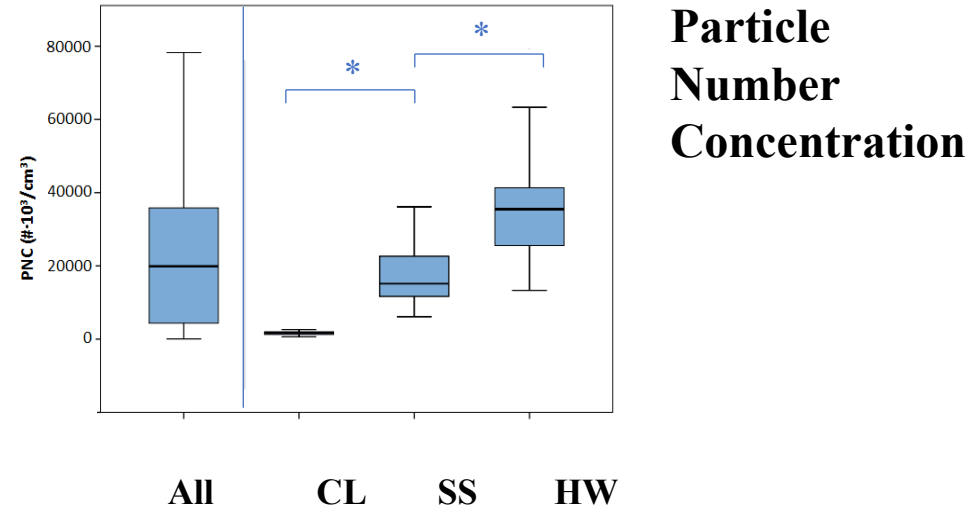
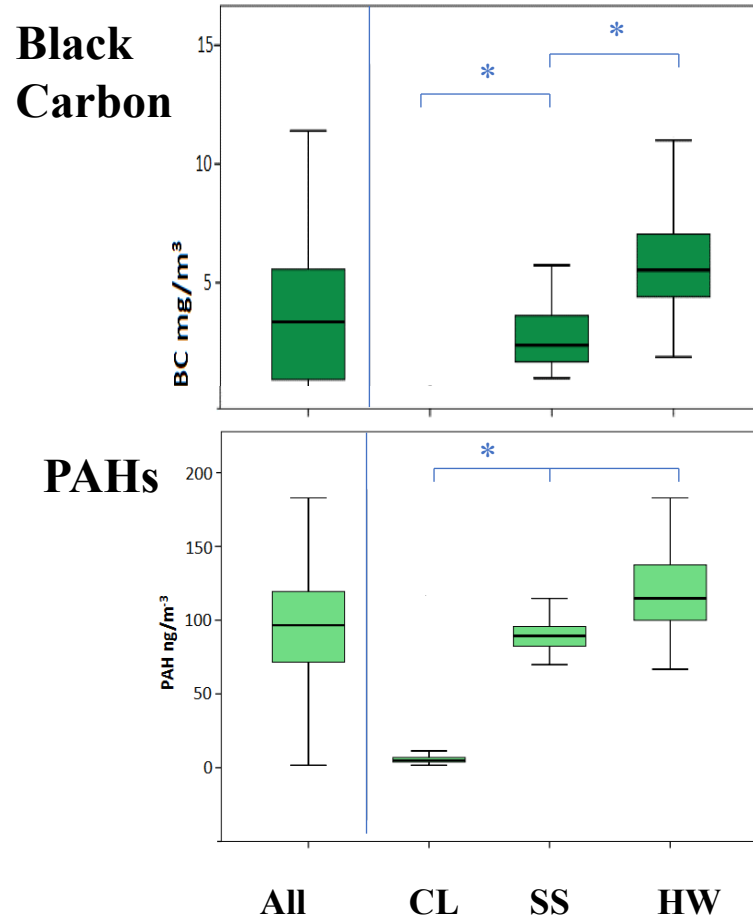


\* Indicates collection of health measurements.

In-vehicle TRAP measurements: PNC, pb-PAH, noise, PM<sub>2.5</sub>, 4 organic compounds and 19 metals of PM<sub>2.5</sub>



# ACE-2 Study: TRAP concentrations by exposure scenarios

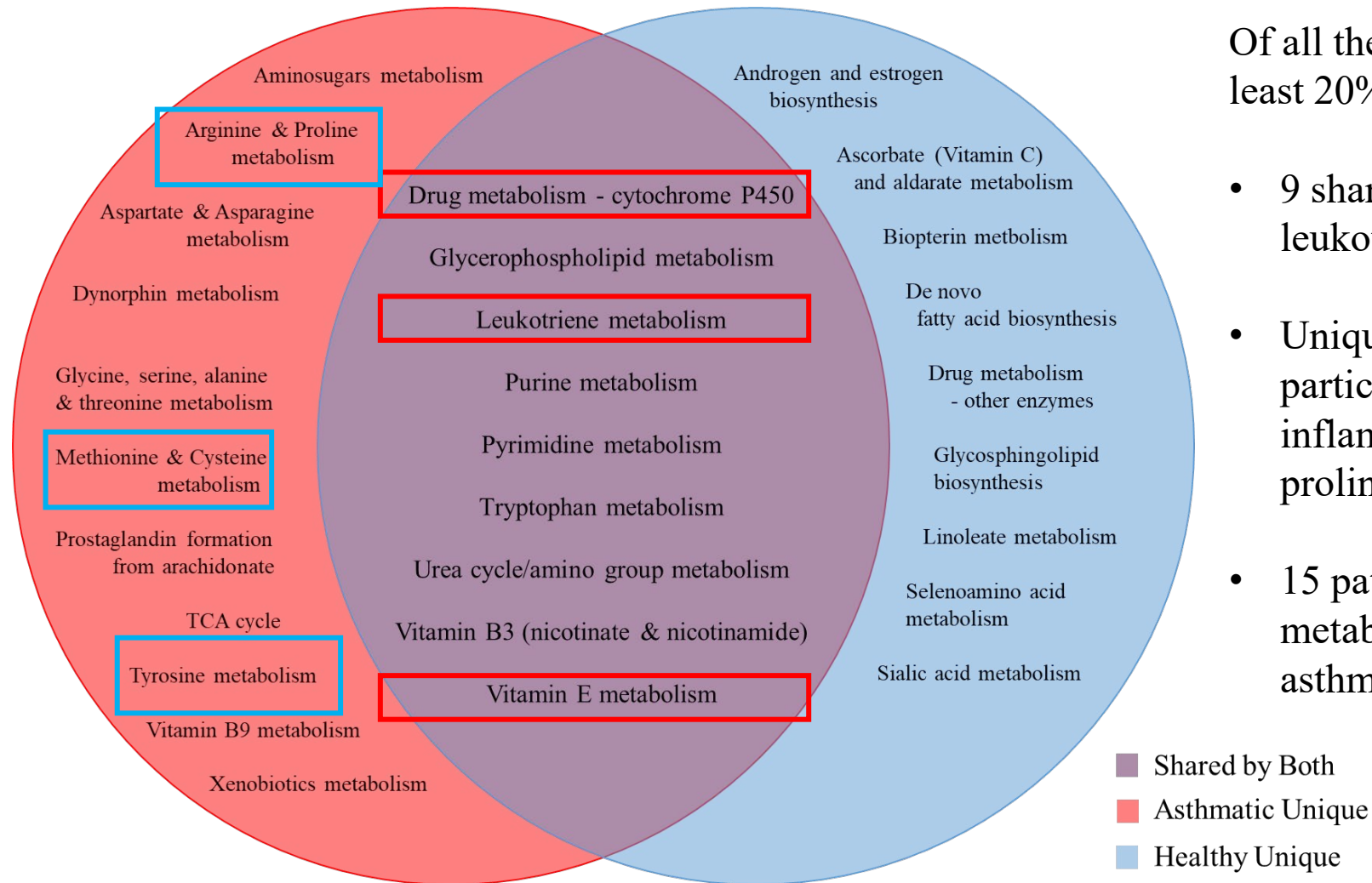


CL = Clinic exposures  
SS = Surface street commute  
HW = Highway commute

\* Indicates significant difference in means at  $p < 0.05$

Golan et, al. 2017

# ACE-2 Study: Pathway Analysis Results



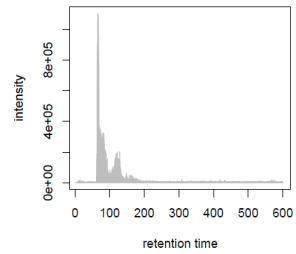
Of all the pathways that are associated with at least 20% of the TRAP indicators

- 9 shared by both subgroups, including leukotriene, cytochrome P450, and vitamin E
- Unique top pathways among the asthmatic participants highly related to acute pulmonary inflammation, including the arginine and proline, methionine, as well as the tyrosine
- 15 pathways associated with differential metabolic responses to TRAP, modified by asthmatic status



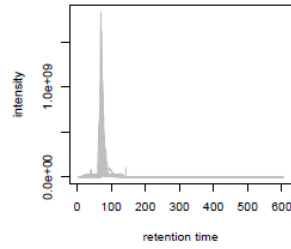
Methionine

EIC for row 893 ,m/z 148.0424



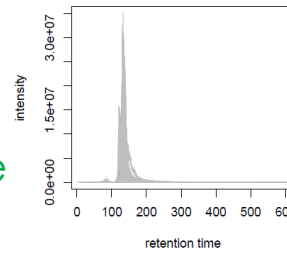
Choline

EIC for row 232 ,m/z 104.1073

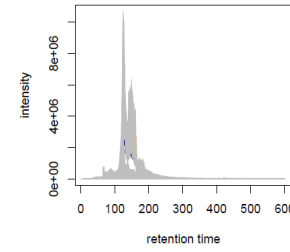


Cystine

EIC for row 2723 ,m/z 241.0309

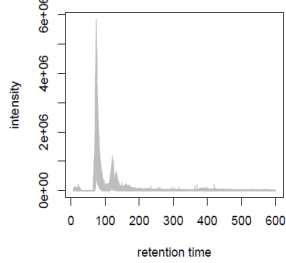


EIC for row 872 ,m/z 146.0446



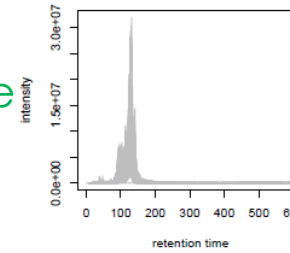
5-oxo-proline

EIC for row 511 ,m/z 128.0339

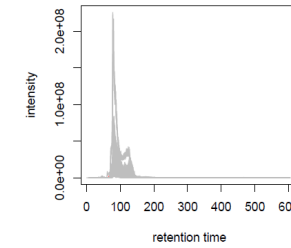


Glutamic Acid

EIC for row 1607 ,m/z 176.1028

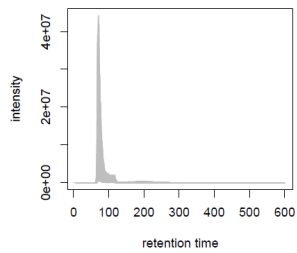


EIC for row 687 ,m/z 132.0767



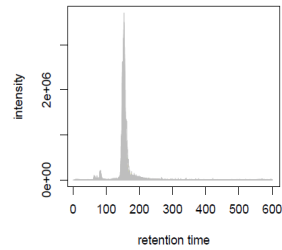
Histidine

EIC for row 999 ,m/z 153.018



AMP

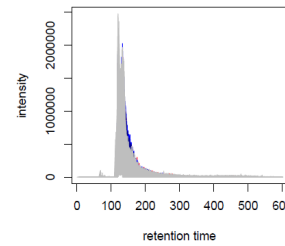
EIC for row 6139 ,m/z 346.0554



Citrulline

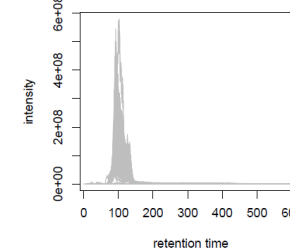
Arginine

EIC for row 1454 ,m/z 173.1031



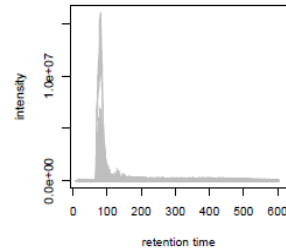
Creatine

EIC for row 411 ,m/z 116.0708



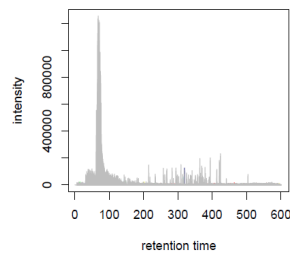
Hypoxanthine

EIC for row 763 ,m/z 137.0456



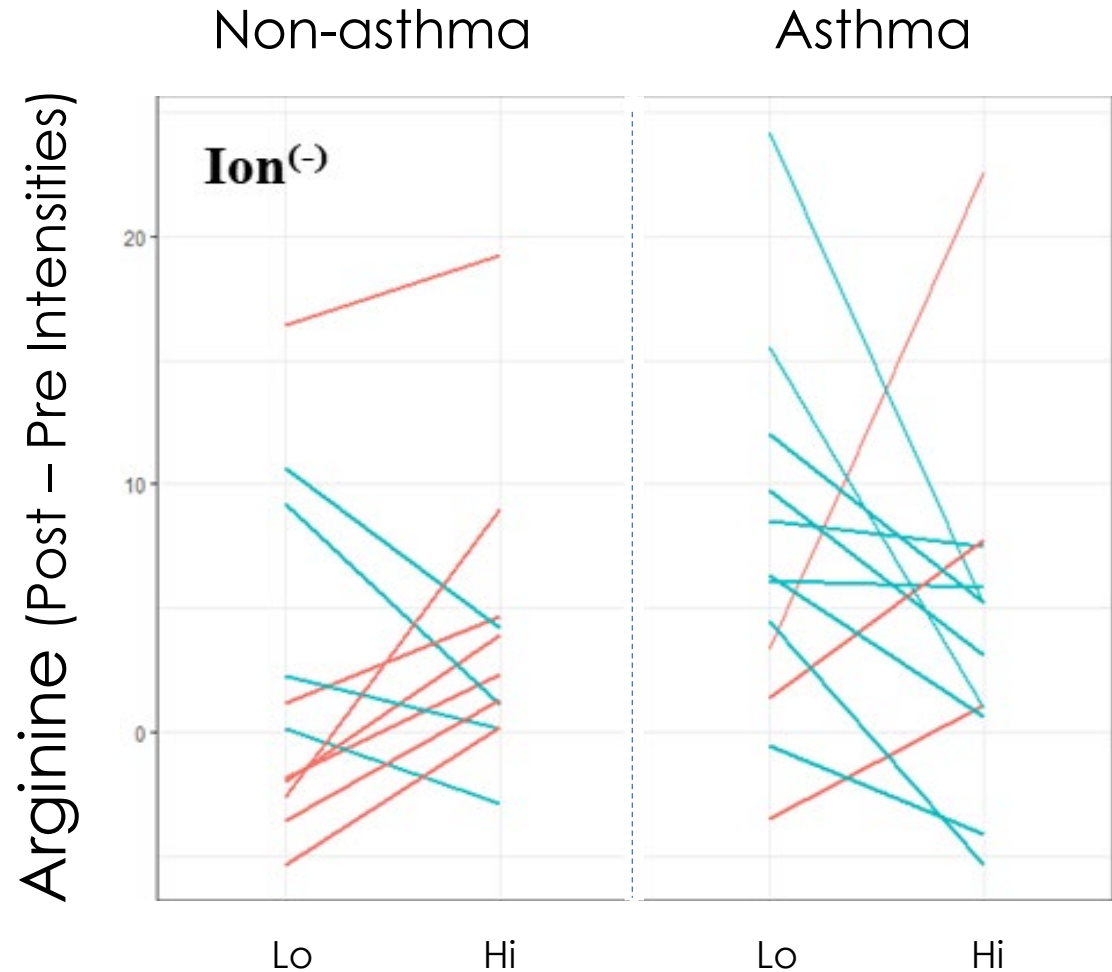
Xanthine

EIC for row 964 ,m/z 151.025



Proline

# ACE-2 Plasma Arginine

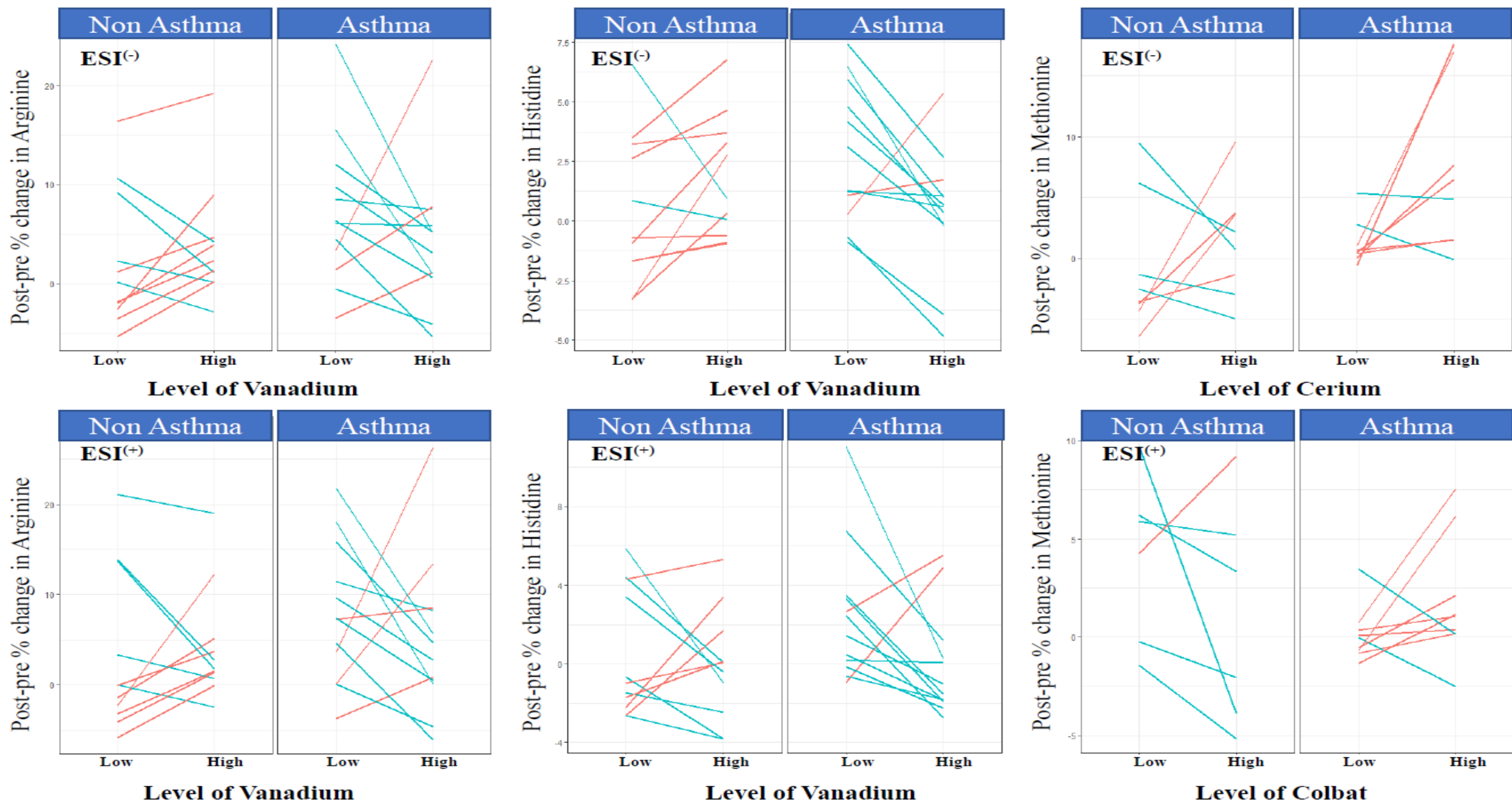


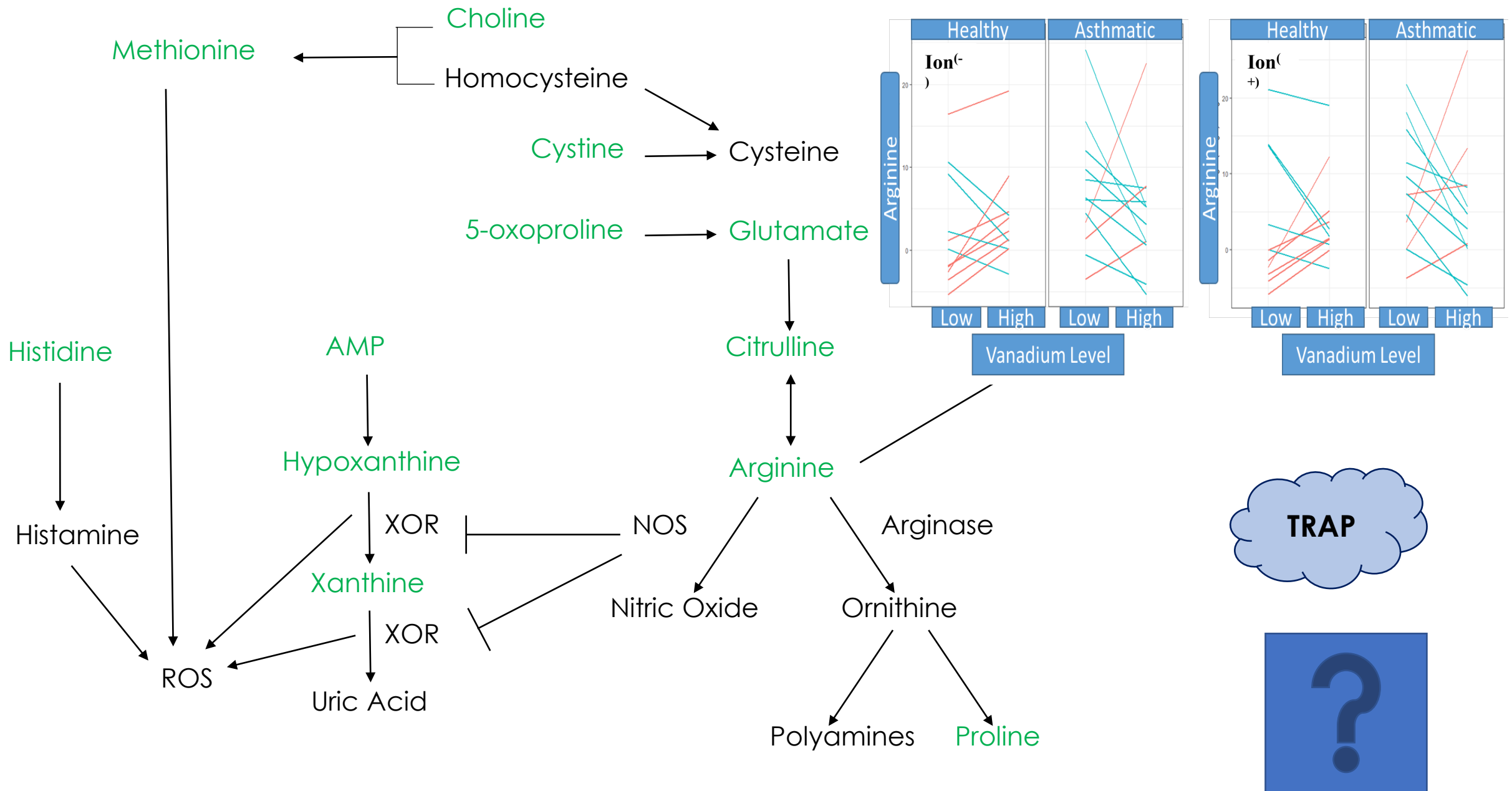
- Within subject differences in post-pre arginine intensities
- By asthma status
- Blue lines = lower relative arginine concentrations following higher TRAP exposures

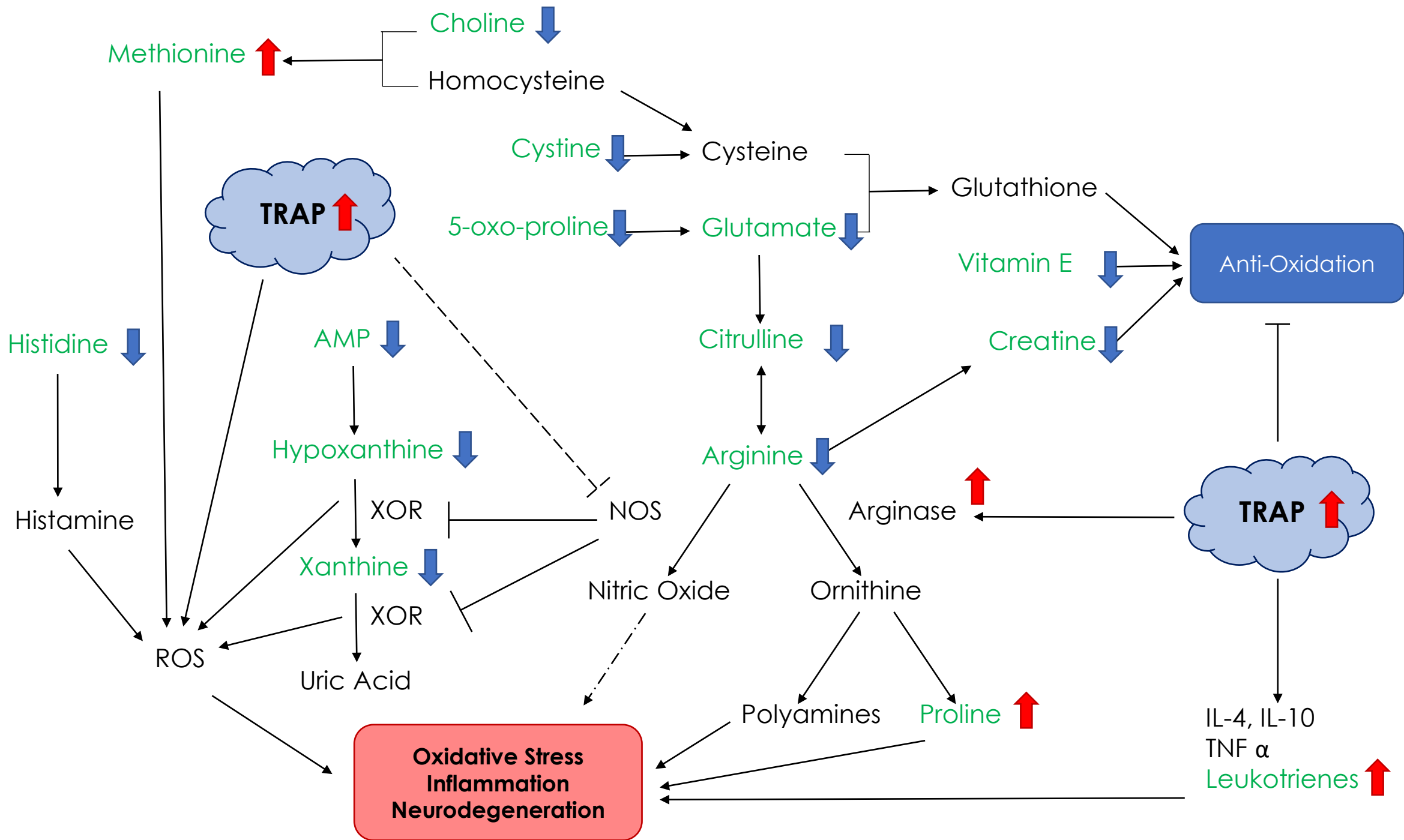
In this study:

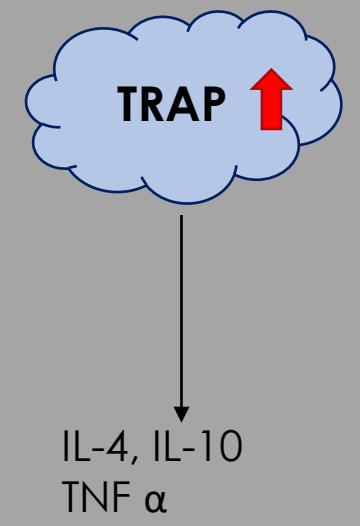
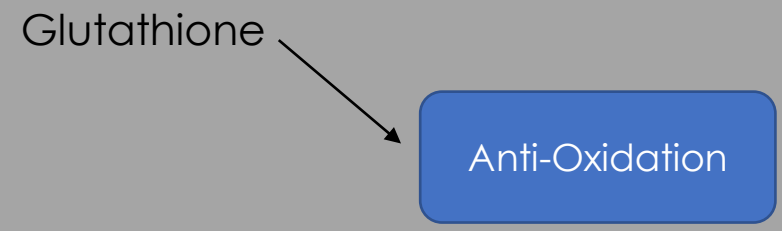
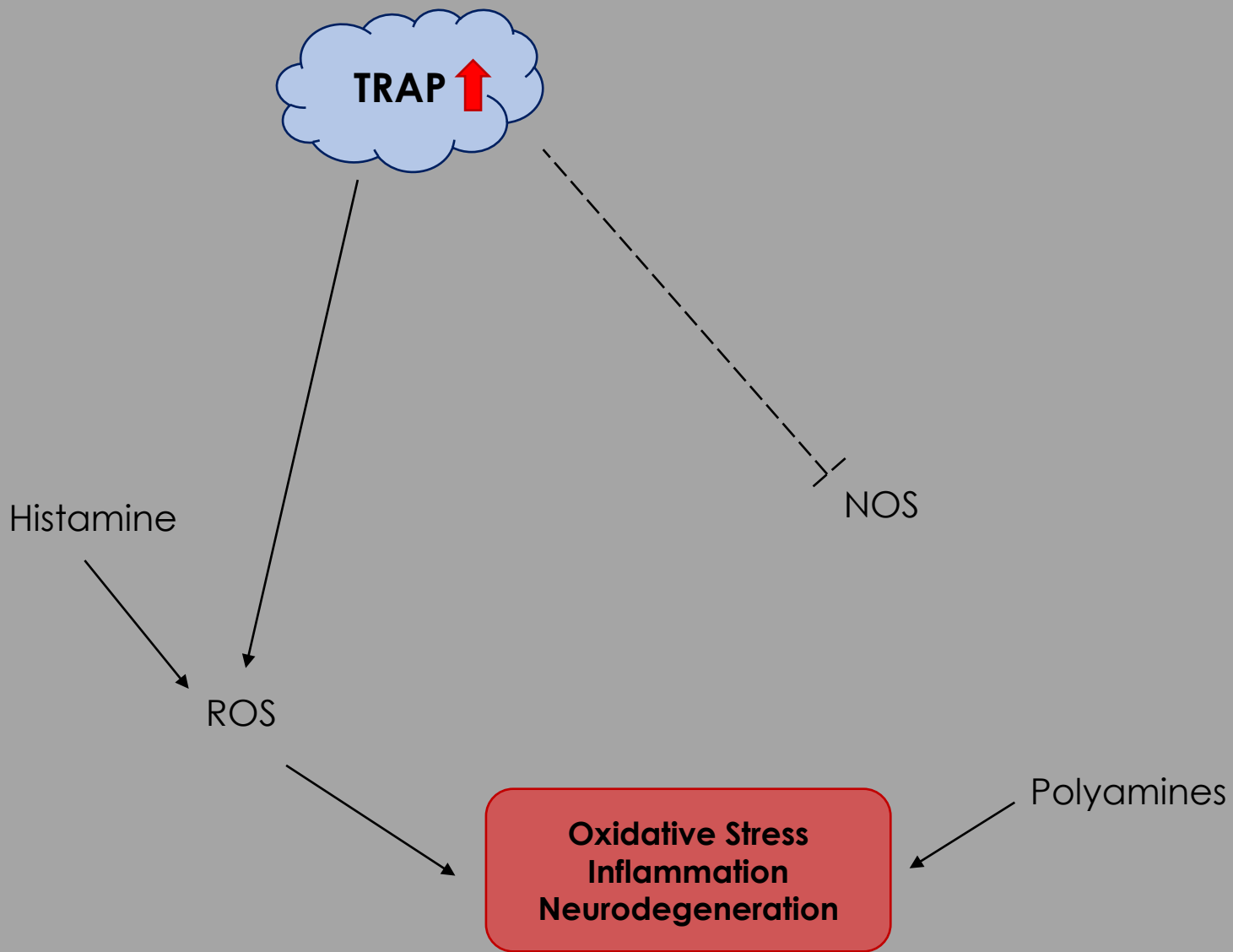
- Significantly associated with TRAP
- Indicator of effect modification

\* Vanadium used as surrogate of TRAP exposures









# Traffic Exposure, Maternal Metabolome and Birth Outcomes (TEMMBO) study

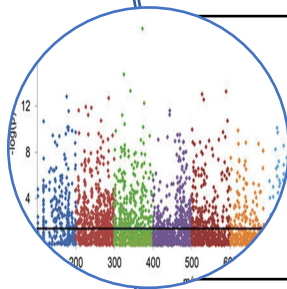
**Overarching Aim:** to apply an advanced untargeted metabolomics workflow to investigate associations between air pollution levels, perturbations in maternal metabolome and adverse birth outcomes in the Atlanta ECHO cohort of 320 African American mother and newborns.



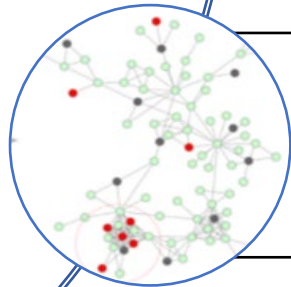
Donghai Liang, PhD, MPH



Characterize **air pollution exposure** among African American pregnant people in Atlanta, USA.



Investigate the **association between air pollution levels and perturbations in maternal metabolome** by using a non-targeted metabolomics approach.

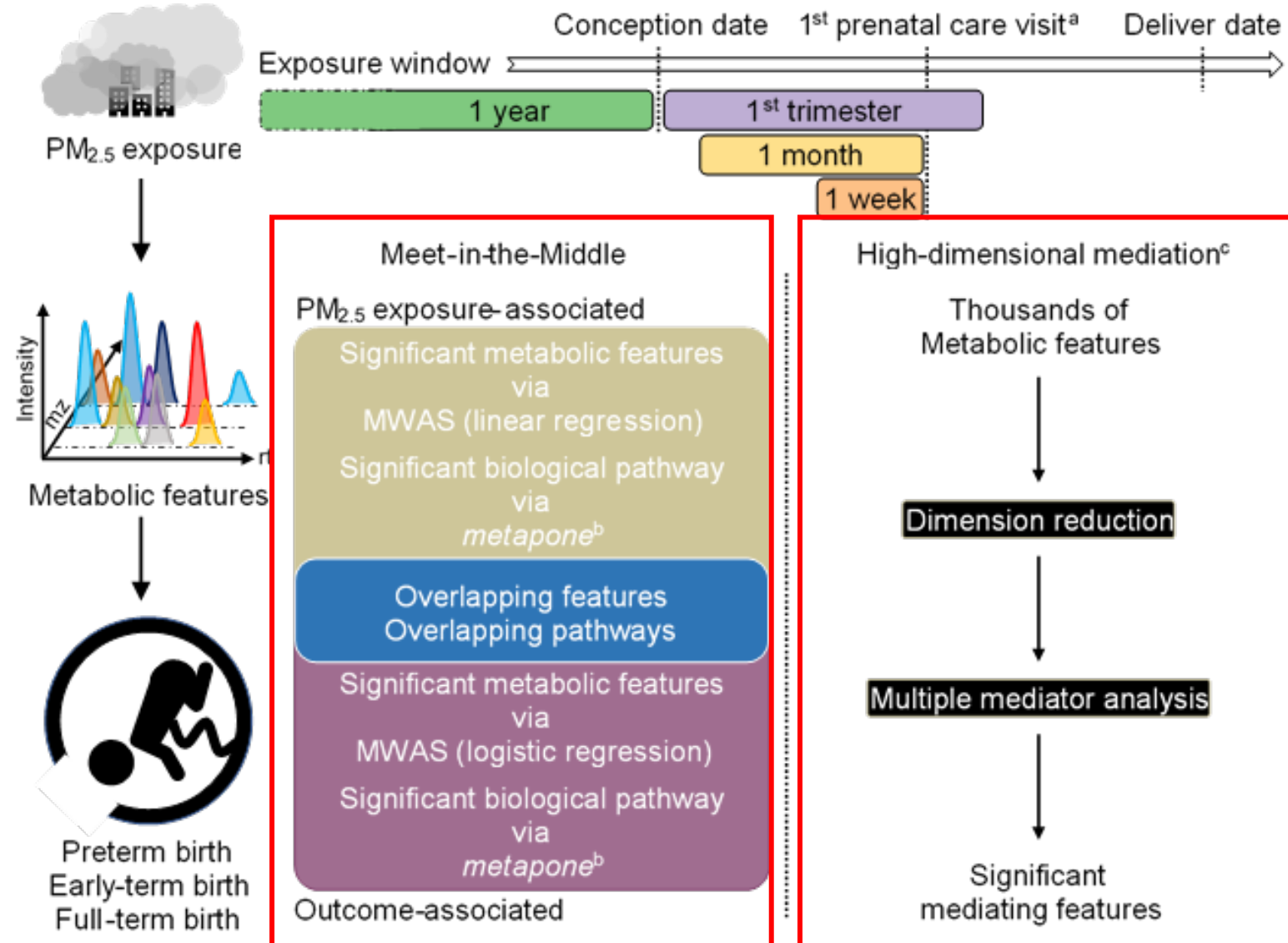


Identify the **potential biological pathways** for adverse pregnancy and birth outcomes.



Anne Dunlop, MD, MPH

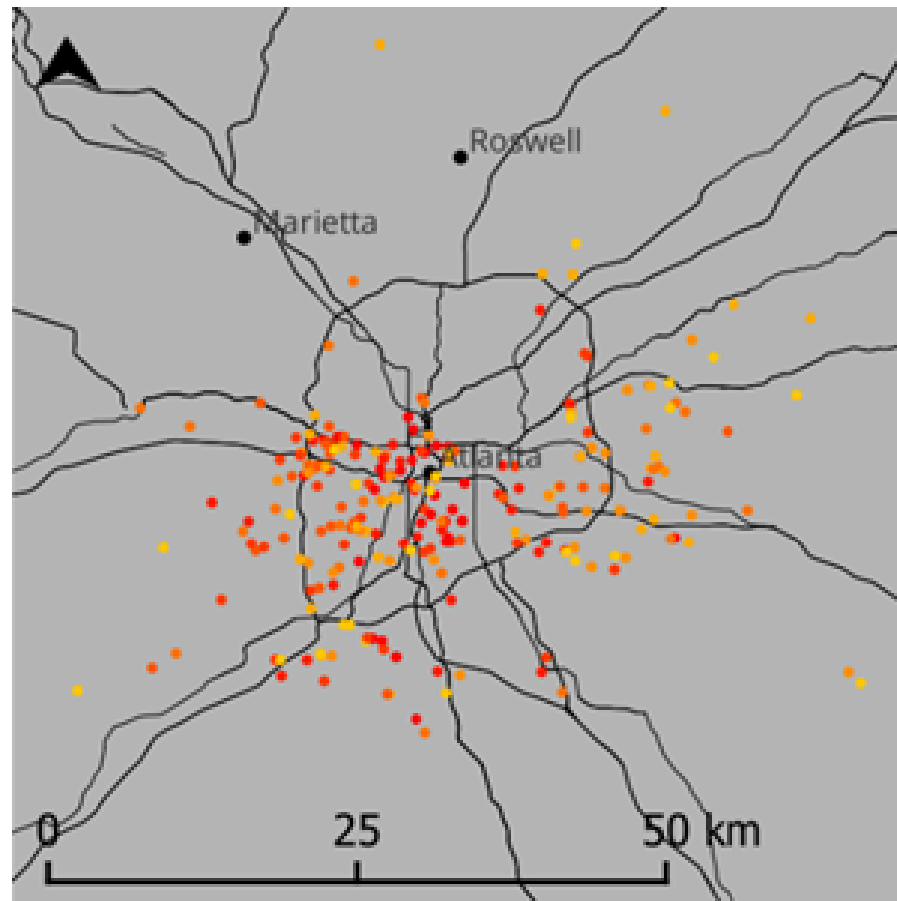
# ANALYSIS FLOWCHART



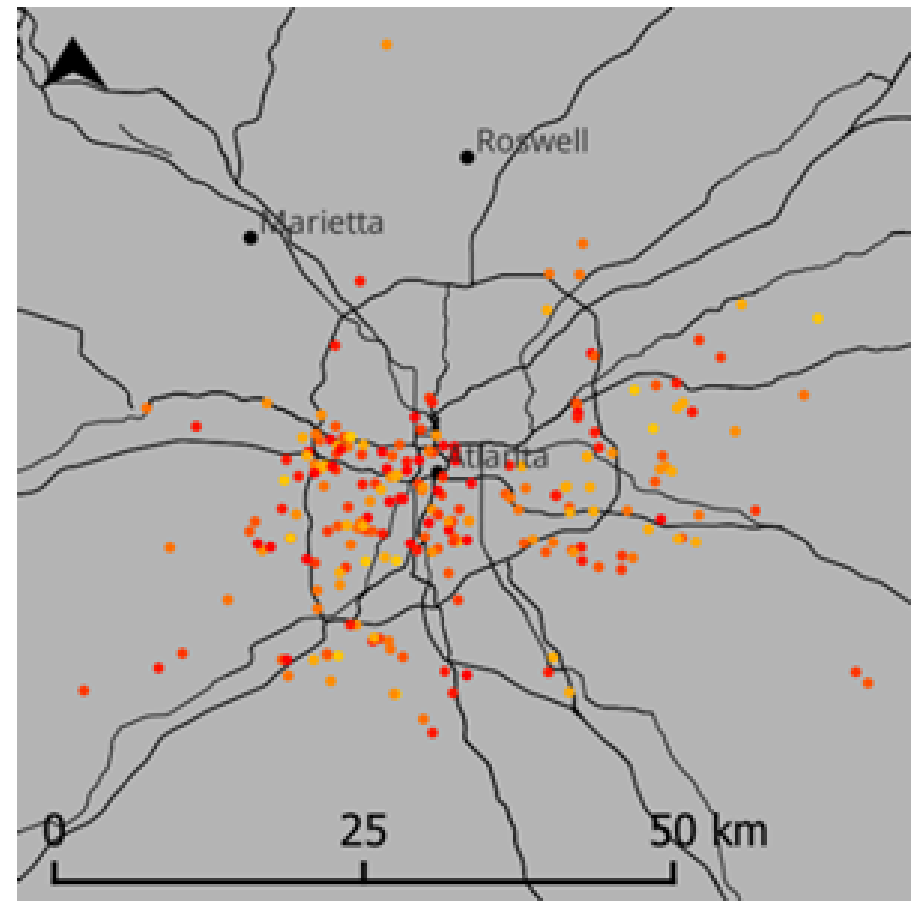




United States Highways:



PM<sub>2.5</sub> exposure for One-year prior to conception

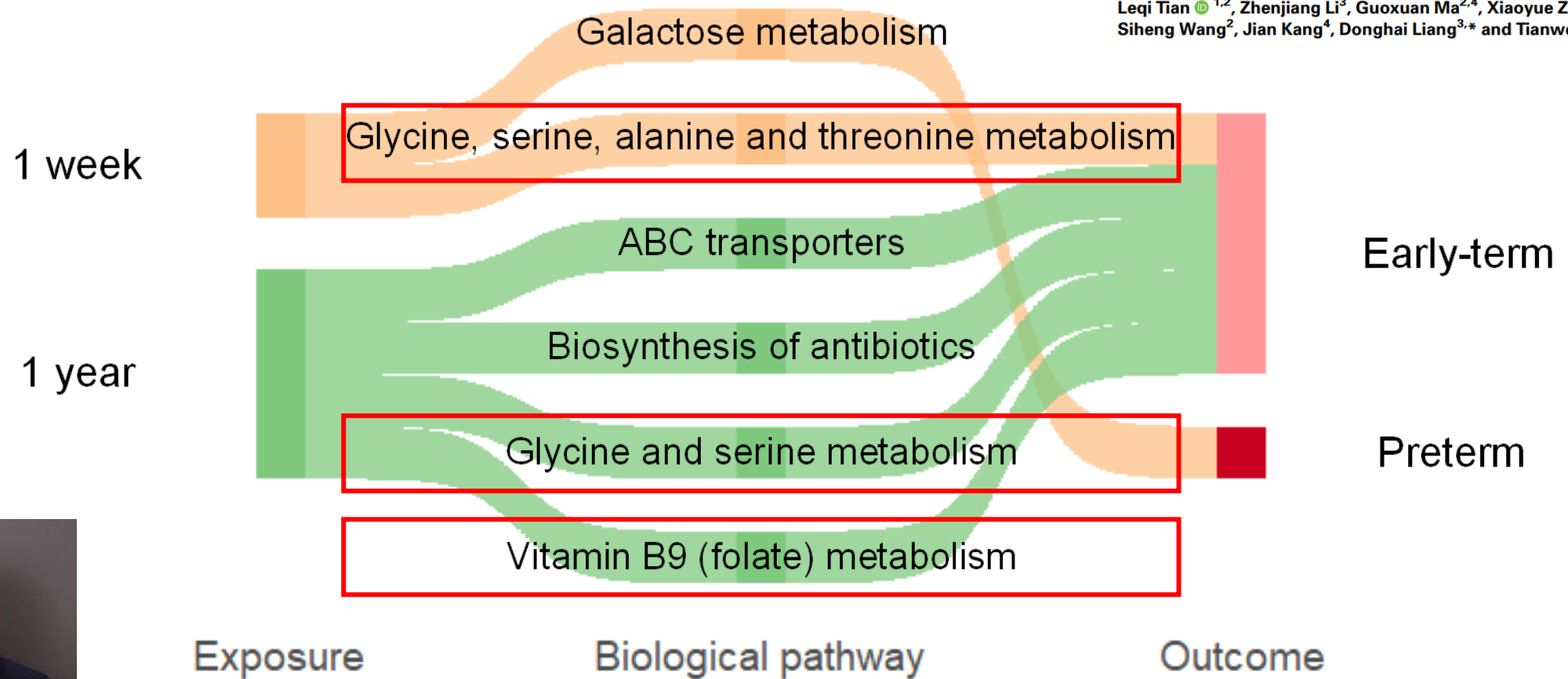


PM<sub>2.5</sub> exposure for 1<sup>st</sup> trimester

Data and text mining

**Metapone: a Bioconductor package for joint pathway testing for untargeted metabolomics data**

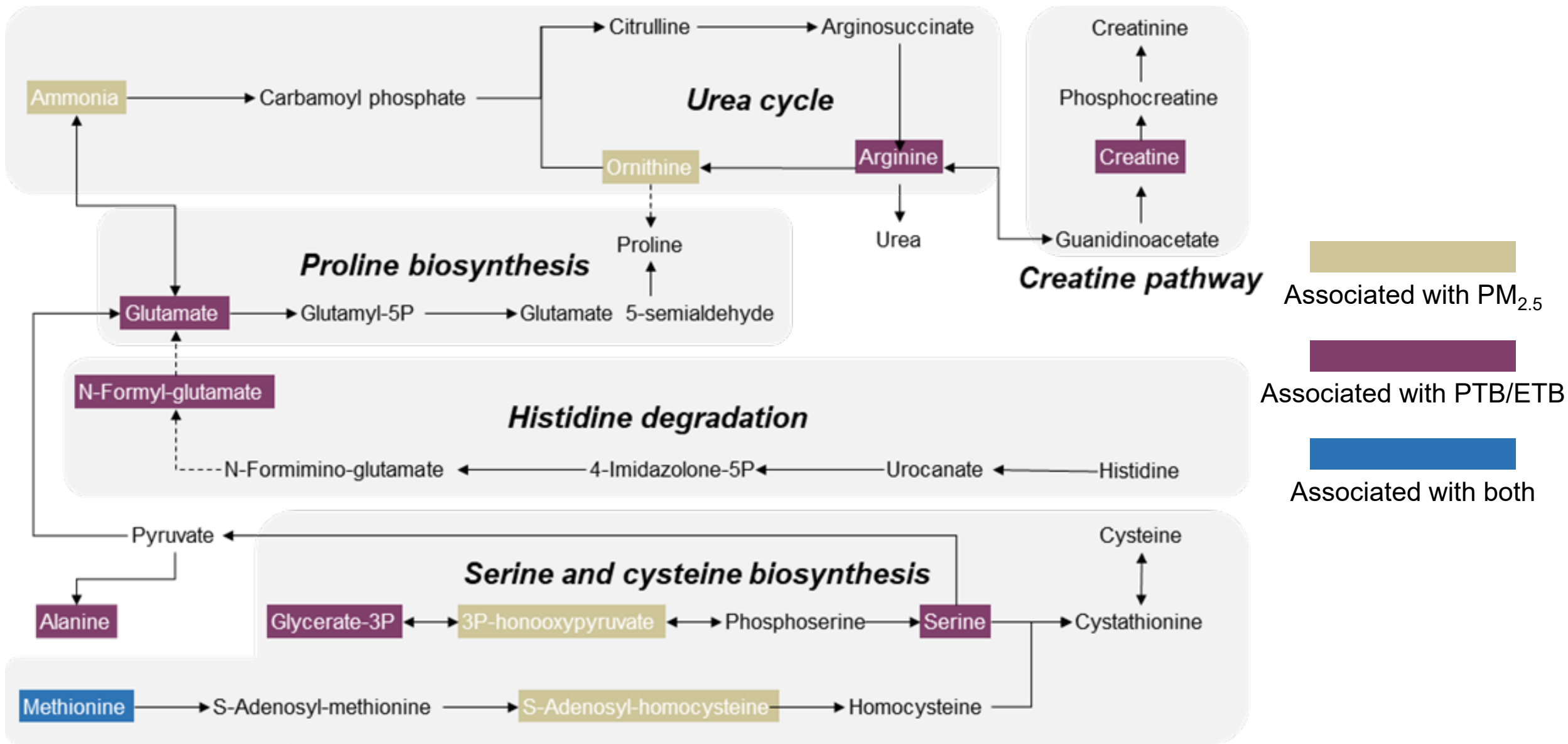
Leqi Tian <sup>1,2</sup>, Zhenjiang Li<sup>3</sup>, Guoxuan Ma<sup>2,4</sup>, Xiaoyue Zhang<sup>3</sup>, Ziyin Tang<sup>3</sup>, Siheng Wang<sup>2</sup>, Jian Kang<sup>4</sup>, Donghai Liang<sup>3,\*</sup> and Tianwei Yu<sup>1,2,5,\*</sup>



Pathway enrichment analysis (via *metapone*)

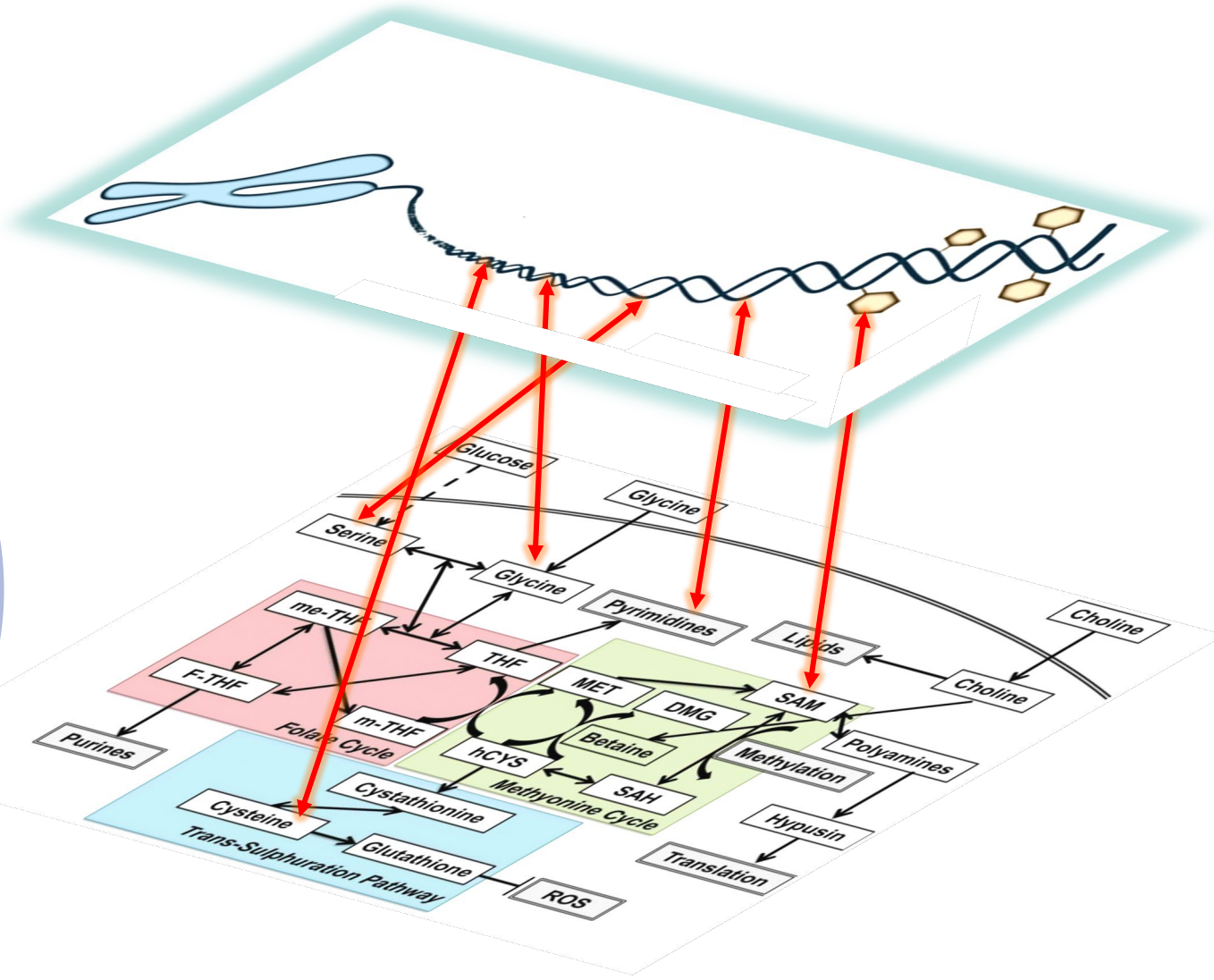
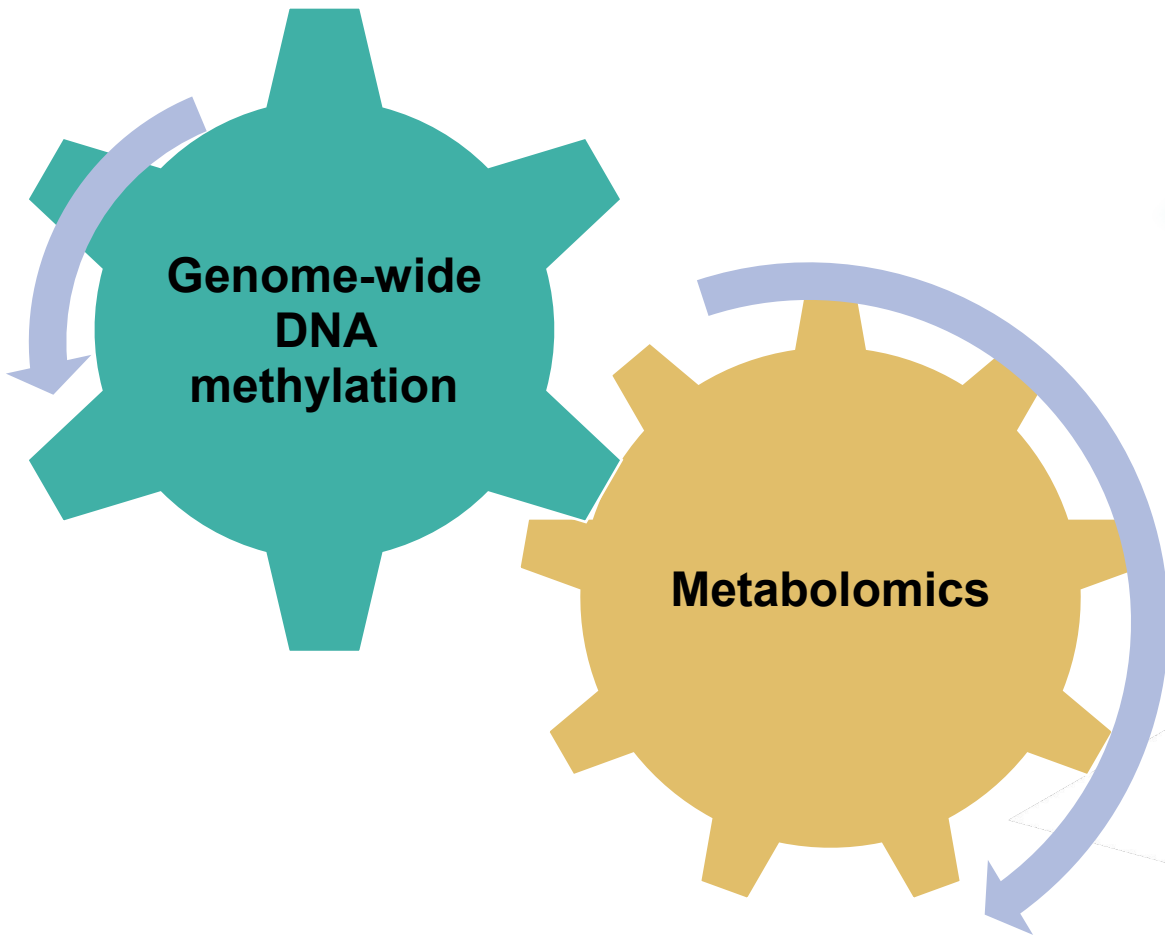


Zhenjiang Li, MSPH



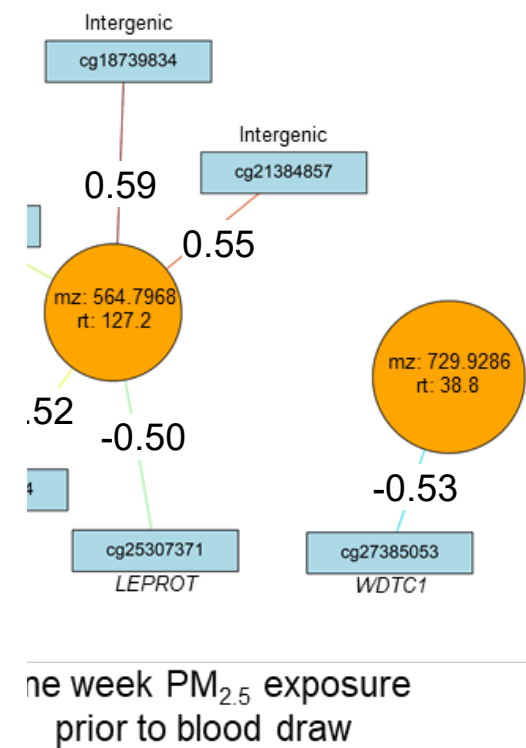
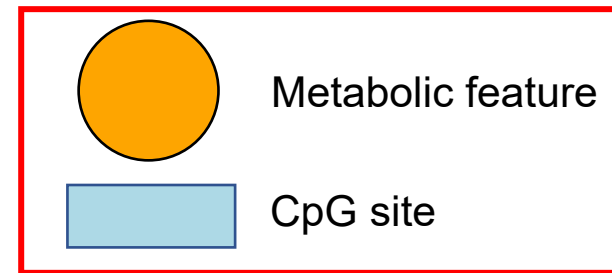
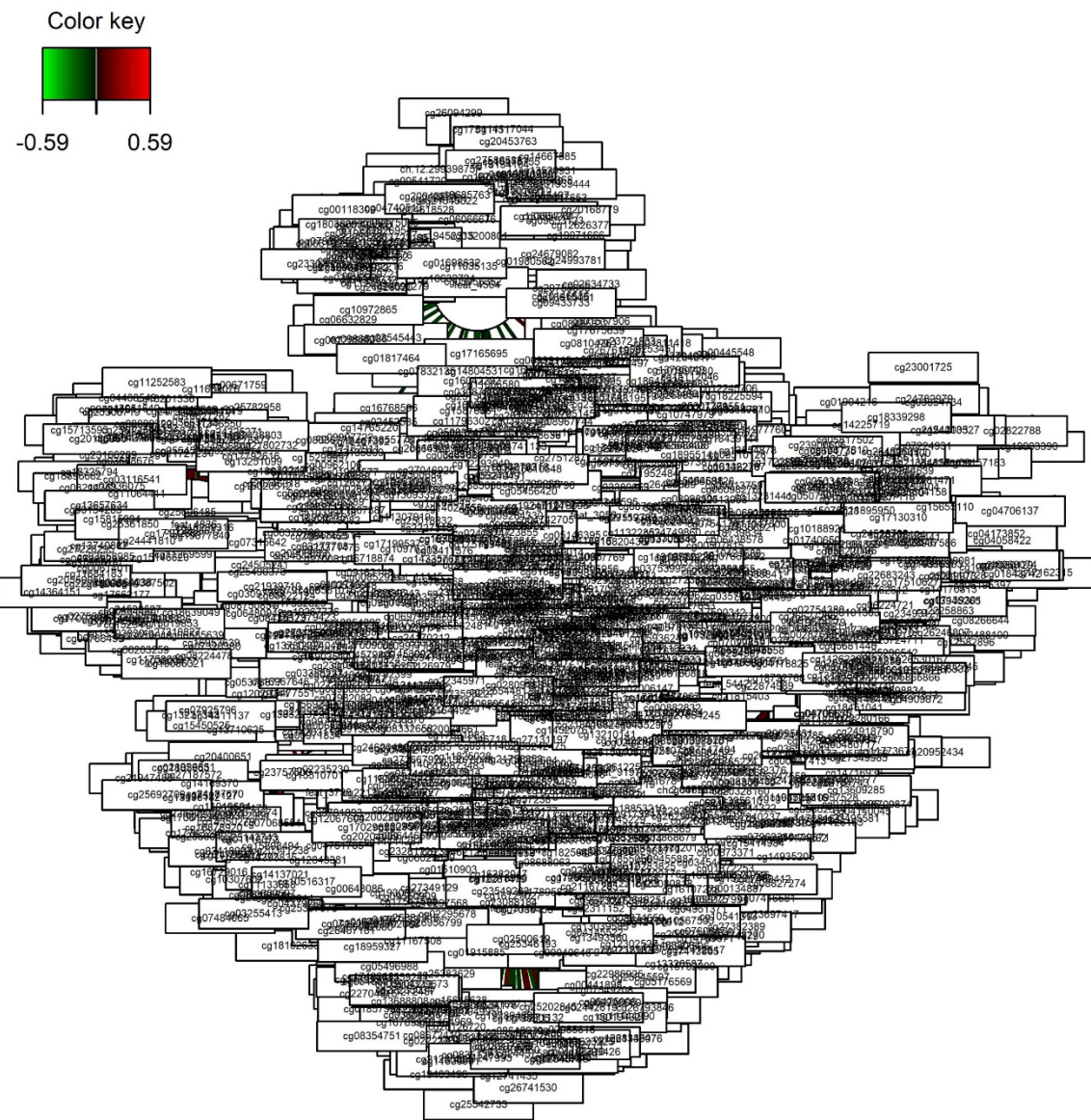
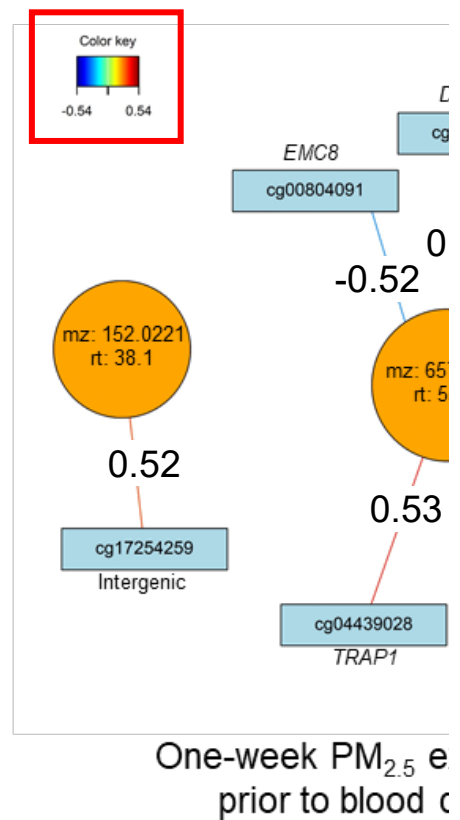
# INTERPLAY OF OMICS DATA

# Multi-Omics Integration Analysis



# SECOND STA Network Analysis

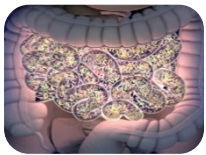
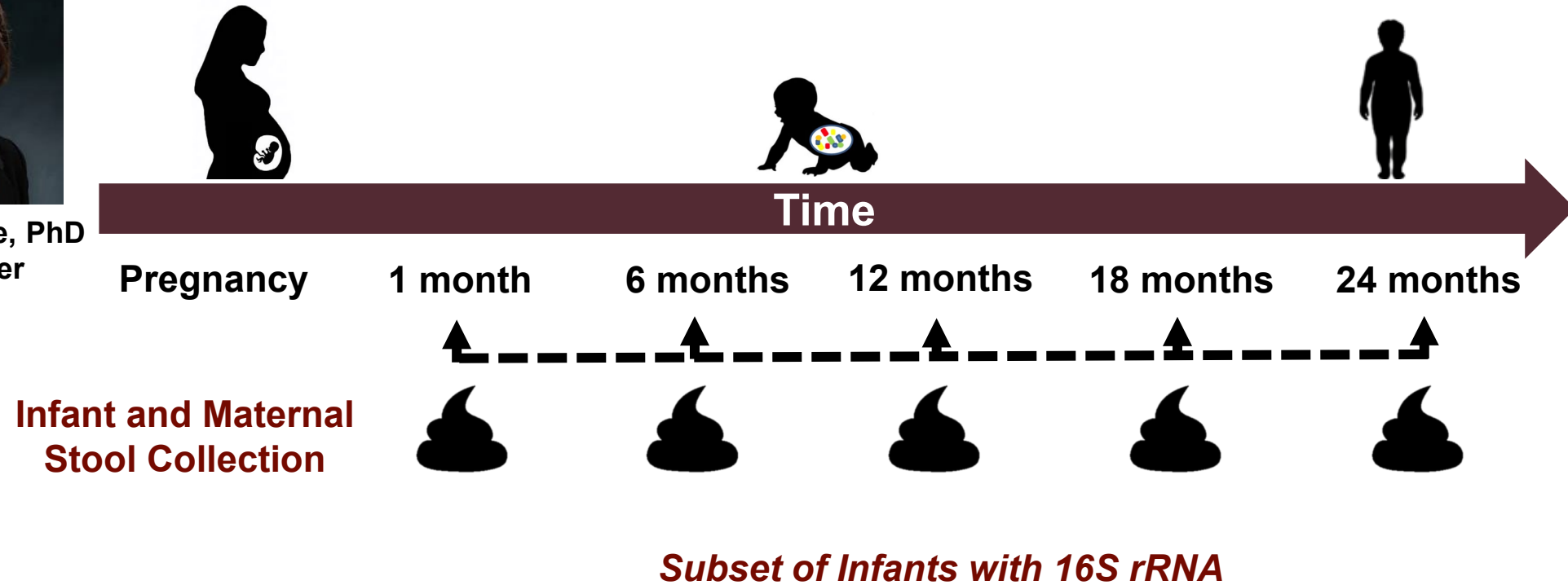
A. HILIC column



# Early Life: Gut Microbiota, Infant Growth, and Childhood Obesity in the Southern California Mother's Milk Study



Tanya Alderete, PhD  
CU Boulder



# Preliminary Analysis: Is Air pollution Exposure Associated with the Infant Fecal Metabolome?

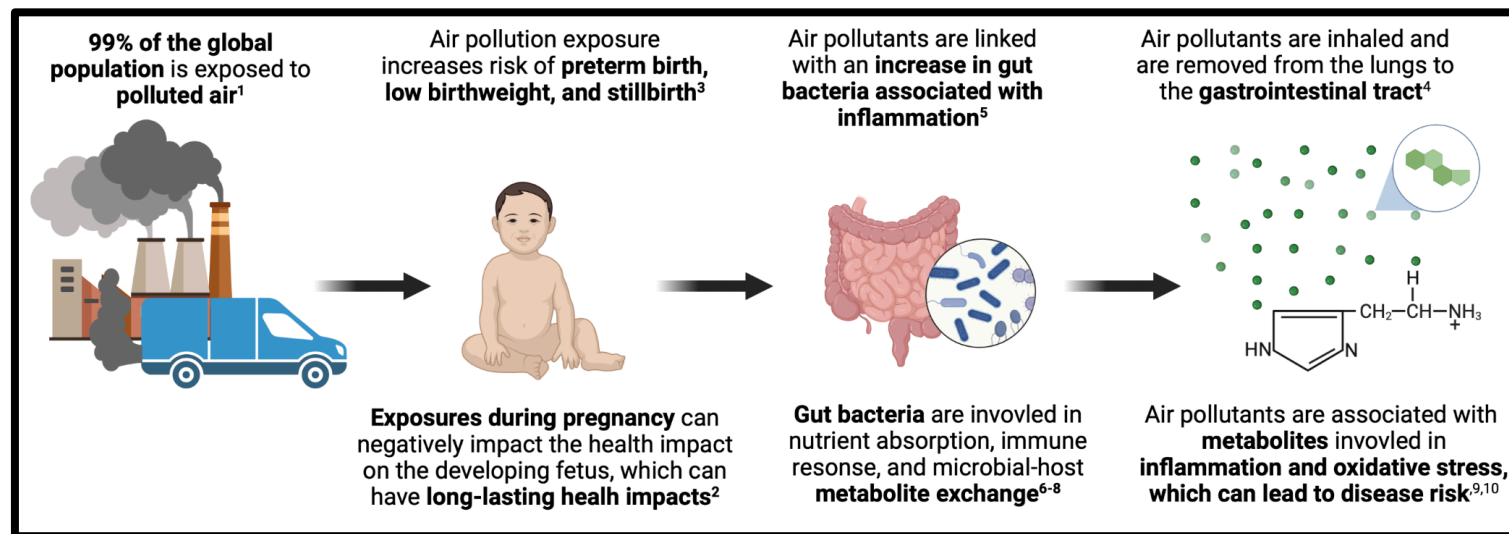
- Infants with **metabolite data** in first 2 years (n=124)
- **Aim:** Explore the the associations between ambient air pollution exposure with fecal metabolites



Tanya Alderete, PhD  
CU Boulder



Ellie Holzhausen, PhD  
CU Boulder



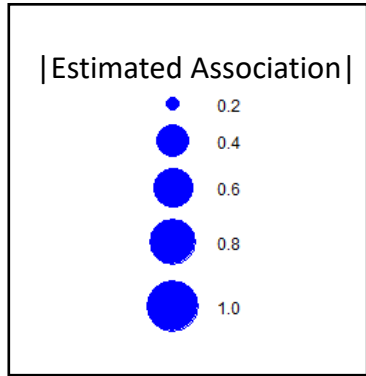
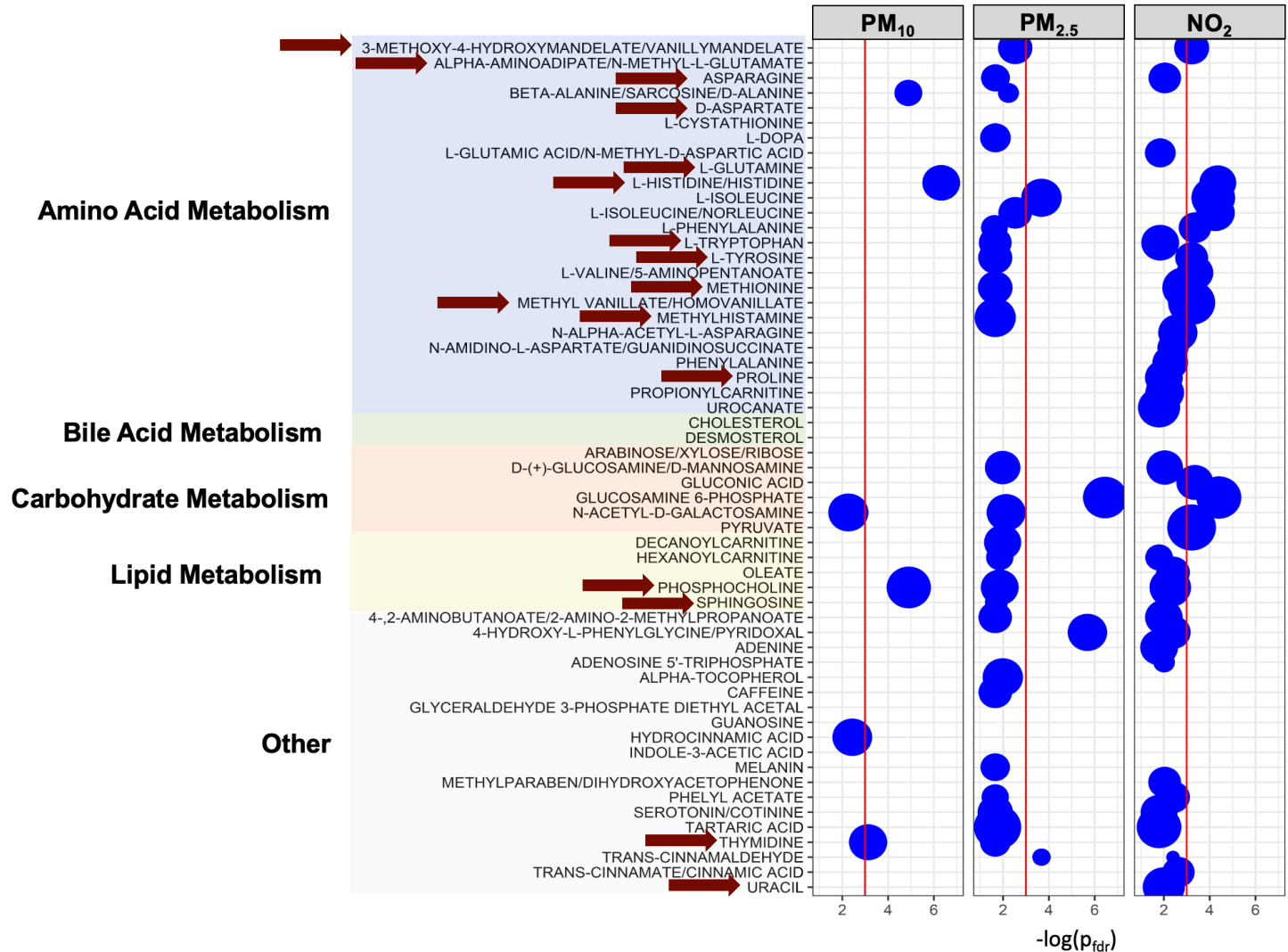
1. [https://www.who.int/health-topics/air-pollution#tab=tab\\_1](https://www.who.int/health-topics/air-pollution#tab=tab_1)  
2. <https://doi.org/10.1016/j.envpol.2017.03.055>  
3. <https://doi.org/10.1001/jamanetworkopen.2020.8243>  
4. <https://doi.org/https://doi.org/10.1016/j.freeradbiomed.2019.12.044>

5. <https://doi.org/10.1080/19490976.2022.2105096>  
6. <https://doi.org/10.1177/0884533611436116>  
7. <https://doi.org/10.3390/ijerph17207618>  
8. <https://doi.org/10.1038/s41467-019-12476-z>

9. <https://doi.org/10.1016/j.envint.2021.106666>  
10. <https://doi.org/10.1038/s41591-022-01688-4>



# Prenatal Air Pollution Exposure is Associated Metabolites Belonging to Amino Acid, Bile Acid, Carbohydrate, and Lipid Metabolism Pathways at 1-Month



$P_{FDR} < 0.2$   
Red line =  $P_{FDR} < 0.05$

Markers of oxidative stress and systemic inflammation

*Metabolites have also been linked with gut bacterial function*

Preliminary / Unpublished Data

$-\log_2(\text{metabolite intensity}_{1 \text{ month}}) = \text{air pollutant}_{\text{pregnancy}} + \text{infant sex} + \text{SES} + \text{season} + \text{breastfeedings}_{1 \text{ month}}$   
Effect estimates scaled to 1-SD in exposures ( $PM_{10}=4.0 \text{ ug/m}^3$ ,  $PM_{2.5}=1.2 \text{ ug/m}^3$ ,  $NO_2=2.5 \text{ ppb}$ ,  $n=124$ ).



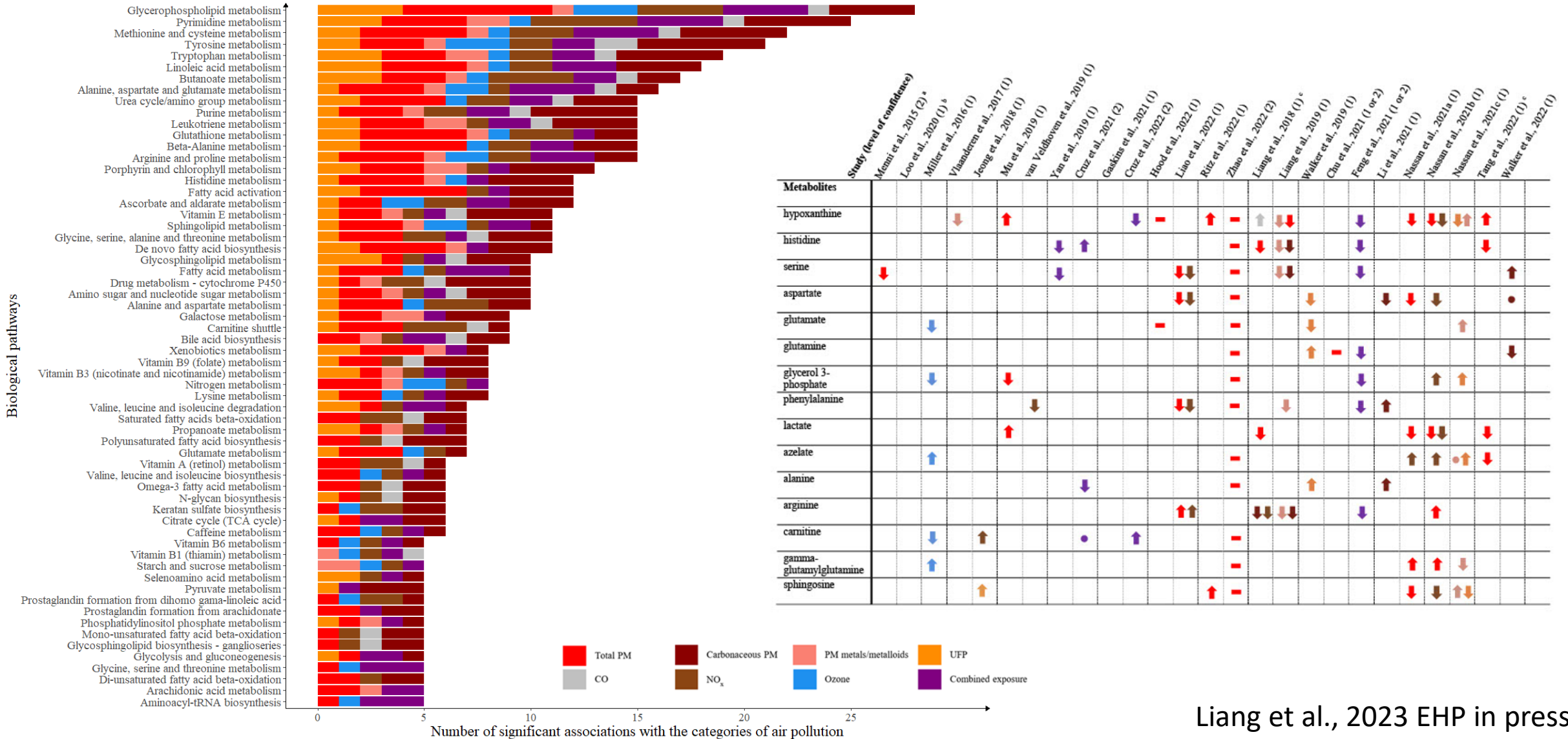


# A Systematic Review of Untargeted Metabolomics Application for Air Pollution Health Research: Current Progress, Analytical Challenges, and Future Direction



EMORY Donghai Liang<sup>1</sup>, Zhenjiang Li<sup>1</sup>, Jelle Vlaanderen<sup>2</sup>, Ziyin Tang<sup>1</sup>, Dean Jones<sup>1</sup>, Roel Vermeulen<sup>2</sup>, Jeremy A. Sarnat<sup>1</sup>

<sup>1</sup> Emory University, Atlanta, USA <sup>2</sup> Utrecht University, Utrecht, Netherlands



# What Have we Learned and Future Directions

- Metabolomics as a sensitive platform linking air pollution exposure to internal dose and biological responses
- Air pollution exposures may induce perturbations in pathways and metabolites, which may in turn increase risk of adverse health outcomes
- The exact mechanisms by which air pollution exposures impact human health remain uncertain – application of multi-omics is critical
- Validation of these findings via hypothesis-driven protocols
- Technical advances needed in metabolic annotation and quantification
- Integration of multi-omics data for comprehensive examination on molecular network
- Future development of sensitive biomarkers in assessing community exposures

# ACKNOWLEDGEMENT



**SCAPE**



**EMORY**

**ROLLINS  
SCHOOL OF  
PUBLIC  
HEALTH**



[donghai.liang@emory.edu](mailto:donghai.liang@emory.edu)

<https://scholarblogs.emory.edu/environmentalmetabolomics>

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Audrey Gaskins Todd Everson  
Carmen Marsit Yang Liu  
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Lauren Mccullough Yijuan Hu  
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Kasthuri Sivalogan James Zhang  
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