

# Outdoor Air Pollution and Asthma

John R. Balmes, MD

University of California, San Francisco  
and Berkeley



# Outdoor Air Pollution

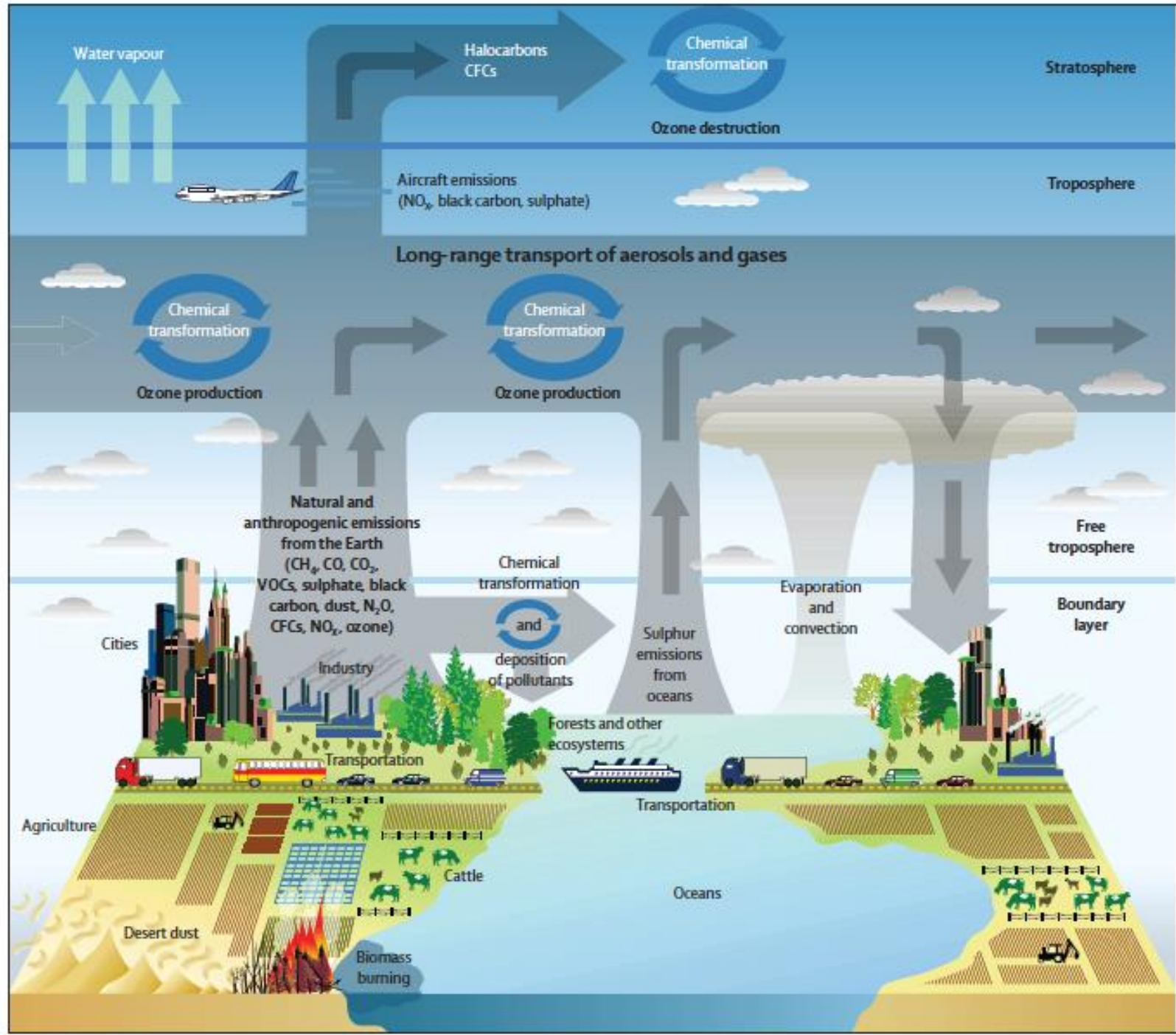
- Increased contribution to the Global Burden of Disease (2010 Comparative Risk Assessment, *Lancet*, 2012)
- 14% of new cases and 15% of exacerbations of childhood asthma attributed to TRAP in a study of 10 European cities (*Eur Respir J*, 2013)
- Rapidly increasing pollution in mega-cities of the developing world

# Outdoor Air Pollution



- Multiple sources
- Mixture of gases and particulate matter
- Traffic-related air pollution





# Air Pollution and Asthma

- Exacerbation
  - Multiple studies support short-term worsening of asthma with exposure to PM, O<sub>3</sub>, NO<sub>2</sub> or traffic emissions
- New onset
  - Evidence less clear-cut, but accumulating for O<sub>3</sub>, NO<sub>2</sub>, and traffic

# WHY THE SAN JOAQUIN VALLEY?

- High air pollution
  - Primarily mobile source
  - Valley topography
- Rapidly growing population
  - Fastest in California
  - 45% Latino
- Economic hardship
  - High unemployment
- High rates of asthma



# Fresno Asthmatic Children's Environment Study (FACES)



- Study of a panel of asthmatic children living within 20 km of the Fresno EPA monitoring station
- Goal: follow course of asthma in relation to air pollution



Funded by CA Air Resources Board and NHLBI

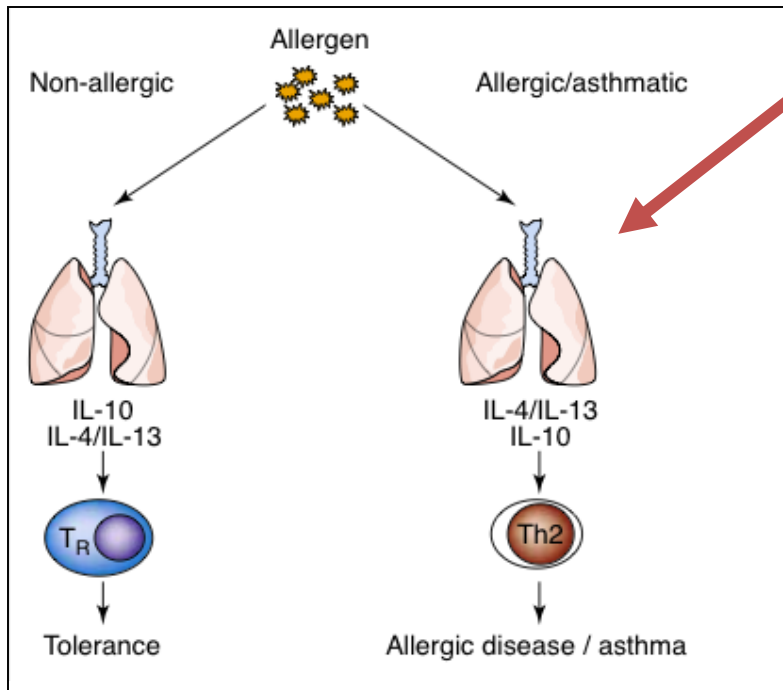
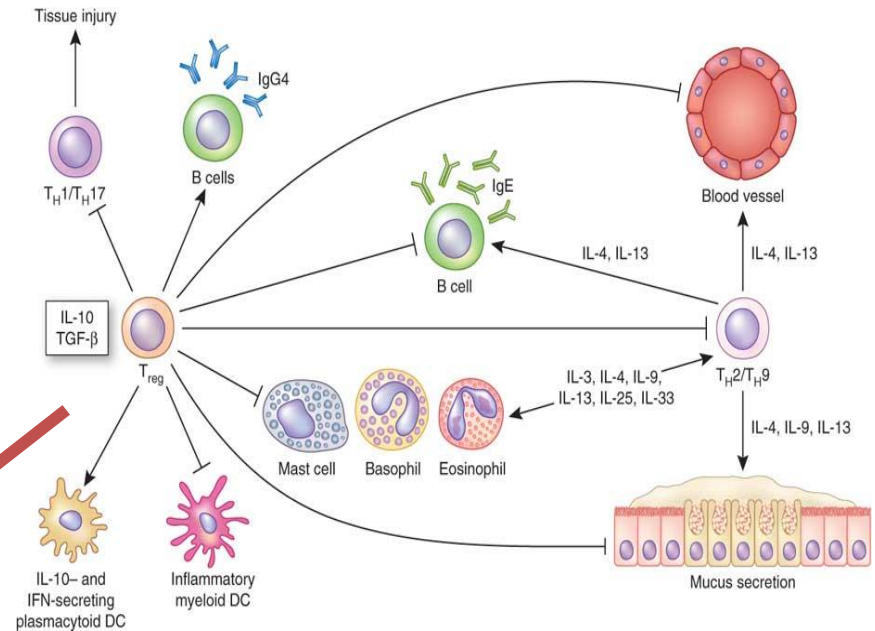
# Short-term effects of air pollution on wheeze in asthmatic children in Fresno

- 315 children with asthma, 6-11 years of age, were recruited for FACES
- Ambient air quality data from the Fresno monitoring station were used to assign exposures to pollutants
- Wheeze was significantly associated with short-term exposures to
  - NO<sub>2</sub> [OR = 1.10 (1.02-1.20)];
  - PM<sub>10-2.5</sub> [OR = 1.11 (1.01-1.22)]



# Regulatory T cells (Tregs) in Asthma

- **Treg** (CD4+CD25<sup>hi</sup>CD127<sup>lo</sup>) cells can control other immune cells
- **Foxp3** is a transcription factor associated with Treg function
- Children lacking Foxp3 have severe allergies, asthma, GI disease, and type 1 diabetes.
- Treg cells can inhibit effector T cells



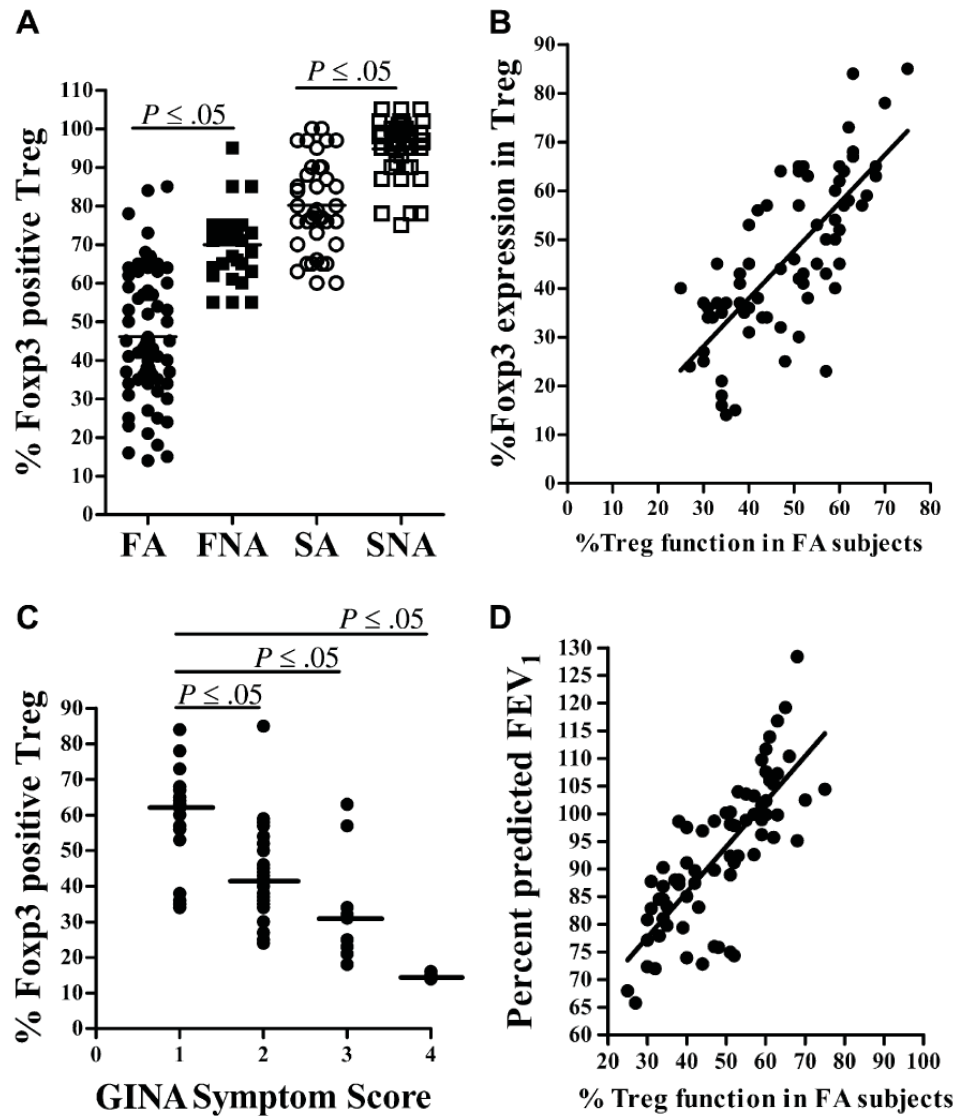
• Does exposure to air pollution decrease Treg function in asthma?

• Is Foxp3 expression altered? If so, how?

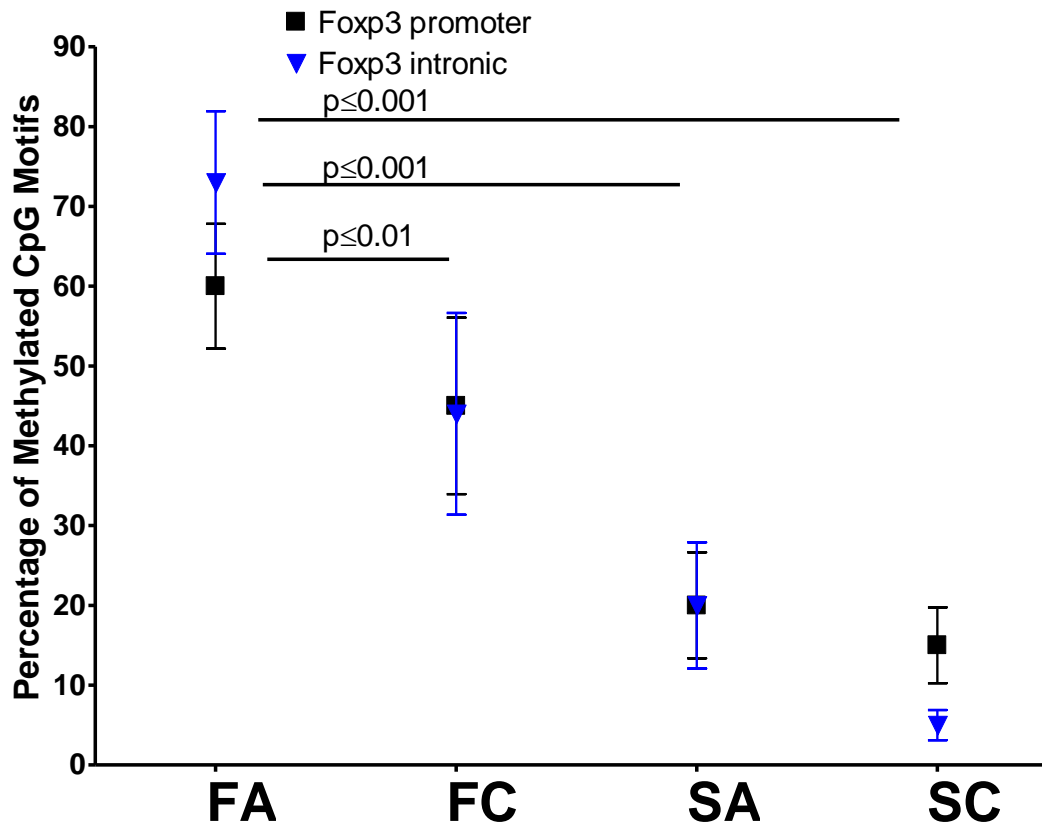
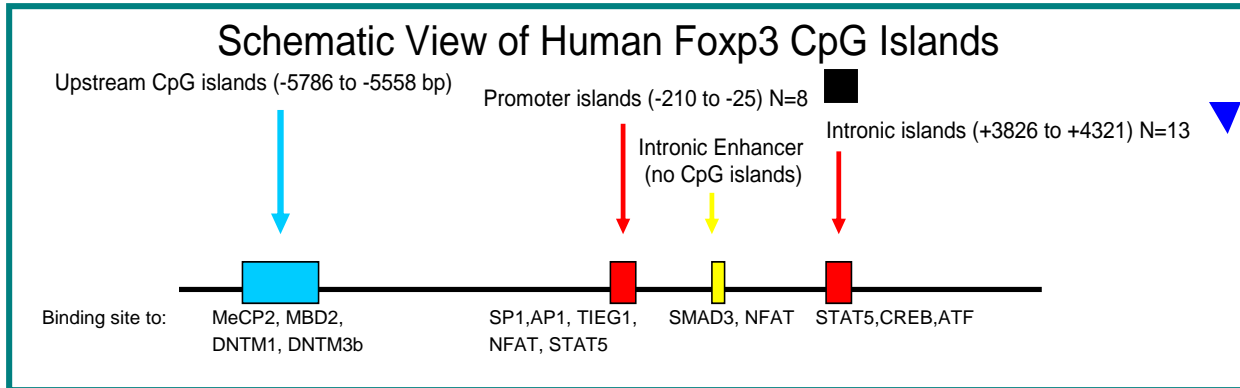
# Ambient air pollution impairs regulatory T-cell function in asthma

- FACES participants
  - Children 8-12 yrs with asthma (FA: n=71)
  - Serial spirometry and clinical symptom score
  - Blood samples
  - Individual estimates of exposure to PAHs
- Age-matched and sex-matched comparison groups
  - Fresno control children with no asthma and no allergies (FC: n=40)
  - Stanford children with asthma (SA: n=30)
  - Stanford control children with no asthma and no allergies (SC: n=30)

# Treg Foxp3 expression is associated with asthma severity

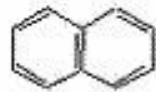


# FOXP3 CpG regions are hypermethylated in FACES subjects

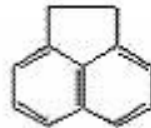


# Polycyclic Aromatic Hydrocarbons (PAHs)

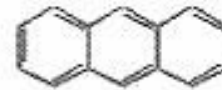
- PAHs are formed by incomplete combustion of carbon-containing materials (wood, coal, diesel, gas; also cooked food and tobacco smoke)



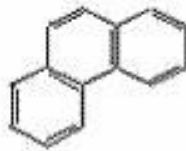
Naphthalene



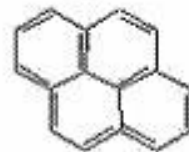
Acenaphthene



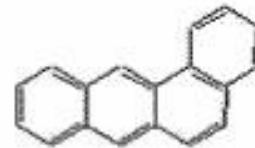
Anthracene



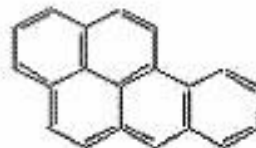
Phenanthrene



Pyrene

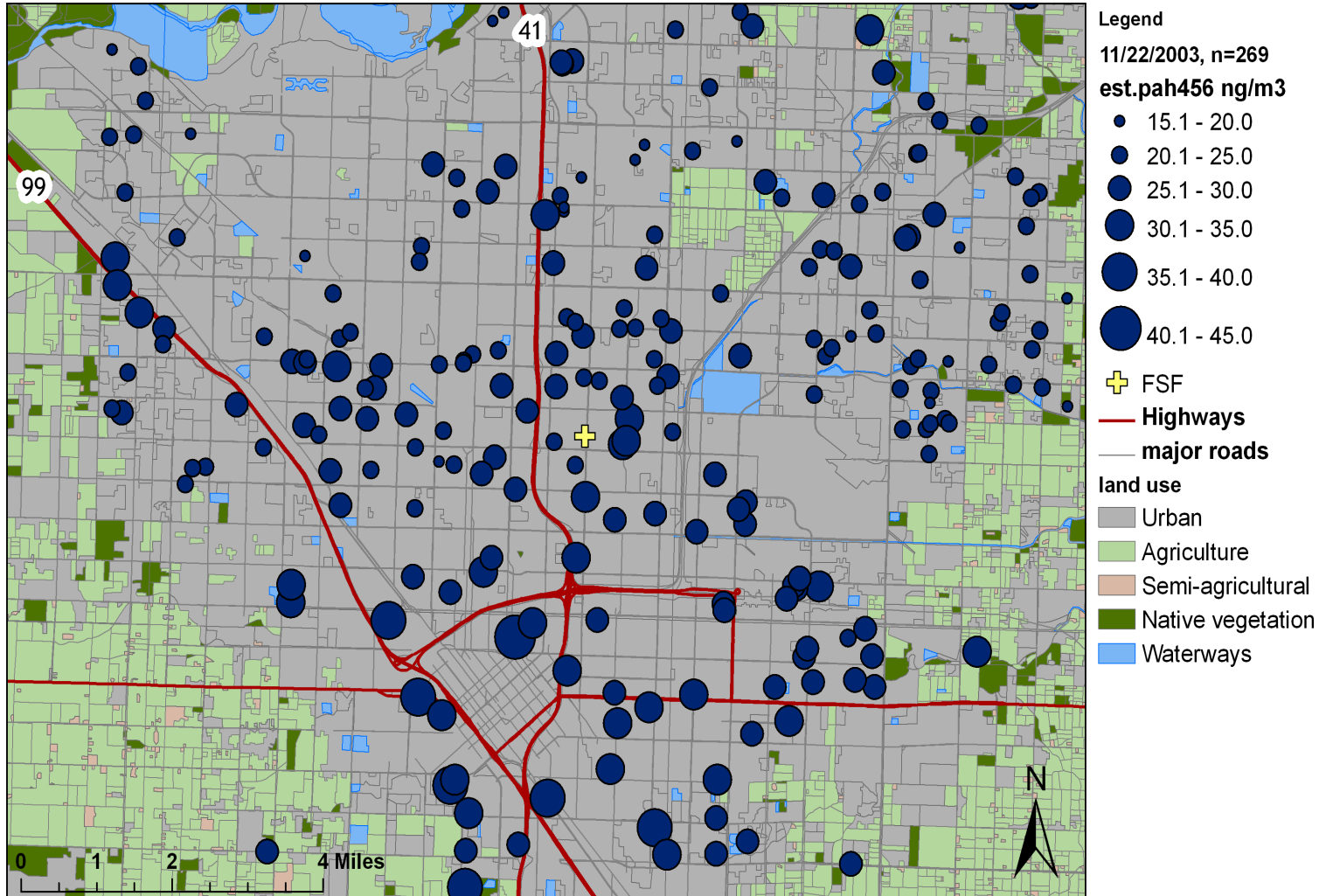


Benzofluoranthene

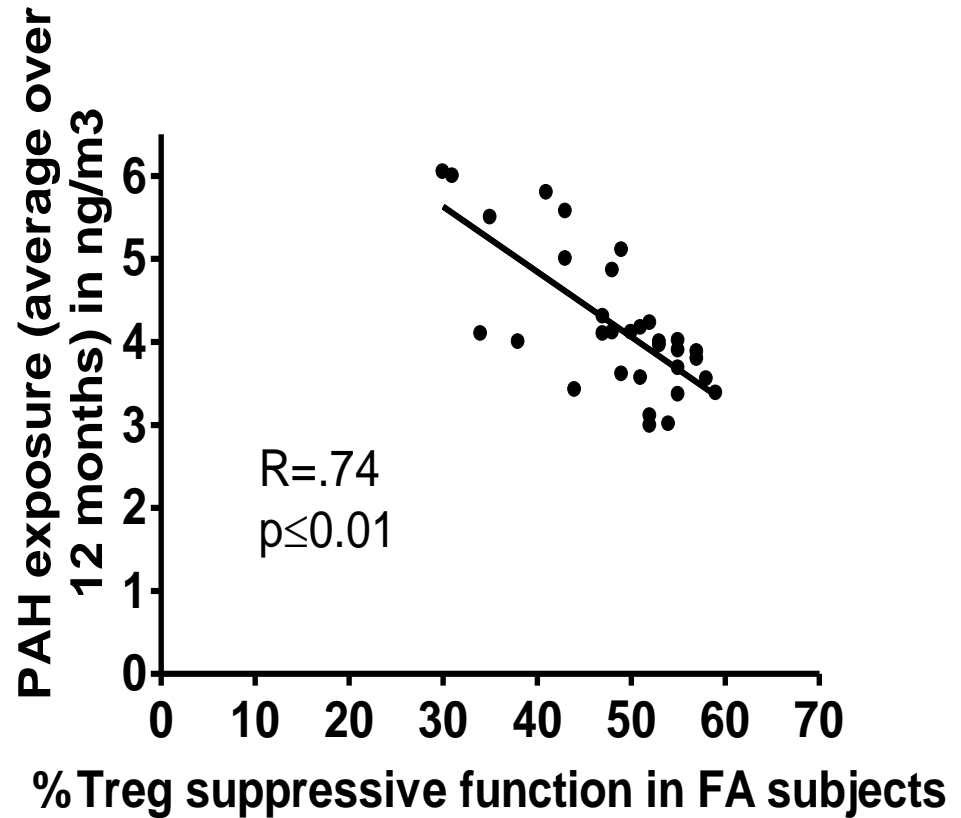
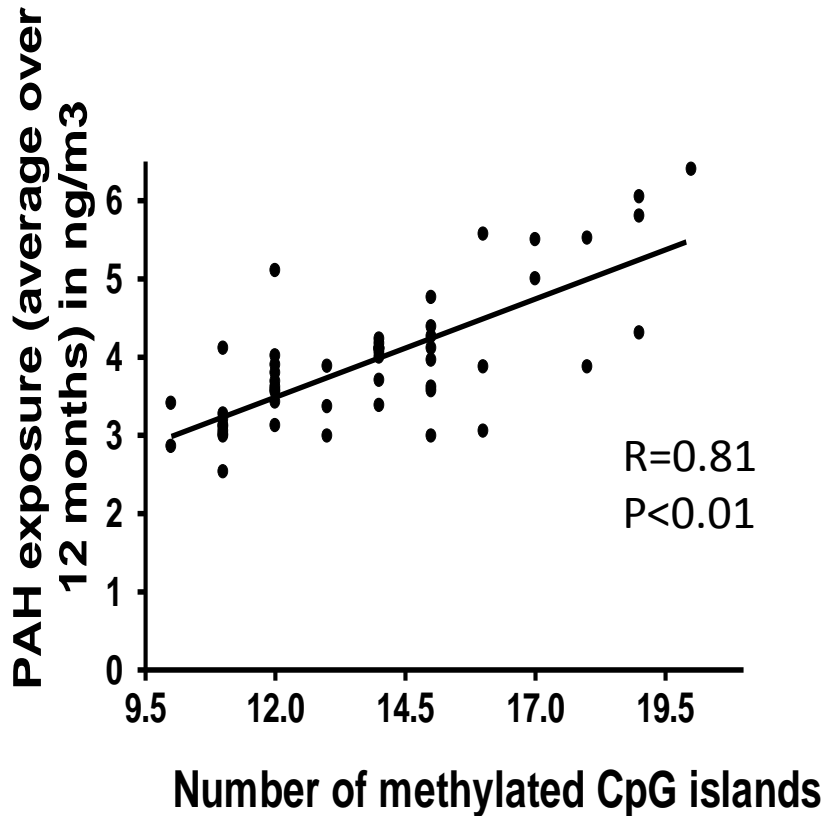


Benzo(a)pyrene

# PAH cumulative exposure over 12 mos



# Association between PAH exposure and methylation of *FOXP3* in FA subjects



# PAH exposure and wheeze in the FACES cohort

- Estimates of PAH exposure were associated with increased wheeze (n=283)
- The odds ratios for asthmatic children exposed to PAHs (ng/m<sup>3</sup>) ranged from 1.01 (95% CI, 1.00-1.02) to 1.10 (95% CI, 1.04-1.17)].
- This trend for increased wheeze persisted among all PAHs measured.
  - Phenanthrene was found to have a higher relative impact on wheeze.



# CHAPS SJV

Children's Health & Air Pollution Study  
San Joaquin Valley

With appreciation to our subjects  
and their families

FACES and CHAPS teams:

Kari Nadeau  
Katharine Hammond  
Elizabeth Noth  
Fred Lurmann  
Ellen Eisen  
Jennifer Mann  
Boriana Pratt  
Gary Shaw  
Ira Tager  
Helene Margolis  
Tim Tyner

**Berkeley**  
UNIVERSITY OF CALIFORNIA

**STANFORD**  
UNIVERSITY

Funded By:



Nadeau Lab:  
Kinjal Hew  
Annett Walker  
Unni Nygaard  
Shu-Chen Lyu  
Rachel Hovde  
Arunima Kohli



National Institute of Environmental Health Sciences  
*Your Environment. Your Health.*