JOHNS HOPKINS
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JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH

Protecting Health, Saving Lives—*Millions at a Time*

The Johns Hopkins PM Research Center

Jonathan M. Samet

Principal Investigator

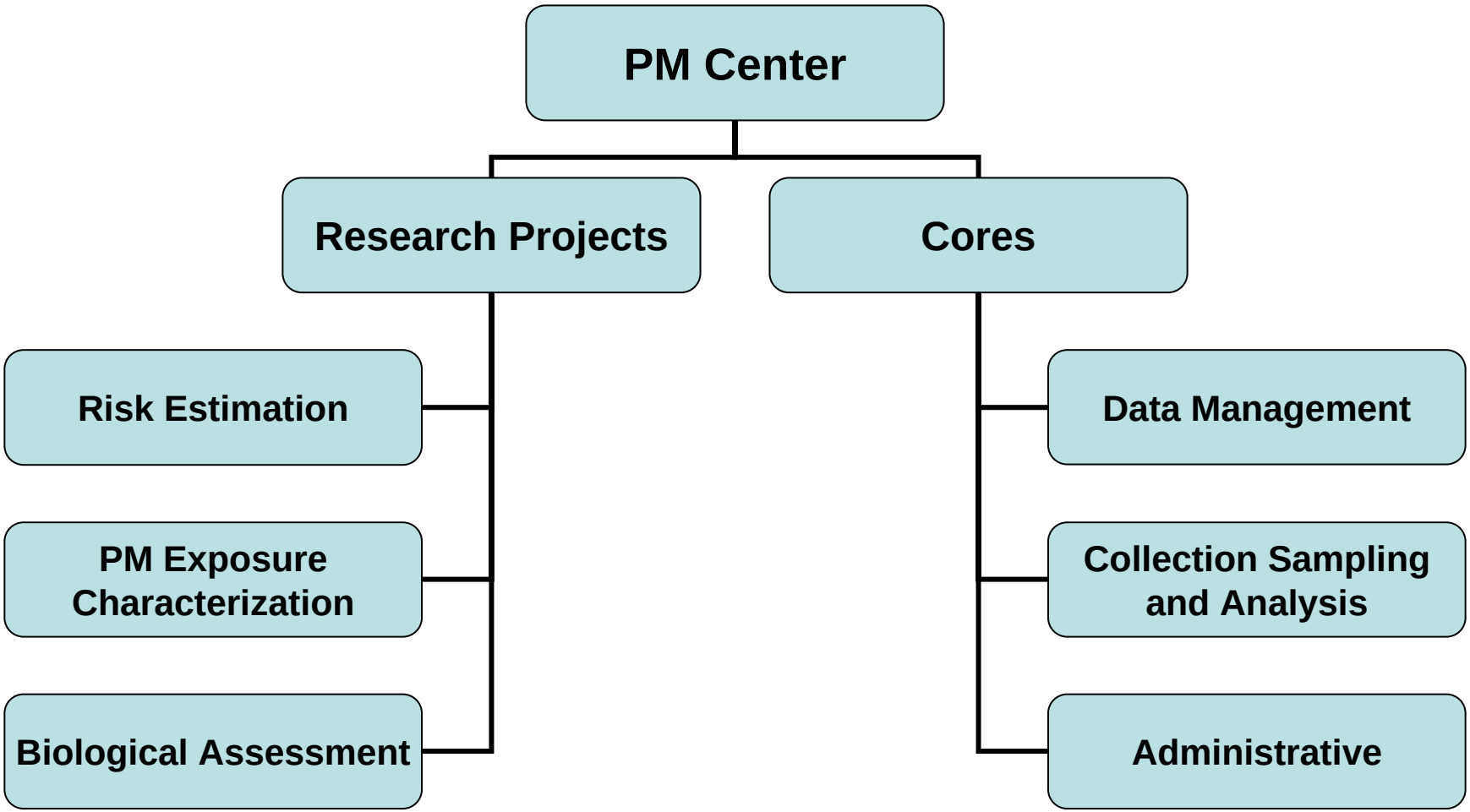
The Johns Hopkins PM Center

“The Johns Hopkins PM Research Center brings together a multidisciplinary research team…to address the most critical gap in current understanding of health and particulate matter (PM)—the physical and chemical characteristics that determine risk to human health.”

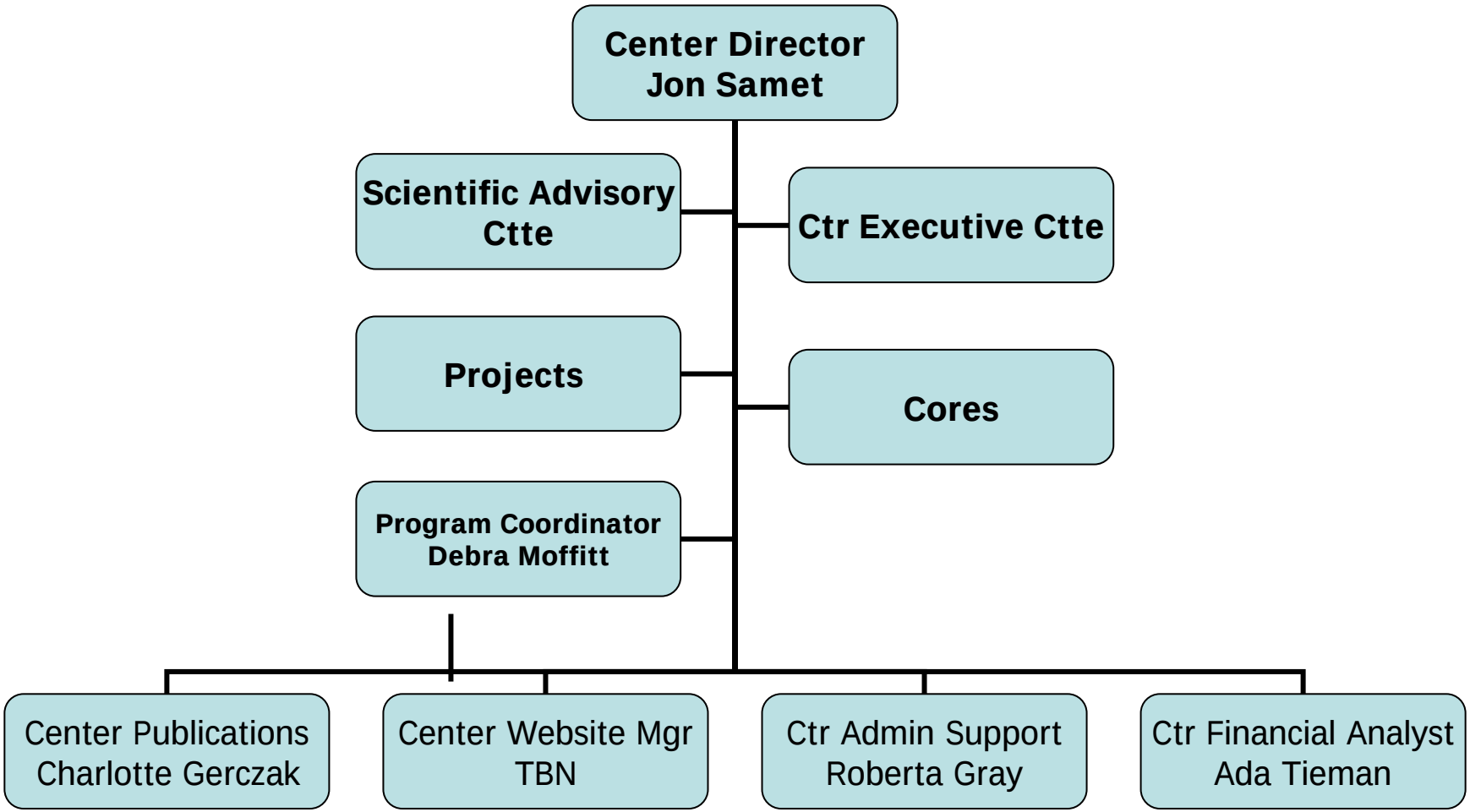
National Risk-Based Approach

- **Map variation in risk of PM across the country using mortality and Medicare hospitalization as outcome**
- **Sample PM in locations with contrasting PM risks**
- **Carry-out biological assays on the PM from the selected locations**

Center Structure



Center Administrative Structure



Three Phases

- ***First phase***
  - **Initial epidemiological analyses and *description* of PM characteristics**
  - **Develop sampling and characterization approaches**
  - **Develop biological assays**
- ***Second phase***
  - **Monitor and collect PM in selected sites**
  - **Evaluate PM toxicity**
- ***Third phase***
  - **Test focused hypotheses**

Project 1.
Risk Estimation

PI: Francesca Dominici

Research Team
(in alphabetical order)

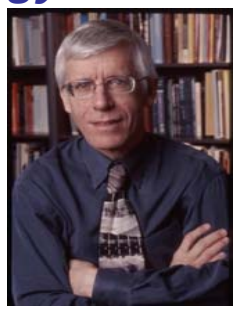
- **Michelle L. Bell - Yale**
- **Francesca Dominici**
- **Aidan McDermott**
- **Roger D. Peng**
- **Jonathan M. Samet**
- **Scott L. Zeger**

A Meta-Analysis of Time-Series Studies of Ozone and Mortality With Comparison to the National Morbidity, Mortality, and Air Pollution Study. *Epidemiology* 2005

Ozone and Short-term Mortality in 95 US Urban Communities, 1987-2000. *JAMA* 2004

Airborne particulate matter and mortality: timescale effects in four US cities. *American Journal of Epidemiology* 2003

REVISED ANALYSES OF THE NATIONAL MORBIDITY, MORTALITY, AND AIR POLLUTION STUDY: MORTALITY AMONG RESIDENTS OF 90 CITIES



J Toxicol Environ Health A. 2005

Fine particulate air pollution and mortality in 20 U.S. cities, 1987-1994. *New England Journal of Medicine* 2000

National maps of the effects of particulate matter on mortality: exploring geographical variation. *Environmental Health Perspectives* 2003

Seasonal Analyses of Air Pollution and Mortality in 100 US Cities

American Journal of Epidemiology 2005

Overall Research Plan

- **Multi-site time series studies for estimating short-term effects of PM and PM components on mortality and hospitalization (Phase I)**
- **Cohort studies based on the National Medicare Cohort for estimating longer-term effects of PM and PM composition in susceptible populations and for cause-specific health outcomes (Phase II)**
- **Assess coherence of evidence from bioassays and epidemiological studies on PM toxicity and susceptibility; and explore linkages of sources of harmful PM components to human health risks. (Phase III)**

Aims of Phase I

1. Characterize spatial and temporal variability of $PM_{2.5}$, $PM_{2.5}$ components, across the US;
2. Estimate short-term effects of fine particles on hospitalization and mortality for cities and regions;
3. Investigate whether spatial and seasonal variability of $PM_{2.5}$ components explains spatio-temporal variability of short-term effects of $PM_{2.5}$

Aim 1: Characterize spatial and temporal variability of $PM_{2.5}$ and $PM_{2.5}$ components

Research Plan

- Acquisition of EPA $PM_{2.5}$ speciation data
- Cleaning of this dataset
- Literature review on sources of various $PM_{2.5}$ components
- Generation of maps (yearly, seasonal) of PM components
- Factor analysis
- Second stage analysis on $PM_{2.5}$ components and hospital admissions

Aim 2: Estimate short-term effects of fine particles on hospitalization and mortality

Aim 3: Investigate whether spatial and seasonal variability of the $PM_{2.5}$ components explains spatio-temporal variability of short-term effects of fine particles on health estimated in Aim 1

Cohort studies based on the National Medicare Cohort for estimating longer-term effects of PM and PM composition in susceptible populations and for cause-specific health outcomes (Phase II)

Project 2:
PM Exposure Characterization

PI: Pat Breysse

Research Team

- **Patrick Breysse**
- **Steven Chillrud - LDEO**
- **Saugata Datta - GC&SU**
- **Alison Geyh**
- **John Ondov - UMD**
- **James Ross - LDEO**

Evaluation of a personal and microenvironmental aerosol speciation sampler (PMASS).
***Research Reports of the Health Effects Institute* 2004**

Accumulation of metals, trace elements and semi-volatile organic compounds on exterior window surfaces in Baltimore. *Environmental Pollution* 2003

Respiratory effects of inhalation exposure among workers during the clean-up effort at the World Trade Center disaster site. *Environmental Research* 2005

Indoor exposures to air pollutants and allergens in the homes of asthmatic children in inner-city Baltimore. *Environmental Research* 2005

Impact of the 2002 Canadian forest fires on particulate matter air quality in Baltimore city. *Environmental Science & Technology* 2005

Ambient Urban Baltimore Particulate-induced Airway Hyperresponsiveness and Inflammation in Mice. *AJRCCM* 2001

Assessing Truck Driver Exposure at the World Trade Center Disaster Site: Personal and Area Monitoring for Particulate Matter and Volatile Organic Compounds During October 2001 and April 2002 *J Occup Environ Hyg* 2005

Project 2 Focus

"*The diversity of PM characteristics and the array of possible health effects define a potentially large and complex matrix for investigation; in fact different features of particles might be relevant to different health outcomes" (NRC 2004)*

- Assessment of specific chemical components and physical characteristics of particulate matter (PM) from samples taken in different areas of the country
  - Locations selected based on a gradient of estimated risks to health (**Project 1**)

Overall Research Plan

- Develop methods for collecting bulk PM and for detailed characterization (Phase I)
- Collect PM samples at selected locations across the country and complete a detailed characterization of the samples (Phase II)
- Assess exposures to $PM_{2.5}$ and selected components and risk for adverse effects (Phase III)

Aims

- **To develop new methods for collecting bulk PM for use in biological assays**
- **To develop a mobile monitoring station for the characterization of chemical and physical properties of ambient PM**
- **To identify specific regional differences in PM characteristics that may contribute to differential biological responses in *in vitro* and *in vivo* bioassay systems**
- **To assess the relationship between human exposure to $PM_{2.5}$ and biological response indicators during high $PM_{2.5}$ and low $PM_{2.5}$.**

Phase I Goals

- **Development of specific methods and protocols that will be used throughout the five years of the Center**
  - **Develop PM collection**
    - **Provide PM for detailed bioassays which will be carried out within Project 3**
  - **Develop a mobile ambient air monitoring station**
    - **Characterization of chemical and physical properties of ambient PM**
  - **Field test in Baltimore and elsewhere**

Bulk Collection

- **Goal is to collect PM from ambient air in sufficiently large quantities for the various biologic assays proposed in Project 3**
- **We have experience in collecting bulk PM from ambient air and occupational settings**
  - **Single cyclones or cyclone cascades**
- **Estimate need for approximately 0.5 – 1.0 g of PM for each cut size**
  - **Using a bulk PM collection flow rate of 1 m^3/min we should be able to collect sufficient mass for testing in approximately 4 weeks**

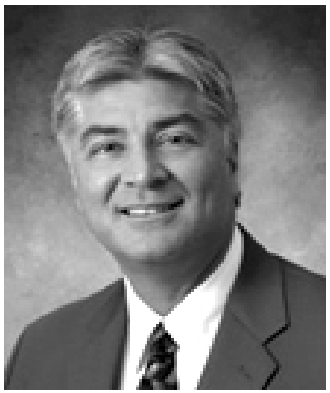
Mobile Air Monitoring Station

- Develop a mobile air monitoring station
  - Characterization of chemical and physical properties of ambient PM
- Collaboration with University of Maryland
  - Baltimore Super Site
- Described in Exposure Assessment Core

Project 3:
Biological Assessment

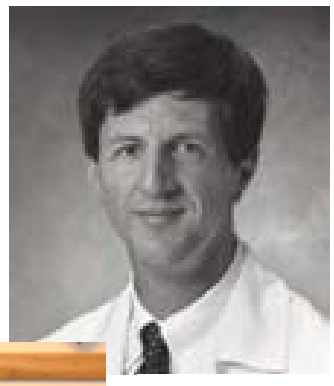
PI's: Skip Garcia

Bill Spannhake

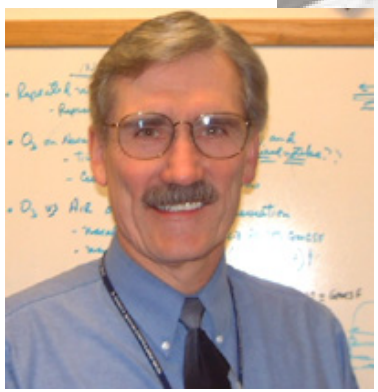


Gene expression analysis of ischemic and nonischemic cardiomyopathy: shared and distinct genes in the development of heart failure
***Physiol Genomics* 2005**

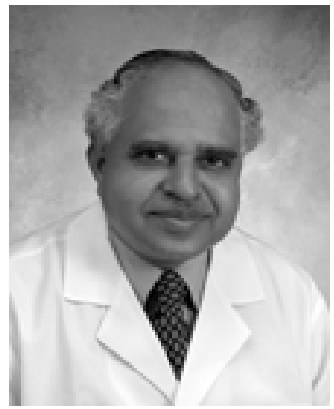
Transcriptional regulation of lysophosphatidic acid-induced interleukin-8 expression and secretion by p38 MAPK and JNK in human bronchial epithelial cells. *Biochem J* 2005



Bioinformatic identification of novel early stress response genes in rodent models of lung injury. *Am J Physiol Lung Cell Mol Physiol* 2005



Signaling Pathways Involved in Adenosine Triphosphate-Induced Endothelial Cell Barrier Enhancement
***Circulation Research* 2005**



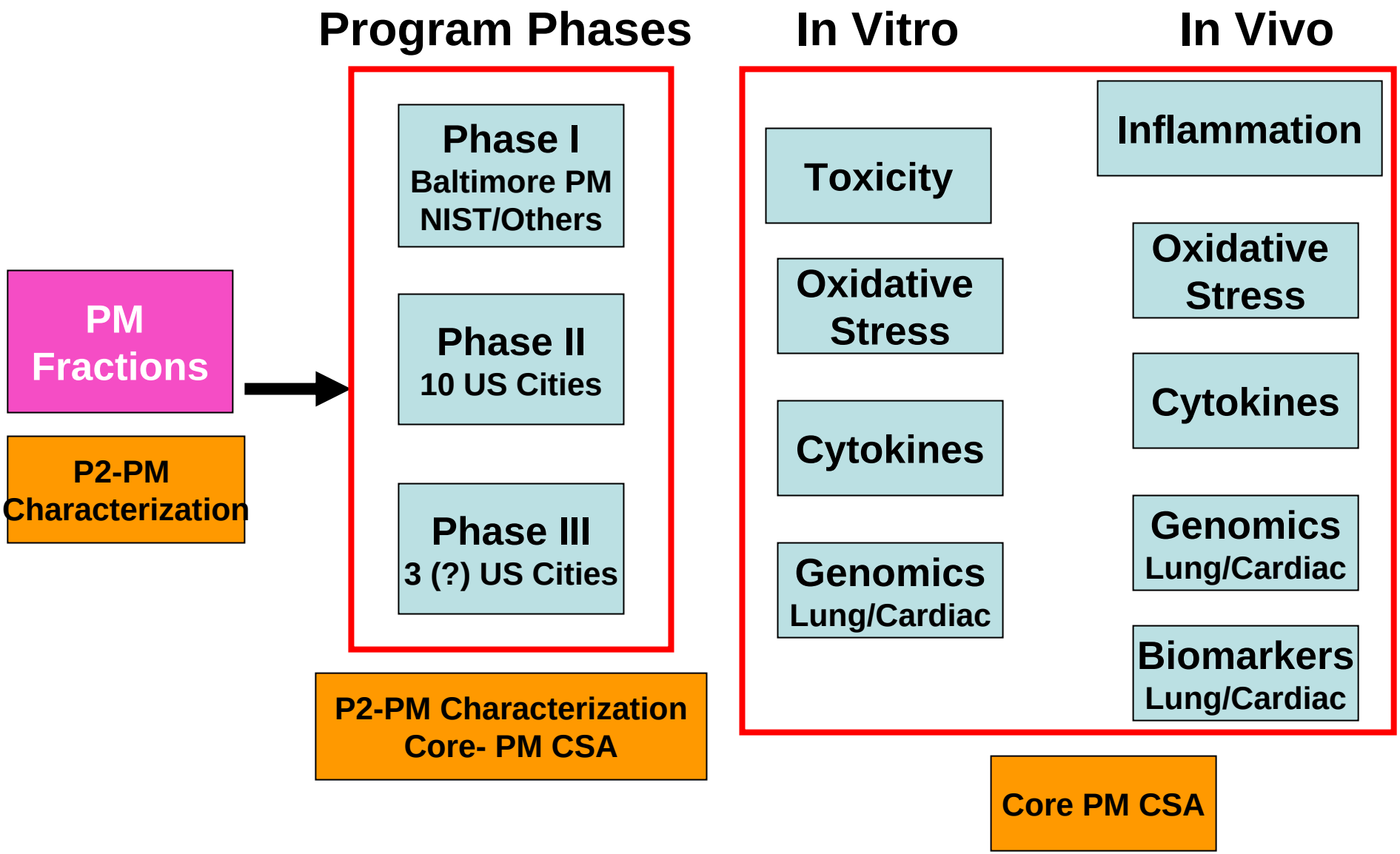
Repetitive Ozone Exposure of Young Adults. Evidence of Persistent Small Airway Dysfunction. *AJRCCM* 2001

Synergism between rhinovirus infection and oxidant pollutant exposure enhances airway epithelial cell cytokine production. *Environ Health Perspect.* 2002

Research Team

- **Rey DeCastro**
- **Joe (Skip) Garcia**
- **Rafael Irizarry**
- **Liliana Moreno**
- **Viswanathan Natarajan**
- **E. (Bill) Spannhake**
- **Eric Svensson**

Integration of Biological Assessments (Project 3) with other JHU Projects/Cores



Overall Research Plan

- **To characterize secretion of inflammatory cytokines/chemokines in human bronchial epithelial cells induced by PM.**
- **To characterize airway inflammation in murine models of lung and cardiac injury induced by PMs.**
- **To evaluate the role of ROS in PM-induced in vitro and in vivo cardiac and airway inflammation and toxicity.**
- **To link in vitro and in vivo gene expression patterns induced by PM with morbidity and mortality rates of the city where the sample was collected.**
- **To link fluctuations in ambient PM levels with relevant biomarkers (cytokines, epithelial/endothelial activation, peripheral blood mononuclear cell gene expression, exhaled breath condensates) in a panel of PM exposed human subjects.**
- **To characterize signaling mechanisms of PM-induced secretion of inflammatory cytokines/chemokines and ROS burden in human bronchial epithelial cells.**

Phase I (Years 1 – 2)

- **Develop in vitro (human epithelial) and in vivo (murine) models of cardiopulmonary effects of particulate matter (PM)**

- **PM having differing characteristics (Project 2) will be evaluated for release of cytokines, ROS/RNS and biomarkers for vascular and cardiac functions:**

- **PM mediated gene expression profiles in human lung epithelial cells and murine lung and cardiac tissues.**

Phase II (Years 2 – 3)

- **Evaluate PM fractions from 10 sites for cellular, animal models and toxicogenomic effects.**

- **PM will be screened for release of cytokines, ROS/RNS, and vascular/cardiac biomarkers and function.**

- **Toxicity of PM components, mechanisms of injury and susceptibility will be studied with in vitro and animal models.**

Phase III (Years 3 – 5)

- **Characterize biochemical, toxicological and molecular mechanisms of signal transduction underlying PM-induced airway inflammation and cardiac dysfunction.**

- **PM from potentially informative locations identified in Projects 1 & 2 will be tested.**

- **In addition to human bronchial epithelial cells, human alveolar epithelial cells/cell lines and human microvascular ECs will be used to evaluate PM mediated signal transduction, toxicity and pulmonary genomics.**

The PM CSA Core

PI: Alison Geyh

Purpose of the Core

- Central resource for PM sampling and analysis to support the research projects.
  - **establishment of the mobile PM monitoring station**
  - **transport and maintenance of mobile monitoring station**
  - **support for bulk PM sample collection**
  - **sample handling and analytical support for evaluation of PM samples**

Resources

Source	Resource
• EPA U MD Baltimore Supersite	• ●8 x 24' Portable Air Monitoring Trailer; ●Sunset ECOC Analyzer; ●Scanning Mobility Particle Sizer (SMPS, TSI Inc., model 3080), ●R&P 8400 N Ambient Particulate Nitrate Monitor; ●Harvard Ambient Sulfate Monitor; ●Marple Virtual Impactor 1000 L/min Filter-based Bulk PM Collector; ●Mico-orifice 10 Stage Cascade Impactor
• NIEHS Center for Urban Environ. Health	• ●TSI Model 3320 Aerodynamic Particle Sizer; ●MSP PM_{10} and $PM_{2.5}$ Sampling Inlets; ●Personal and Microenvironmental Sampling Pumps; ●DataRam Nephelometers; ●Field/Laboratory Technician; ●Mettler MT-5 Microbalance; ●Primary gas flow calibrator Bios DryCal DC-2
• EPA/NIEHS CCAUE	• ●Baltimore Ambient Monitoring Station including Davis Met. Station, R&P TEOM, R&P $PM_{2.5}$ FRM, Andersen Dichot Sampler; ●PM_{10} and $PM_{2.5}$ MSP inlets; ●BGI 5 L/min Pumps; ●Cyclone PM Bulk Collector
• EPA Baltimore Traffic Study	• ●Particle-bound PAH (EcoChem PAS2000); ●Therm Electron 48C CO monitor; ●Therm Electron 42C NOx monitor; ●Thermo Electron Model 146C Dynamic Gas Calibrator; ●BGI 5 L/min pumps; ●Medo 30 lpm pumps; ●10 L/min PM_{10} and $PM_{2.5}$ Harvard Impactors

Planned analyses

Filter and bulk PM samples will be analyzed for:

- **mass**
- **inorganic ions**
- **organic components**
- **PAHs**
- **elements**
  - **oxidation states of elements of importance**

The Data Core

PI: Aidan McDermott

Objectives

- **Maintain and update existing pollution database**
- **Update other data**
- **Integrate PM Characterization data and Biological studies**
- **Relation Builder**
- **Web based interface**

Meanwhile, back in Baltimore….