

# Organization

## EPA Airborne Particulate Matter Center, Univ. of Rochester

### *Source Specific Health Effects of Ultrafine/Fine Particles*

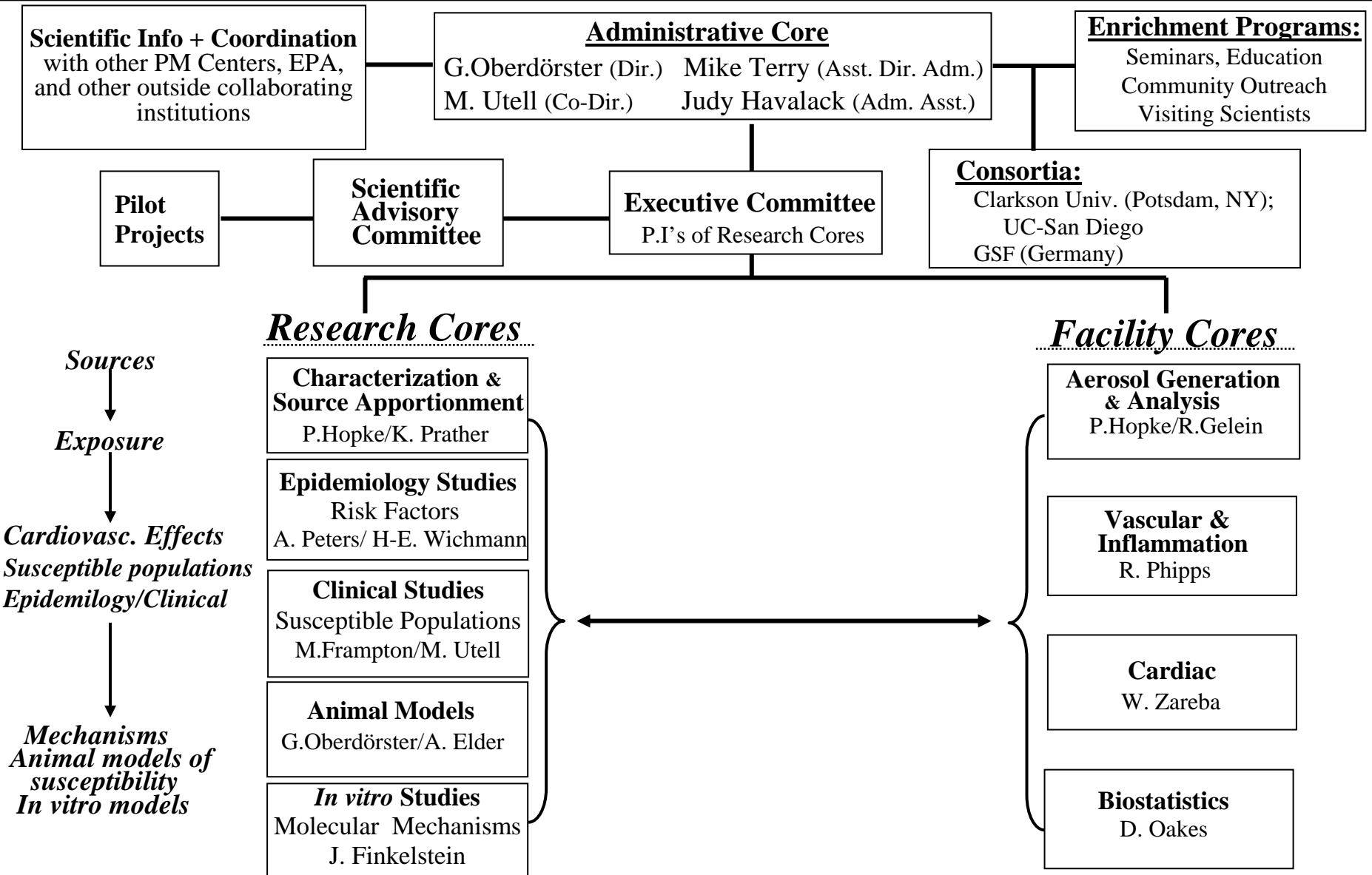
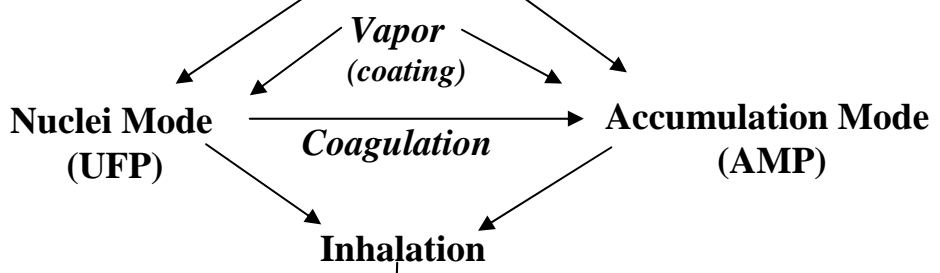


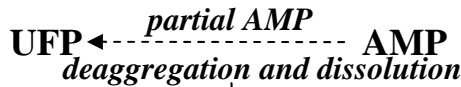
Figure 3.1

*EMP - endothelial microparticles*  
*PMP - platelet microparticles*  
*EPC - endothelial precursor cells*  
*ANS - autonomic nervous system*  
*CNS - central nervous system*  
*TB - tracheobronchial*  
*NP - nasopharyngeal*

**SOURCES OF FINE PM**



**Respiratory Tract Deposition**



**Translocation of UFP to interstitium, capillaries, heart** *(direct effects)*

**Uptake by endothelium; platelets**

**Activation/interaction of endothelial cells, platelets and leukocytes**

**Release of EMP, PMP, cytokines**

**Increased coagulability thrombus formation**

**Plaque rupture**

**Endothelial dysfunction, vasoconstriction**

**Cardiac events**

**Stroke**

**Acceleration of atherosclerosis**

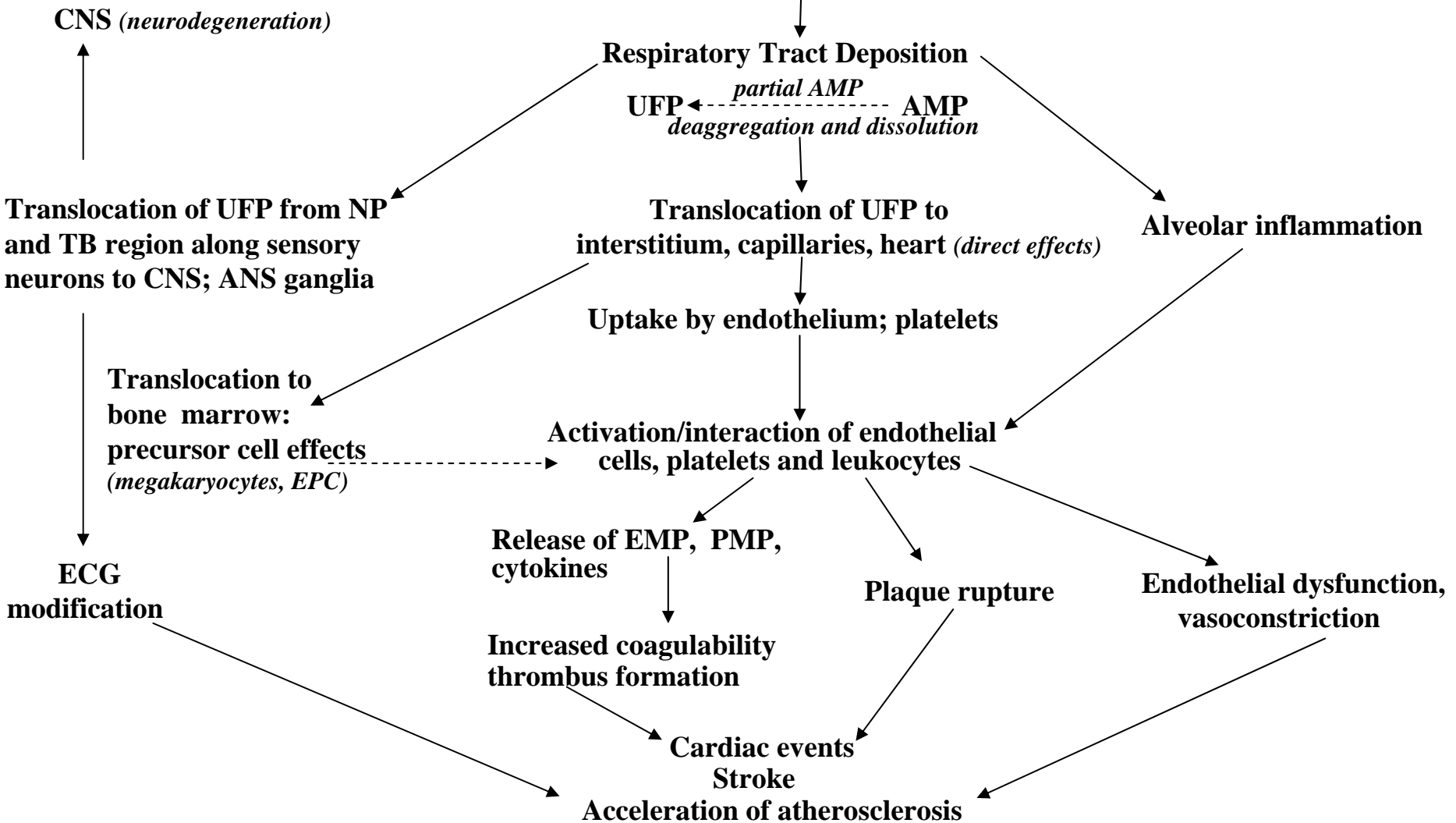
**Alveolar inflammation**

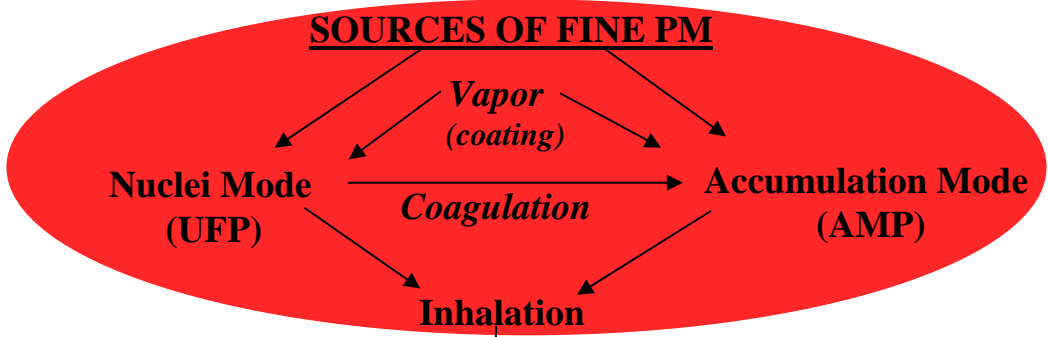
**CNS** *(neurodegeneration)*

**Translocation of UFP from NP and TB region along sensory neurons to CNS; ANS ganglia**

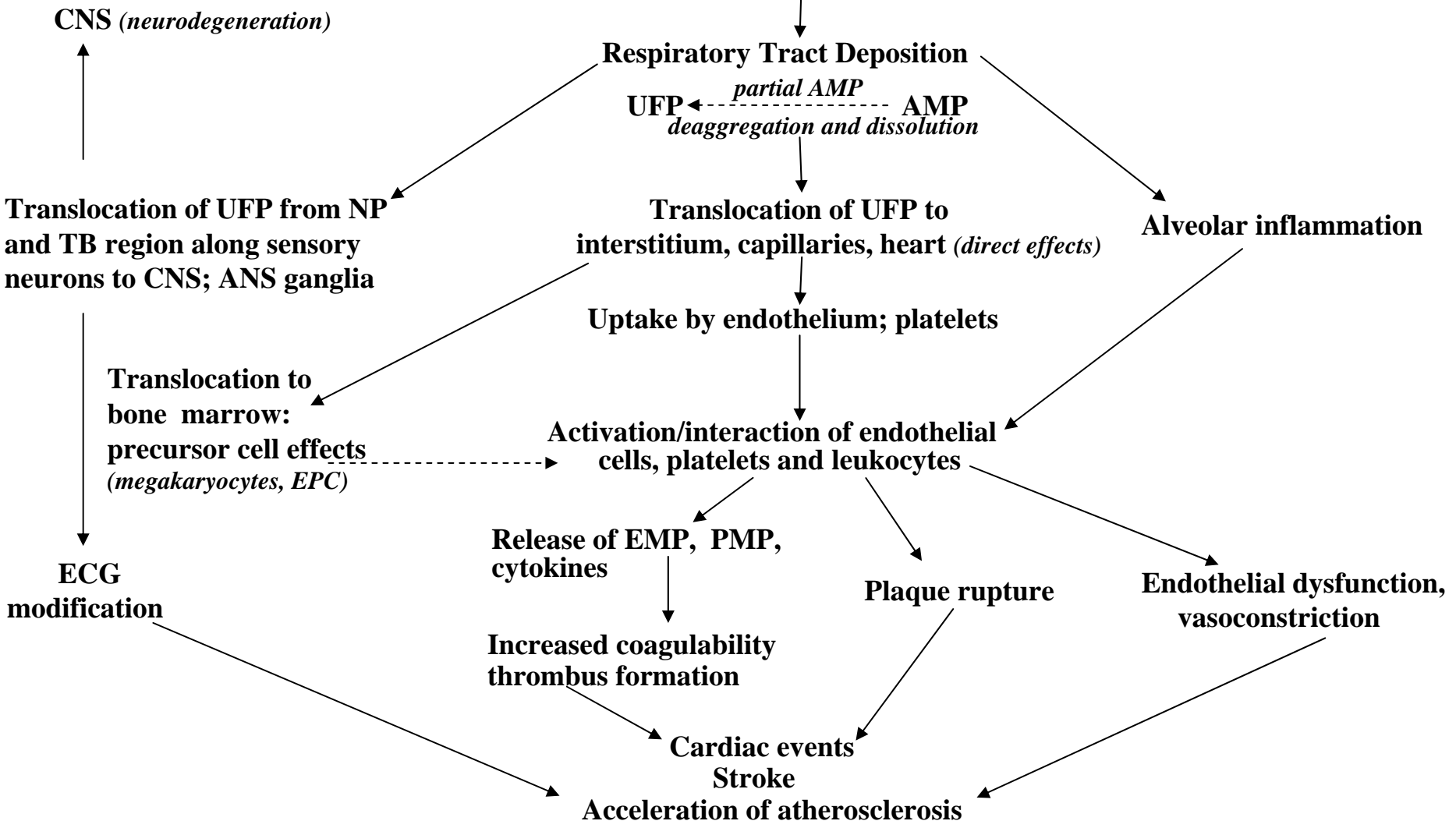
**Translocation to bone marrow: precursor cell effects** *(megakaryocytes, EPC)*

**ECG modification**

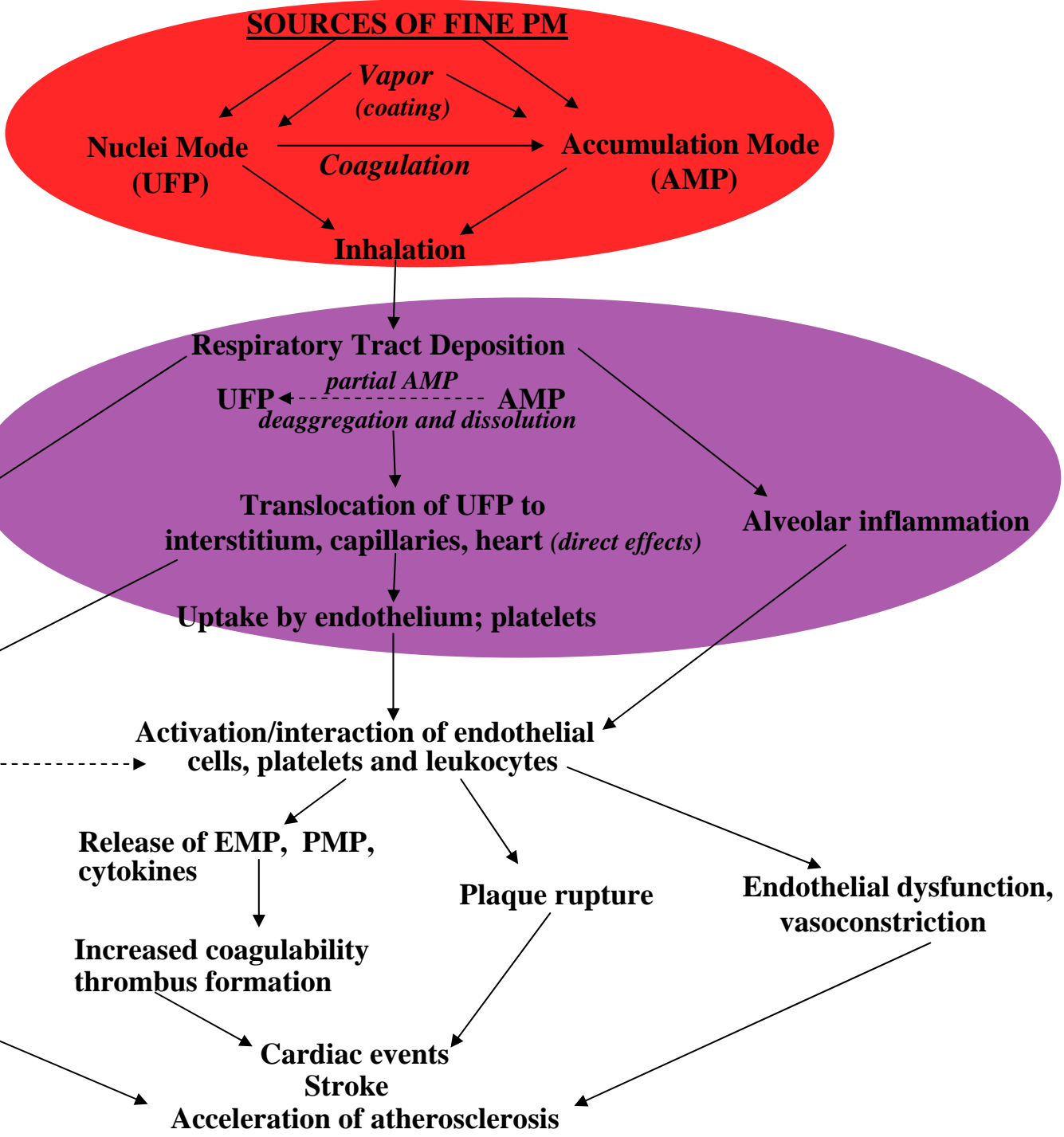




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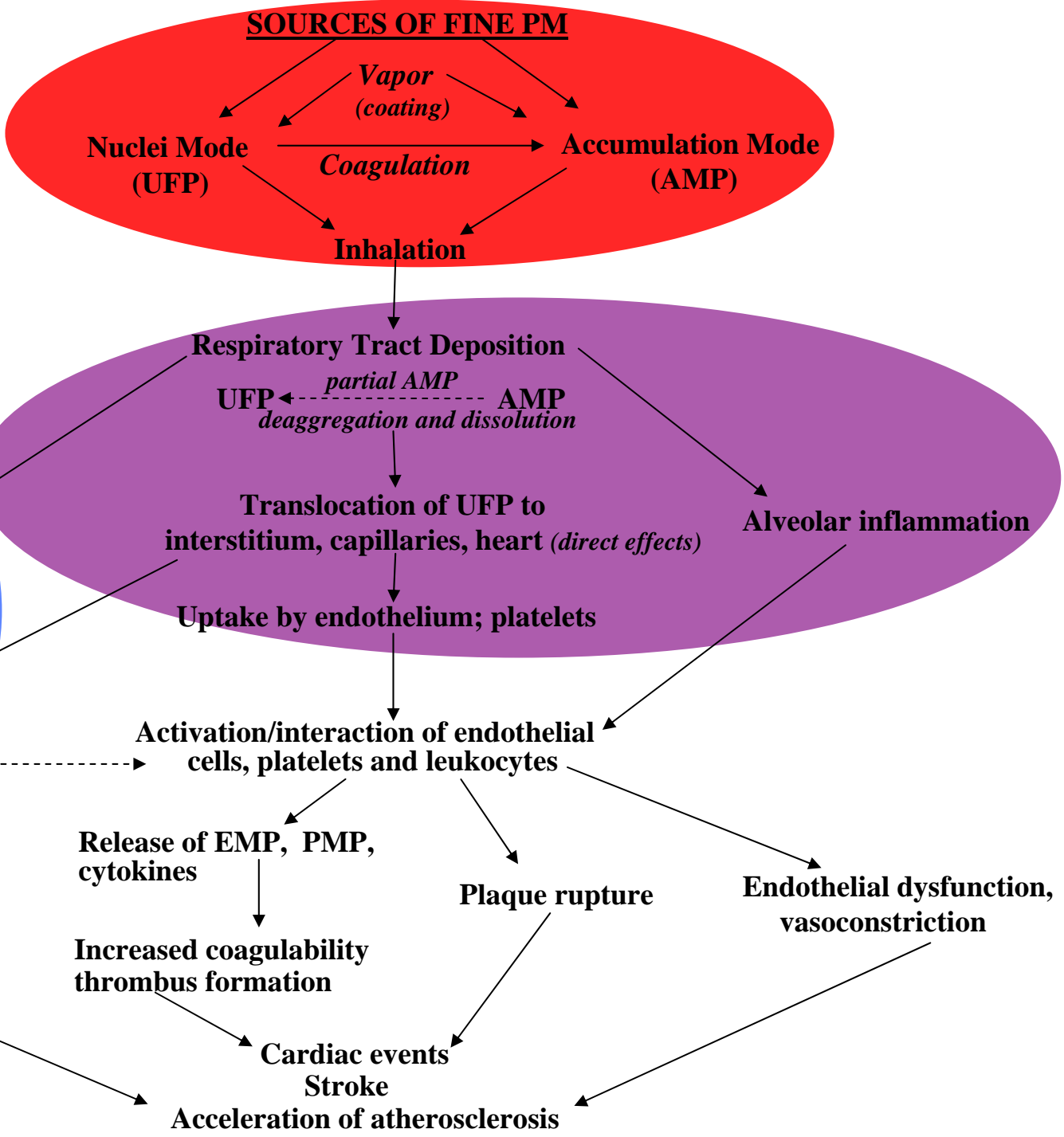
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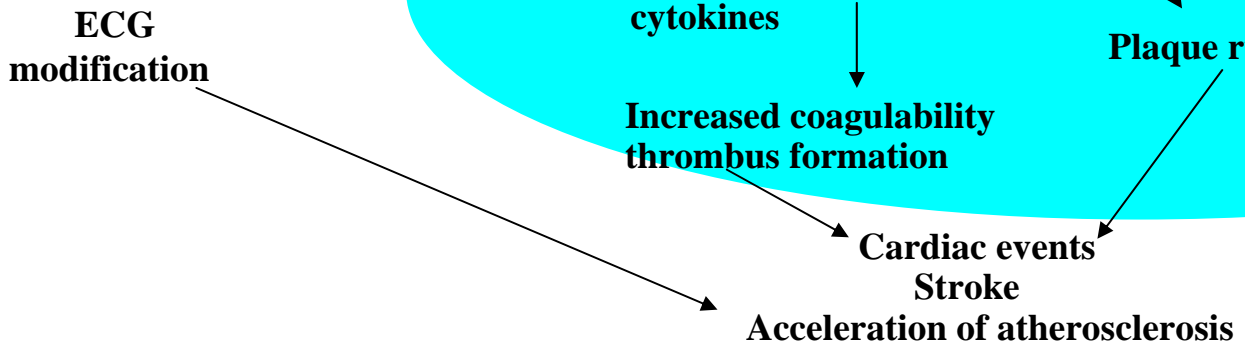
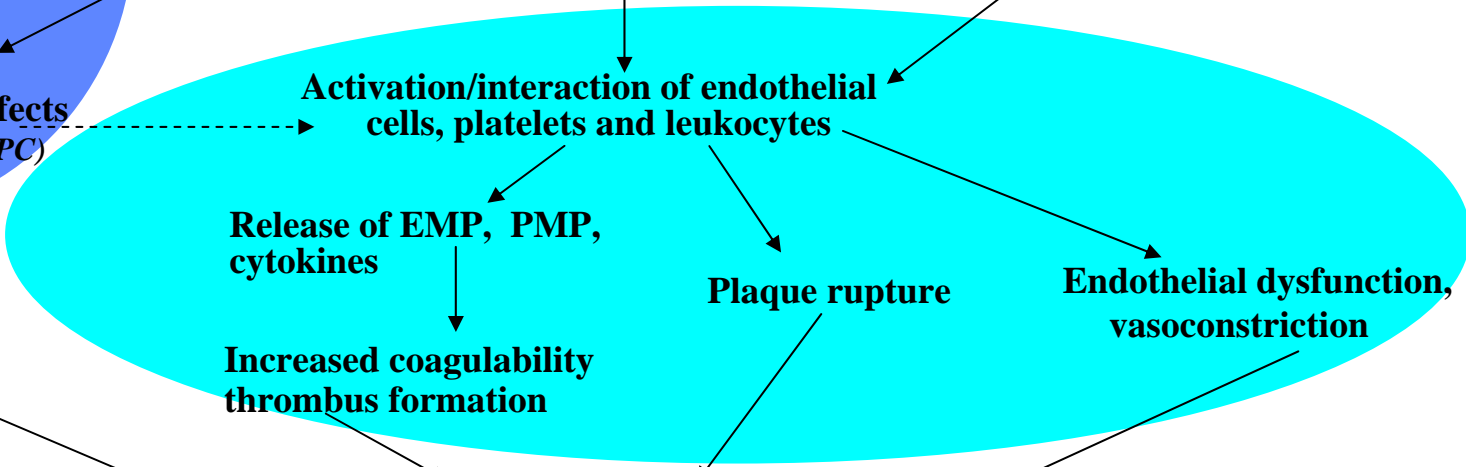
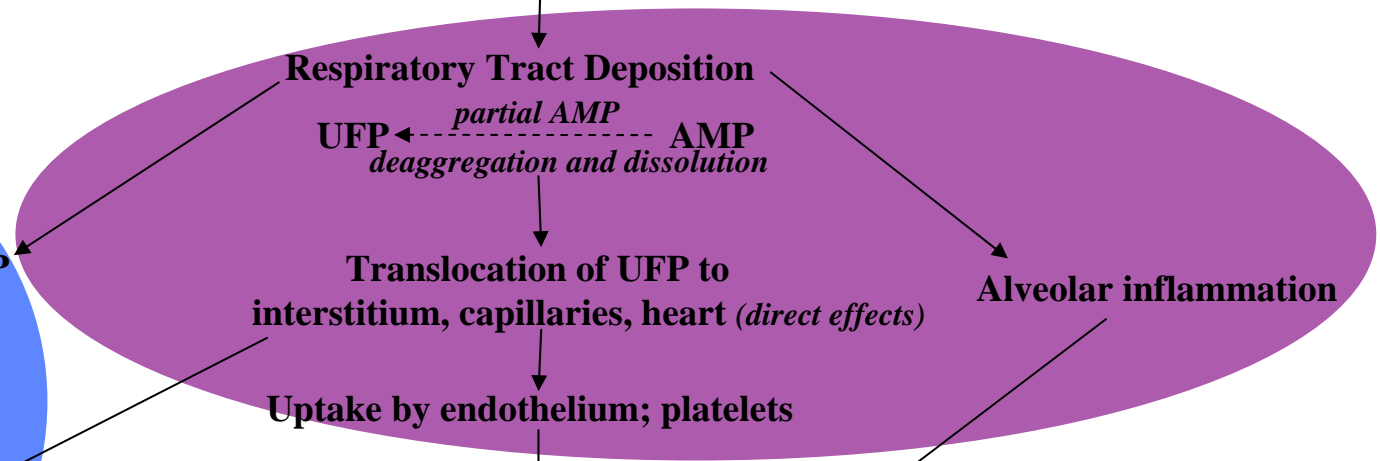
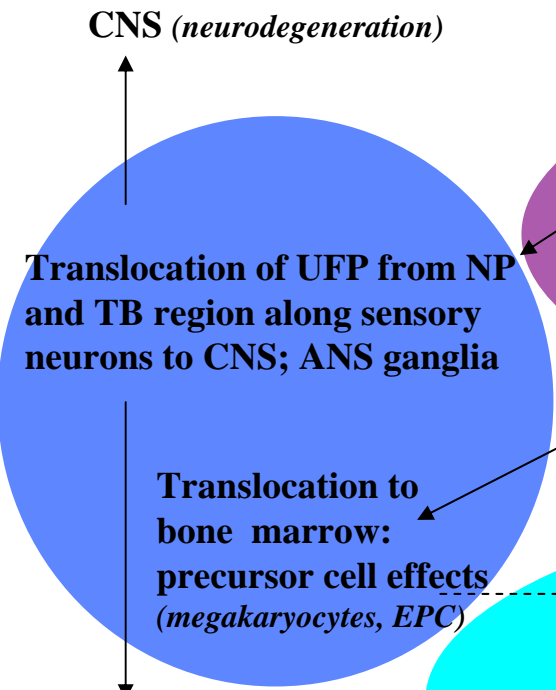
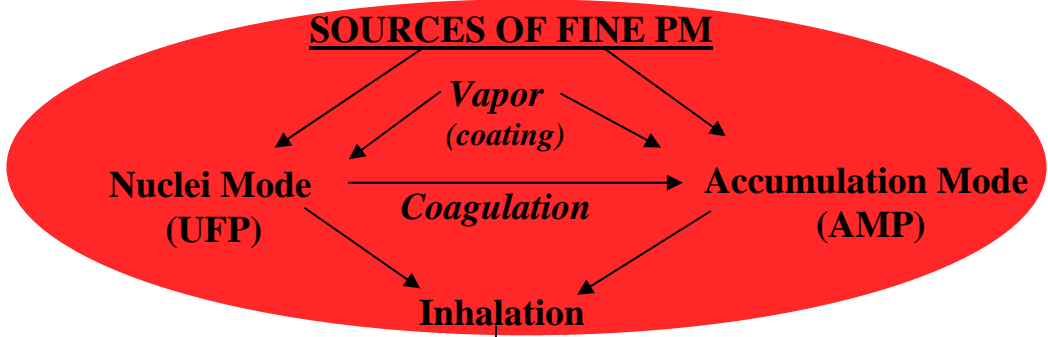
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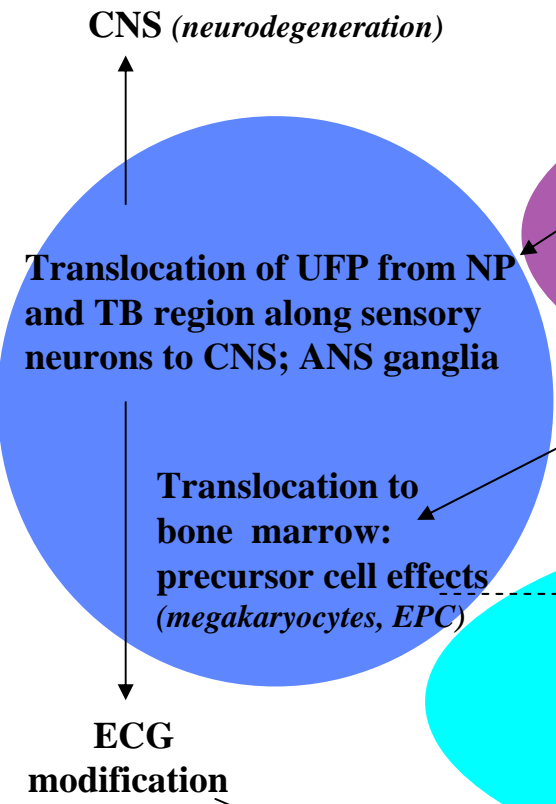
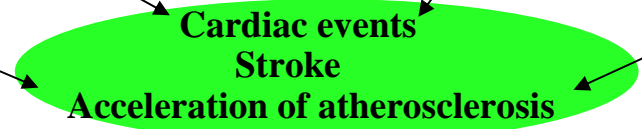
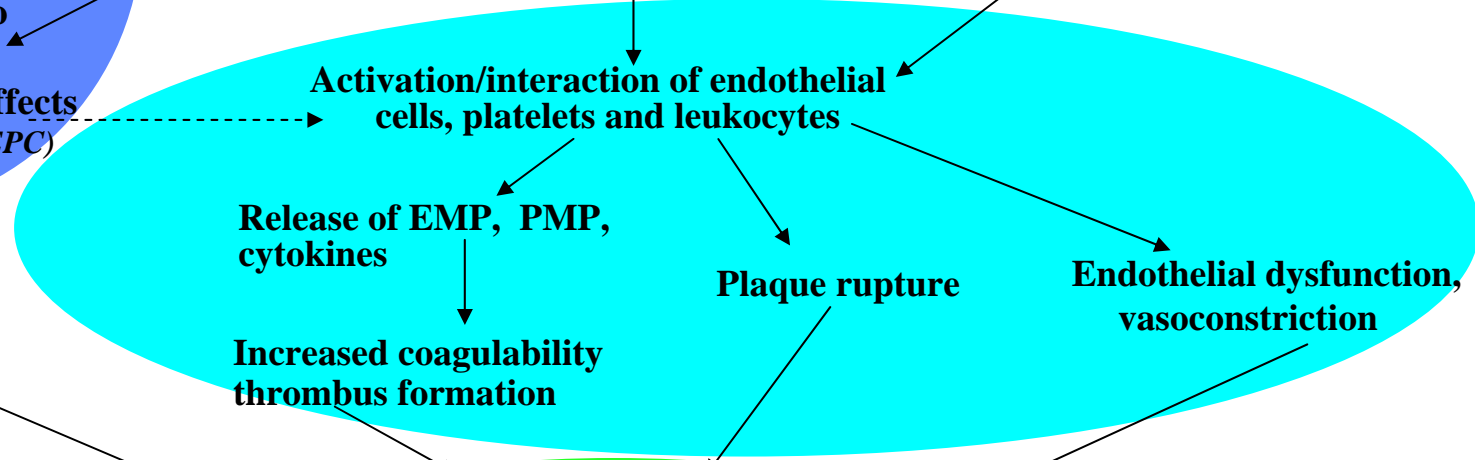
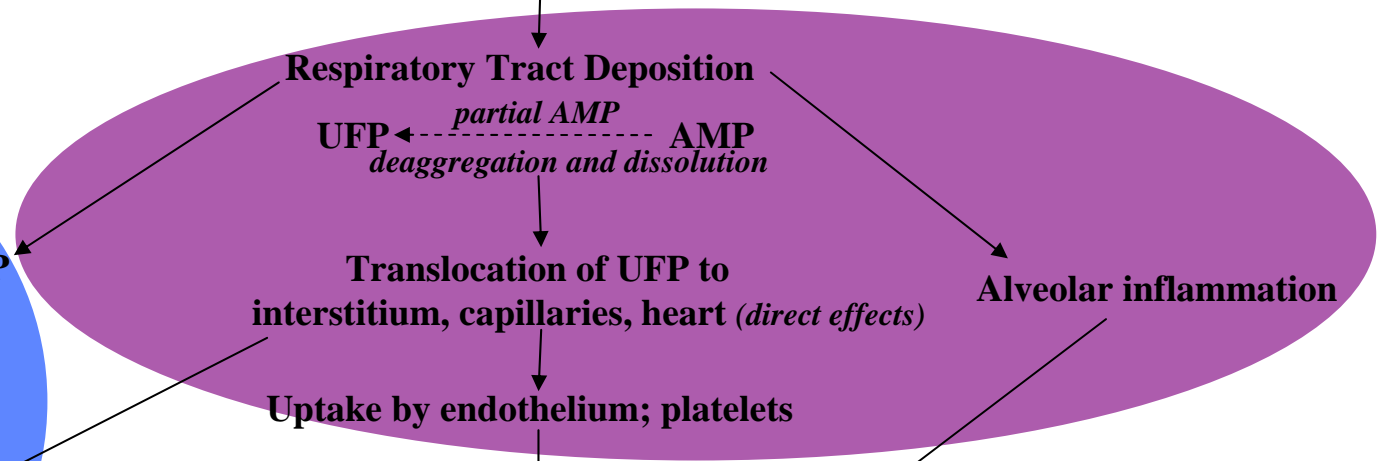
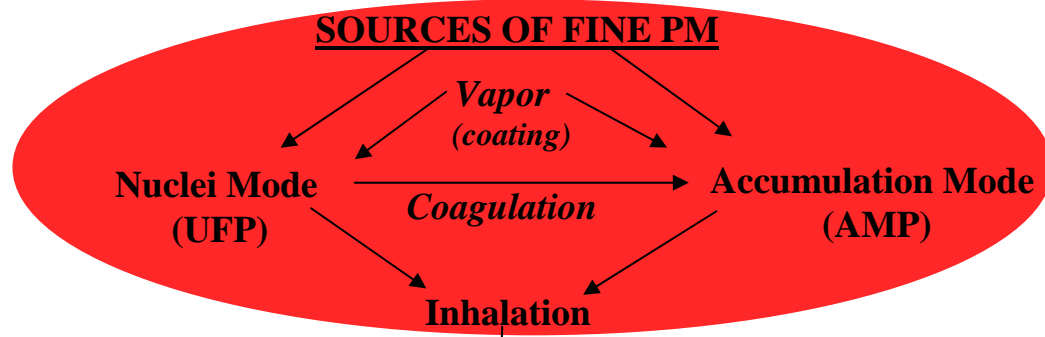
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ECG modification

Translocation of UFP from NP and TB region along sensory neurons to CNS; ANS ganglia

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CNS (neurodegeneration)

# Research Core 1: Characterization of Particle-Bound ROS

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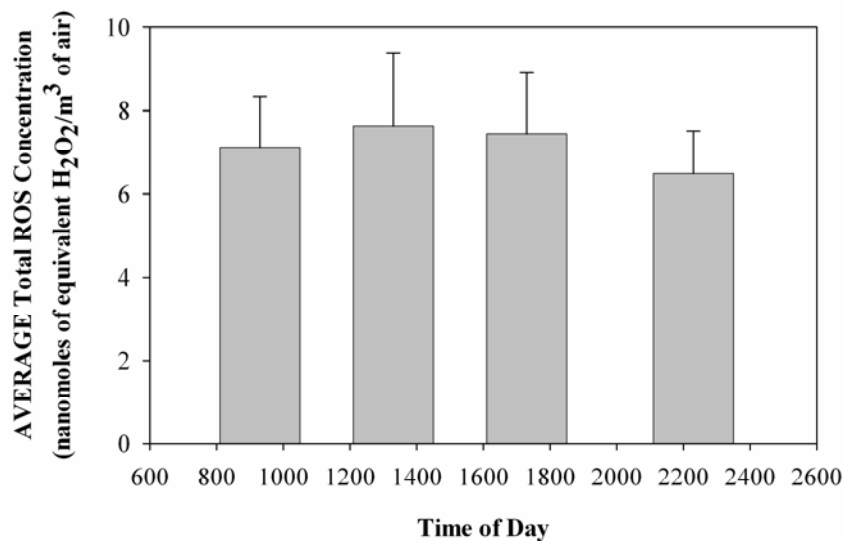
## Specific Aims

- **Aim #1. To understand the evolution of ambient particle compositions as they are transported from the sources to the receptor site with particular emphasis on the concentrations of particle-bound reactive oxidative species.**
- **Aim #2. To develop methods to characterize the sources and nature of reactive oxidative species associated with the ambient PM<sub>2.5</sub> and PM<sub>0.1</sub> particle aerosol using high resolution EPR and LC/MS.**

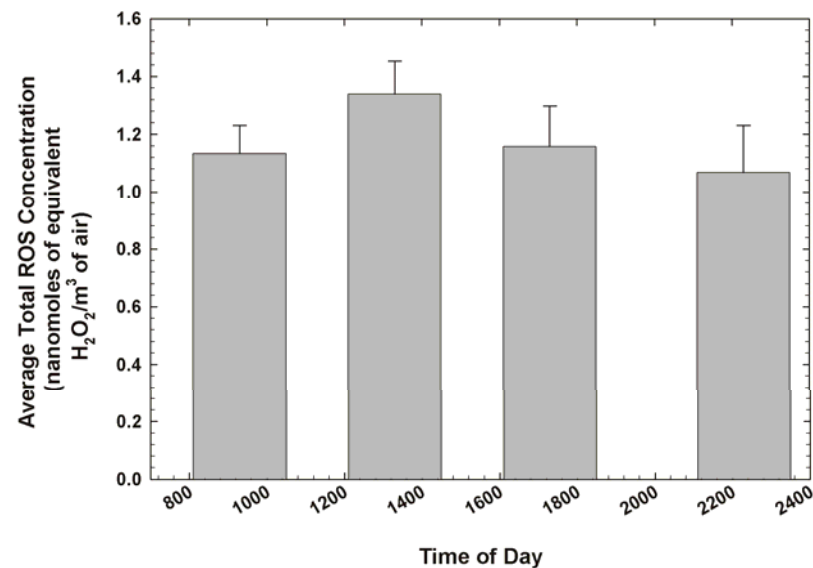


# Characterization of Particle-Bound ROS

Rubidoux July 2003

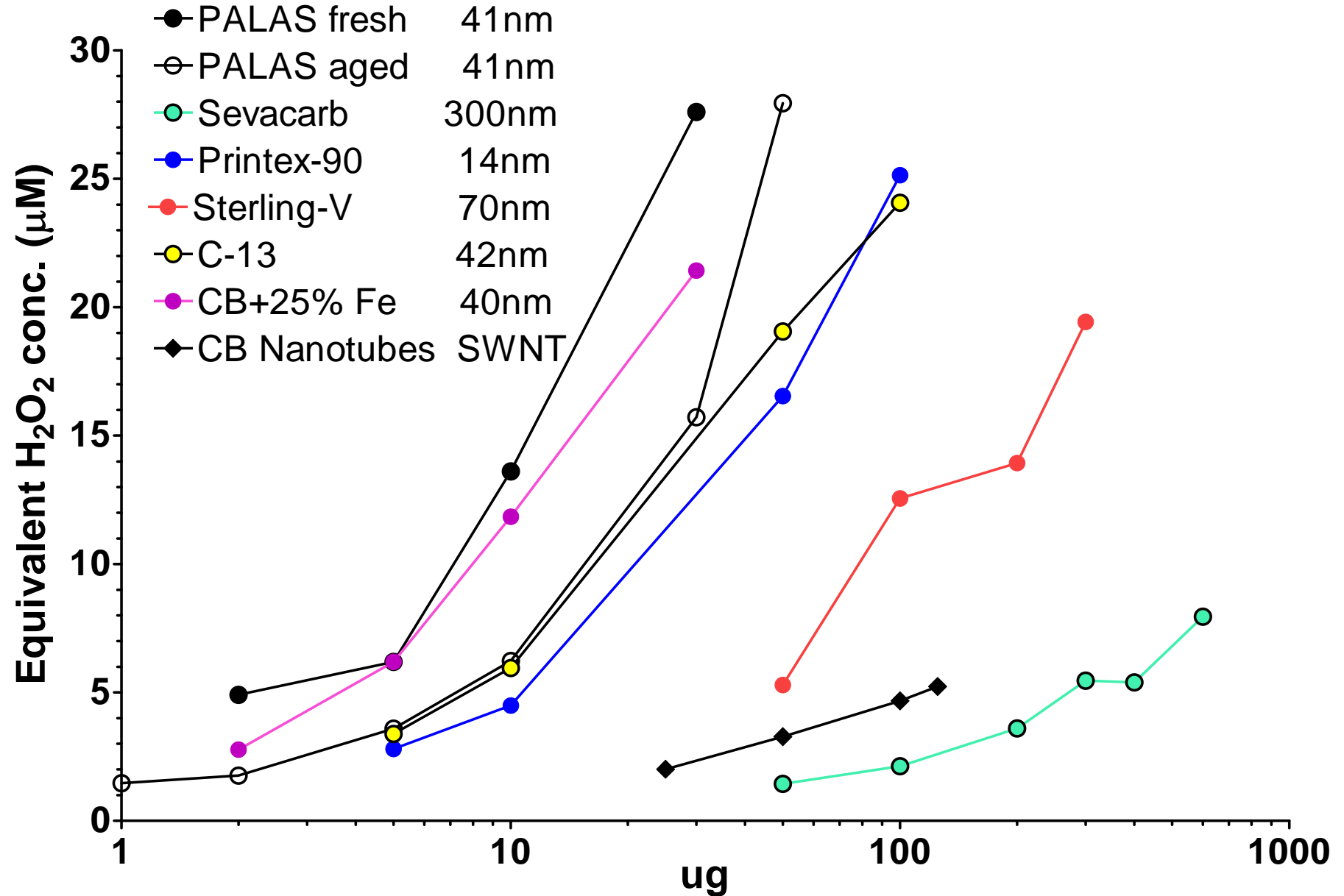


NYC January 2004



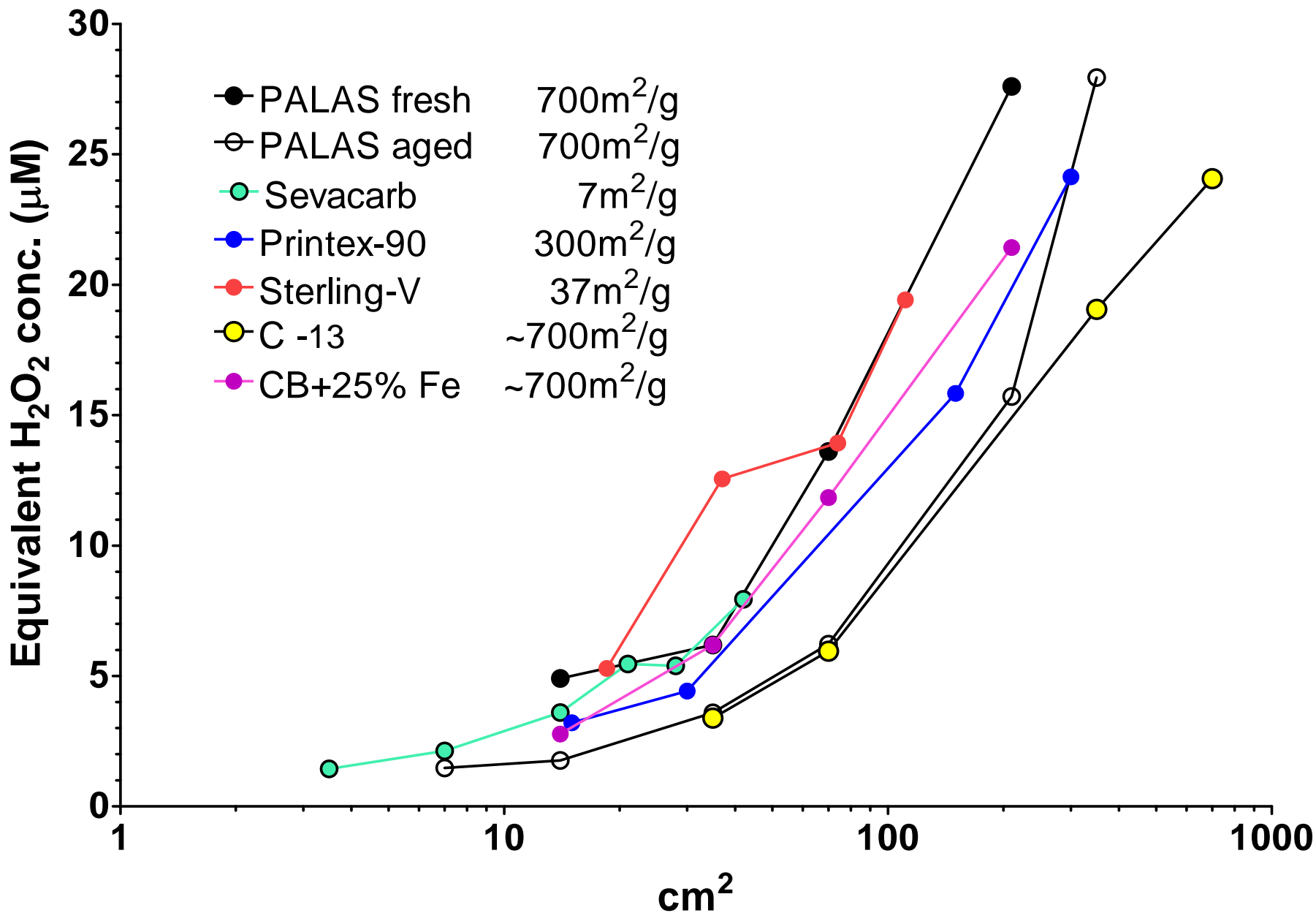
# Noncellular ROS Summary *(Carbon Particles)*

## *Particle Mass Correlation*



# Noncellular ROS Summary (Carbon Particles)

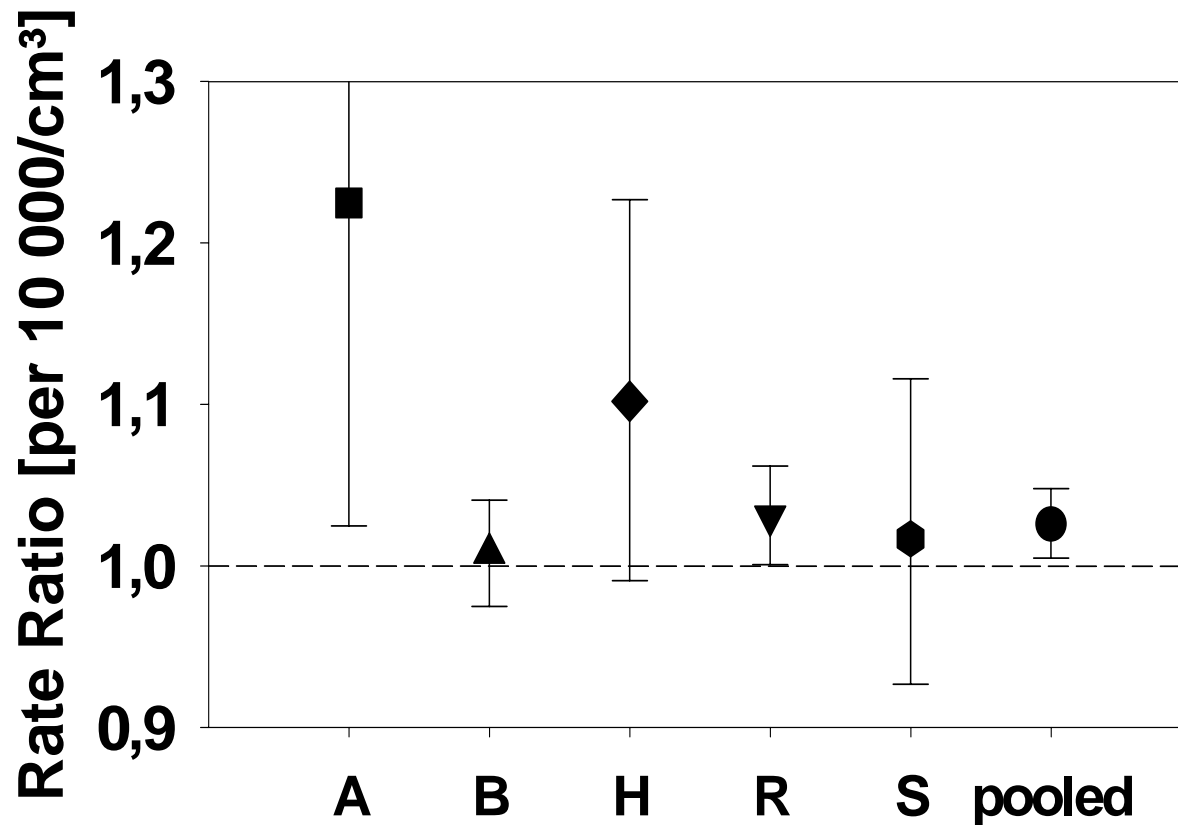
## Particle Surface Area Correlation



# Research Core 2 – Epidemiological Studies

- Panel studies in potentially susceptible subgroups
  - Diabetics
  - Myocardial infarction survivors
  - Genetically predisposed subjects
- Associations between sources of fine and ultrafine particles and inflammation and endothelial dysfunction
- ECG-sub-study assessing associations between personal particle exposures, stress and cardiac function

# Ultrafine particles and cardiac readmission in myocardial infarction survivors



Klot et al. *Circulation* 2005



# Core 2 Studies

<b>Cardiac Rehabilitation (Rochester) N=80</b>	<b>Diabetes/Myocardial Infarction (Augsburg) N=100/100</b>	<b>Inflammatory/Detoxification Polymorphisms/Controls (Augsburg) N=100/100</b>
<b>Air Monitoring</b>		
Criteria pollutants (PM <sub>2.5</sub> , SO <sub>2</sub> , CO, O <sub>3</sub> )	Criteria pollutants (PM <sub>2.5</sub> , SO <sub>2</sub> , CO, O <sub>3</sub> )	Criteria pollutants (PM <sub>2.5</sub> , SO <sub>2</sub> , CO, O <sub>3</sub> )
Particle size distribution	Particle size distribution	Particle size distribution
Particle composition (STN Network site)	Volatile particle distributions	Volatile particle distributions
Indoor particle number	Sulfates, Nitrates	Sulfates, Nitrates
	EC/OC	EC/OC
	Surface area	Surface area
<b>Measurements</b>		
Symptoms	Symptoms	Symptoms
ECG	ECG	ECG
BP & HR, rest & exercise	BP, HR	BP, HR
Blood biomarkers	Glycosylated hemoglobin	Glycosylated hemoglobin
	Genetic polymorphisms	Genetic polymorphisms
	Blood biomarkers	Blood biomarkers
	Endothelial dysfunction	Endothelial dysfunction

# Research Core 3: Human Exposures

## Objectives

### **Effects of inhaled ambient UFP in healthy and diabetic subjects:**

- Blood coagulation via effects on platelets and circulating microparticles
- Cardiac output
- Cardiac rhythm and repolarization
- Role of reactive oxygen species
- Antioxidant prevention
- Comparison to carbon particles

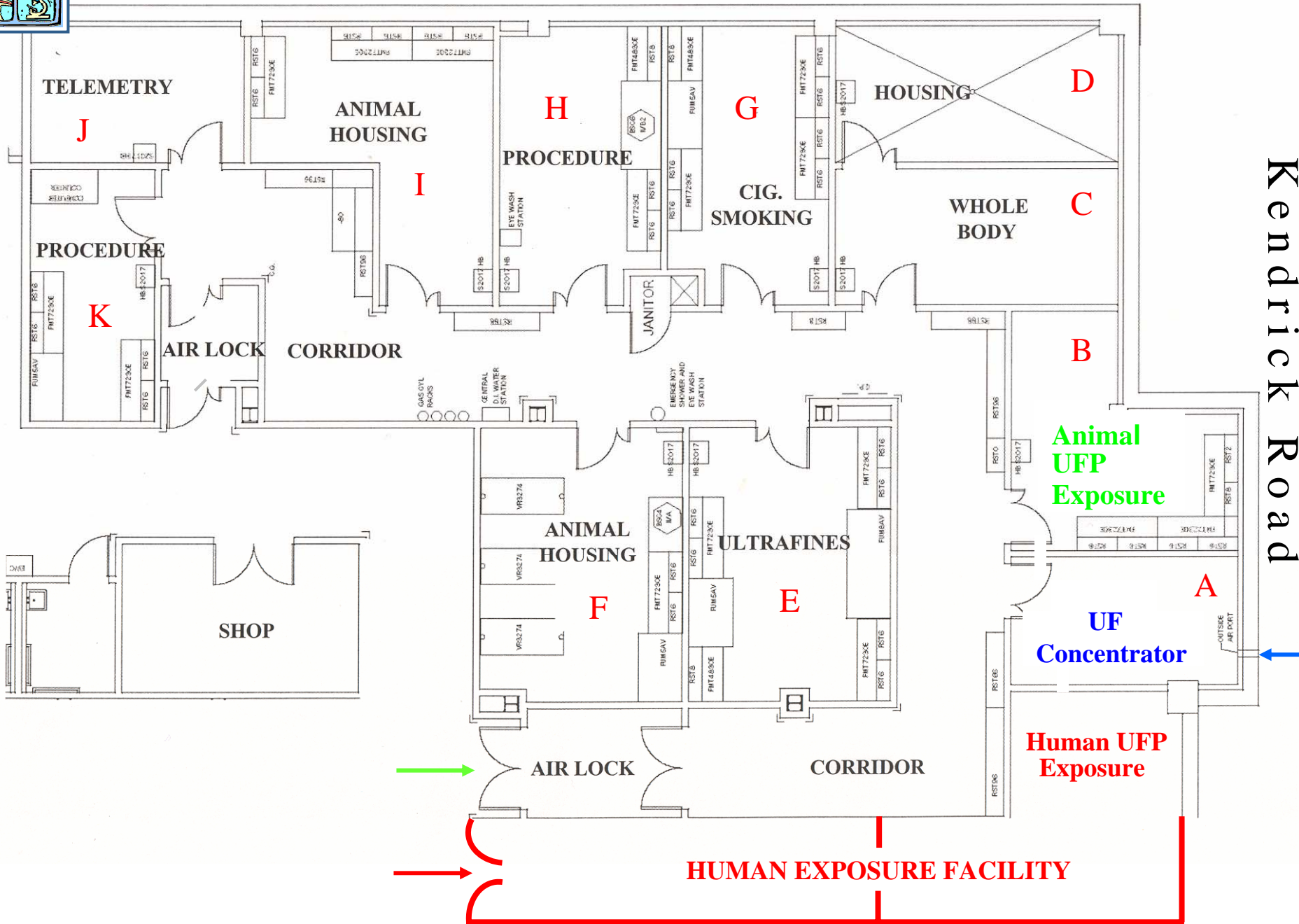
# Human Studies of Exposure to Carbon UFP

- Changes in leukocyte adhesion molecule expression
- Reduction in DLCO
- Reduced brachial flow-mediated vasodilatation
- Suggests both pulmonary & systemic vascular effects
- Preliminary findings: effects in type 2 diabetics, *at rest*
- Implications for cardiovascular disease





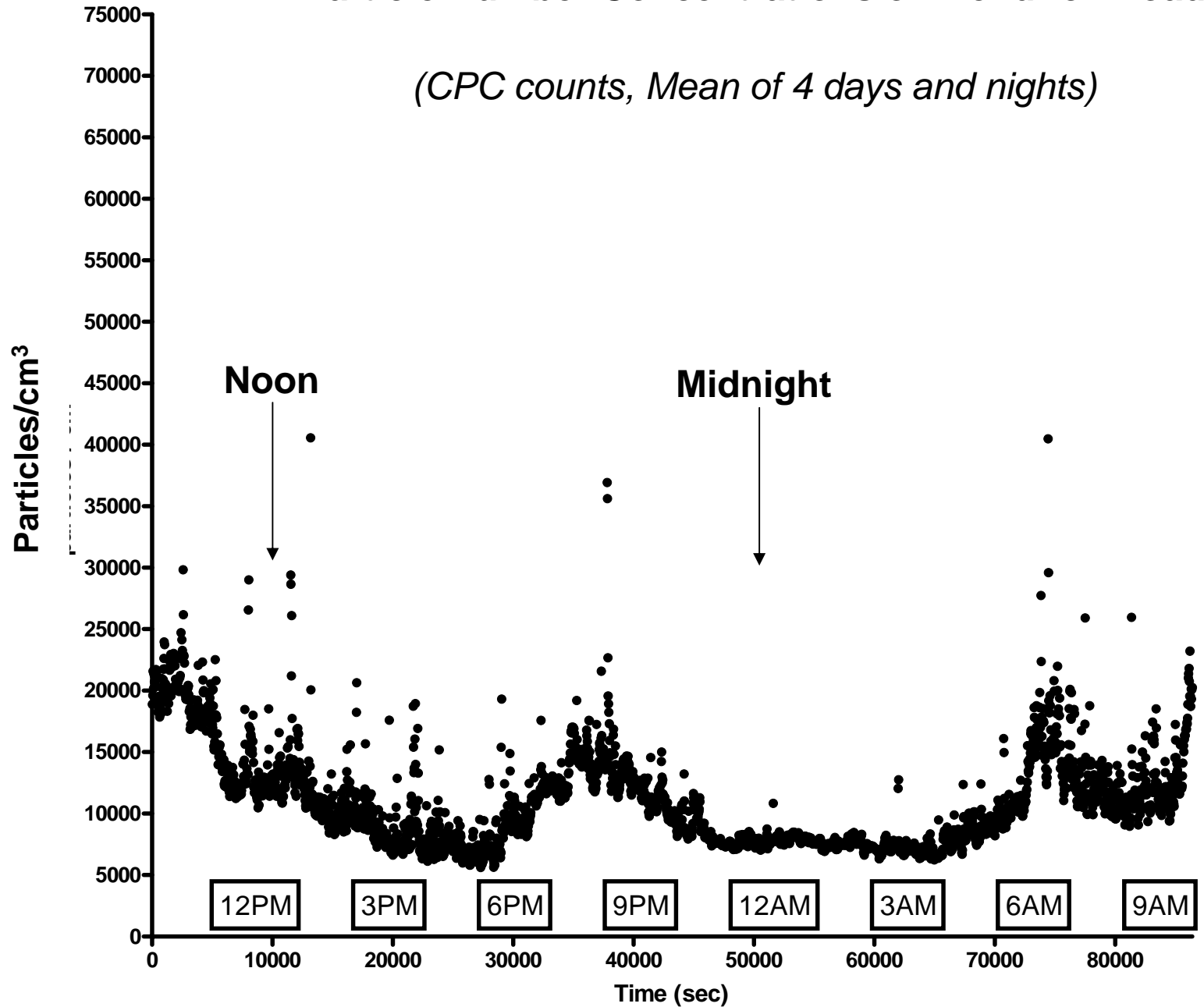
# MRBx-Inhalation Facility





# Particle Number Concentrations on Kendrick Road

*(CPC counts, Mean of 4 days and nights)*



# Research Core 4: Animal Models

**Focus on: Cardiovascular Disease; CNS injury; particle biokinetics**

- **Exposures of diabetic rats (JCR): Concentrated UFP exposures** (*acute/subchronic*)
  - On-road exposures (truck study)**
  - Intratracheal microspray exposures to UF/Fine PM** (*different sites and sources*)
    - PM physico-chemical analyses and ROS measurements
    - pulmonary and cardiovascular endpoints (*inflammatory; oxidative stress, acute phase proteins, microparticles, ECG analyses*)
    - impact of: ultra-low sulfur fuel (*less nucleation, NPs*); after device (*filter*) + NO<sub>x</sub> catalyst
- **Translocation and clearance kinetics of model and ambient UF/Fine PM** (*heart; platelets; bone marrow; spleen; brain*)
  - model particles: gold (TEM; ICPMS); <sup>13</sup>C UFP
  - neutron activation of UF/Fine PM: GeLi detector analysis; organ retention kinetics
- **Neurotoxic effects of UF/Fine PM, rats and mouse model of neurodegeneration**
  - MPTP model; mitochondrial effects (*electron transport chain function and activities; membrane potential; ROS production*)

# University of Minnesota Mobile Emissions Laboratory (MEL)

air-conditioned  
compartment



**Year 1**



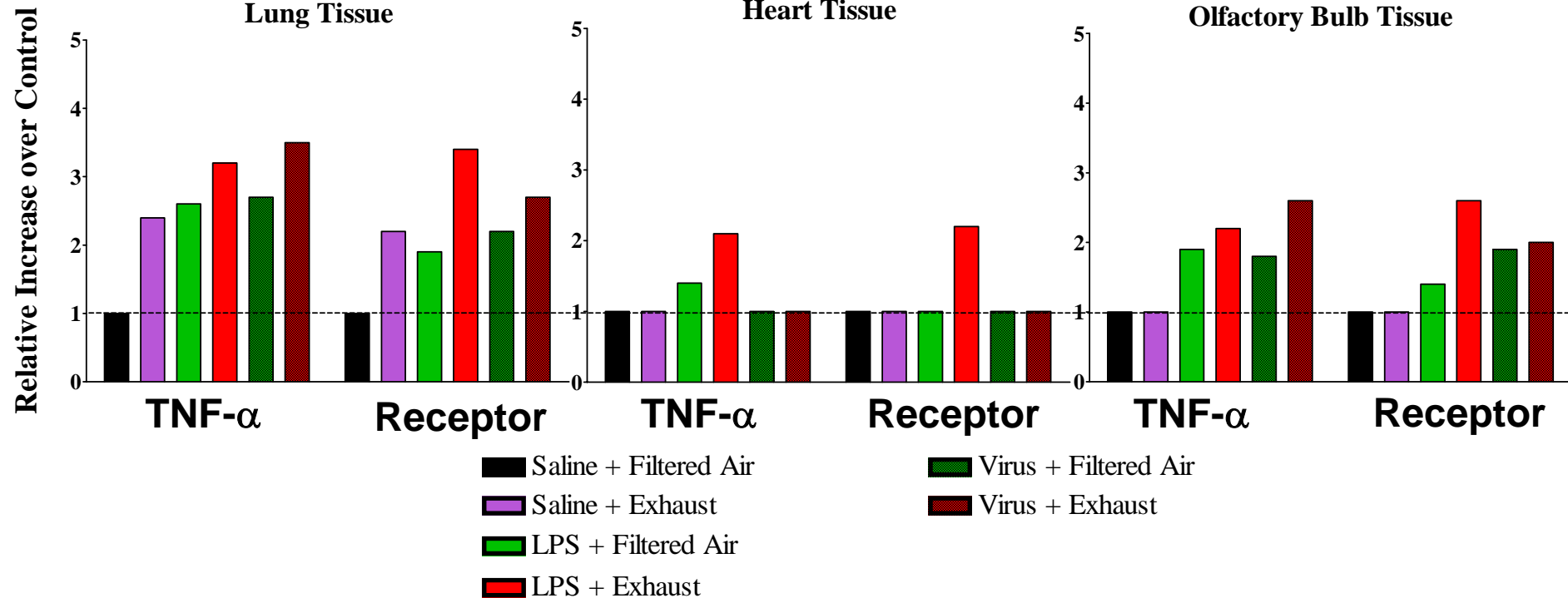
**Year 2**

**exhaust intake**

# MEL 6 hr exposure of rats on Rochester-Buffalo Thruway: *Aerosol and Atmospheric Characteristics*

<b>Atmospheric Monitoring Data, <i>in truck</i></b>		
<b>Plume number concentration</b>		1.6-4.3 x 10 <sup>6</sup> particles/cm <sup>3</sup>
<b>Exposure cage number concentration</b>		<b>1.3-7.6 x 10<sup>5</sup> particles/cm<sup>3</sup></b>
NO		0.95-1.85 ppm
NO <sub>2</sub>		0.05-0.15 ppm
<b>Elemental carbon concentration</b>		<b>0-2.7 μg/m<sup>3</sup></b>
<b>Organic carbon concentration</b>		<b>7.1-12.9 μg/m<sup>3</sup></b>
CO <sub>2</sub>		485-581 ppm
CO		3.1-6.4 ppm
<b>Particle size (DGN)</b>		<b>13-19 nm</b>
Filtered air controls ( <i>n</i> )		<4.5 x 10 <sup>3</sup> particles/cm <sup>3</sup>
Chamber temperature		19-27 °C
<b>Atmospheric Conditions, <i>outside</i></b>		
Outside temperature (high)		10-23 °C
Wind speed		3-12 mph

# TNF- $\alpha$ and TNF- $\alpha$ Receptor I Gene Expression in 21 month-old Rats Exposed for 1 Day in MEL

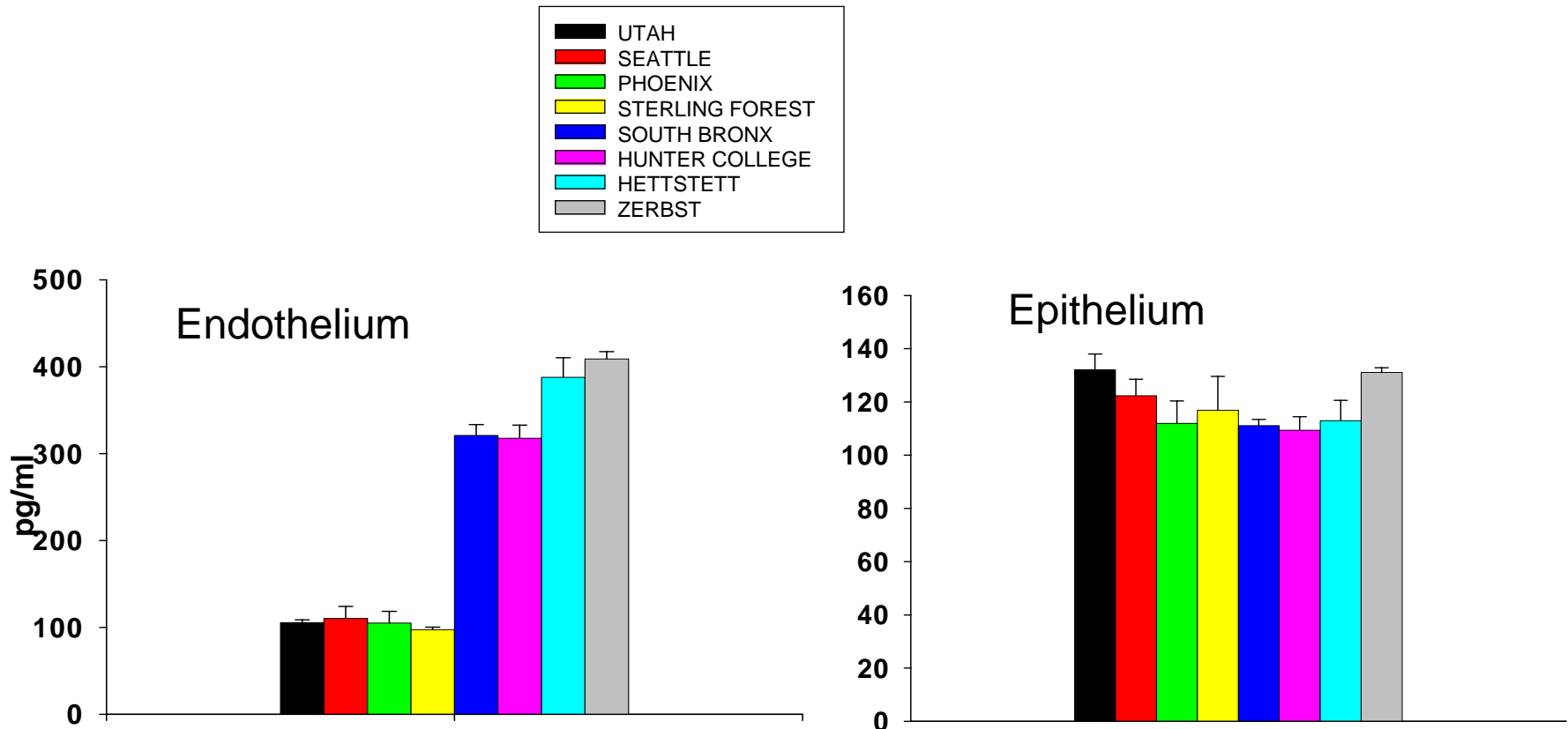






# Ambient UF PM stimulation of IL-6 Expression

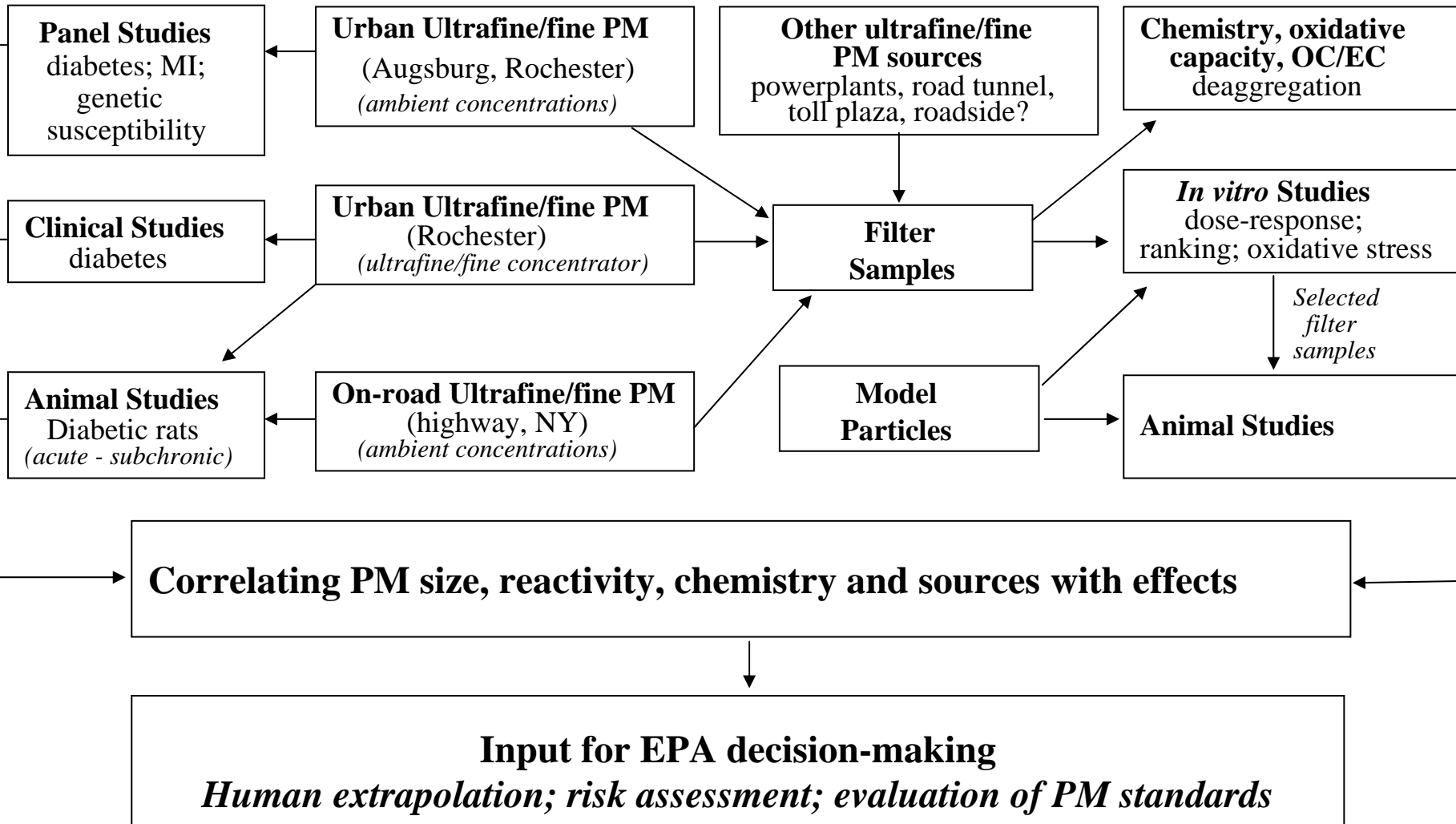
## Endothelial and Epithelial Response ( $4,7\mu\text{g}/\text{cm}^2$ ): Source effects



# INTEGRATION OF PARALLEL AND SEQUENTIAL STUDIES

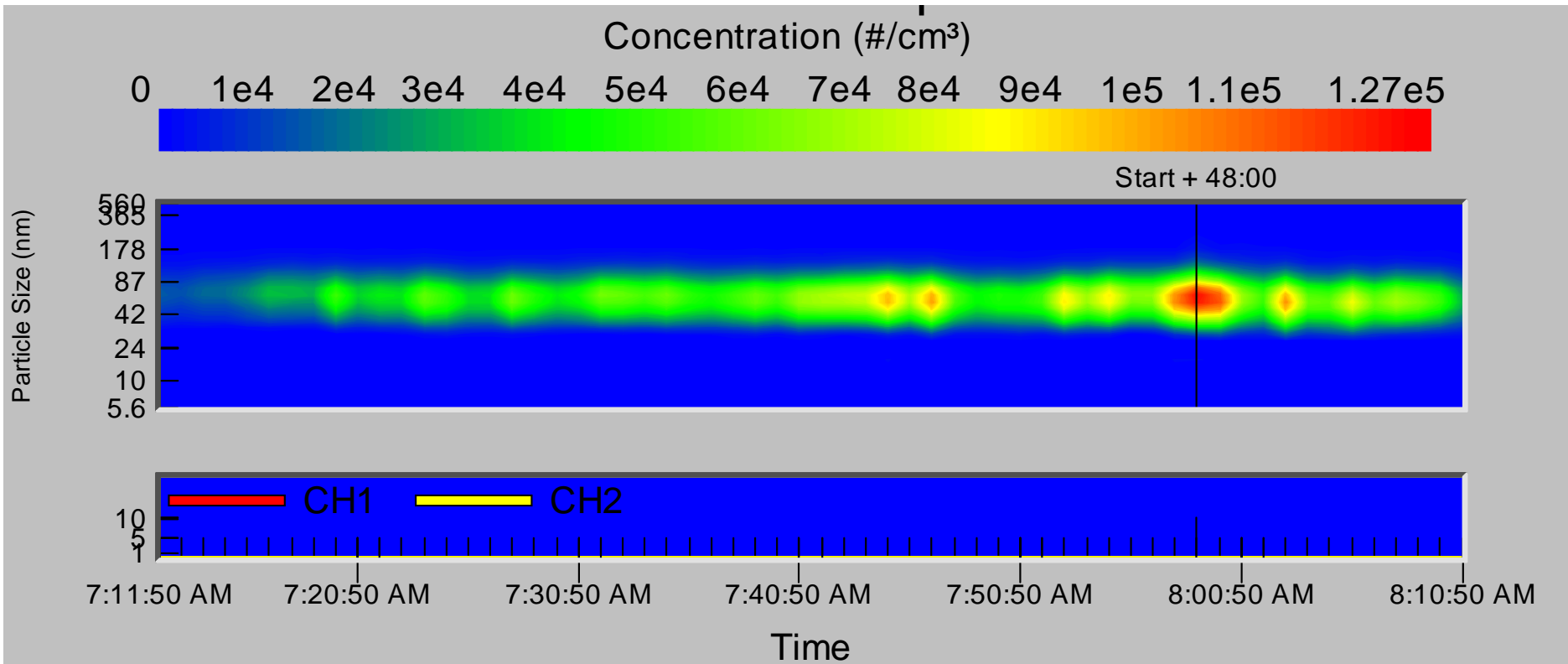
Similar Biological Endpoints — Real Time PM Size Measurements

## Sources

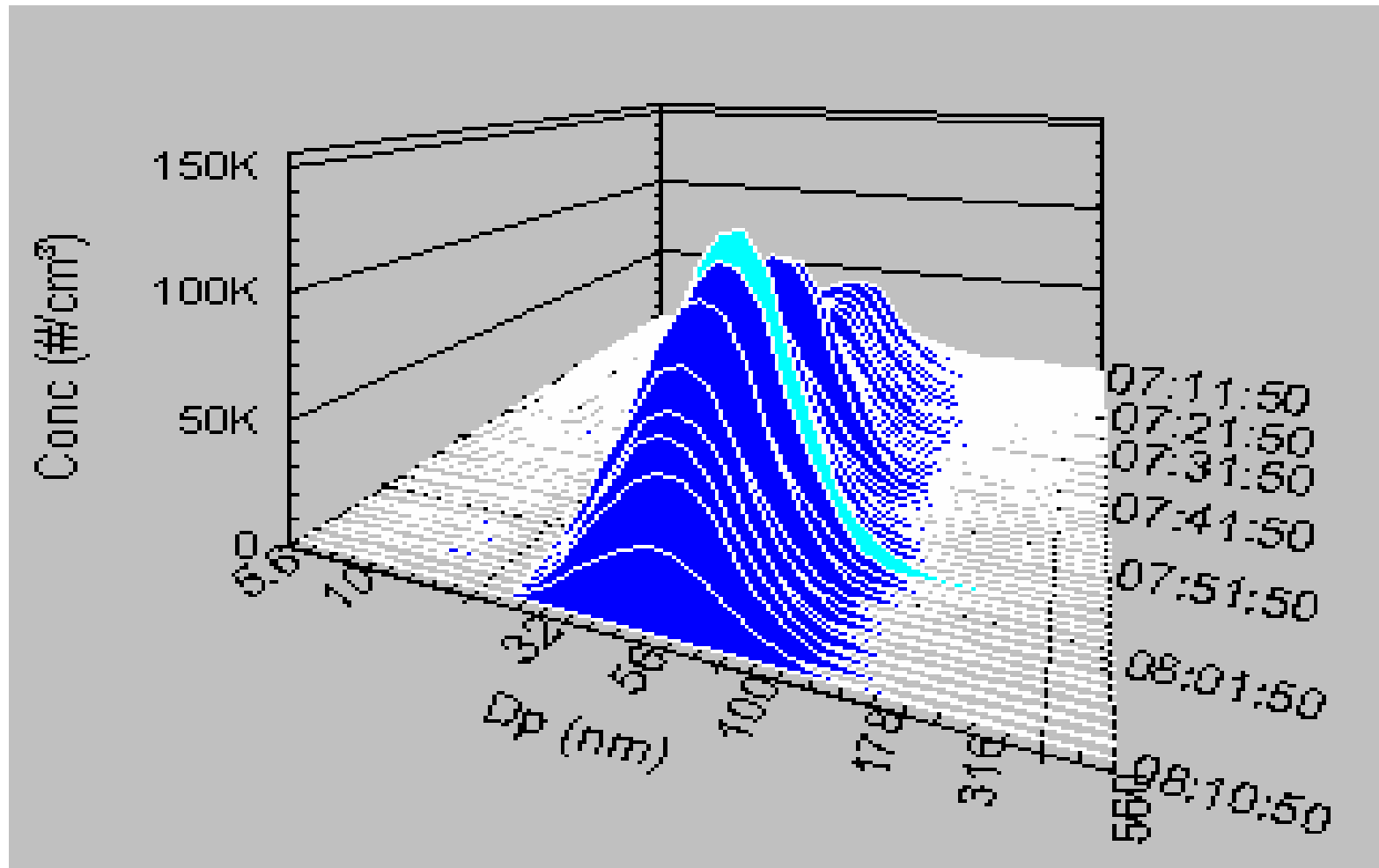




# Concentrated Ultrafine Particles, Rochester Exposure Facility FMPS display



# Fast Scan Array of Particle Size distribution



# Fast Scan Array of Particle Size distribution

