US EPA ARCHIVE DOCUMENT

Organization
EPA Airborne Particulate Matter Center, Univ. of Rochester
Source Specific Health Effects of Ultrafine/Fine Particles

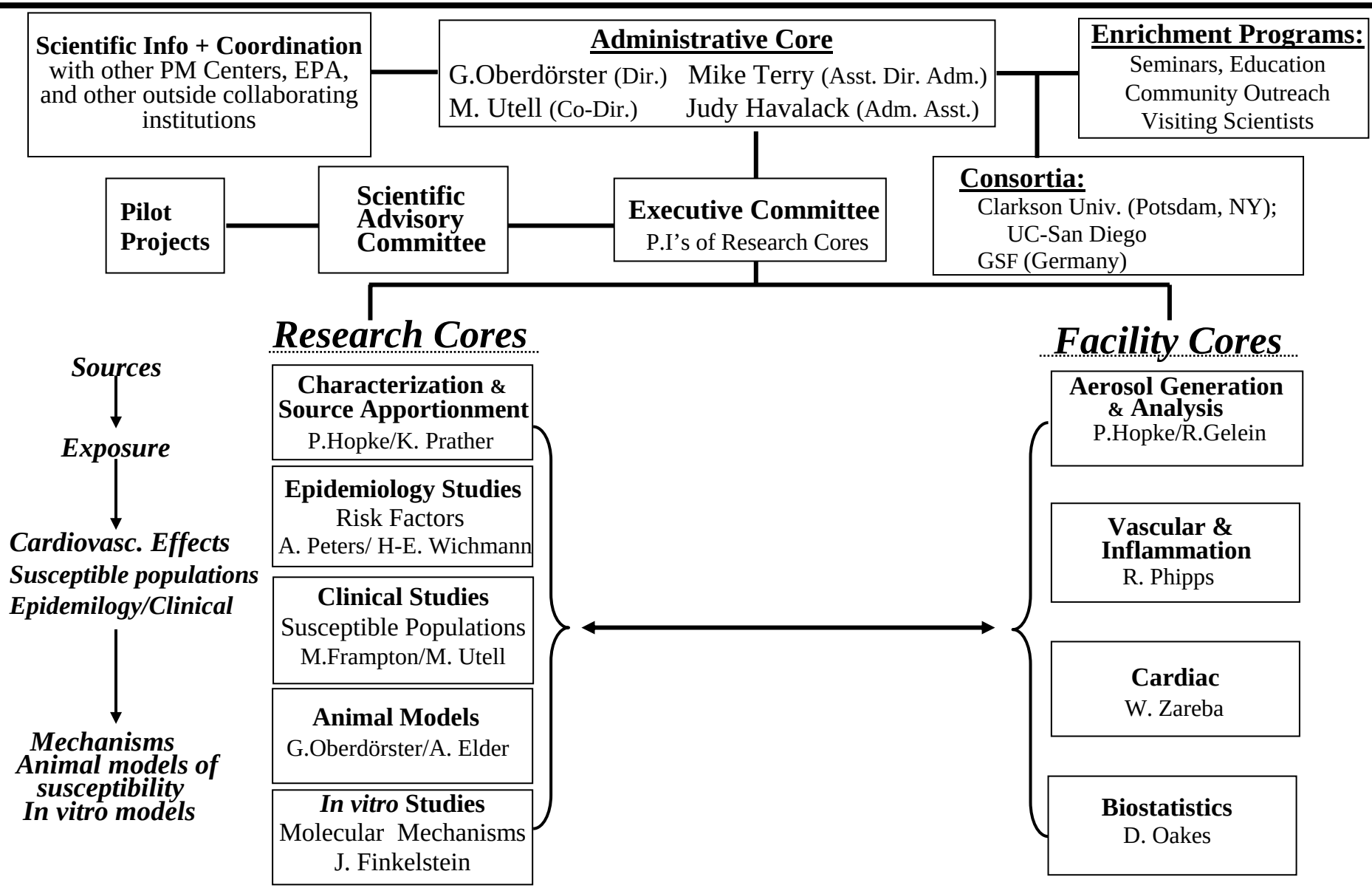
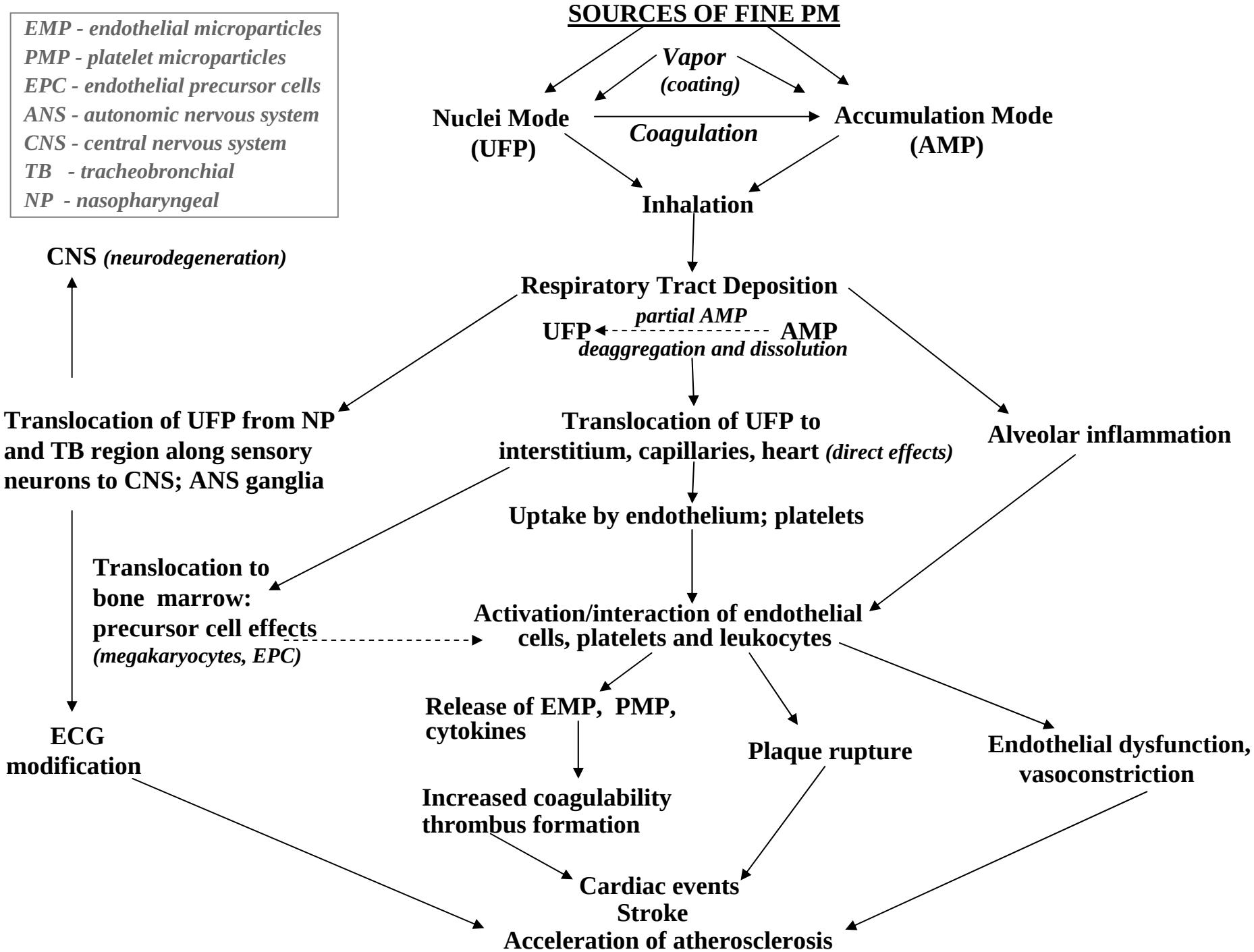


Figure 3.1

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



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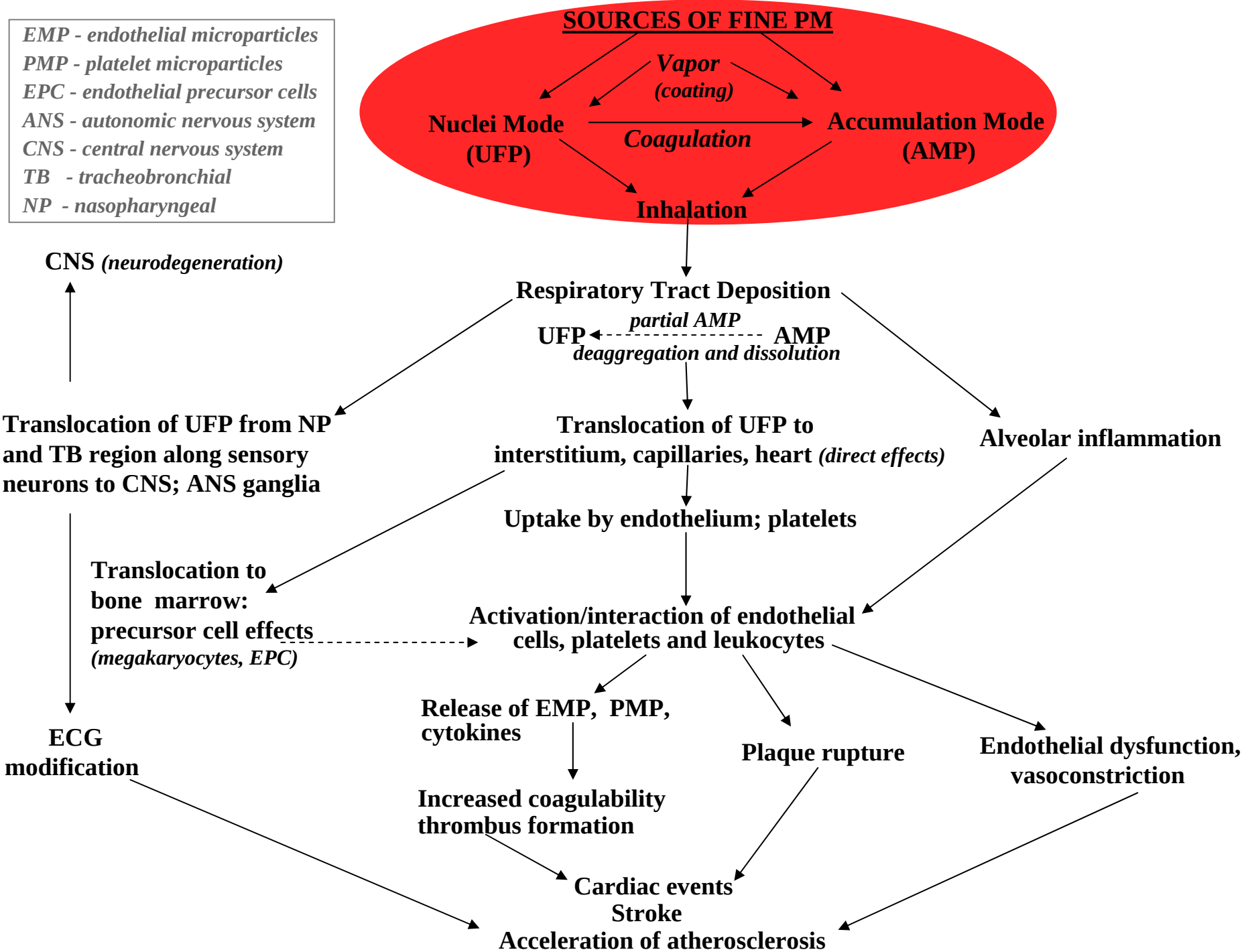

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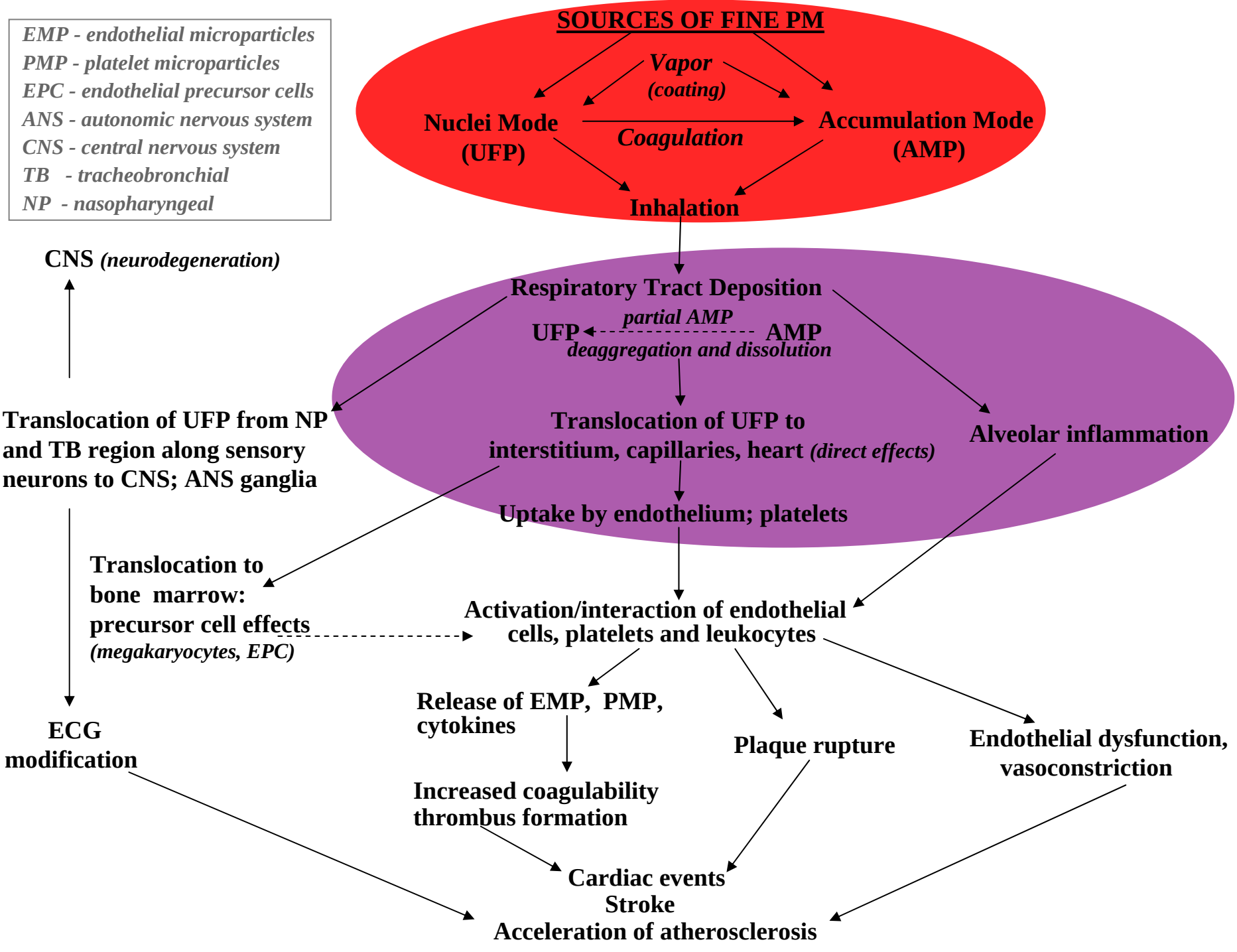

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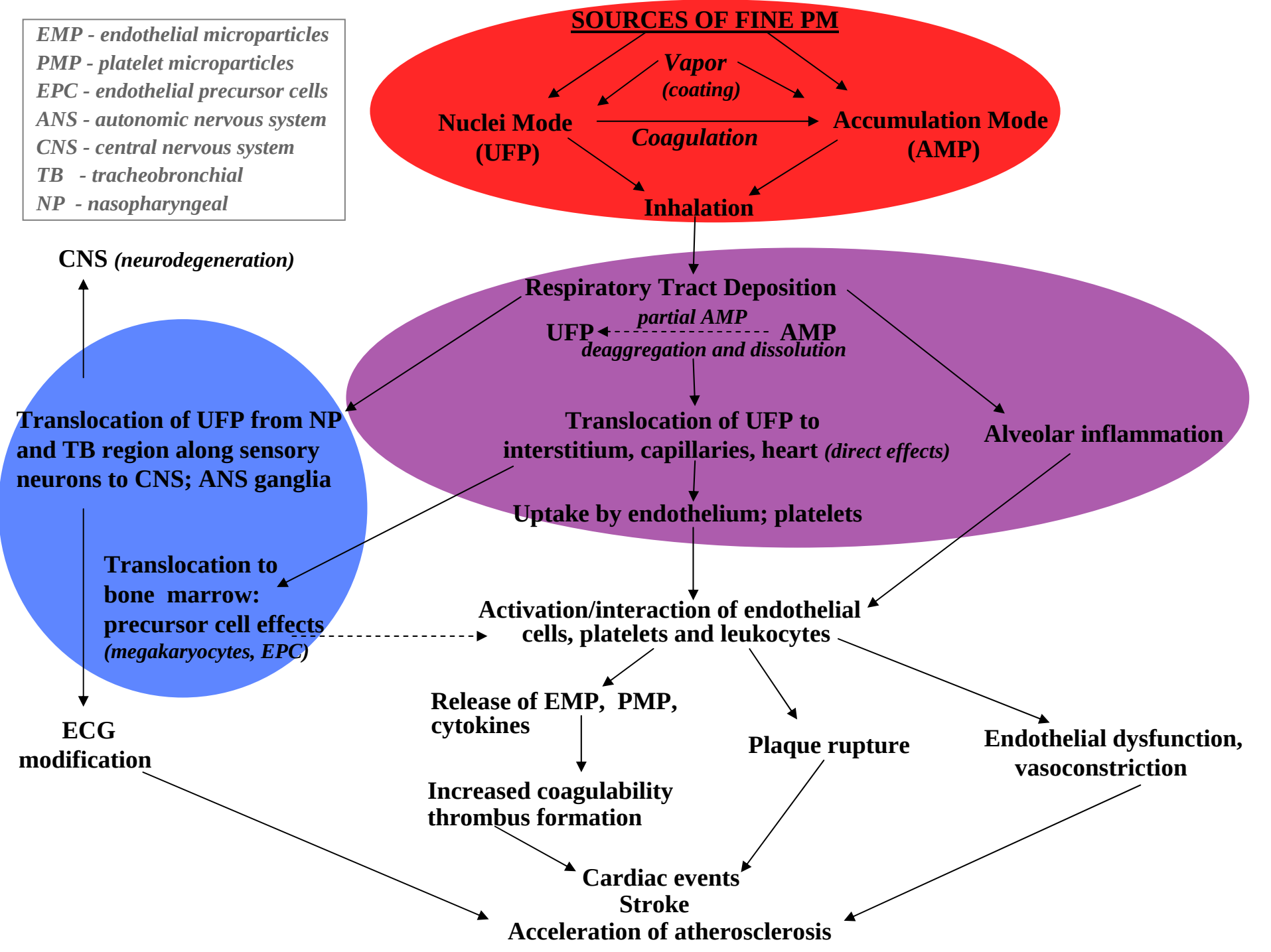

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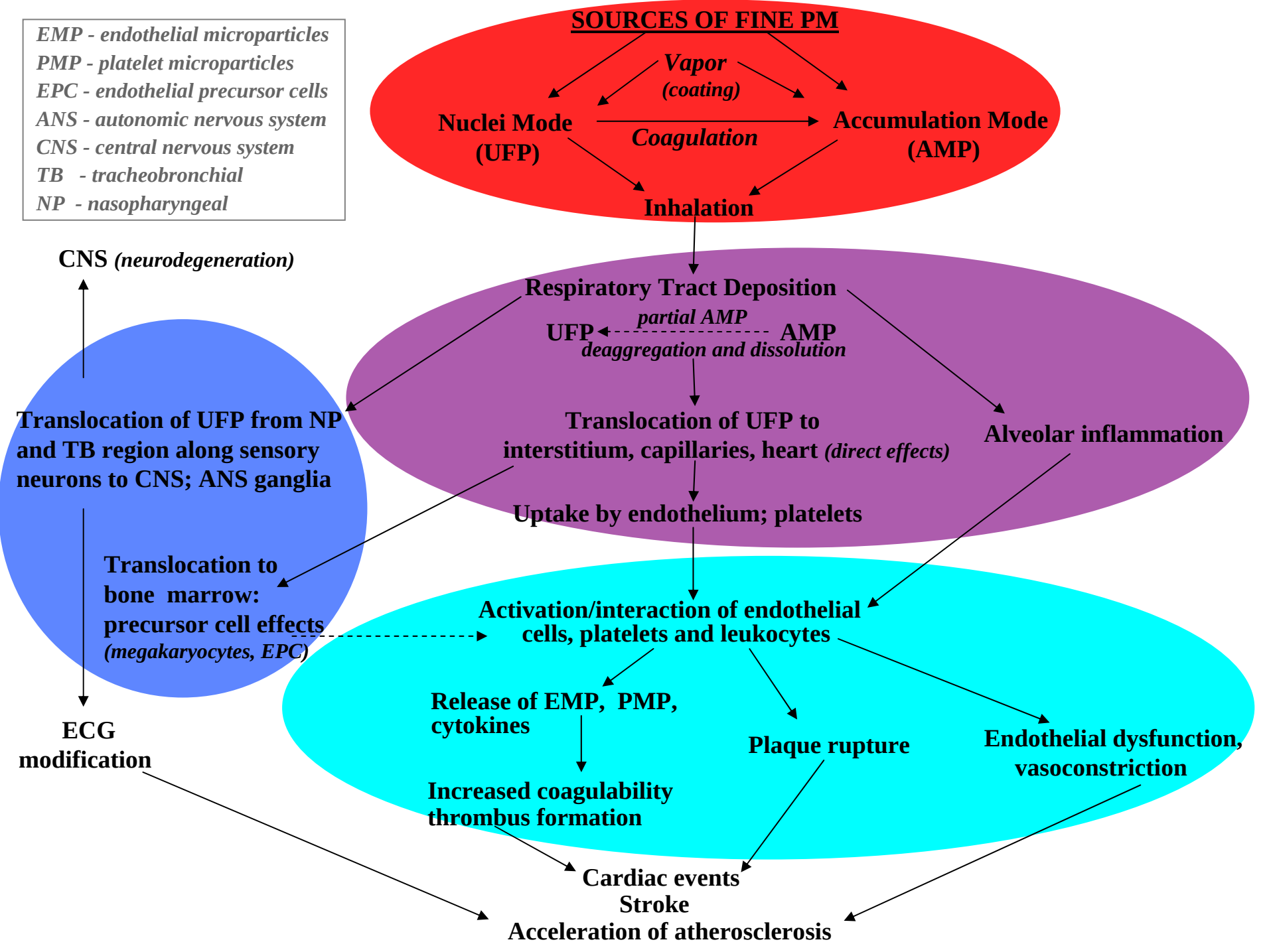

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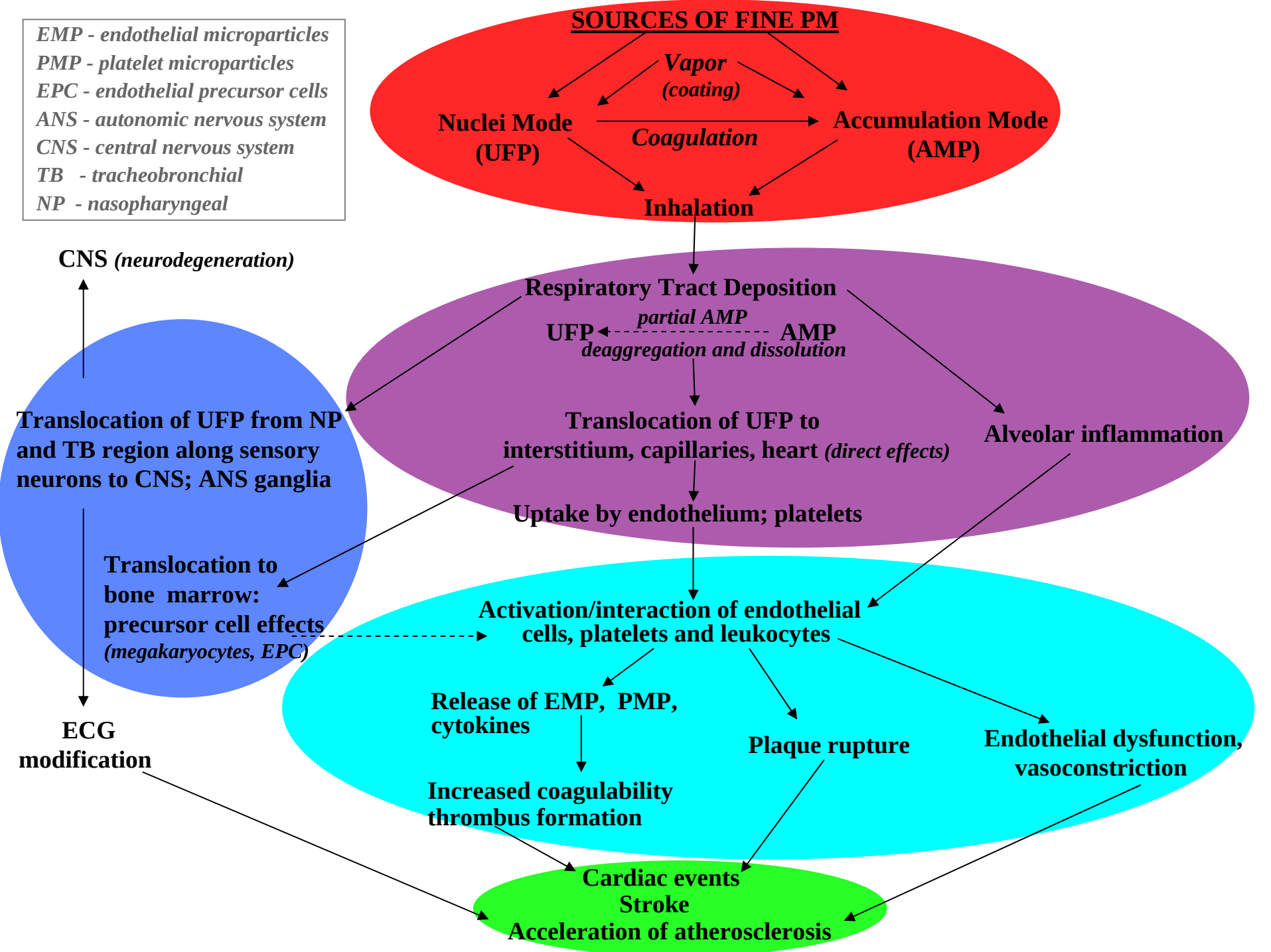


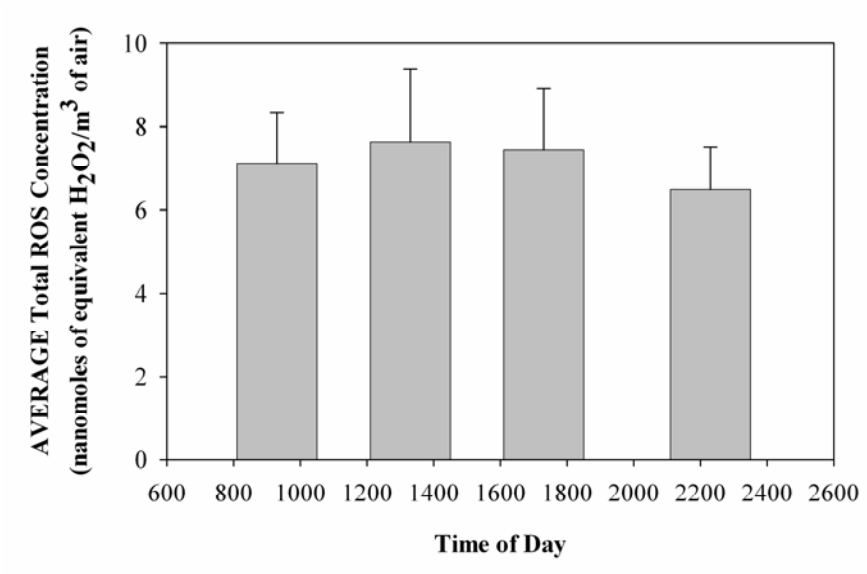
Research Core 1: Characterization of Particle-Bound ROS

Specific Aims

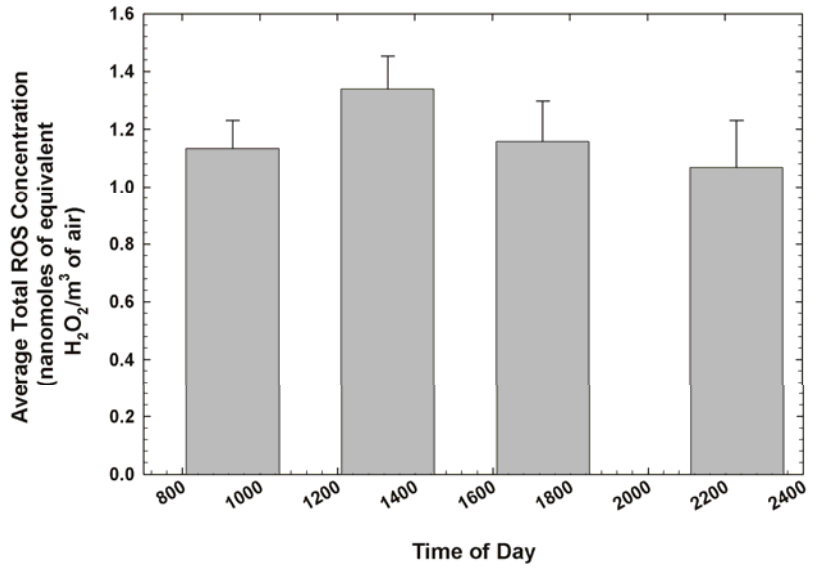
- **Aim #1. To understand the evolution of ambient particle compositions as they are transported from the sources to the receptor site with particular emphasis on the concentrations of particle-bound reactive oxidative species.**
- **Aim #2. To develop methods to characterize the sources and nature of reactive oxidative species associated with the ambient PM2.5 and PM0.1 particle aerosol using high resolution EPR and LC/MS.**

Characterization of Particle-Bound ROS

Rubidoux July 2003

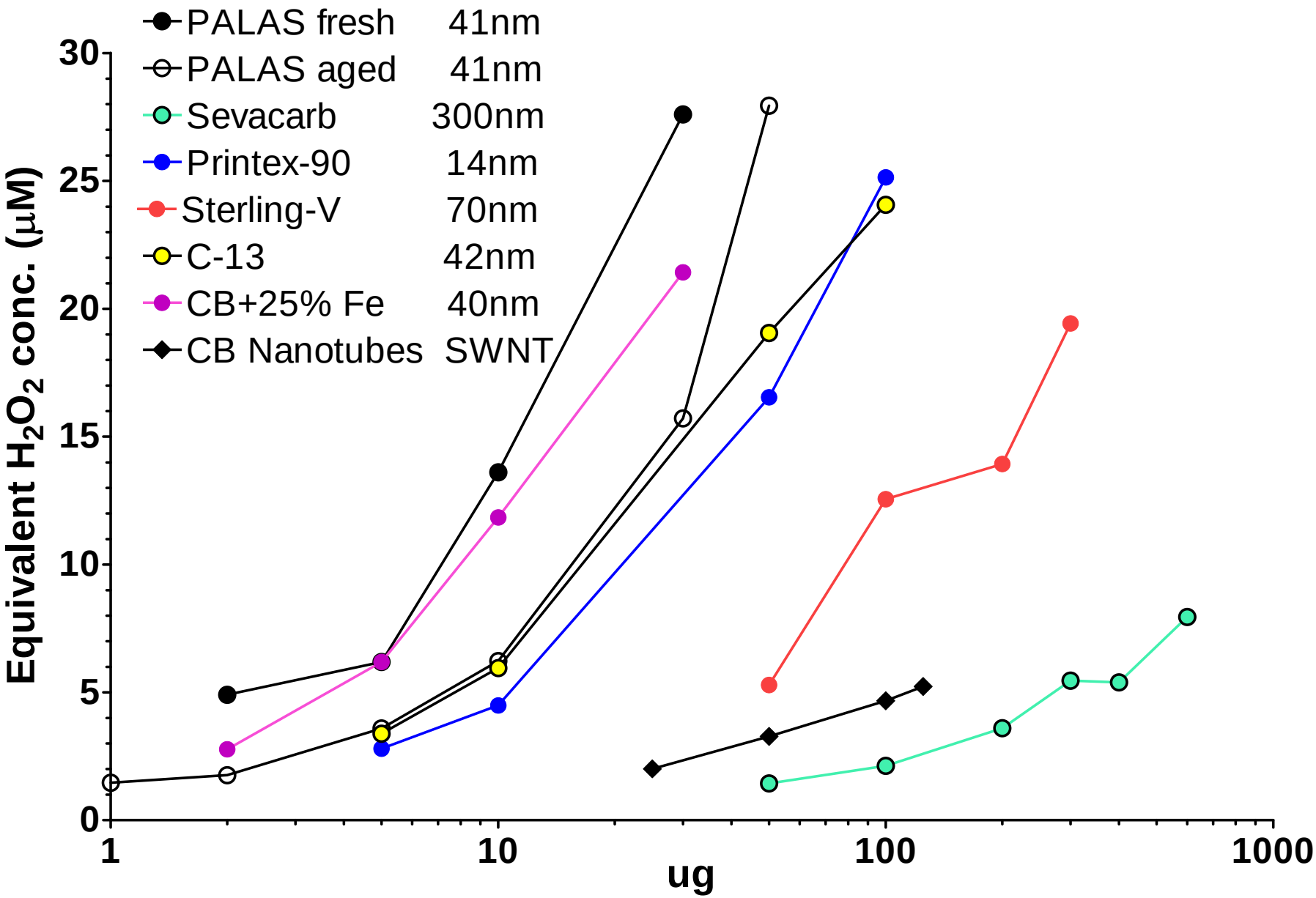


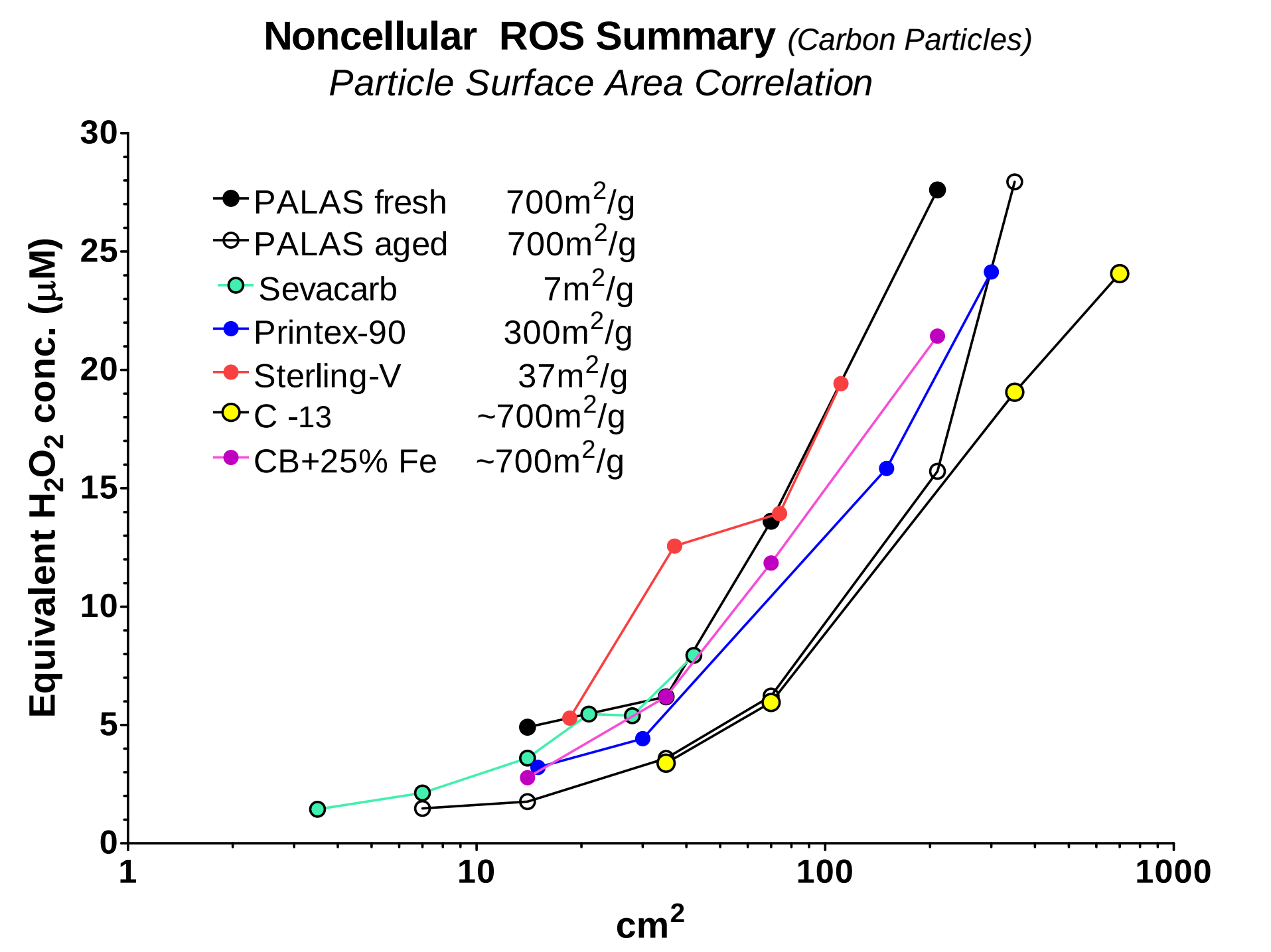
NYC January 2004



Noncellular ROS Summary *(Carbon Particles)*

Particle Mass Correlation

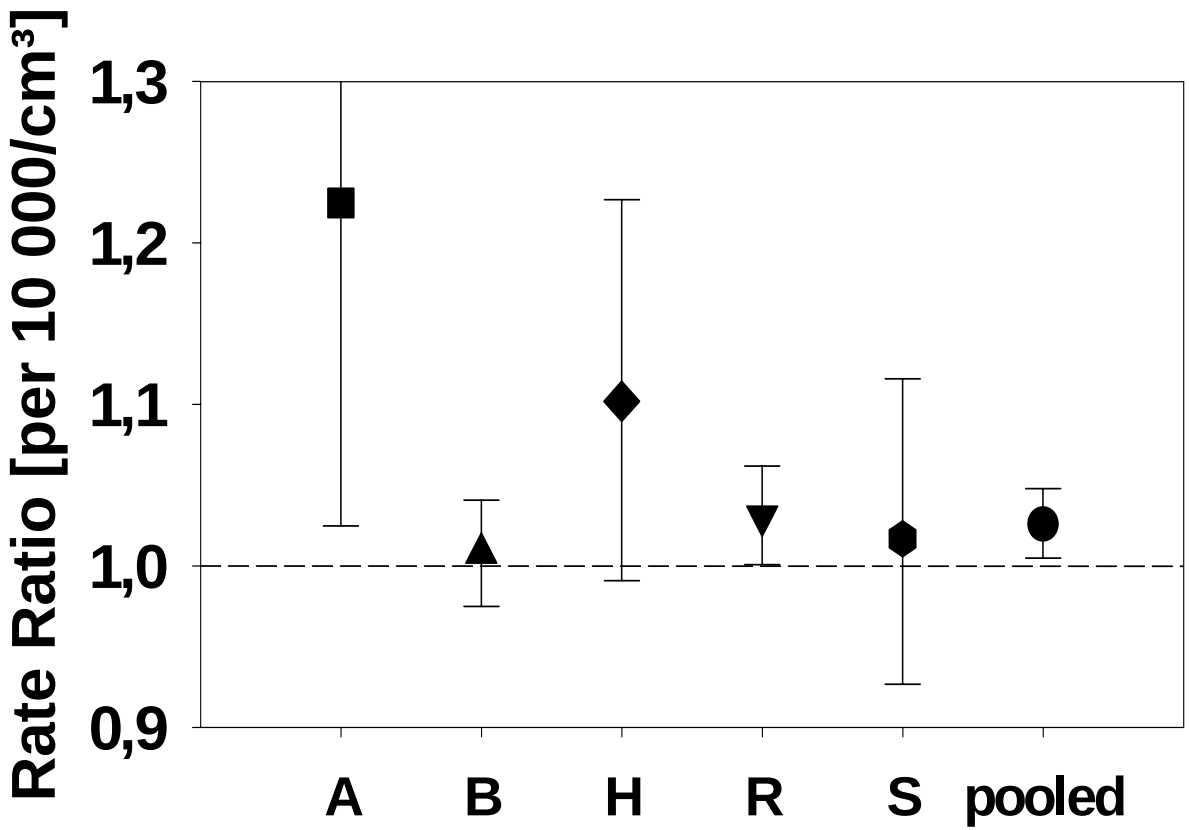



Noncellular ROS Summary (Carbon Particles)
Particle Surface Area Correlation
PALAS fresh 700m2/g
PALAS aged 700m2/g
Sevacarb 7m2/g
Printex-90 300m2/g
Sterling-V 37m2/g
C -13 ~700m2/g
CB+25% Fe ~700m2/g
Equivalent H2O2 conc. (µM)
0
5
10
15
20
25
30
1
10
100
1000
cm2

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

Cardiac Rehabilitation (Rochester) N=80	**Diabetes/Myocardial Infarction (Augsburg) N=100/100**	**Inflammatory/Detoxification Polymorphisms/Controls (Augsburg) N=100/100**
	Air Monitoring	
Criteria pollutants ($PM_{2.5}$, SO_2, CO, O_3)	Criteria pollutants ($PM_{2.5}$, SO_2, CO, O_3)	Criteria pollutants ($PM_{2.5}$, SO_2, CO, O_3)
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
	Measurements	
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

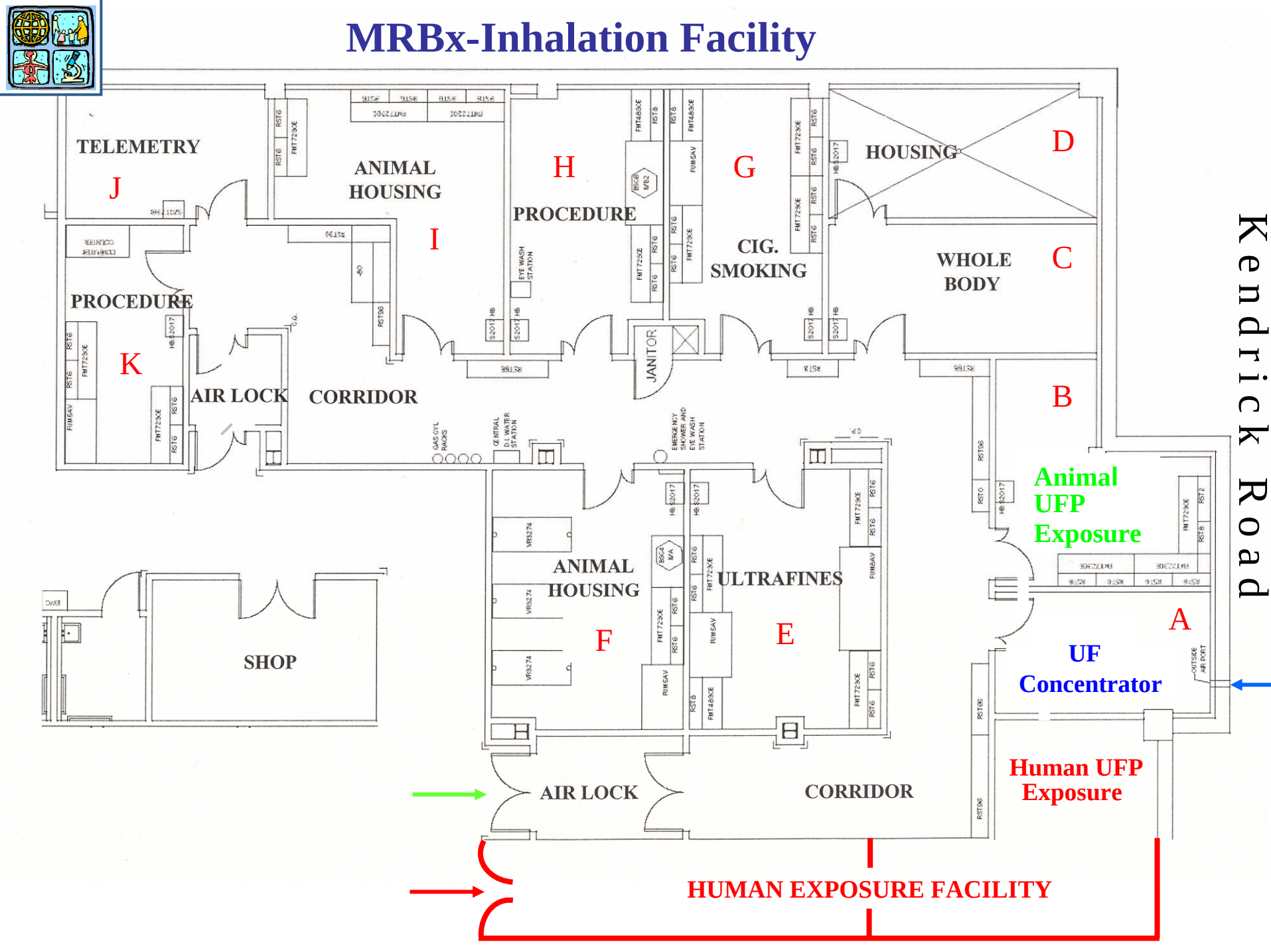
Effects of inhaled ambient UFP in healthy and diabetic subjects:

- 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

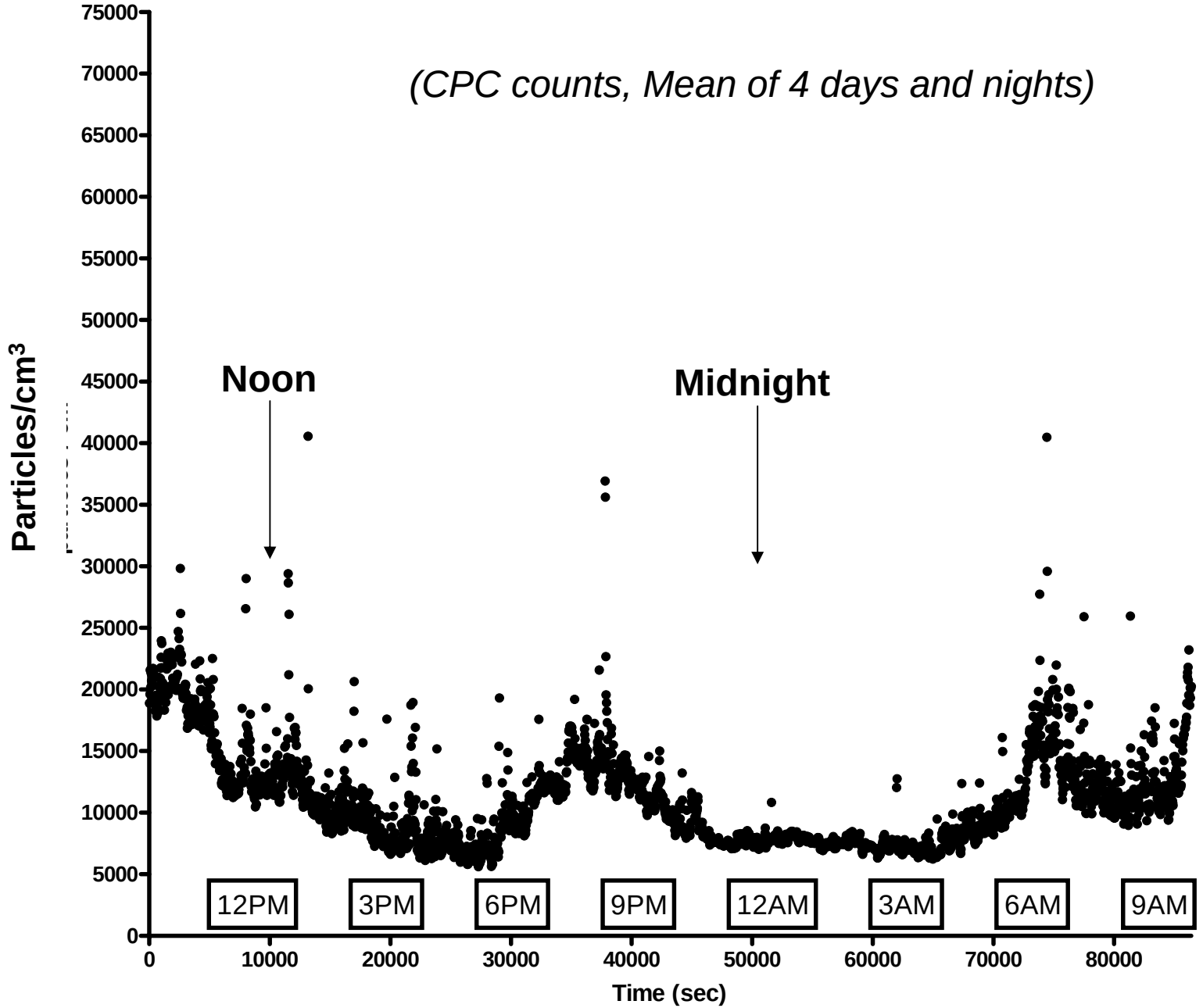
- Changes in leukocyte adhesion molecule expression
- Reduction in DLCO
- Reduced brachial flow-mediated vasodilatation
- Suggests both pulmonary & systemic vascular effects
- Preliminary findings: effects in type 2 diabetics, *at rest*
- Implications for cardiovascular disease

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_x catalyst

- **Translocation and clearance kinetics of model and ambient UF/Fine PM**
  (heart; platelets; bone marrow; spleen; brain)

  – model particles: gold (TEM; ICPMS); ^{13}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

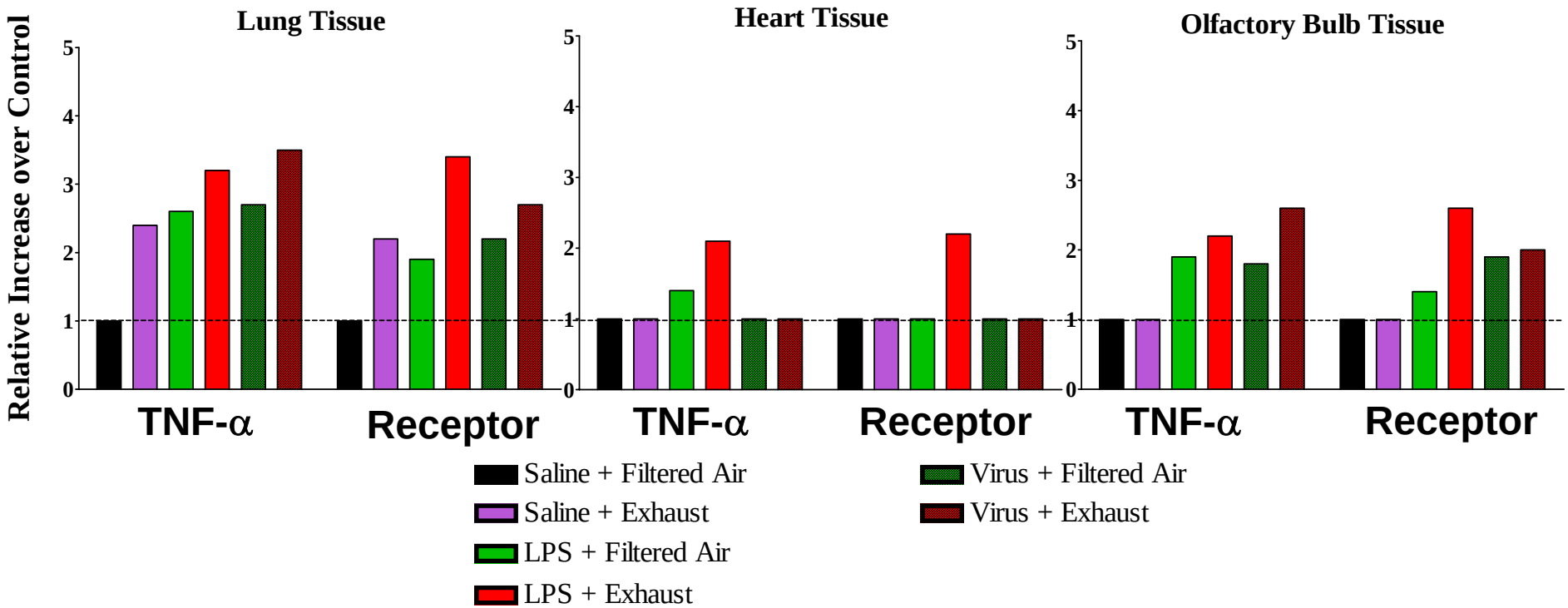
Year 2

exhaust intake

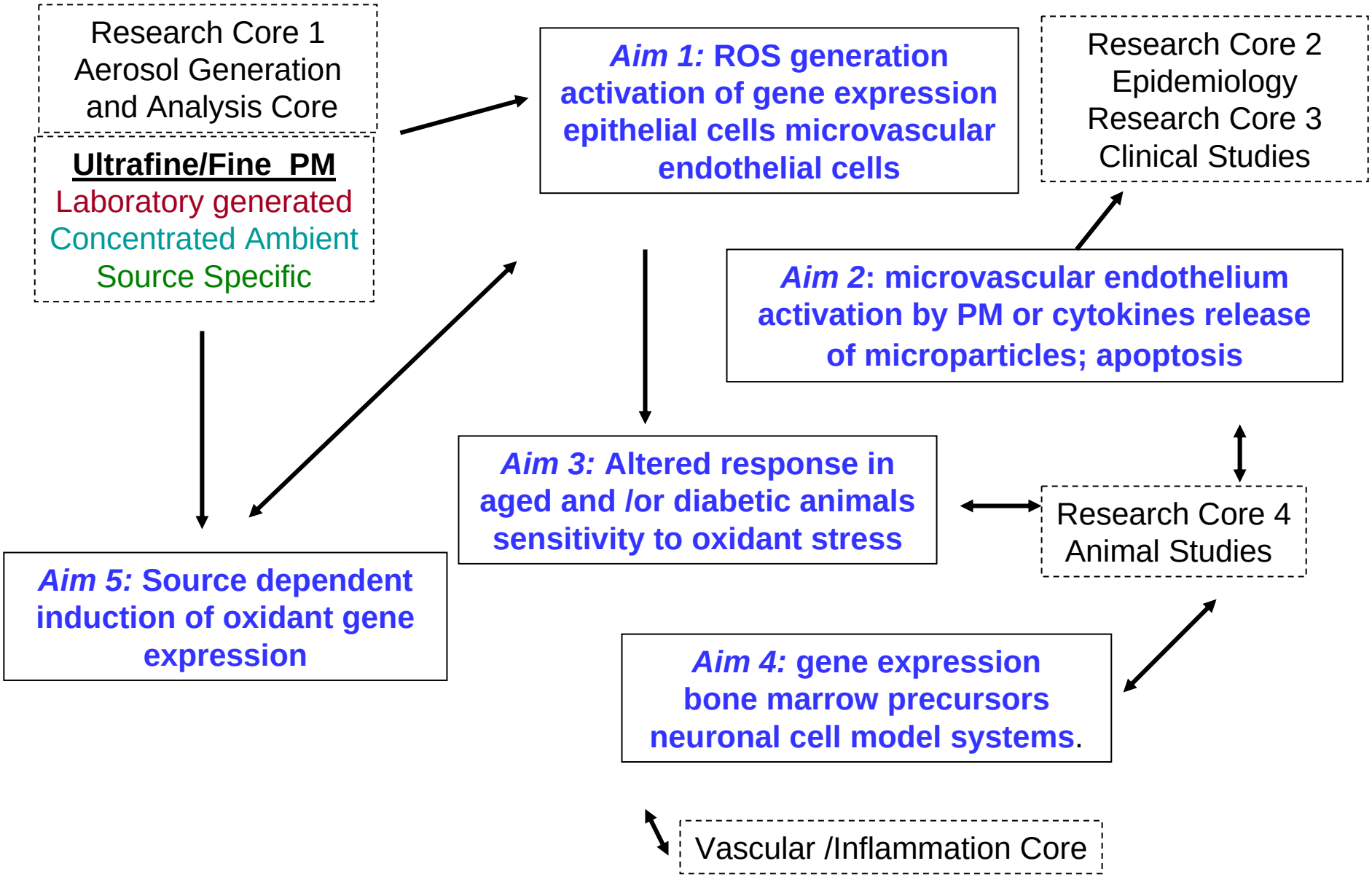
MEL 6 hr exposure of rats on Rochester-Buffalo Thruway: *Aerosol and Atmospheric Characteristics*

Atmospheric Monitoring Data, ***in truck***		
Plume number concentration		1.6-4.3 x 10^6 particles/cm^3
Exposure cage number concentration		**1.3-7.6 x 10^5 particles/cm^3**
NO		0.95-1.85 ppm
NO_2		0.05-0.15 ppm
Elemental carbon concentration		**0-2.7 µg/m^3**
Organic carbon concentration		**7.1-12.9 µg/m^3**
CO_2		485-581 ppm
CO		3.1-6.4 ppm
Particle size (DGN)		**13-19 nm**
Filtered air controls (*n*)		<4.5 x 10^3 particles/cm^3
Chamber temperature		19-27 ºC
Atmospheric Conditions, ***outside***		
Outside temperature (high)		10-23 ºC
Wind speed		3-12 mph

TNF-α and TNF-α Receptor I Gene Expression in 21 month-old Rats Exposed for 1 Day in MEL

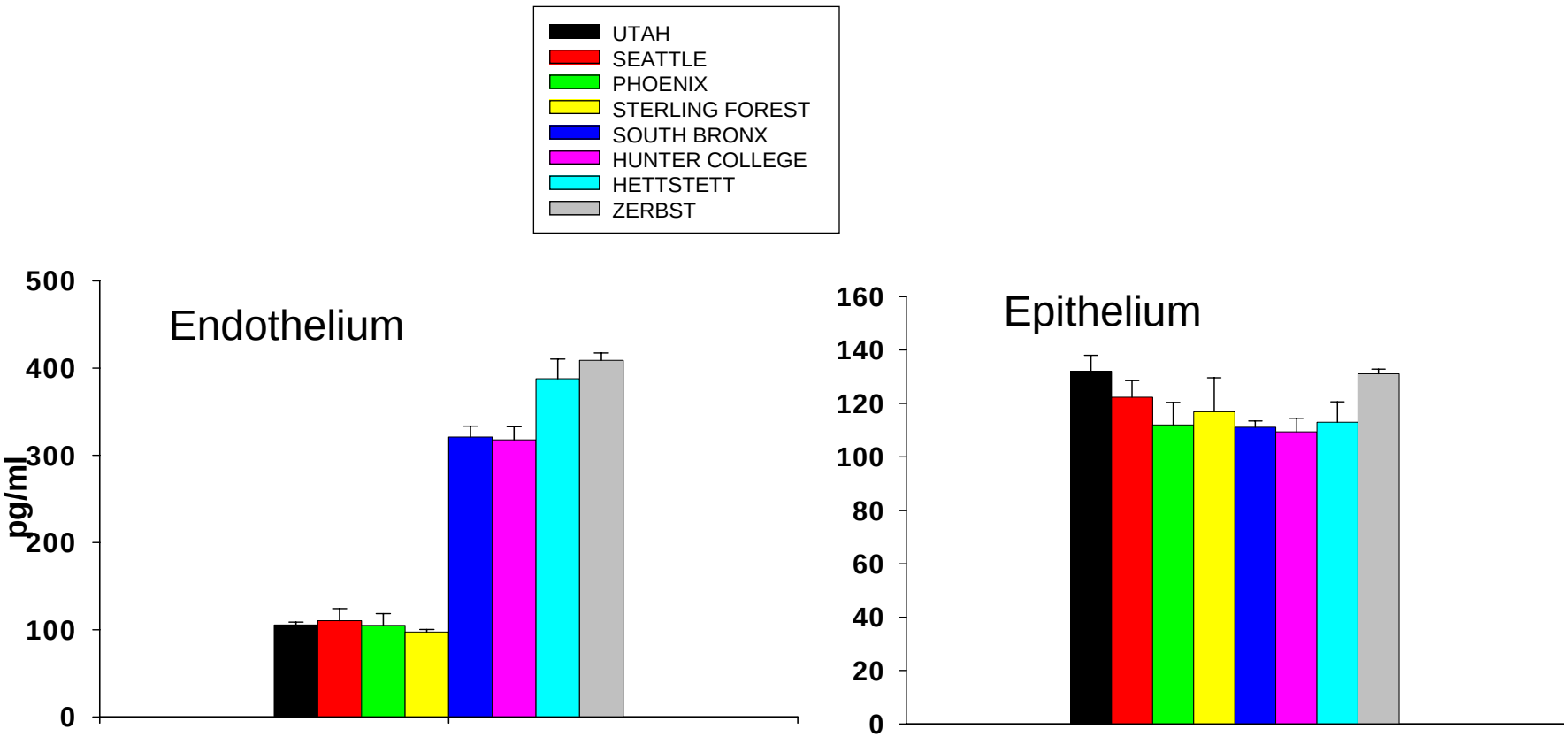


Research Core 5: In vitro Studies

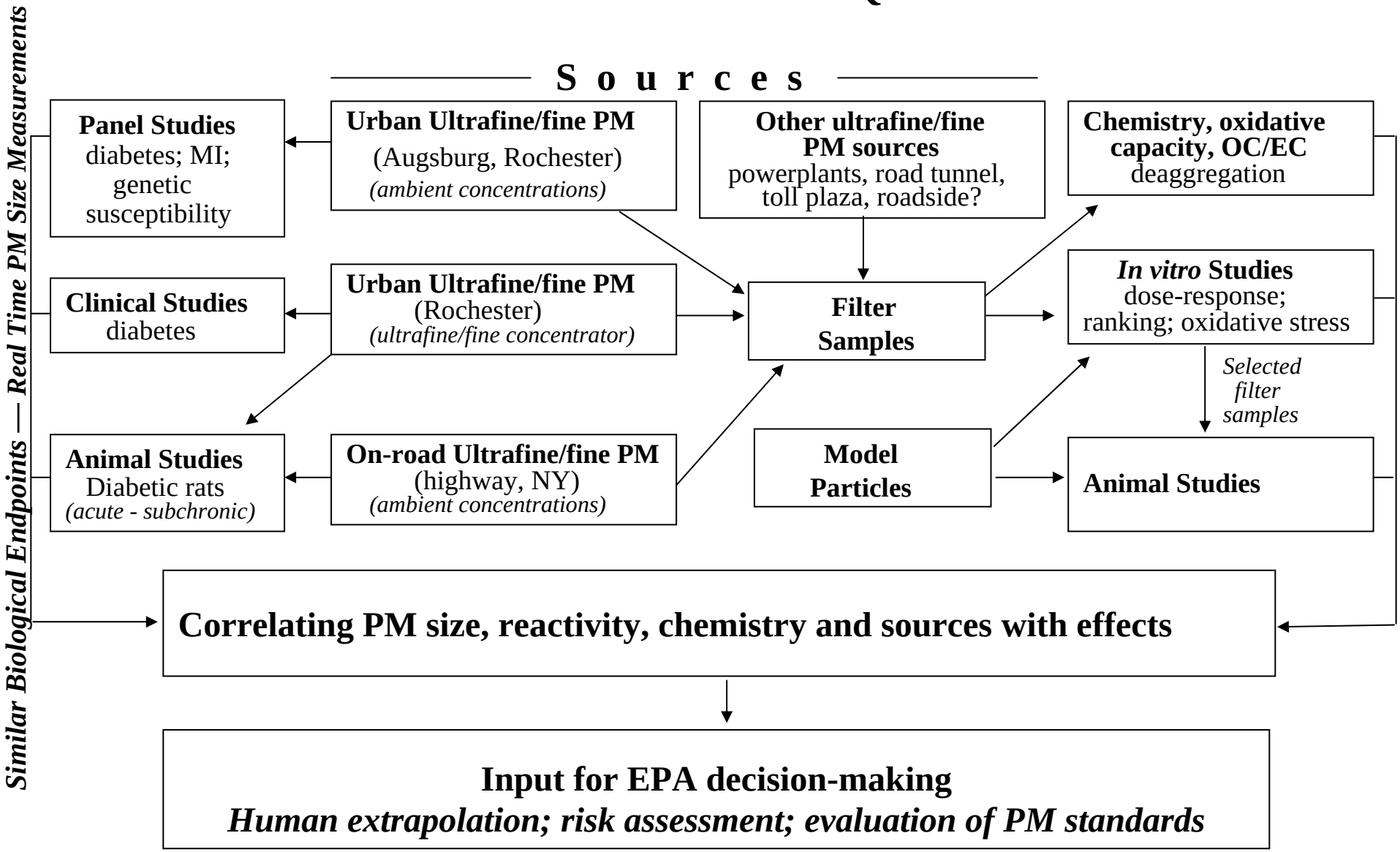


Ambient UF PM stimulation of IL-6 Expression

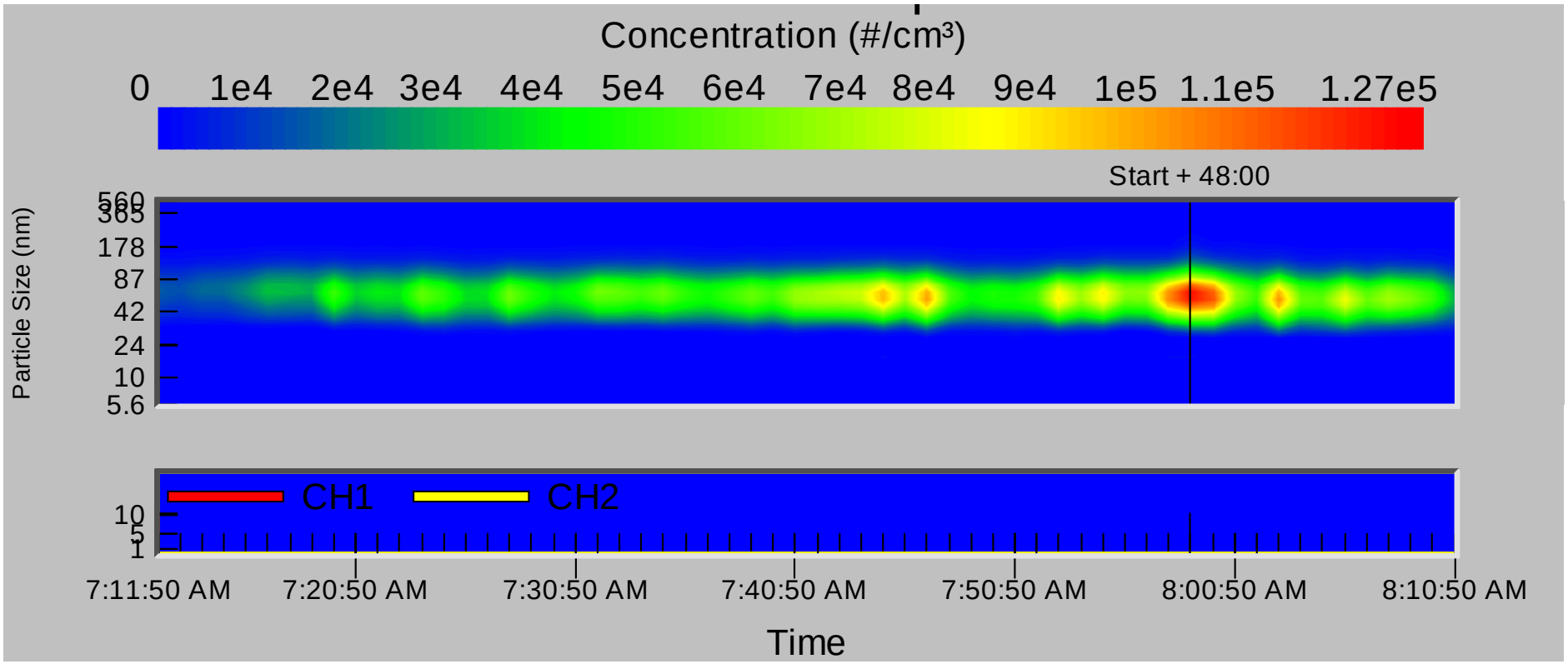
Endothelial and Epithelial Response *(4,7ug/cm²):* Source effects



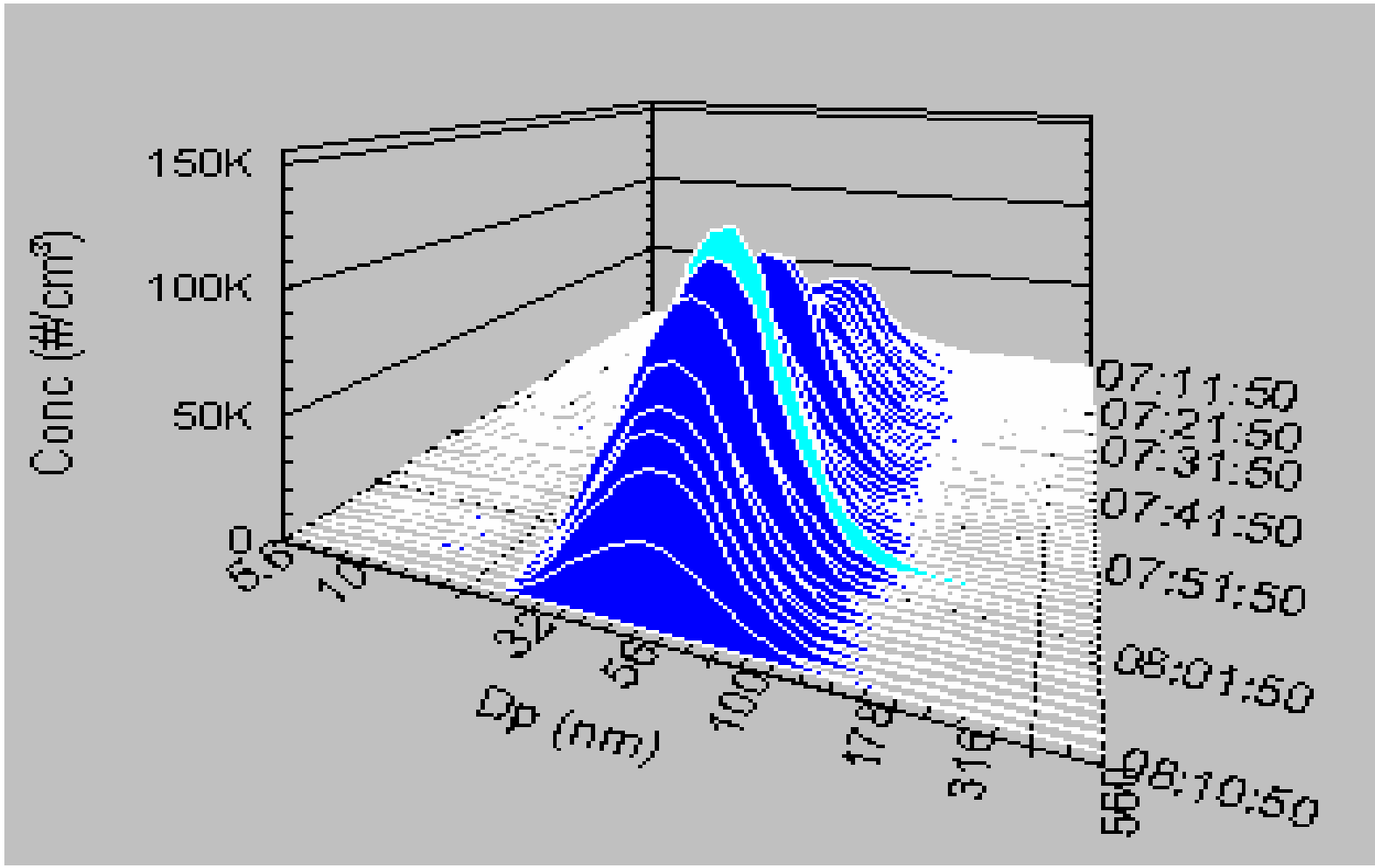
INTEGRATION OF PARALLEL AND SEQUENTIAL STUDIES



Concentrated Ultrafine Particles, Rochester Exposure Facility
FMPS display



Fast Scan Array of Particle Size distribution



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