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# Ambient Particles, Their Toxic Components, Sources and How They Impact Health

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# Accomplishments Reviewed in this Presentation

*Variation in source, season and atmospheric processes influence chemical and toxicological characteristics of particles*

- PM sources and particle characteristics
- Freeway/mobile source associated health effects
- PM toxicity in relation to mechanistic hypotheses
  - Oxidative stress and catalytic ROS generation
  - Cellular uptake of ultrafines
- Key accomplishments and future research questions

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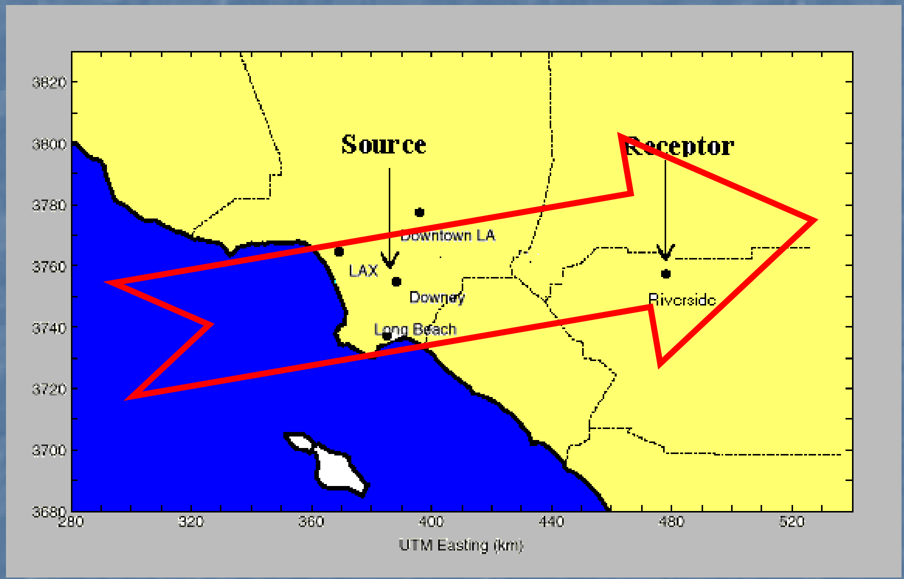
# Studies of PM Sources and Atmospheric Chemistry

Three Zones of PM Exposure:

- Zone of influence: adjacent to primary emissions sources
- Source sites: influenced by a variety of sources
- Receptor sites: influenced by transport and atmospheric chemistry

West → East

Prevailing winds in the Los Angeles Basin




**Dispersion**

**Transformation Chemical reaction**

**Zone of Influence of Emissions/Sources**

**Freeways**

→

**Urban/Downtown Los Angeles, beyond immediate zones of influence**

**"Source" areas**

→

**Inland-Eastern Los Angeles Basin regions**

**"Receptor" areas**

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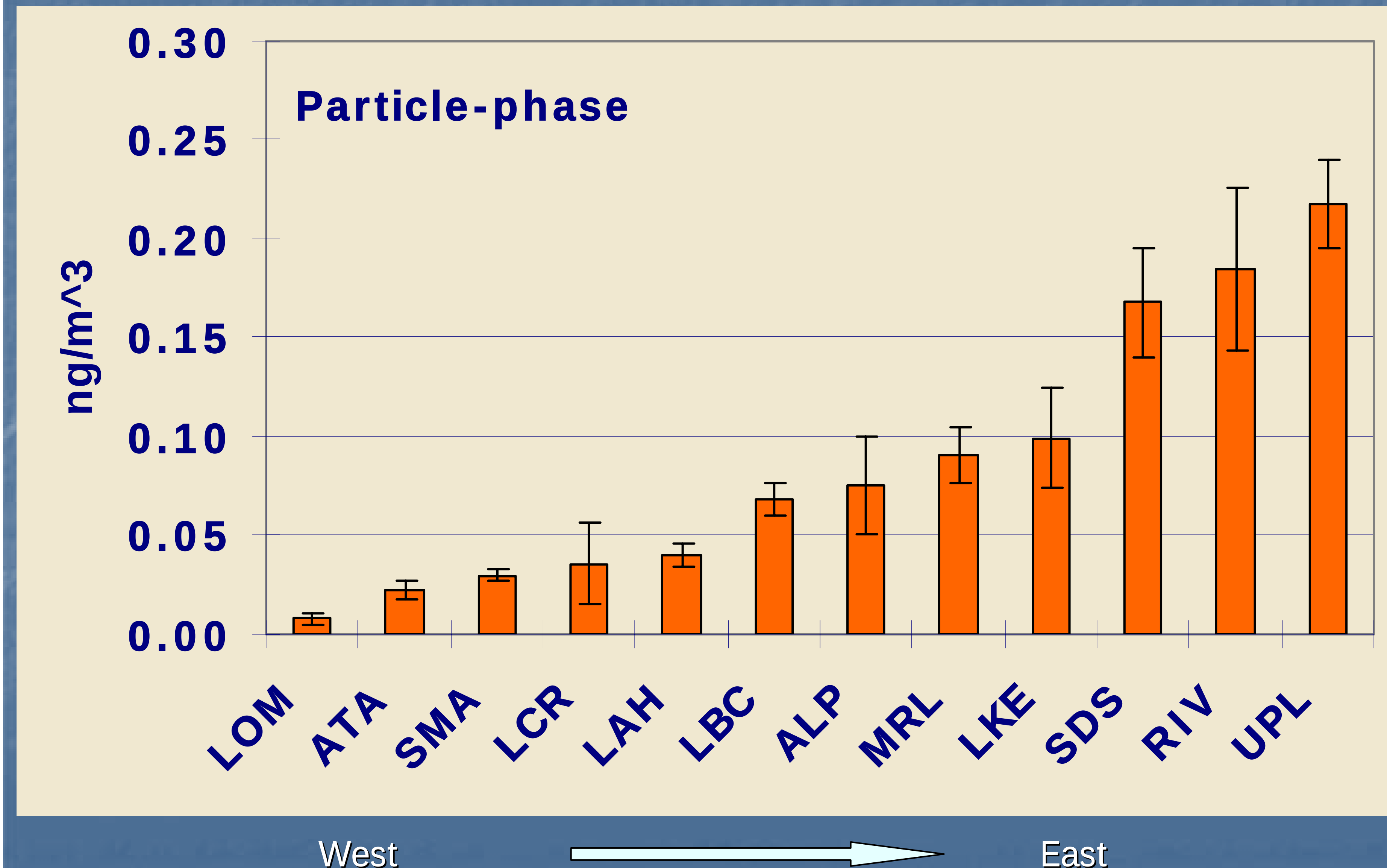
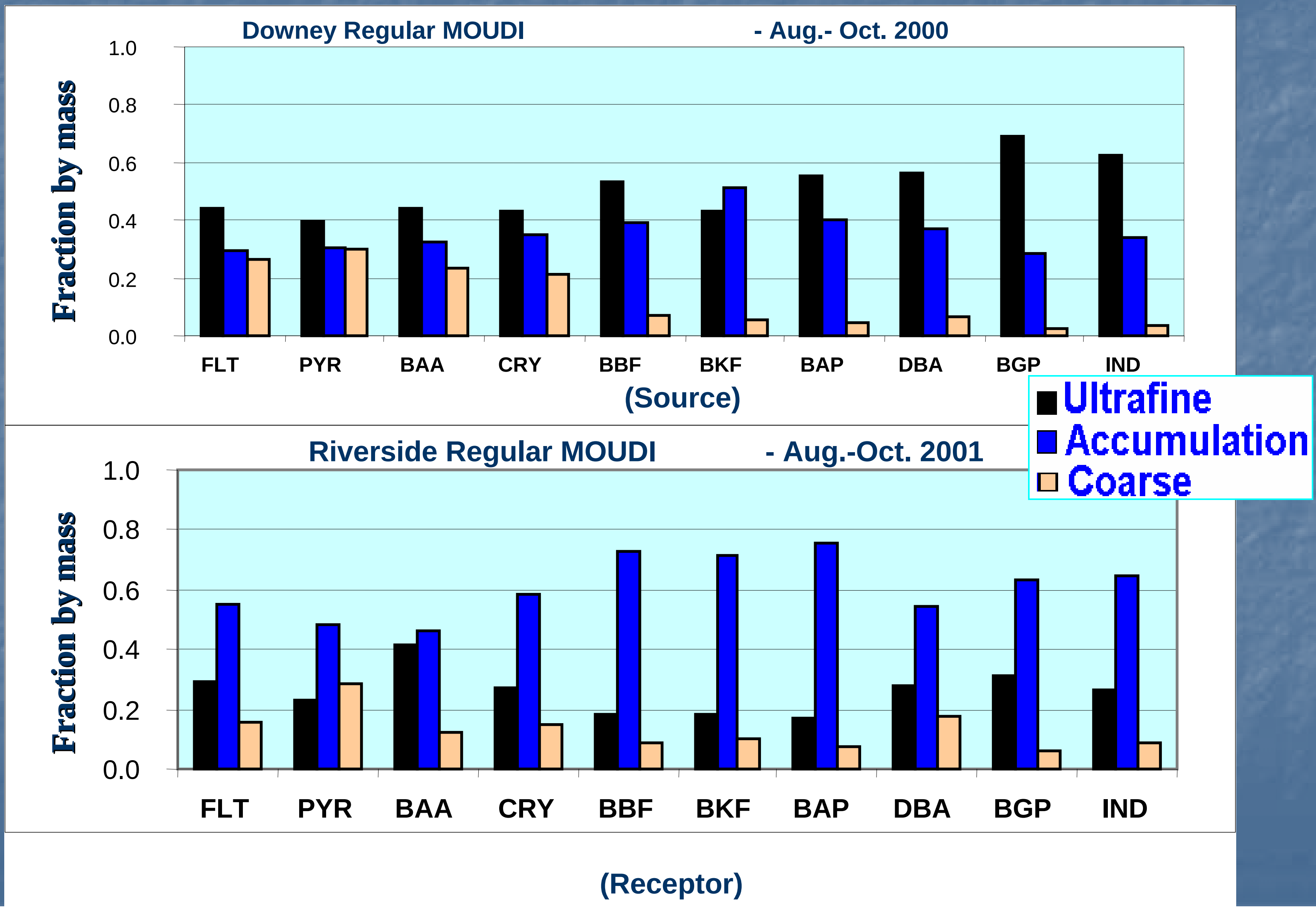
# Spatial Distribution of Particle Phase Phenanthroquinone in the LA Basin



# Effect of Transport on PAH Size Distribution (Source/Receptor)

Eiguren-Fernandez A., Miguel A.H, Jaques, P. and Sioutas, C. *Aerosol Science and Technology*, 2003

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# Use of Source Tracers in PM Exposure and Toxicology Research

**Which sources pose the greatest risks to public health?**

- Characterize physical/chemical characteristics including source tracers
- Conduct toxicological studies to differentiate toxicity
- Analyze associations between toxicity and source tracers to determine relative source toxicity

**How do source contributions to ambient PM samples vary from:**

- Site to site?
- Over the course of the day? Seasons?
- Between size fractions?

**Approach: Evaluate concentrations/size distribution of individual organic compounds to trace primary and secondary sources of PM:**

Markers have been developed for vehicles, cooking, wood smoke and photochemistry

**Fine, P.M., Chakrabarti, B, Krudysz M., Schauer J.J. and Sioutas*, C. *Environmental Science and Technology*, 2004.**

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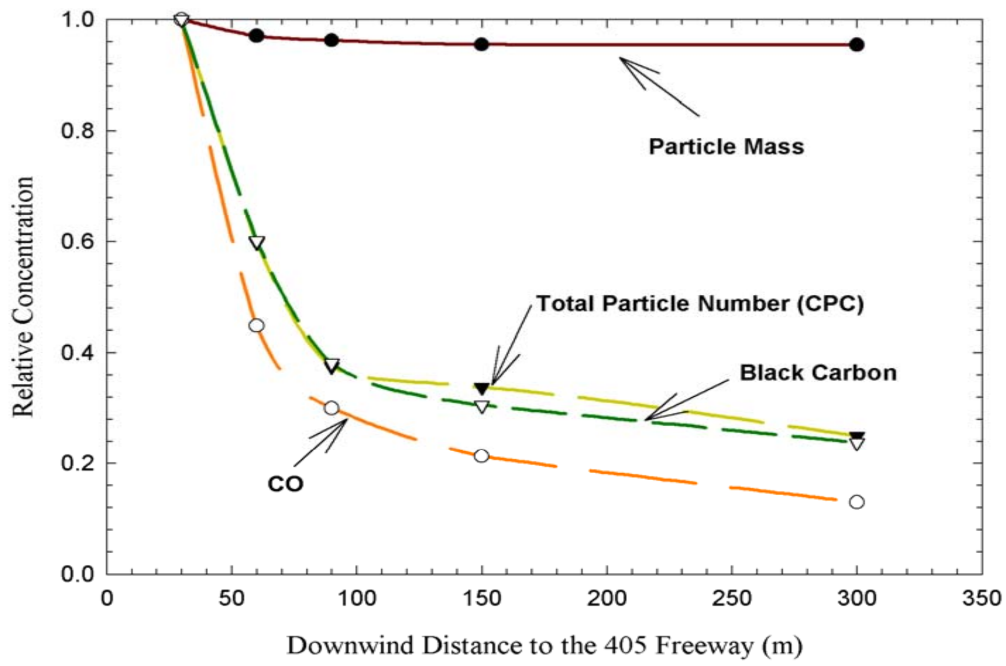


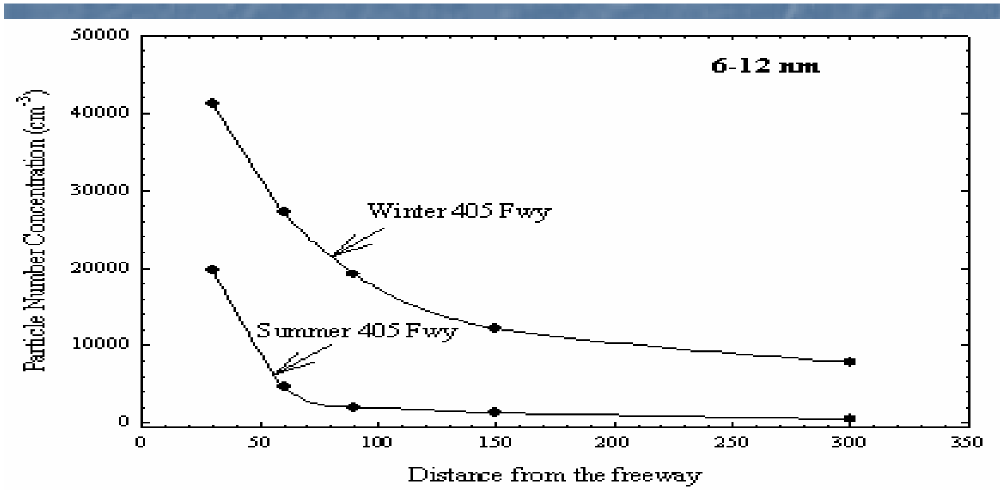


(a)

**Figure 4.** Comparison of decay of particle number concentrations in summer and winter in the size range of (a) 6-12 nm, (b) 12-25 nm, (c) 25-50 nm, (d) 50-100 nm, and (e) 100-200 nm near the 405 freeway.

# Mobile Source Studies

- Particle mass remains relatively constant with distance from freeway; size distribution changes considerably.

- Concentrations of nanoparticles (<20 nm) are much higher in winter than summer, suggesting that these particles are volatile, formed by condensation of organic vapors after they leave the tailpipe.

- **Zhu, Y., Hinds, W.C., Kim, S., Shen, S. and Sioutas*, C. "*Aerosol Science and Technology,* 38, 5-13, 2004.**

- Highway study found "Most of the particles consisted of volatile material."

- **Kittleson et al., Inhal. Tox.-16, 2004:**

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# Recent Studies from PM Centers and EPA:
## Freeway Exposures and Mobile Source Effects

Studies in mice, rats and humans have reported effects of health endpoints in several target tissues/organ systems:

1. **Cardiovascular effects** in aged rats (2 studies) and in humans (3 studies)
2. **Allergic airways responses** in sensitized mice
3. Children's Health Study **asthma prevalence**
4. Children's Health Study **lung development**
5. Traffic density study of effects on **human fetal development**
6. **Brain inflammation responses** in mice

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# Exposure to Traffic and the Onset of Myocardial Infarction

- **Results:** An association between exposure to traffic and myocardial infarction onset one hour later was observed (odds ratio: 2.9; 95% confidence interval: 2.2 to 3.8, $p<0.001$).
- Time spent in cars, public transport and on bicycles was consistently connected with an increased risk for myocardial infarction.
- **Conclusions:** Transient exposure to traffic might pose a risk in persons vulnerable to myocardial infarctions.

**Peters et al., NEJM, 2004, In press**

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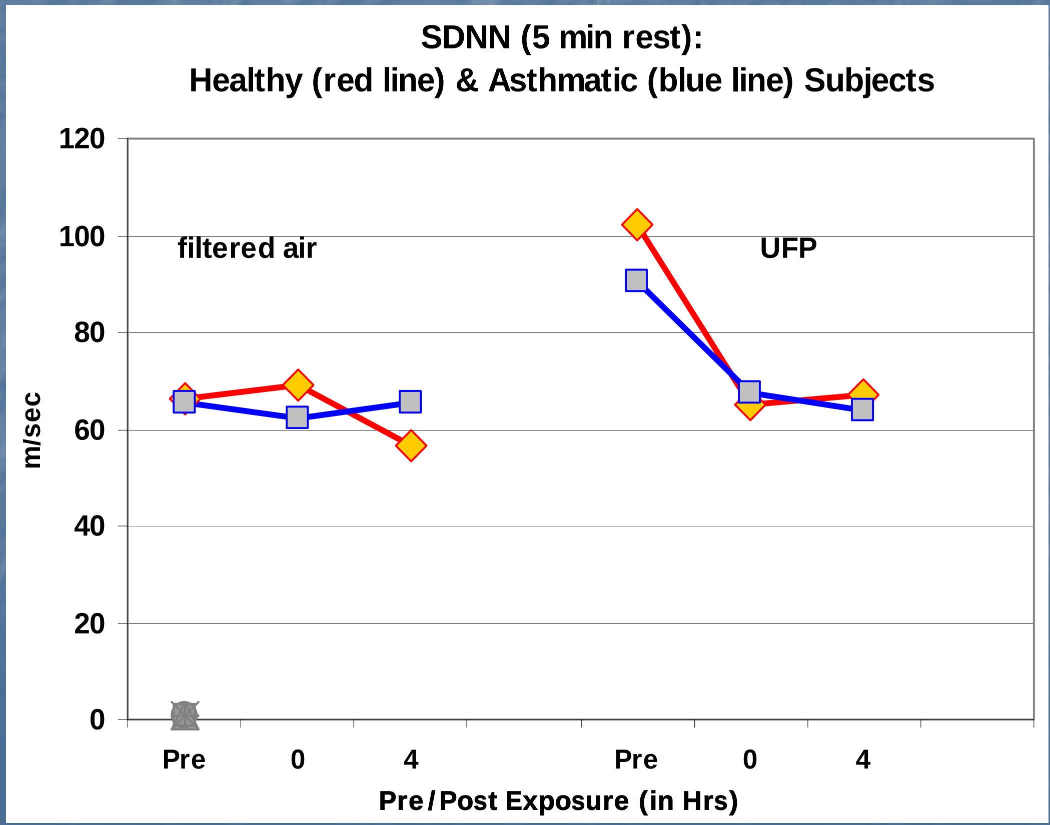
# Recent Studies of Freeway Exposures and Mobile Source Effects:

## Cardiovascular effects

- Exposures to on-road particles produce effects on the pulmonary and cardiovascular system in compromised aged rats, including observed acute phase response and inflammatory cell activation (Elder et al. *Inh Tox* 2004) as well as changes in heart rate and blood pressure (Kleinman et al. *In Preparation*).

- Study of healthy men exposed during driving (the "Trooper Study") noted a significant association between in- vehicle PM 2.5 exposure levels and changes in heart rate variability (HRV) and other cardiac endpoints. (Riediker et al., *AJRCCM* 2004)

- Gong et al. have completed the first ultrafine exposures on human subjects (healthy and asthmatic) and have seen a significant change in heart rate variability.



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# Recent Studies of Freeway Exposures and Mobile Source Effects: **Pulmonary and Allergic Airways Responses**

- Markers of **allergic and inflammatory airways responses** increased in sensitized mice sensitized exposed to mobile source emissions short distances from a freeway. *Kleinman et al, 2004*
  - Greater responses at 50m compared to 150m from the freeway

- **Asthma prevalence** in the Children's Health Study is associated with residential distance to freeway, both within and across communities. *Gauderman et al, 2004.*

- Current levels of air pollution associated with mobile sources have chronic, adverse effects on **lung development** from the age of 10-18 years leading to clinically significant deficits in attained FEV1 as children reach adulthood. *Gauderman et al, 2004*

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# Recent Studies of Freeway Exposures and Mobile Source Effects:

## Children's Health Study - Prevalence of Asthma by Distance to the Freeway

| Distance to the Nearest Freeway (Kilometers) | All Subjects | | |
|---|---|---|---|
| | Total | Asthma | |
| | N | (%) | OR[a] |
| >0.5 | 104 | (13.5) | 2.00 |
| 0.5 – 1.0 | 169 | (18.9) | 2.92 |
| 1.0 – 1.5 | 146 | (16.4) | 2.33 |
| 1.5 – 2.0 | 102 | (10.8) | 1.48 |
| 2.0 - 3.0 | 138 | (15.9) | 2.38 |
| 3.0 – 7.0 | 210 | (7.6) | 1.00 |
| Trend test[b] | | | p=0.01 |

a Odds ratio relative to the 3.0 – 7.0 km group, based on the combined model with adjustment for sex, race, Hispanic ethnicity, and cohort

b Test of trend in odds ratio across distance groups

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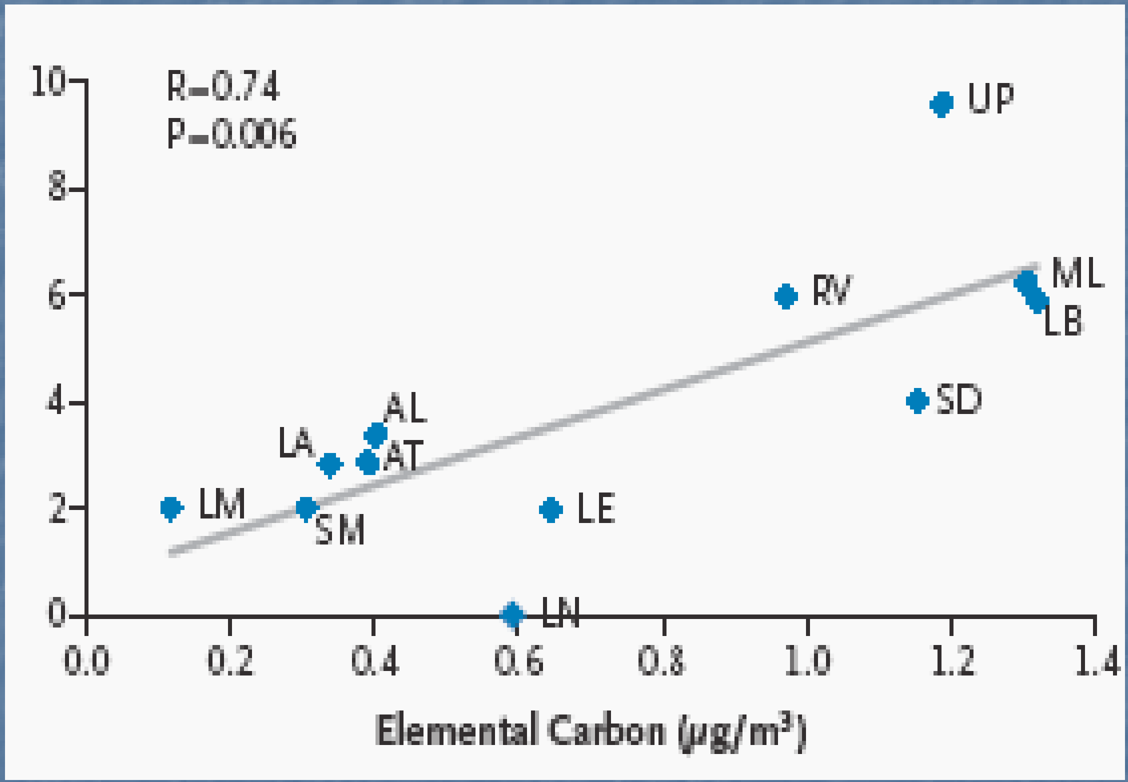
# Recent Studies of Freeway Exposures and Mobile Source Effects:

## Children's Health Study - Lung Development and Exposure to Air Pollution

Proportion of 18-year olds with FEV1 below 80 % of the predicted value




*Gauderman, et al. 2004 New England Journal of Medicine*

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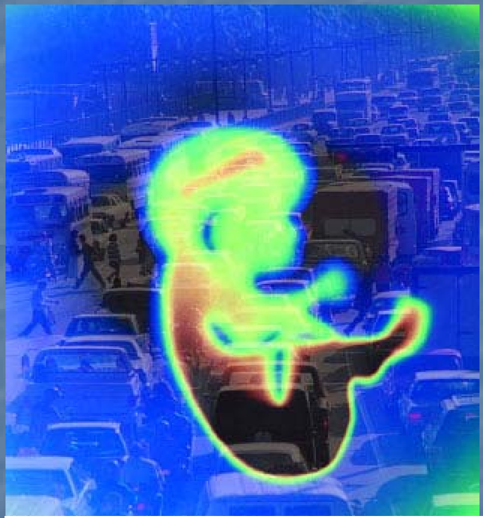
# Recent Studies of Freeway Exposures and Mobile Source Effects:

## Residential Proximity to Freeway Truck Traffic and Pre-term and LBW Babies



Infants born between 1997-2000 in Los Angeles County

| Number of freeway trucks passing within 750 feet of a home per day | Odds Ratio (95% CI) |
|---|---|
| | (n=4,346; 26,606) |
| ≥ 13,290 trucks | 1.23 (1.06-1.43) |
| ≥ 8,684 heavy-duty diesel vehicles | 1.18 (1.02-1.37) |

Model adjusted for all maternal risk factors as covariates, background air pollution concentrations and census block-group level socio-economic status

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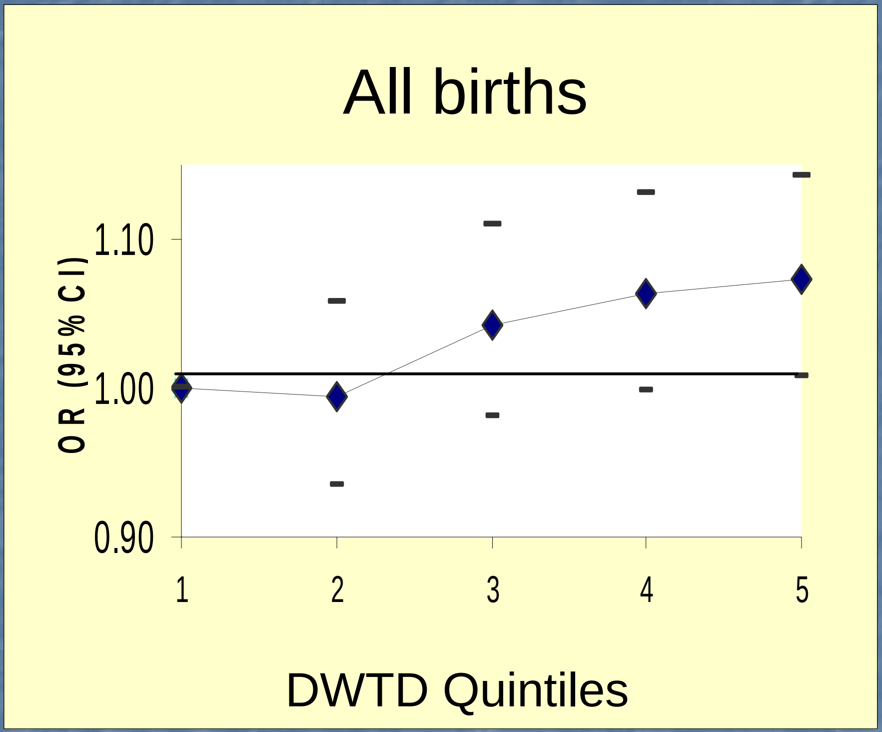
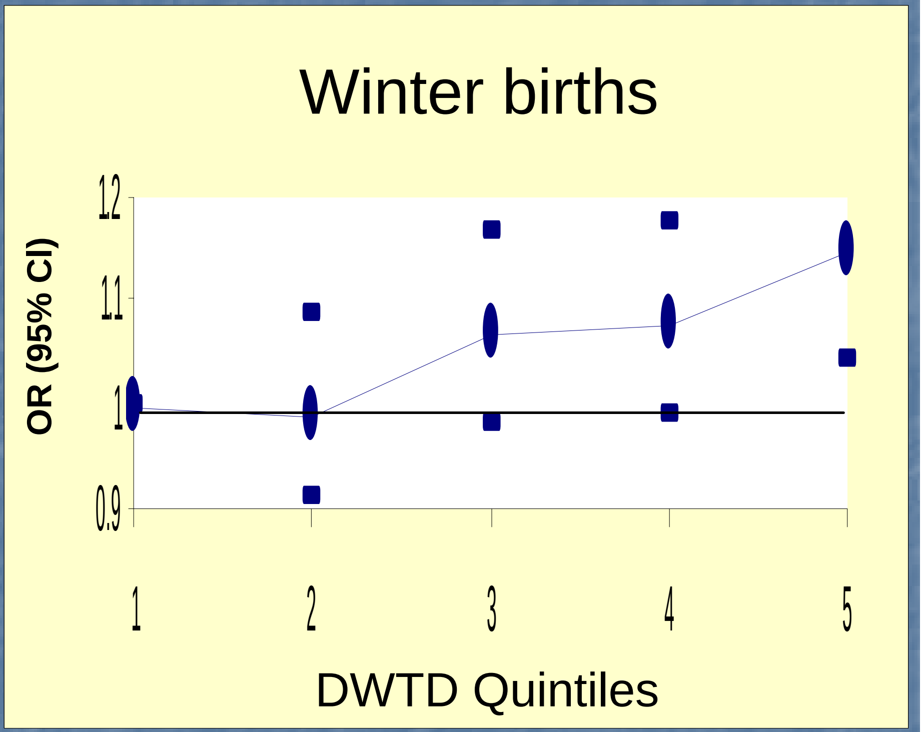
# Distance Weighted Traffic Density and Preterm Birth in LA: 1994-1996

**(Case N=17,706; Control N=26,005)**




Wilhelm M, Ritz B. Residential Proximity to Traffic and Adverse Birth Outcomes in Los Angeles County, California, 1994-1996. Environ Health Perspect 2003 Feb;111(2):207-16.

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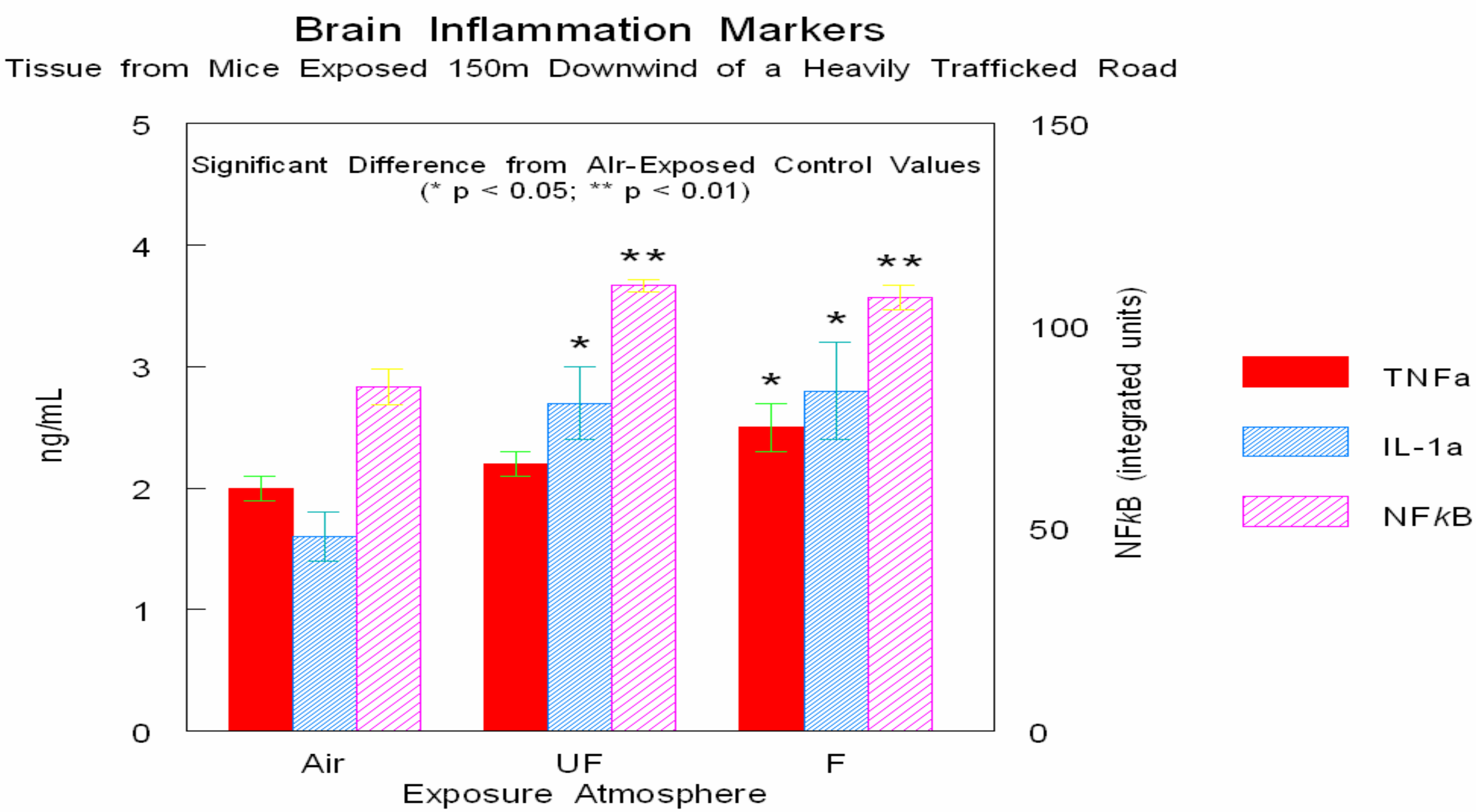
# Recent Studies of Freeway Exposures and Mobile Source Effects: **Central Nervous System**

**Kleinman et al., in preparation, 2004**



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# Mechanistic Hypotheses as a Basis for Studying PM Toxicity and Health Effects

- PM contains pro-oxidative chemicals
- Organic chemicals and metals located on the PM matrix are responsible for toxicity
- PM generates reactive oxygen species → oxidative stress
- Oxidative stress → pro-inflammatory effects
- Inflammation → adjuvant effects in asthma, cardiovascular disease and other endpoints
- Susceptibility to oxidative stress-related health effects may be modulated by anti-oxidant defenses

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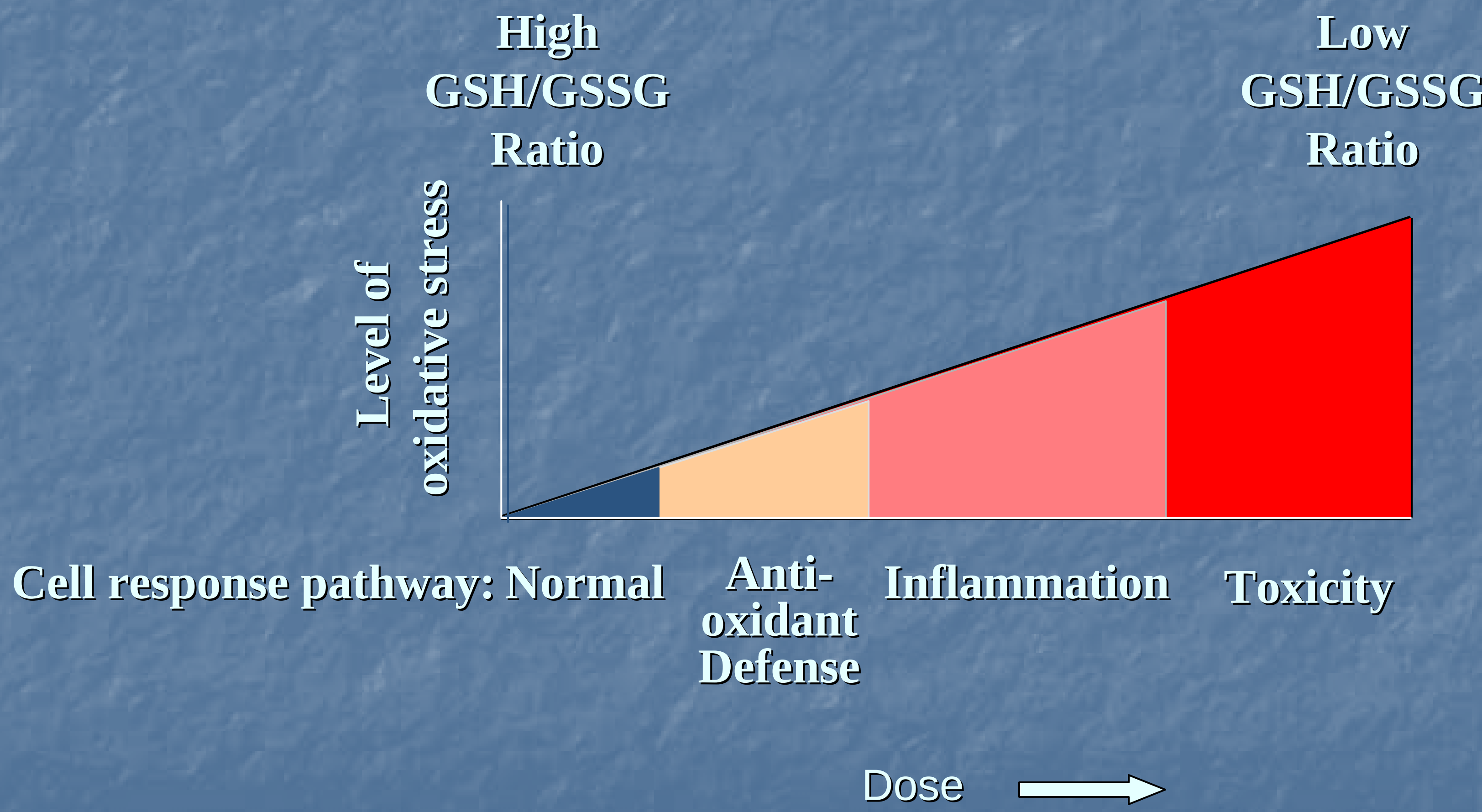
# Pathways of Oxidative Stress




Xiao, et al.

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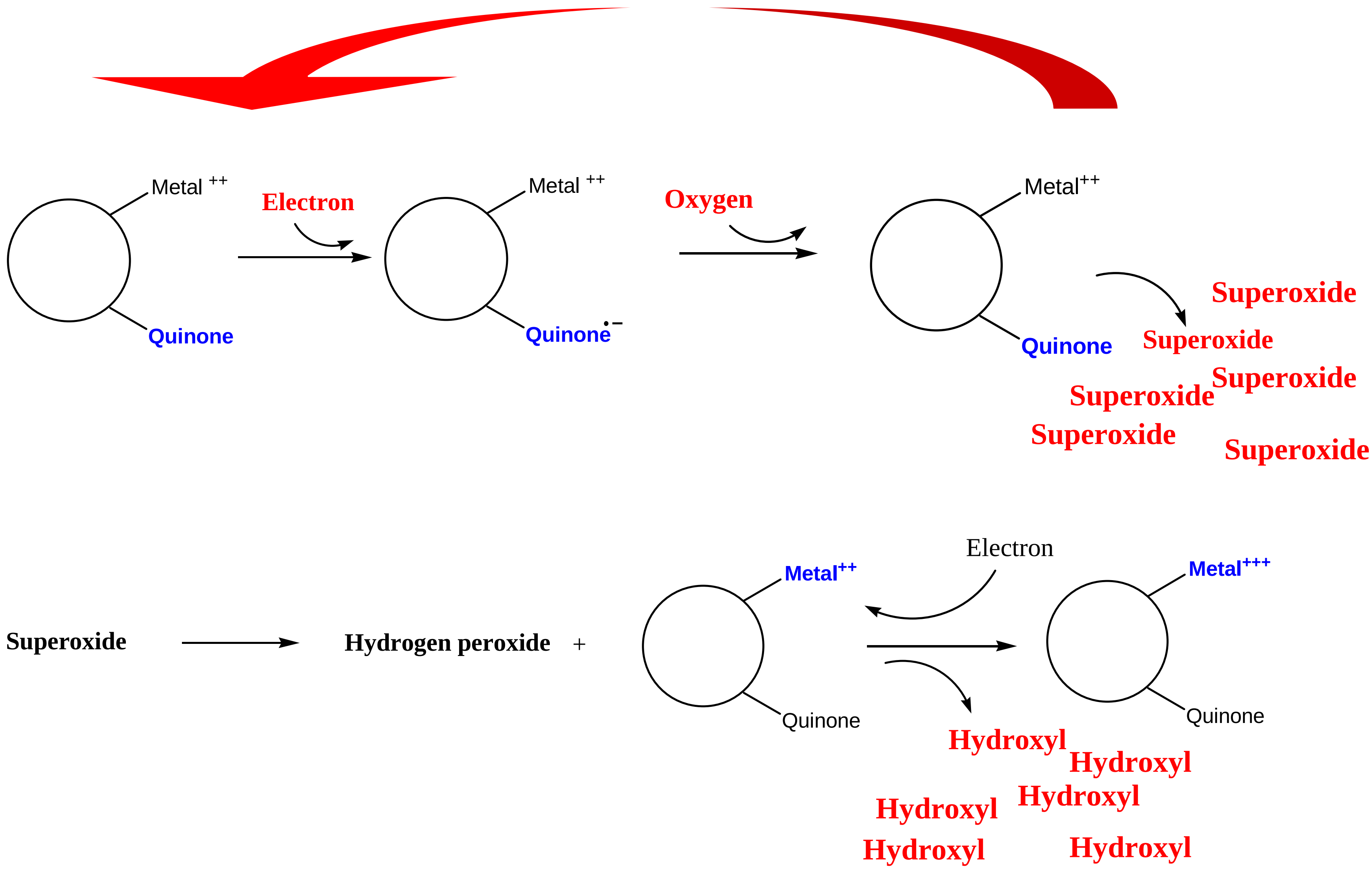
# Compounds Capable of Catalytic Redox Activity and Oxidative Stress Production



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# Particle Size and Composition: Relation to Toxicity

Table 5
Contrasting features of coarse, fine, and ultrafine particles[a]

| Parameters | Particle mode | | |
|---|---|---|---|
| | Coarse ($PM_{10}$) | Fine ($PM_{2.5}$) | Ultrafine |
| Size | 2.5–10 μm | 2.5–0.15 μm | <0.15 μm |
| Organic carbon content | + | ++ | +++ |
| Elemental carbon content | + | ++ | +++ |
| Metals as % of total elements | +++ | ++ | + |
| PAH content | + | + | +++ |
| Redox activity (DTT assay) | + | ++ | +++ |
| HO-1 induction | + | ++ | +++ |
| GSH depletion | + | +++ | +++ |
| Mitochondrial damage | None | Some | Extensive |

[a] [85].

(sampled at source site)

From: Li, N., Hao, M., Phalen, R., Hinds, W., Nel, A. (2003). "Particulate air pollutants and asthma: A paradigm for the role of oxidative stress in PM-induced adverse health effects." Clinical Immunology 109: 250-265.

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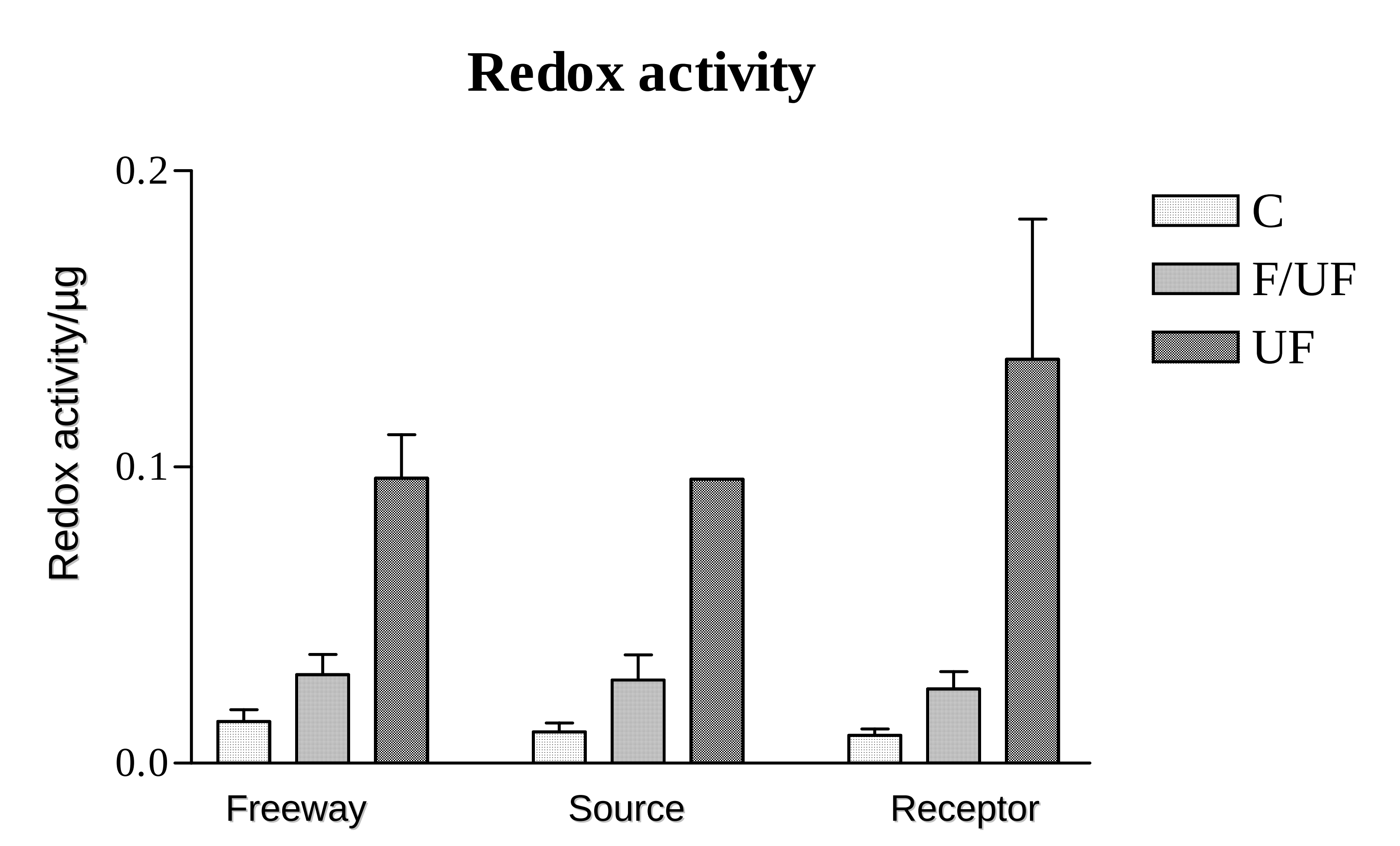
# Redox Activity of Ambient PM: Effect of Location and Size Fraction



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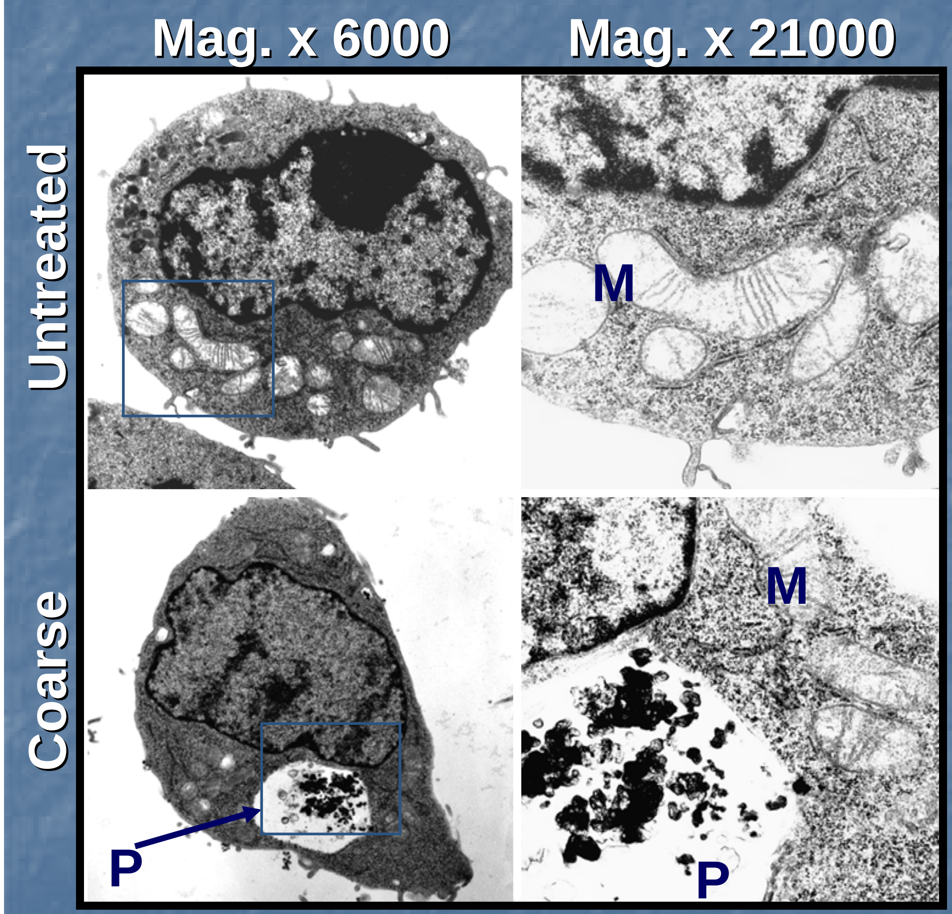
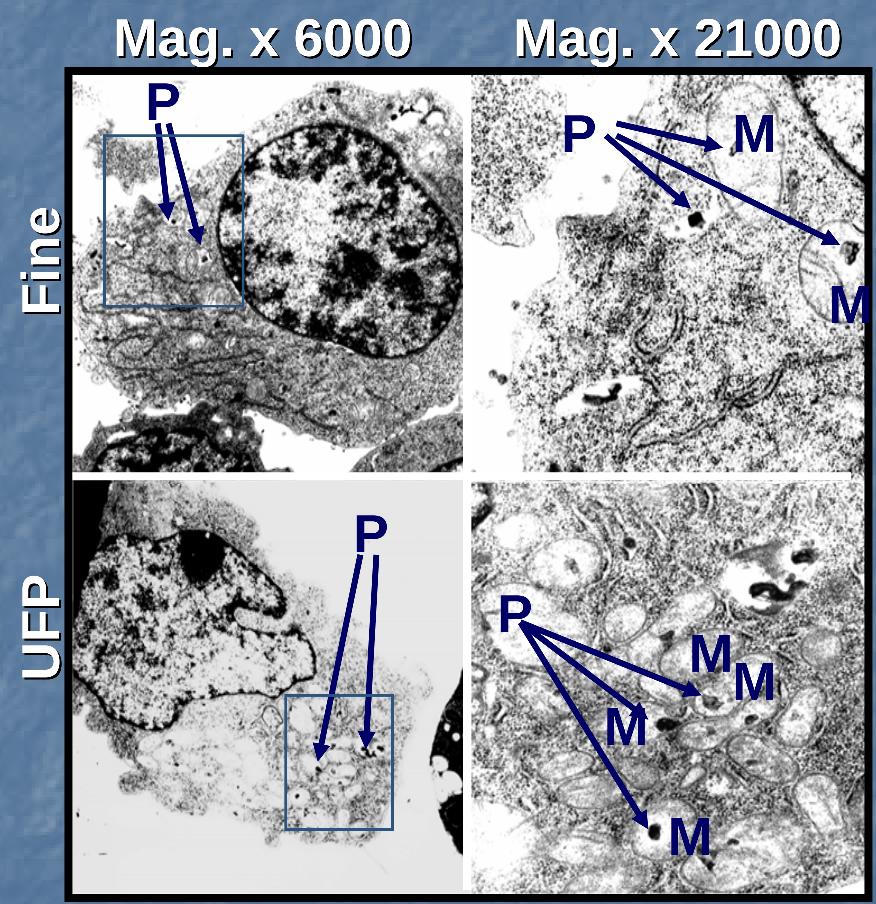
# Mitochondria: An Important Subcellular Target of PM and a Source of ROS Generation




RAW 264.7

Li, N., Sioutas S, Cho A, Schmitz D, Misra C, Sempf J, Wang M, Oberly T, Froines J, Nel A (2003). "Ultrafine Particulate Pollutants Induce Oxidative Stress and Mitochondrial Damage." Environmental Health Perspectives 111(4): 455-460.

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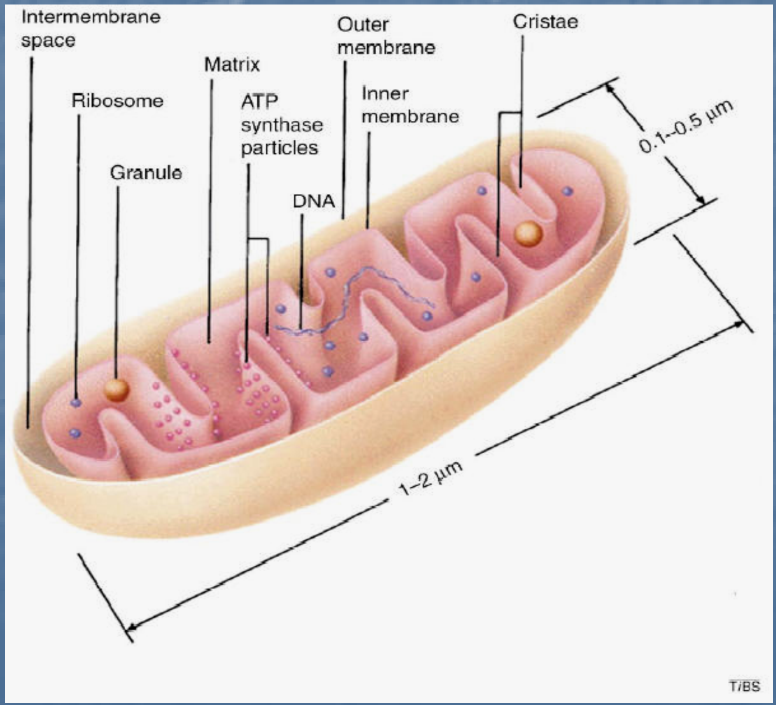
# Hypothesis:

## Differential Cytotoxic Effects of Diesel Exhaust Particulate Fractions Are Caused by Selective Perturbation of Mitochondrial Functions

DEP, ultrafine PM fractions → Mitochondrial functional assays → Cell death




- Potential changes in the mitochondrial membrane
- Mitochondrial PTP opening
  - -swelling
  - -calcium retention capacity
  - -oxygen uptake

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# Recent Findings from the PM Centers Augment the Literature that Associates PM and Reactive Oxygen Species/Oxidative Stress

- **ROS activity in ambient PM samples:**
  - Vary by location and time-of-year.
  - Vary by size fraction: Smaller PM fractions (10-56 nm ) had dramatically higher ROS concentrations. *Venkatachari et al, Atm. Chem. 2004*
- **Biological markers of ROS production:**
  - Increased oxidative stress markers and inflammatory effects in rat lung after exposure to concentrated ambient particles (CAPs). *Rhoden et al, Tox Sci 2004*
  - Oxidative damage (TBARS) was correlated with the metal content of CAPs. *Rhoden et al, Tox Sci 2004*
  - Increased ROS in heart and lung of rats with short term CAPs exposure. *Gurgueira et al, 2002*

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# Summary of PM Center Accomplishments

- **Atmospheric chemistry** has a significant effect on PM composition.
- A wider range of **target tissues and health endpoints are associated with PM exposure** than was known in 1997.
- Results from diverse types of studies has strengthened the evidence that **mobile sources are highly relevant** to the public health risks posed by ambient PM.
- **Improved mechanistic understanding** of PM toxicity has evolved:
  - Ultrafine particles
  - Mitchondrial uptake
  - Organic compounds and metals capable of catalytically generating oxidative stress has been shown.

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# Key Questions for Future Work

- **Which sources pose the greatest risks to public health?**
  - → Need for studies of the relationships among specific sources, including mobile sources, atmospheric chemistry products, wood smoke, cooking and others, and toxicity-health effects

- **What are critical characteristics of PM in relation to toxicity?**
  - → Further evaluation of size fractions needed; implications for PM regulation
  - → Relationship between toxic mechanisms and specific toxic components

- **Which health effects are most sensitive to low levels of PM?**
  - → More quantitative exposure-response data are needed
  - → Role of susceptibility findings including gene-environment interactions in determining most sensitive endpoints