



Cardiopulmonary Health Effects of San Joaquin Valley Fine/Ultrafine Particulate Matter

What Can We Learn From Experimental Research?

Laurel Plummer

Kent Pinkerton

Center for Health and the Environment

San Joaquin Valley Aerosol Health Effects Research Center

University of California, Davis

Particulate Pollution in the San Joaquin Valley: Translating Science Into Policy

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Particle-Induced Health Effects

- Exposure to elevated levels of ambient fine /ultrafine particulate matter ($PM_{2.5}$) is associated with increased morbidity and mortality due to cardiopulmonary health effects.
- In the San Joaquin Valley, a **10 $\mu\text{g}/\text{m}^3$ change in $PM_{2.5}$ concentration** is associated with elevations in mortality due to respiratory and cardiovascular disease.
- Individuals with asthma living in areas of the SJV with high levels of particulate pollution levels are more likely to have frequent asthma symptoms and asthma-related ER visits and hospitalizations—influence of traffic related $PM_{2.5}$.

Particle-Induced Inflammation

- Inhalation of ambient particulate matter induces an **inflammatory response** that is currently regarded as a main mechanism for disease exacerbation .
- Cardiopulmonary inflammation provides a **causative link** between PM exposure and the diverse health effects found in epidemiologic and population based studies.
- **Inflammation is a hallmark of a number of respiratory and cardiovascular conditions** that contribute to morbidity and mortality including asthma, chronic obstructive pulmonary disease, bronchitis, emphysema and atherosclerosis.

What Can We Learn From Experimental Research?

Study Aims:

1. Does inhalation of elevated concentrations of ambient particles induce cardiopulmonary inflammatory or cytotoxic effects in a healthy mouse model?
2. Does the nature of these effects change with increasing duration of exposure?
3. Do these effects correlate with particle physicochemical characteristics?

CAPs Field Studies in Fresno, CA

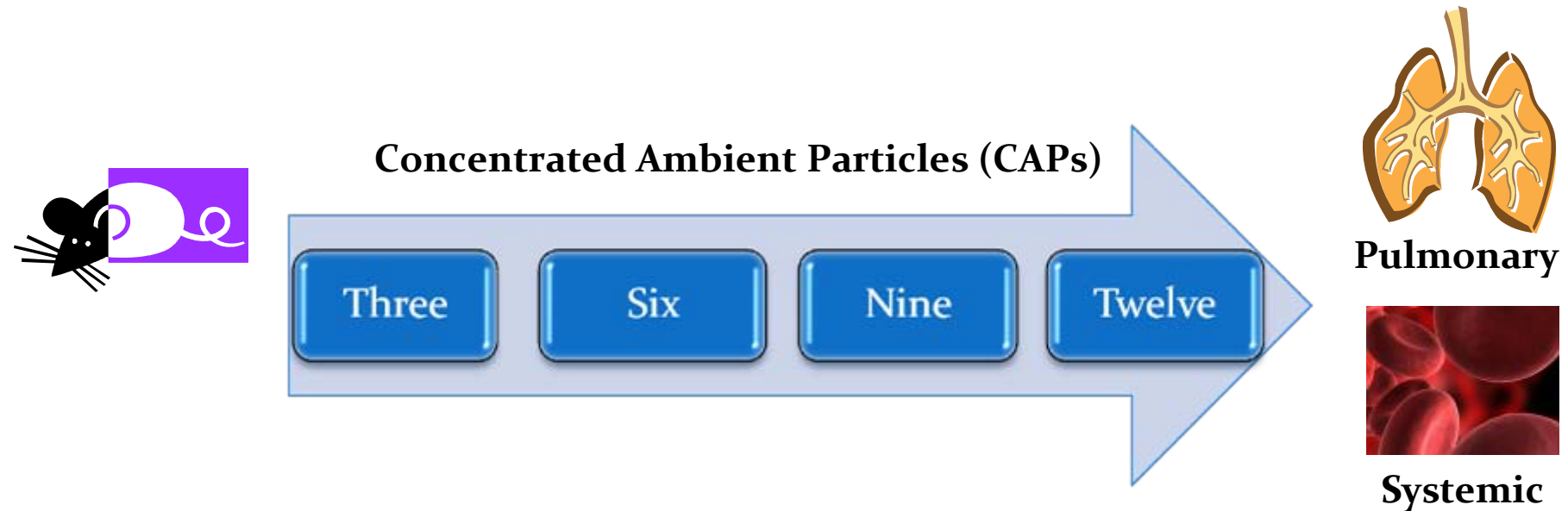


500 West Shaw Avenue

- The Versatile Aerosol Concentration Enrichment System (VACES) concentrates ambient fine/ultrafine particles.
- Exposure to concentrated ambient fine/ultrafine particles (CAPs) in Fresno is associated with mild, but significant, cellular effects in the lungs of healthy adult rats.
- Seasonal/regional differences in lung inflammation have been observed at 24 and 48 hours post-exposure to CAPs.

(Kim et al. 2001, Smith et al. 2006, Plummer et al. unpublished data)

Experimental Design: Progressive Exposure to CAPs



Daily CAPs exposure for six hours at a mean concentration of $150 \mu\text{g}/\text{m}^3$. Cardiopulmonary inflammation was measured **24 hours post exposure**.



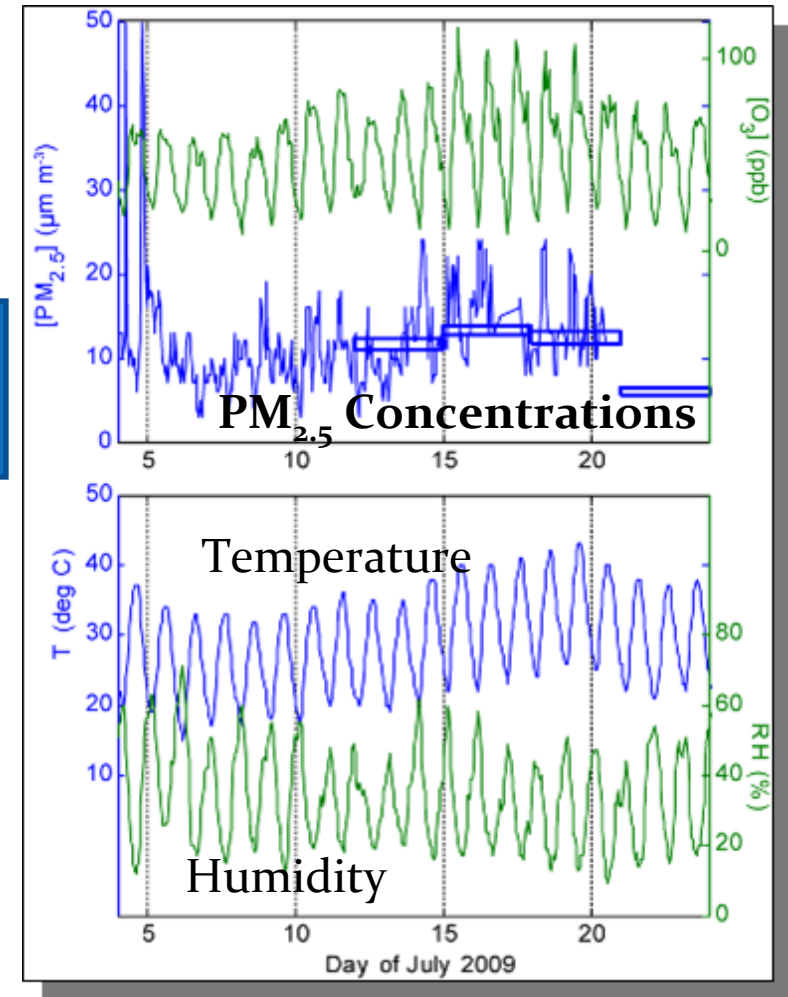
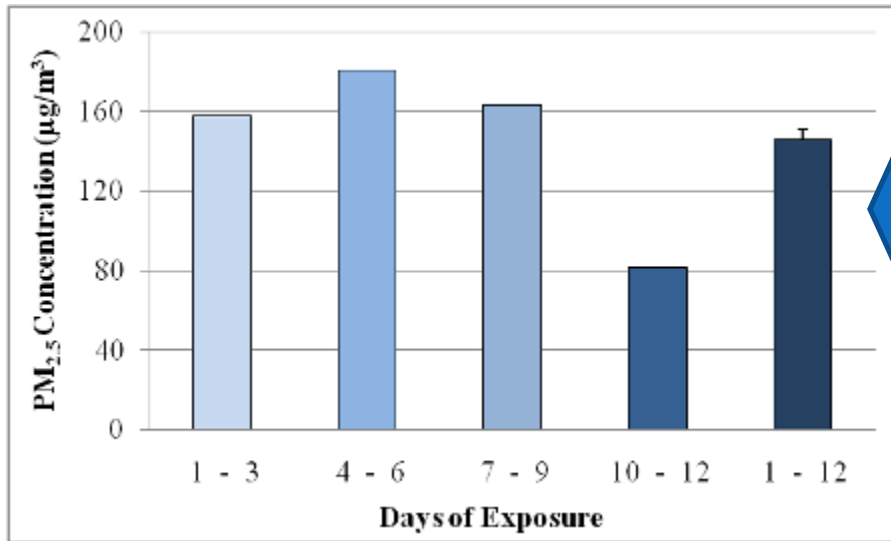
CAPs exposure was conducted over twelve consecutive summer days.



The urban emission profile is influenced by mobile (diesel and gasoline) and stationary (residential and industrial) sources.

Results: Gravimetric Analysis of Particles

A: PM_{2.5} Concentrations

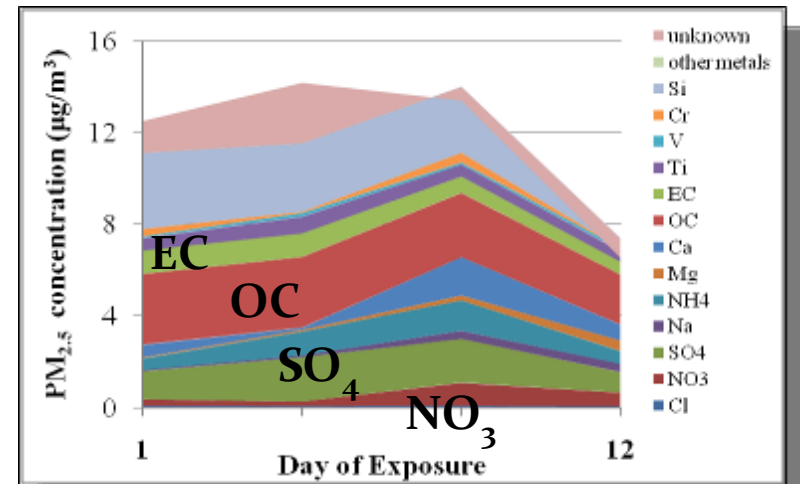


B: Meteorological and Gravimetric Data from CARB Fresno First Street Station

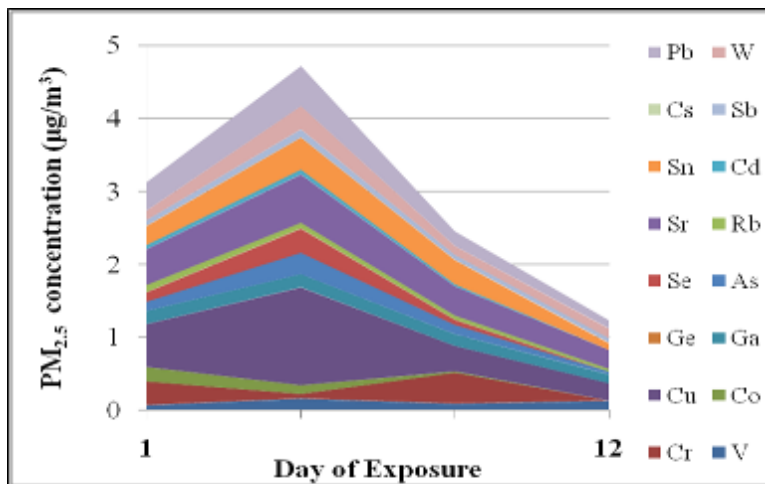
Results: Chemical Analysis of Particles



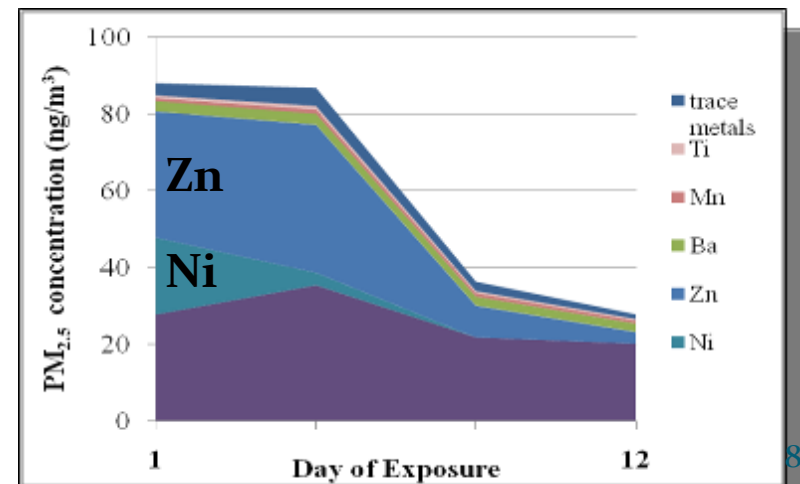
A: Major Ion Aerosol Concentrations



B: Metal Concentrations

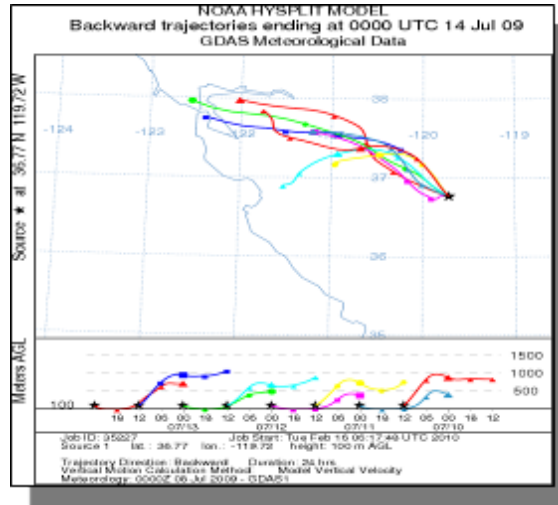


C: Trace Metal Concentrations

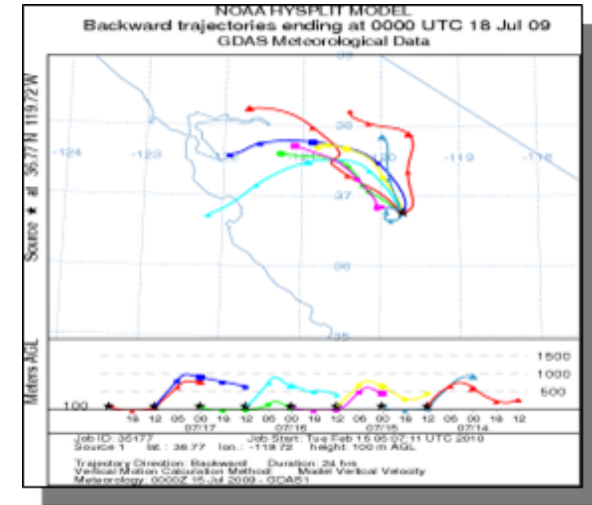


Calculated Wind Pattern Back Trajectories

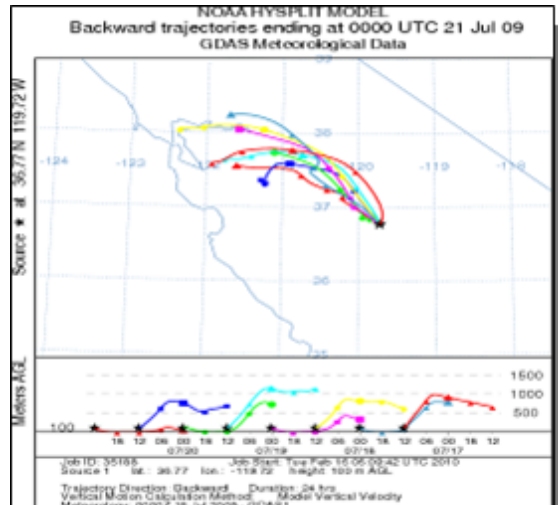
Days 1 - 3



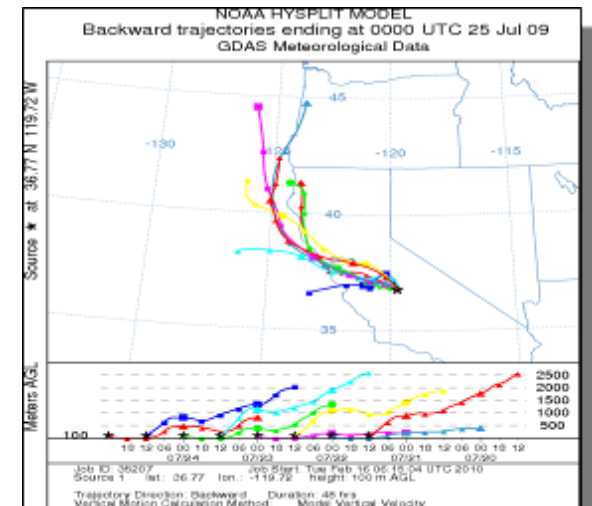
Days 4 - 6



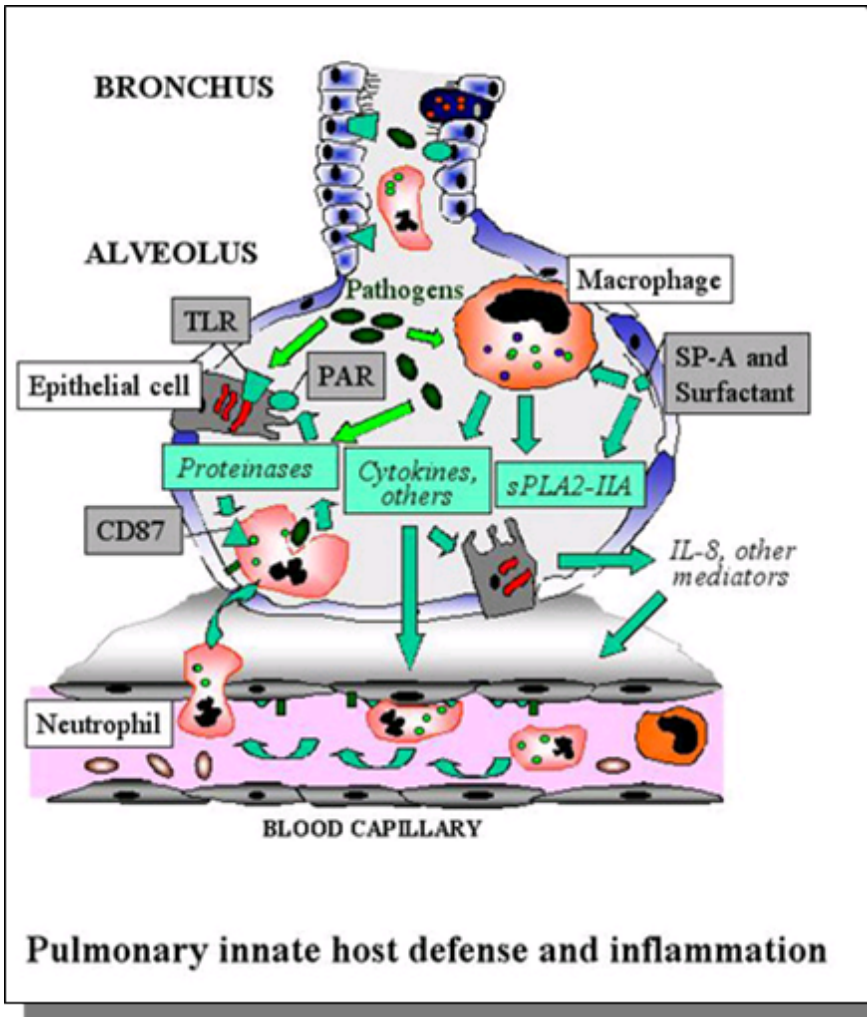
Days 7 - 9



Days 10 - 12

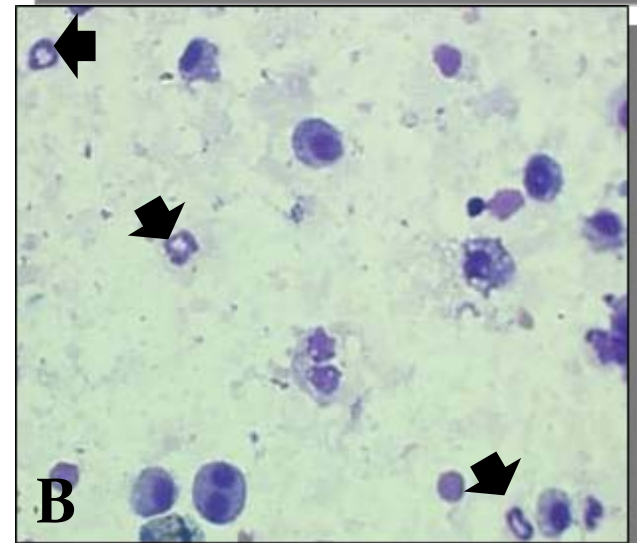
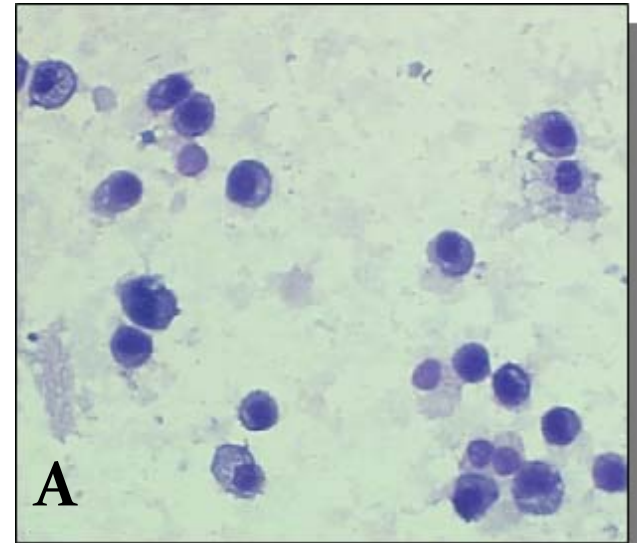
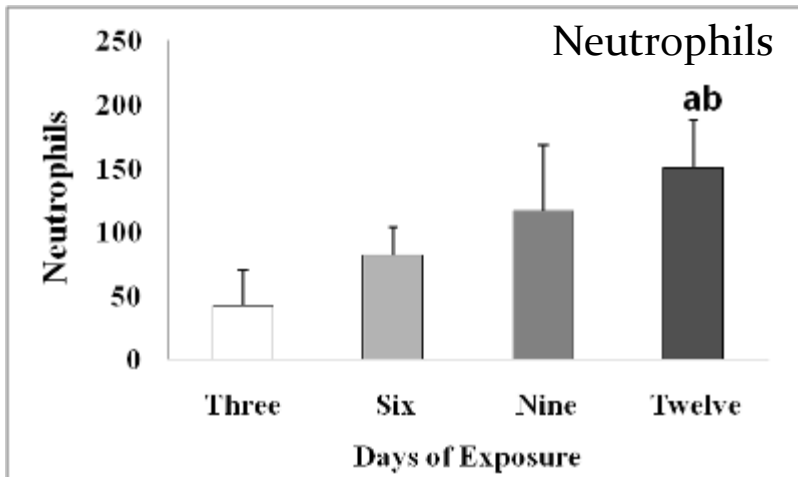
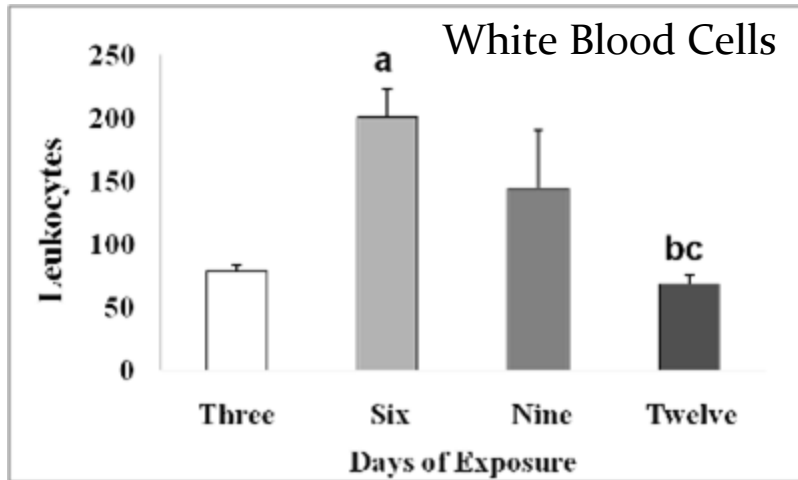


Cardiopulmonary Inflammation: Key Endpoints



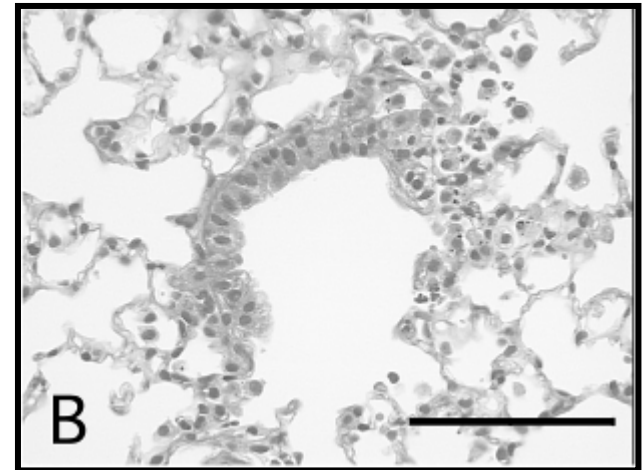
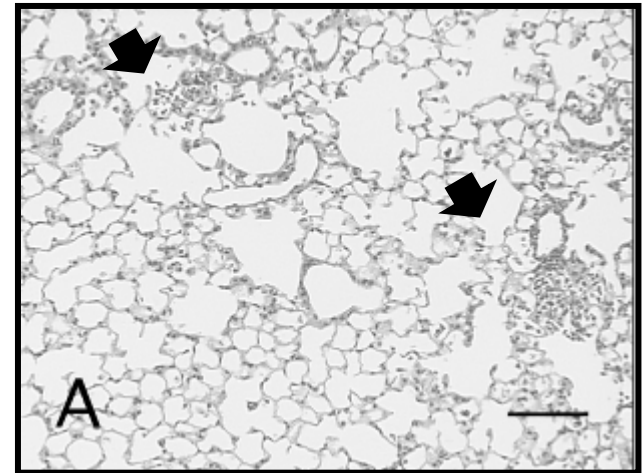
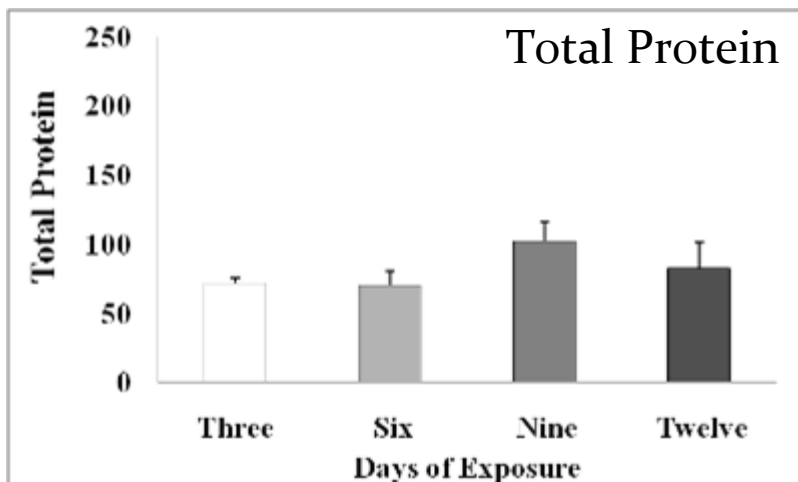
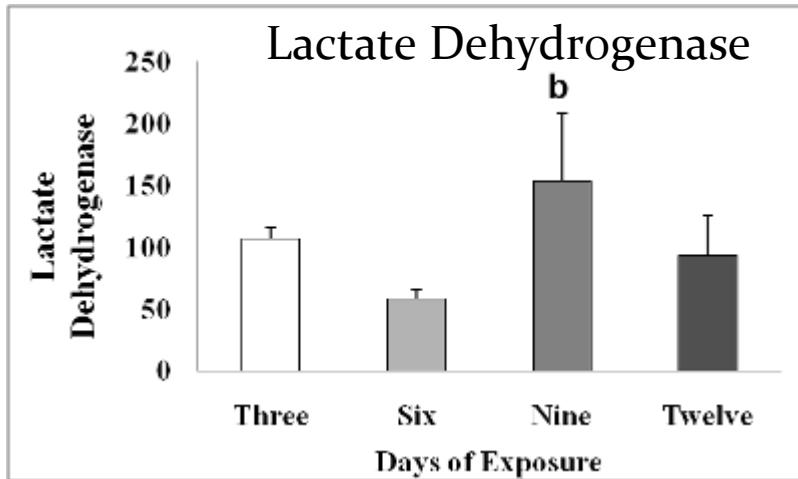
- ❑ Inflammatory Cells
 - Monocytes/Macrophages
 - Neutrophils
 - Lymphocytes
- ❑ Signaling Molecules
 - Cytokines
 - Chemokines
 - Growth Factors

Lung Response: Inflammatory Cell Profile



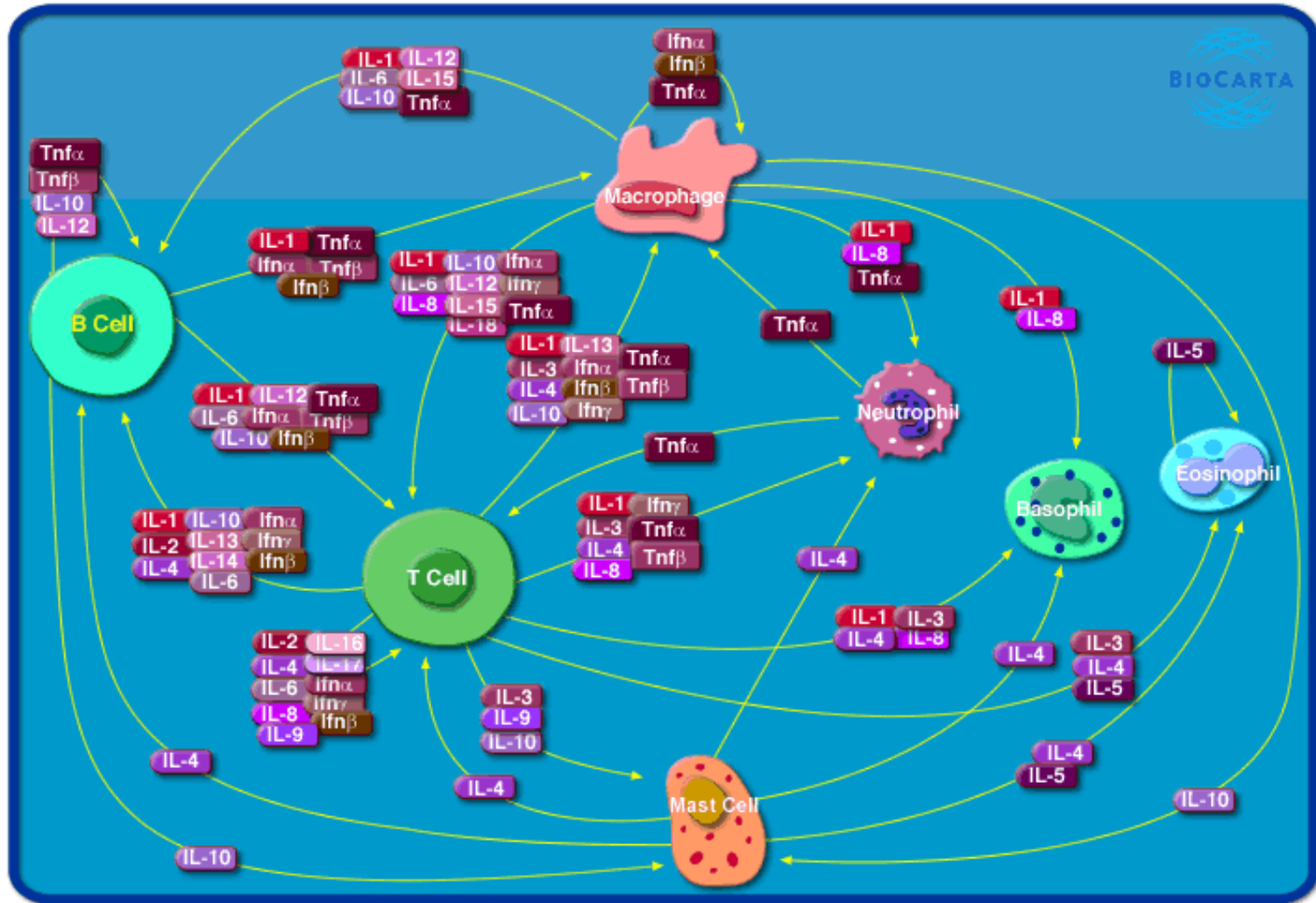
Data is expressed as percent of day matched control $\pm$ standard error. Significance is noted relative to CAP exposure for three days (a), six days (b), or nine days (c).

Lung Response: Cell Damage

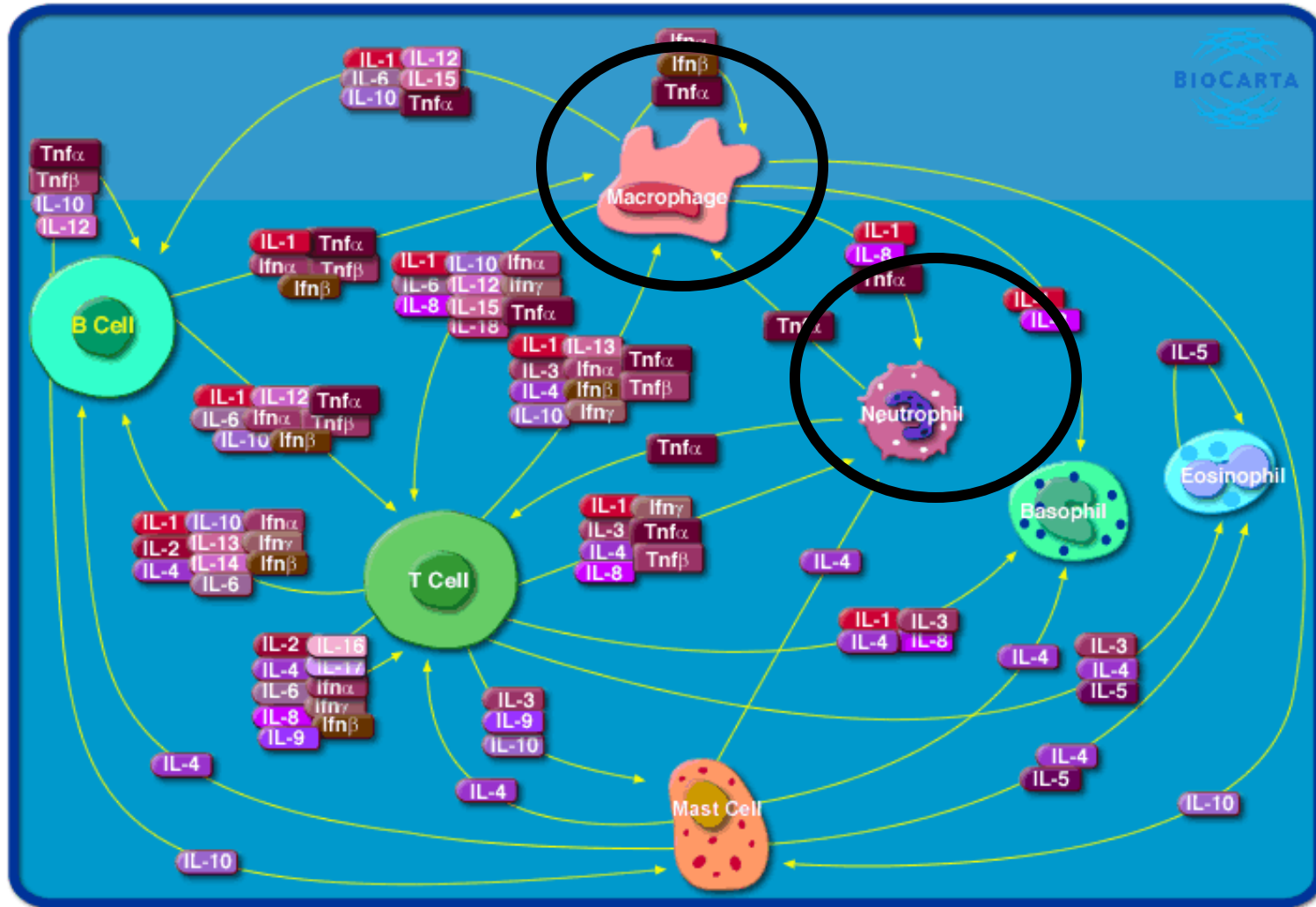


Magnification Bar = 10 μm ₁₂

Inflammatory Mediators: Cytokines and Chemokines

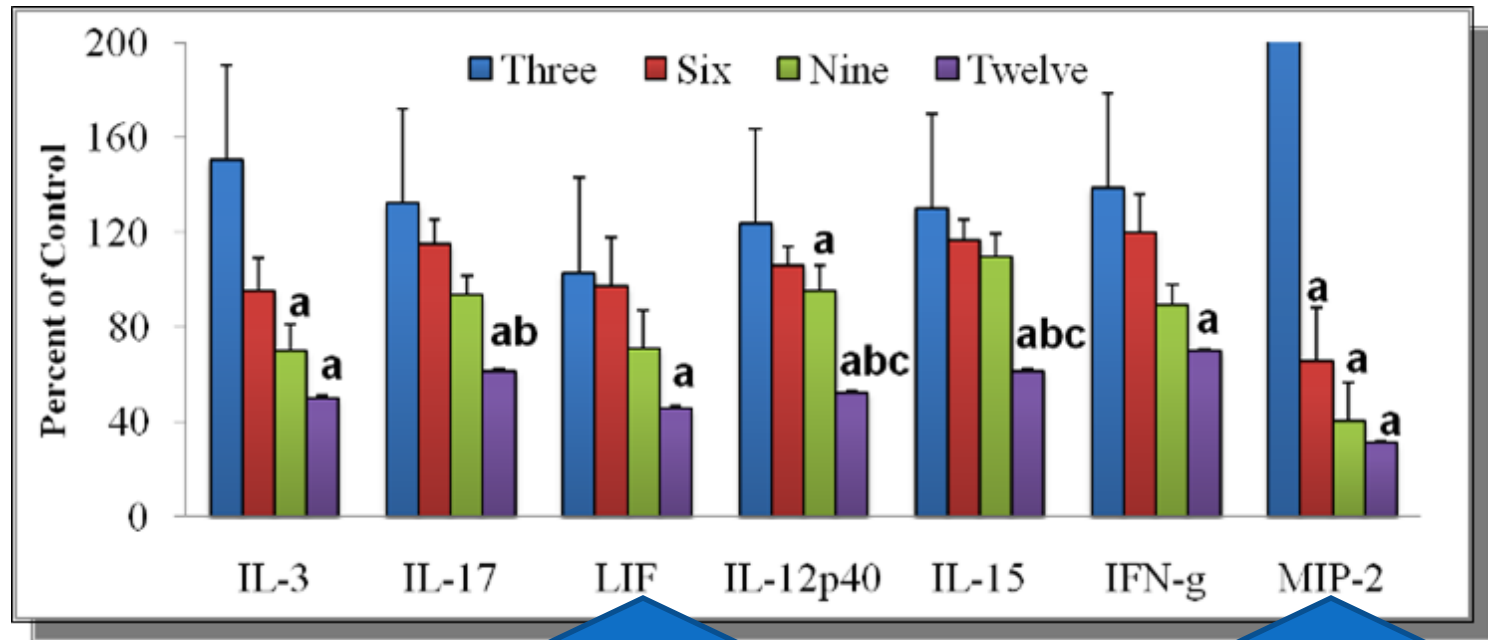


Inflammatory Mediators: Cytokines and Chemokines



Lung Response: Inflammatory Mediators

After THREE days of CAPs exposure....

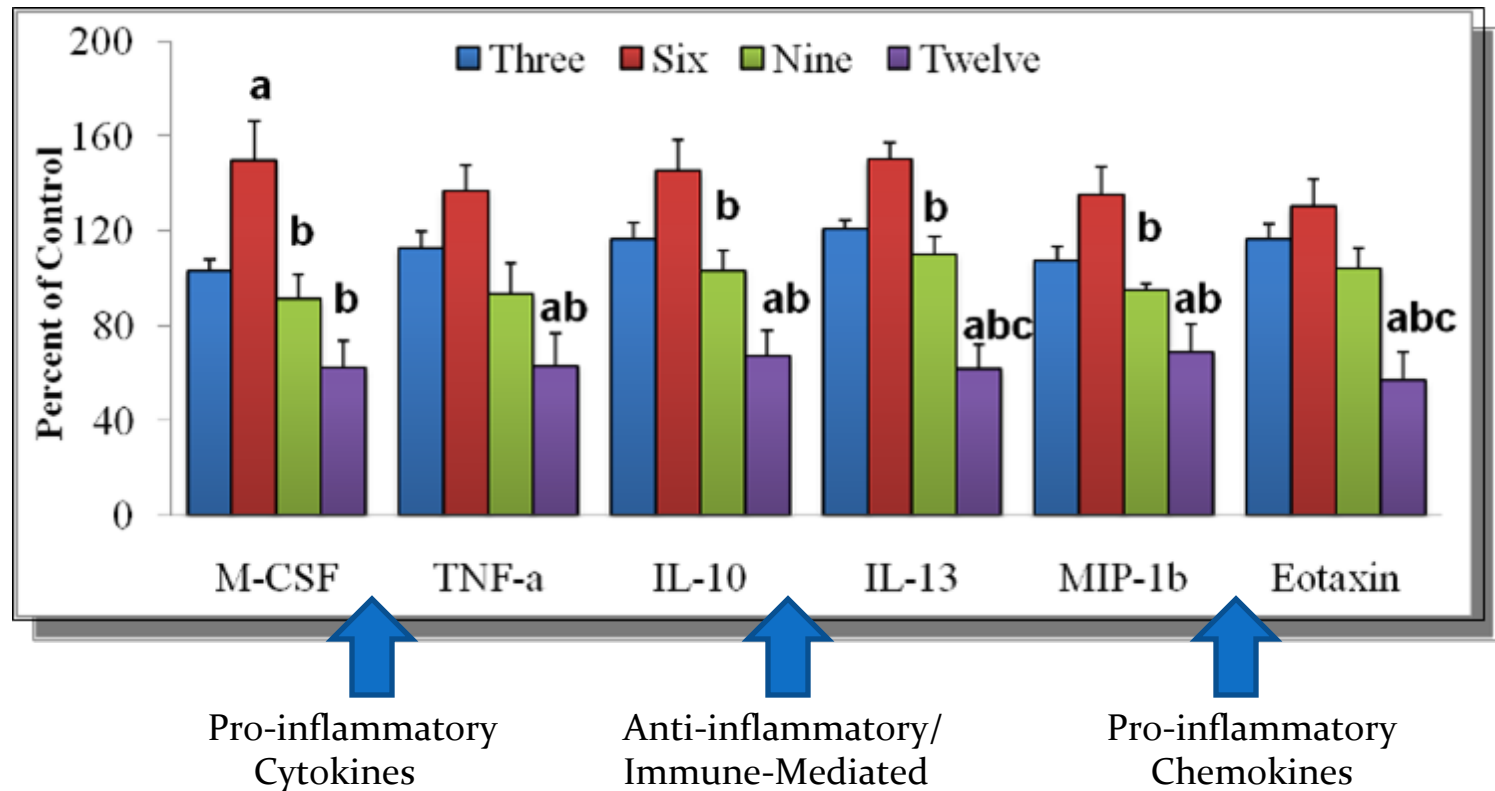


Pro-inflammatory cytokines augment macrophage function and phagocytosis.

Pro-inflammatory chemokine that recruits neutrophils to the lung.

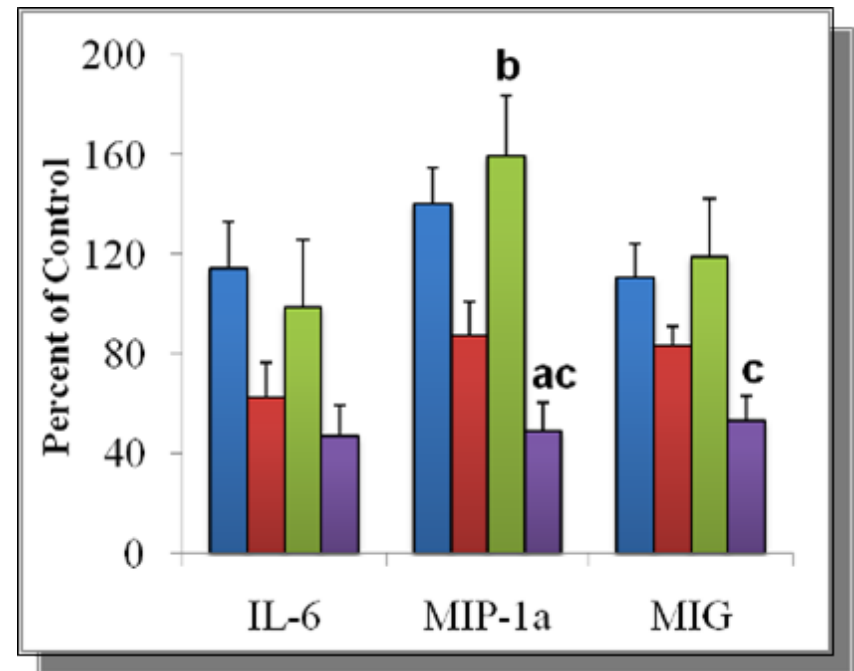
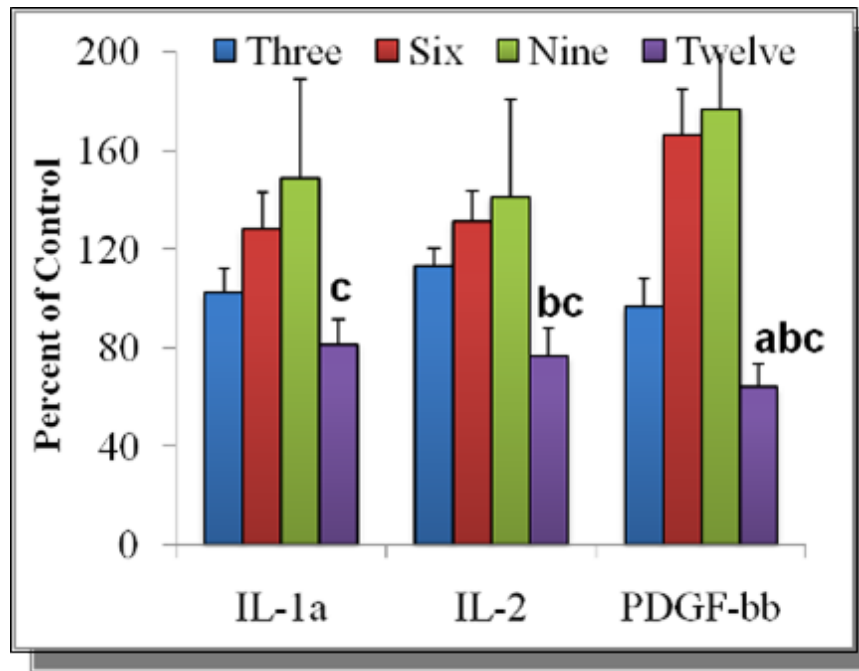
Lung Response: Inflammatory Mediators

After SIX days of CAPs exposure....



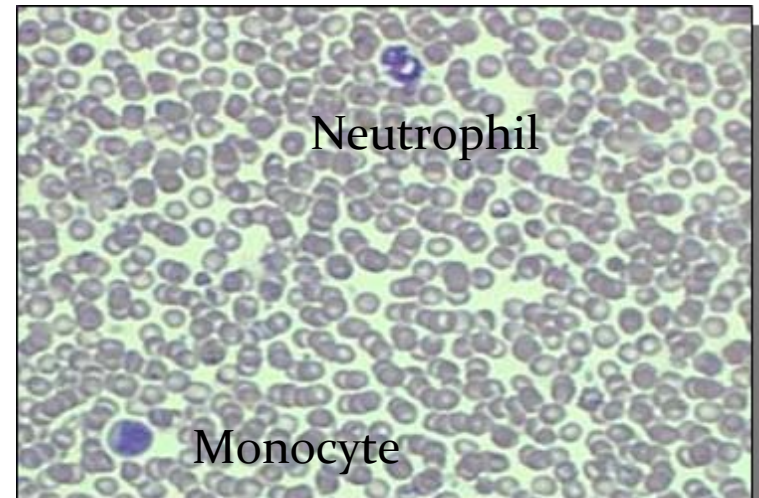
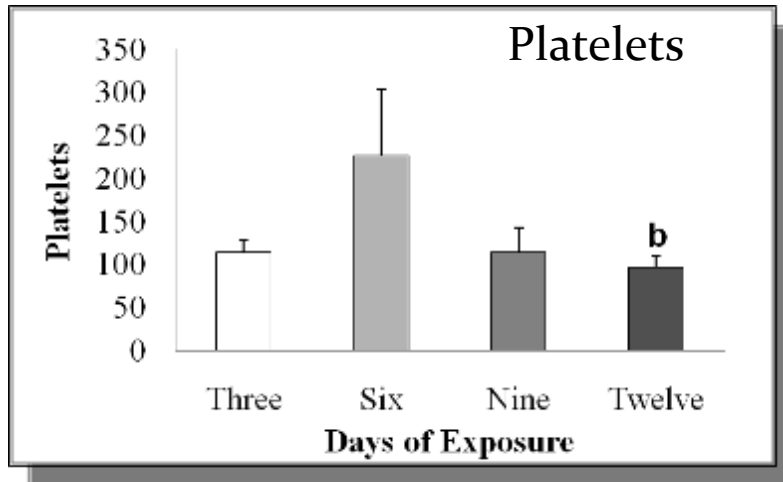
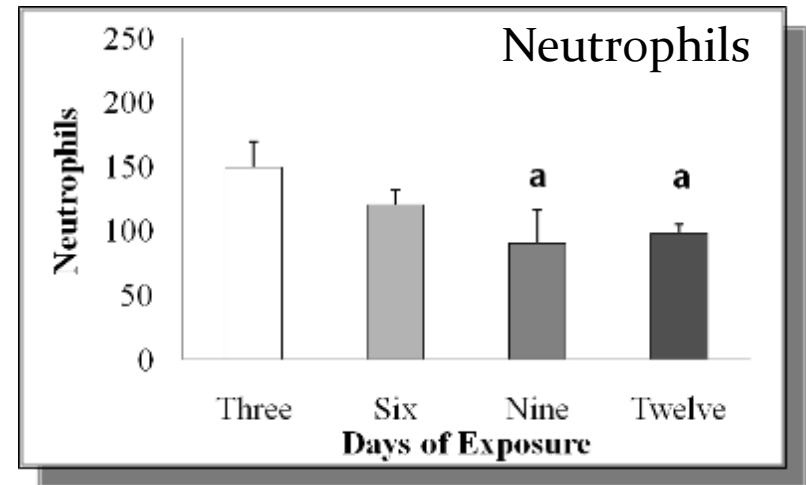
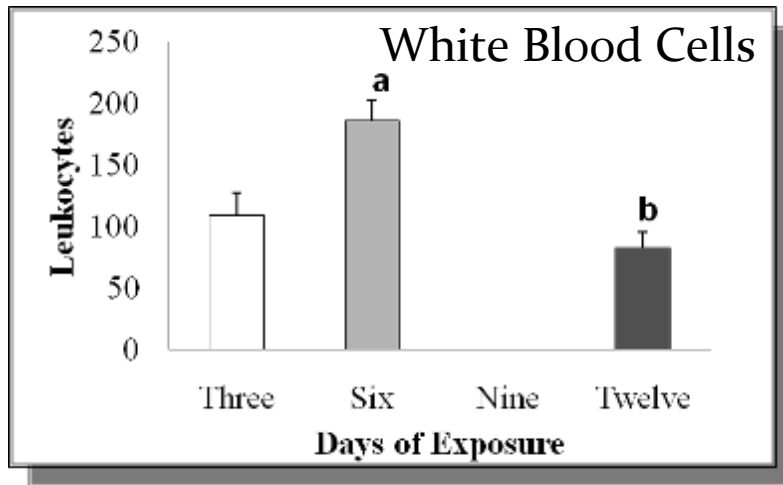
Lung Response: Inflammatory Mediators

After NINE days of CAPs exposure....



These include pro-inflammatory (IL-1a, IL-2) and immune-mediated (IL-6) cytokines, chemokines (MIP-1a, MIG) and growth factor (PDGF-gg).

Systemic Response: Blood Parameters



Summary and Conclusions

Does acute inhalation of elevated concentrations of ambient particles induce cardiopulmonary inflammatory or cytotoxic effects in a healthy mouse model?

Significant pulmonary and systemic inflammation and lung cytotoxic and immune responses are observed following exposure to concentrated ambient San Joaquin Valley PM.

Summary and Conclusions

Does the nature of these effects change with increasing duration of exposure?

Particle-induced pulmonary and systemic responses are strongly influenced by exposure duration and respond in a wave-like fashion to PM exposure.

Progressive exposure to CAPS induced a consistent temporal increase in neutrophils in the respiratory tract in the presence of transient increases in total white blood cells and a variable lung immune response

Adaptation?

Summary and Conclusions

Can we attribute these inflammatory and cytotoxic effects to particle physicochemical characteristics?

Presence of inflammatory cells in the lung and circulation and cytokine and chemokine levels were consistently attenuated during the last three days of exposure when CAPS mass concentrations were also reduced.

Inflammatory and cytotoxic responses cannot be solely predicted by particle chemical composition of main players (EC, OC, nitrates, sulfates, ammonia, transition metals).

Acknowledgements

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