



# **Workplace exposures to polycyclic aromatic hydrocarbons (PAHs) and potential mechanisms driving adverse signaling events in lung**

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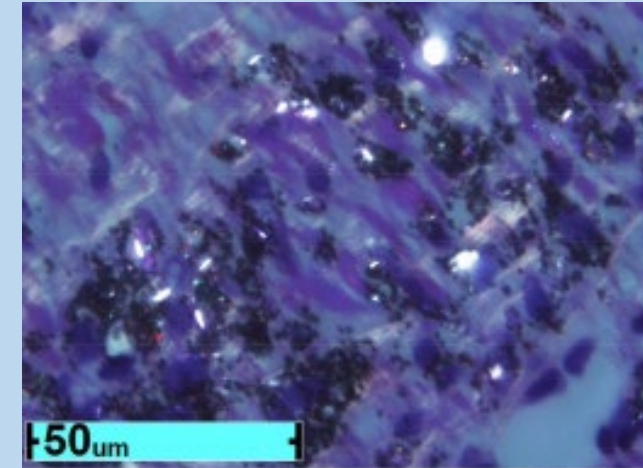


# What are PAHs and where are we exposed?

- PAHs constitute a major group of pollutants
  - Widespread in the environment, including indoor and outdoor environments
  - Workplace exposures due to prevalence in DE, and in industries involving coal tar (i.e. roofers, chemical oil), coal, coke and steel, among others.
  - Formed during incomplete combustion of carbon sources, such as wood, coal, heavy fuel oil, etc
- Due to their bioaccumulation, PAHs are persistent organic pollutants that do not easily degrade in the environment and are subject to long-range air transport (e.g., burn pit plumes; wildfire smoke plumes)
  - Evidence of PAH exposure in soldiers exposed to burn pits (Olsen et al., 2022)
- Sixteen PAHs have been labeled as priority pollutants by the U.S. EPA, owing to their frequency of detection, and potential for human exposure leading to adverse health effects.
  - All 16 found in burn pit ash (Masiol et al., 2016; Kim et al, 2021)
  - Many of these 16 PAHs are IARC carcinogens
  - However, many other species exist that are poorly studied

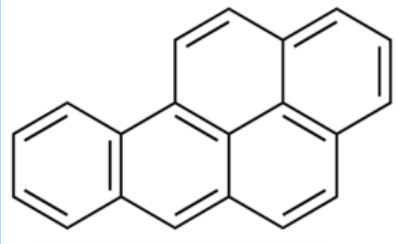
# PAHs were detected in the lung biopsies of soldiers exposed to airborne hazards

- Olsen et al, 2022:
  - All non-smokers and healthy prior to military service
  - Deployed to Iraq and Afghanistan since 2003
    - Airborne hazards include burn pits, sandstorms, etc
  - Identified burned products from incomplete combustion from lung biopsies five soldiers
    - Used Raman Spectrometry to identify spectra that were consistent with PAHs in these samples
    - Metals also found (iron and titanium)
    - Fibrosis and inflammation noted –all had new onset dyspnea

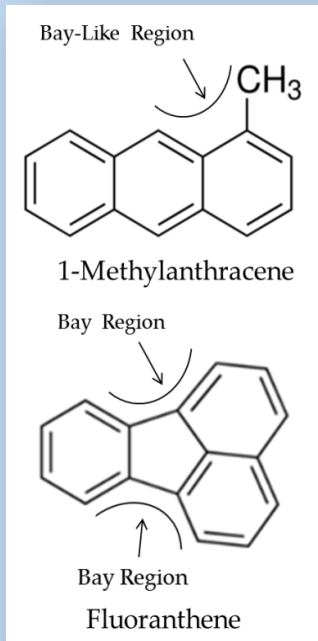


**Figure 1.** Representative lung biopsy from soldier exposed to burn pits has black carbonaceous particles and white refractile dust crystals amidst fibrosis. These black and white particles have polycyclic aromatic hydrocarbons and contain oxidized metals titanium and iron.

# Hypothesis: LMW PAHs have adverse biological effects on lung that lead to increased potential for lung diseases



Benzo[a]pyrene (B[a]P) is the classic PAH used to base all PAH toxicity



Lower molecular weight PAHs (2-4 ring PAHs; LMW; < 202 g/mol)  
Not currently classified as carcinogens by IARC  
More prevalent in indoor and outdoor air pollution

## Signaling events and pathways altered in response to PAH exposures: *in vitro lung cell studies*

- Gap junctional Intercellular Communication (GJIC)
- Inflammation (cytokines/chemokines)
- Bioactive lipids (eicosanoids)
- Cell signaling events (MAP kinases)
- Immune system (macrophage function)
- DNA adducts (anti-BPDE adduct formation)/genotoxicity
- Mouse carcinogenesis studies

# In vitro lung cell models

- Use several *in vitro* cellular models
  - **C10** and E10 mouse alveolar type II cell lines
  - **BEAS2B** and HBE1 human bronchial epithelial cell lines

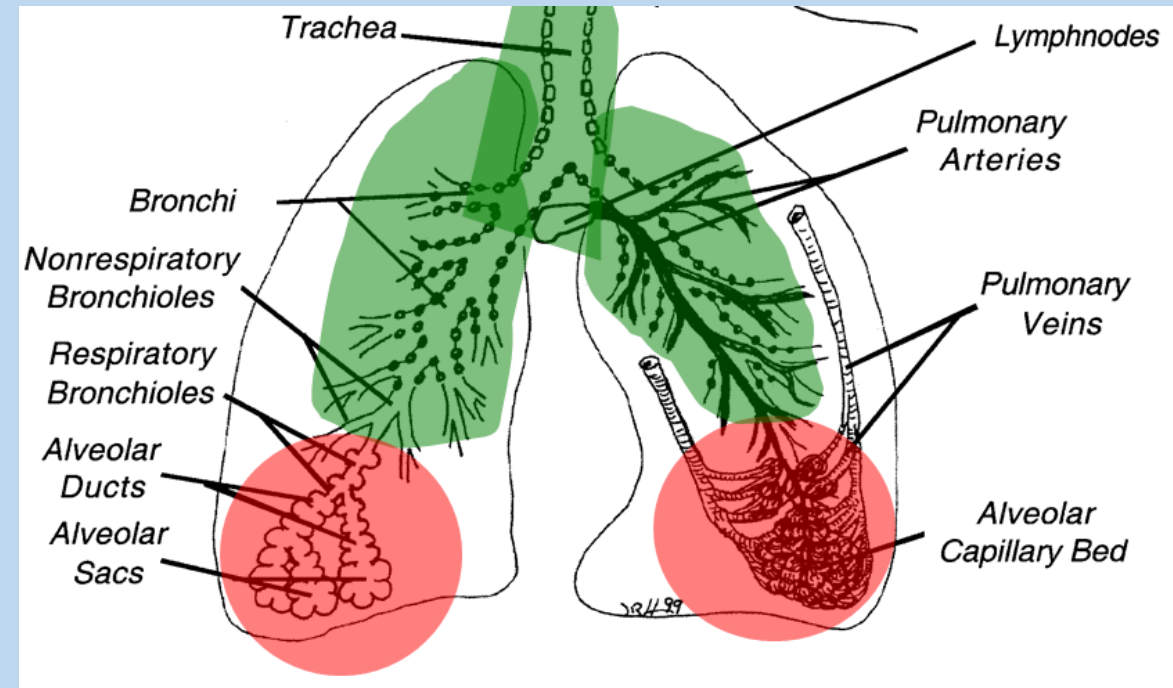
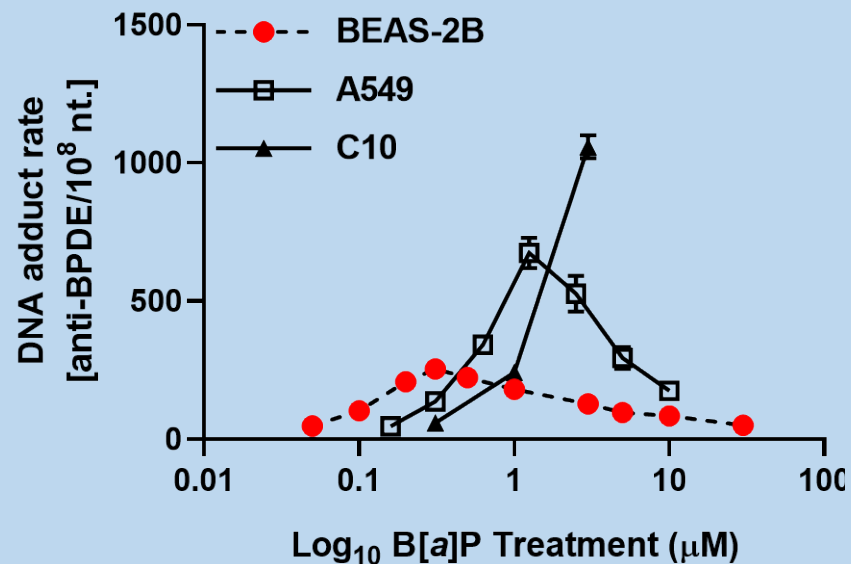
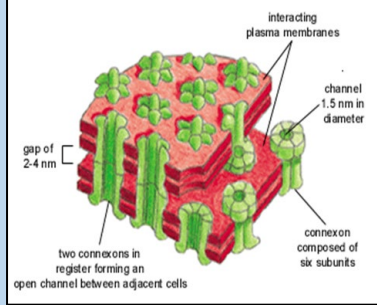
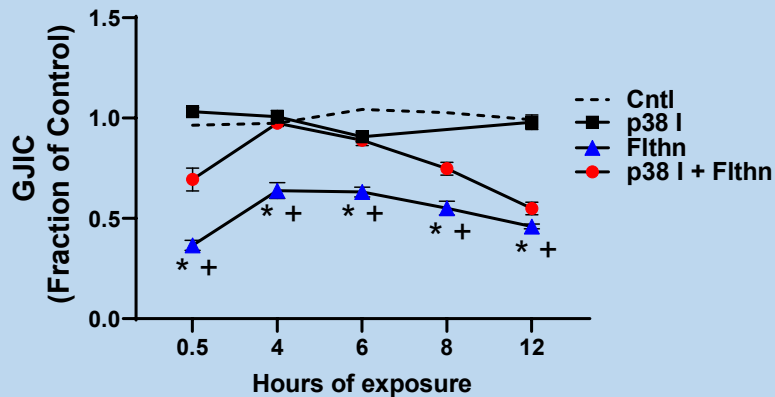


Figure courtesy of J.Harkema

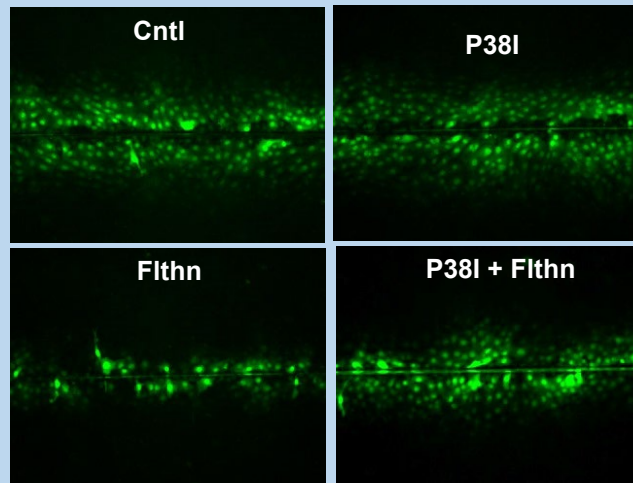
# PAHs inhibit gap junction activity through p38MAPK



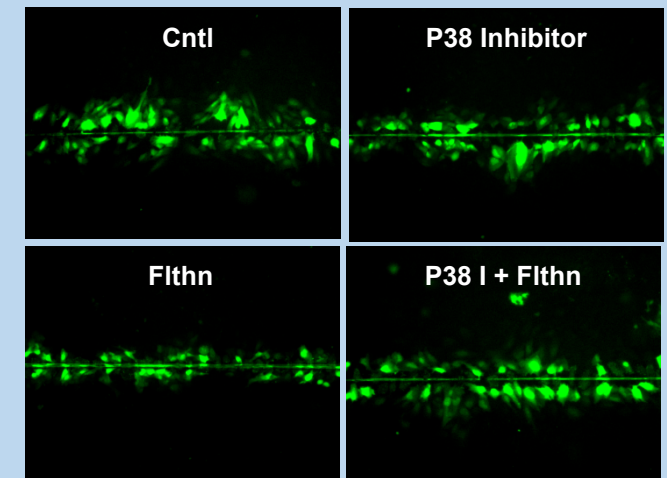
- GJIC suppression is implicated in disease due to homeostatic imbalances
  - Growth factors, environmental toxicants, including carcinogens



C10 cells



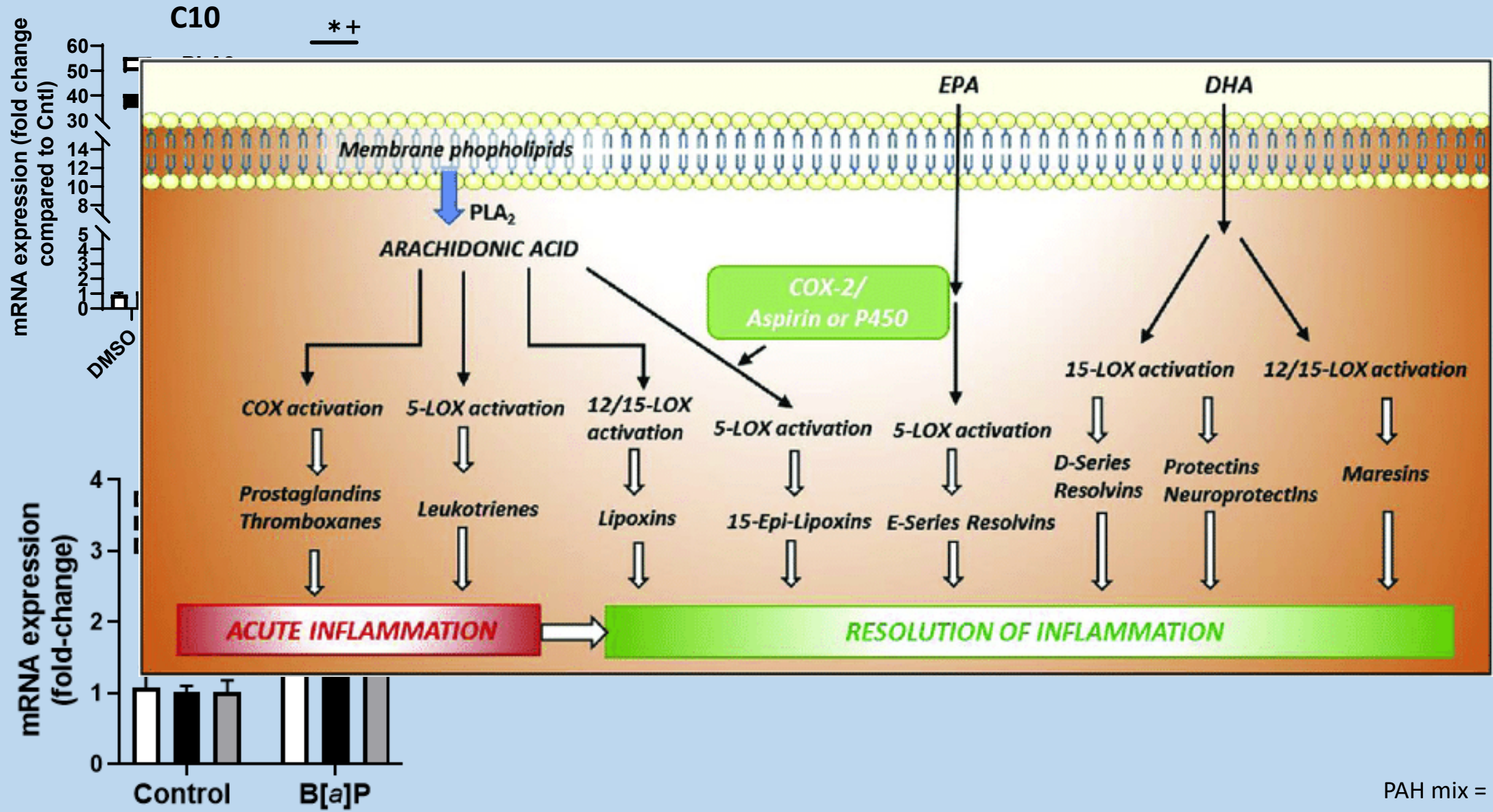
BEAS2B cells



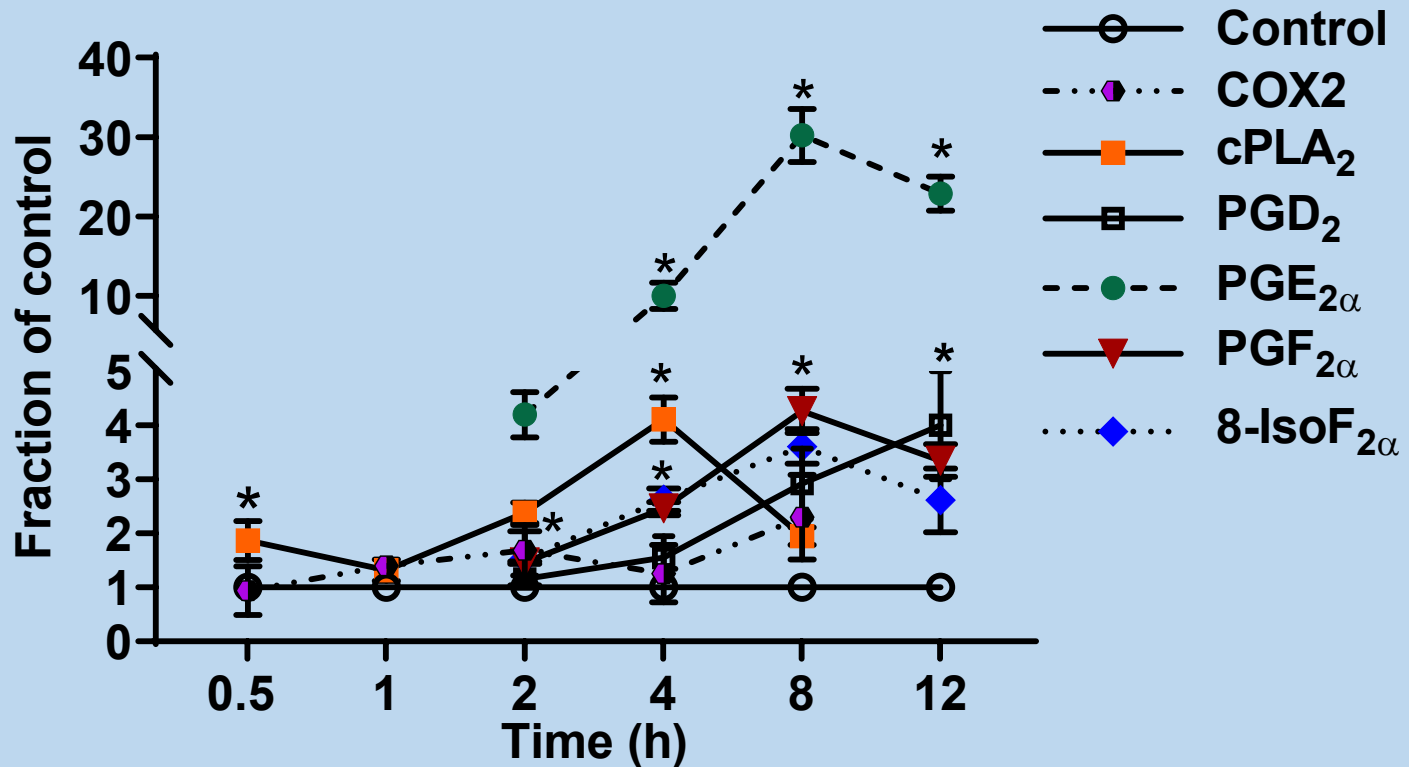
- P38MAPK is linked to several inflammatory mediator pathways, among other pathways



# Eicosanoid pathway involvement downstream of p38MAPK

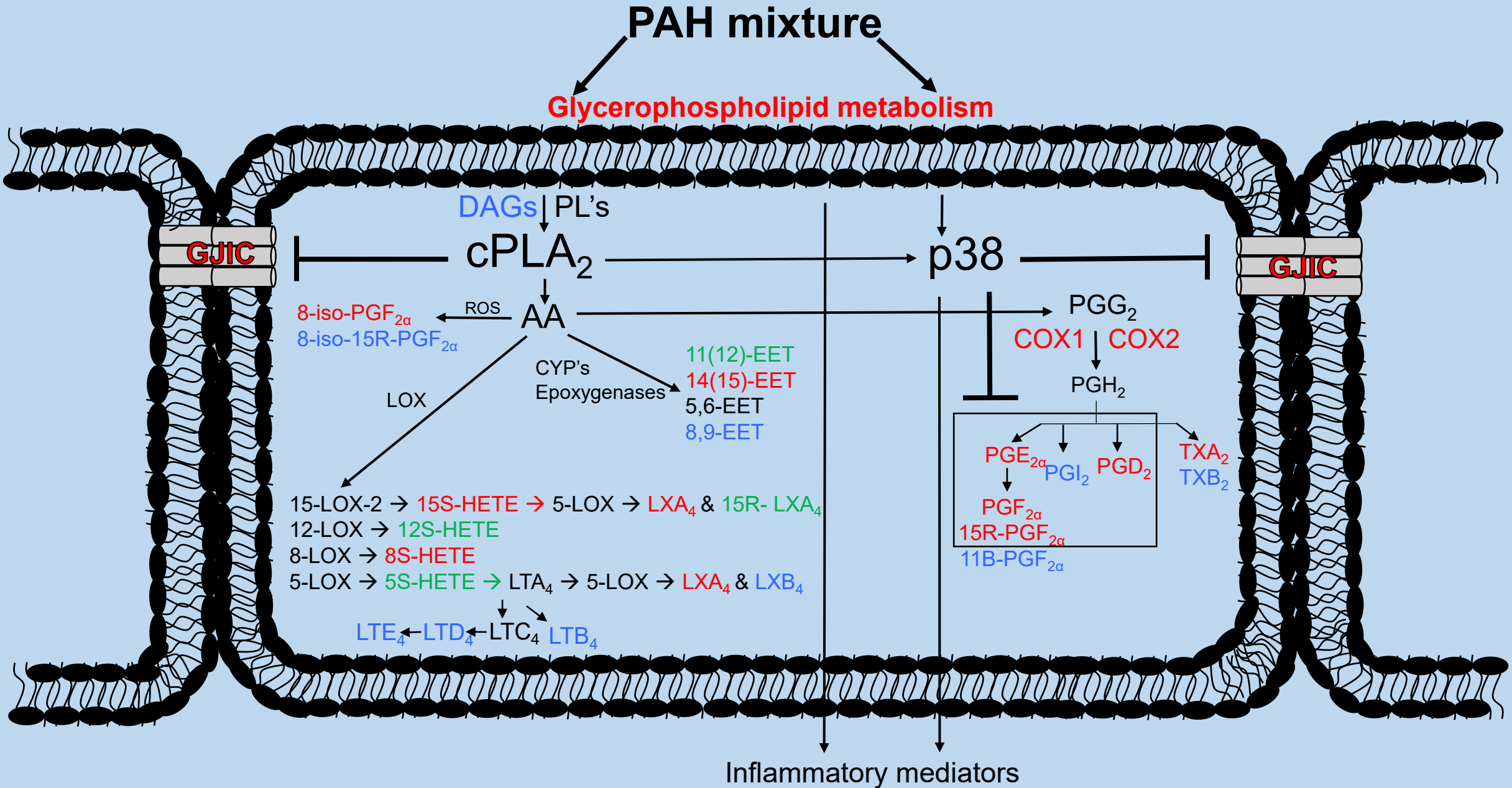


# Kinetics of bioactive lipid signaling events following C10 cell exposure to the binary PAH mixture



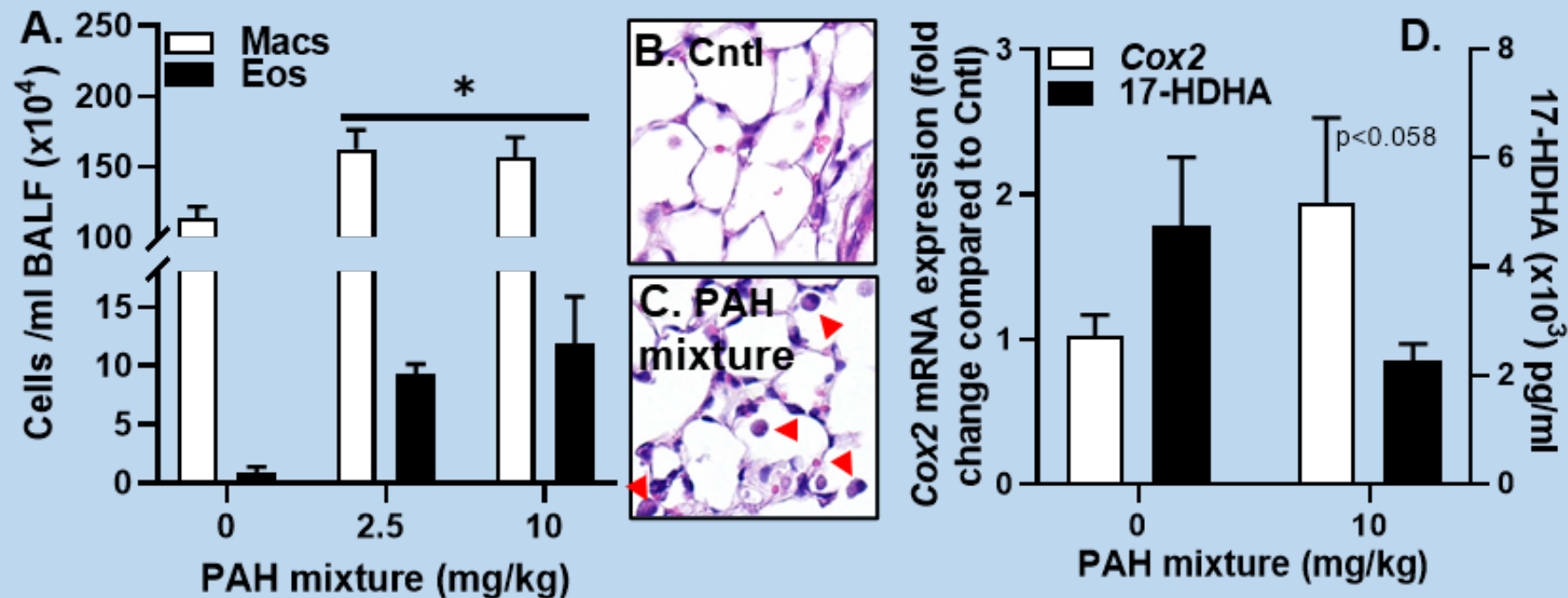
All are, in part, p38MAPK dep.





Red=upregulated    green=downregulated    blue=measured but no change    black=not measured

# Pilot study in female BALB mice with a 5 PAHs\* in NIST diesel exhaust



\*B[a]P, pyrene, fluorene, phenanthrene, and fluoranthene

# Conclusions and Future Directions

- Our studies in human lung epithelial cells support the potential role of PAHs (LMW/HMW) in eliciting adverse health effects in humans, such as the potential to exacerbate allergic airways in addition to co-carcinogenic or tumor promoting effects
  - Our *in vivo* data (not shown) provide evidence that these LMW PAHs can act as tumor promoters in the lung when combined with B[a]P.
    - Future studies will evaluate the balance between pro-inflammatory and pro-resolving/anti-inflammatory bioactive lipids in our *in vitro* and *in vivo* models
      - Potential interventions for future → Pro-resolving mediators, probiotics, etc
- Collectively, these studies linking multiple LMW PAHs to adverse lung effects, are critical to assess potentially upcoming **public health risks** such as exposures due to burn pits and the increasing numbers of wildfires.

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