



THE UNIVERSITY OF ARIZONA

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College of Public Health

# Firefighter Cancer

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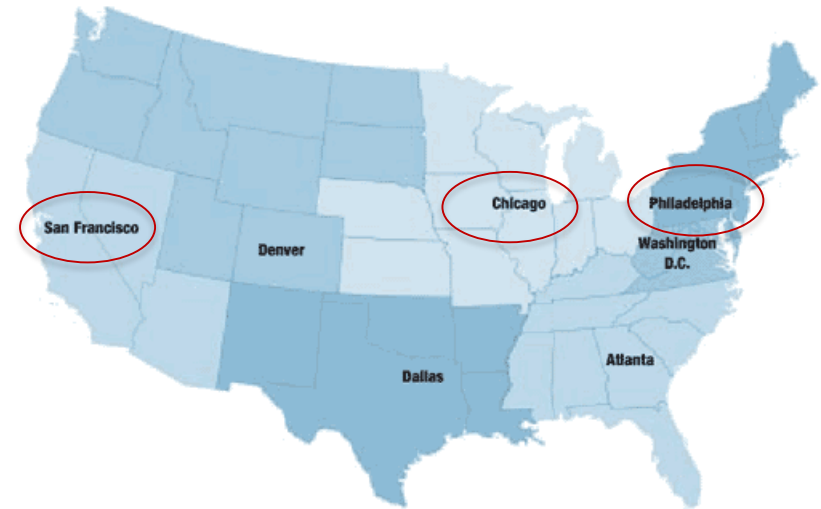
Aircraft Rescue and Fire Fighting Leadership Conference

Jacksonville, FL

January 30<sup>th</sup>, 2019


# US Firefighter Cancer Study

- NIOSH (Daniels et al., 2014) demonstrated excesses in US firefighter cancer mortality:
  - lung (10%)
  - gastrointestinal (30-45%)
  - kidney (29%)
  - mesothelioma (100%)
  - similar increases in cancer incidence.
- Further analyses (Daniels et al., 2015) demonstrated significant associations:
  - fire hours and lung cancer incidence and mortality
  - fire runs and leukemia mortality



Daniels et al. *Occup Environ Med* 2014;71:388-397.  
Daniels et al. *Occup Environ Med* 2015 Epub ahead of print.

# California Cancer Study

- NIOSH (Tsai et al., 2015) study of California firefighters with cancer 1988-2007
  - Cancer excess (all firefighters combined):
    - melanoma (80%)
    - multiple myeloma (40%)
    - acute myeloid leukemia (40%)
    - adenocarcinoma of the esophagus (60%)
    - prostate (50%)
    - brain (50%)
    - kidney (30%)
  - Cancer excess (minority firefighters only):
    - Tongue cancer, testicular cancer, bladder cancer, non-Hodgkin lymphoma, chronic lymphocytic leukemia, and chronic myeloid leukemia
- 
- A map of California divided into various fire districts. The districts labeled include Applegate, Redding, Arcata, Rogue Lake, Northern California District, Central California District, Modesto, Central Coast, Bakemead, Ridgecrest, California Desert District, San Bernardino, San Diego, Santa Springs/South Coast, and El Centro. The map uses different colors to distinguish between the districts.



# Tucson Fire Department



On March 14, 2014, TFD Fire Cause Investigator **Tom Quesnel** died after a battle with leukemia. He spent 20 years investigating nearly 3,000 fires.



[http://tucson.com/news/blogs/police-beat/photos-tucson-fire-investigator-tom-quesnel/collection\\_61f9f48a-b60c-11e3-91b0-0019bb2963f4.html](http://tucson.com/news/blogs/police-beat/photos-tucson-fire-investigator-tom-quesnel/collection_61f9f48a-b60c-11e3-91b0-0019bb2963f4.html), accessed 3/14/18

# Study Aims

Partner with TFD to:

- 1) Evaluate exposure to carcinogens
- 2) Measure biomarkers of carcinogenic (epigenetic) effect
- 3) Reduce carcinogenic exposures and effects

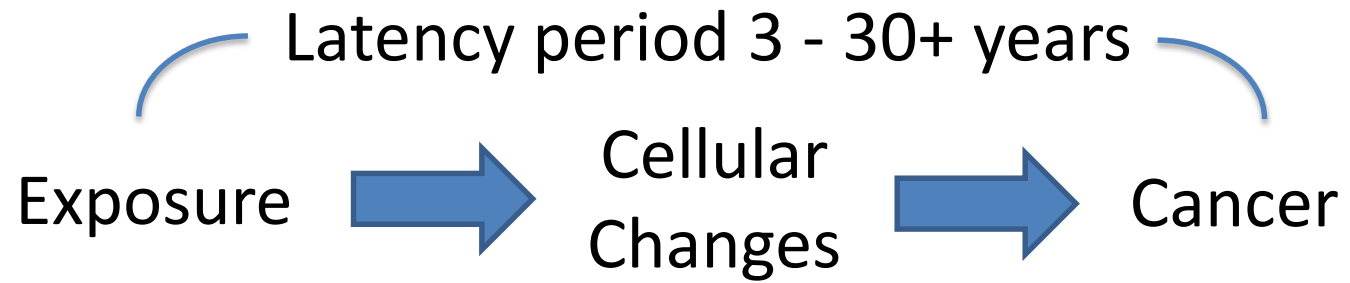
Funding: FEMA AFG EMW-2014-FP-00200



# Biomarkers of Carcinogenic Effect (or Cellular Changes)

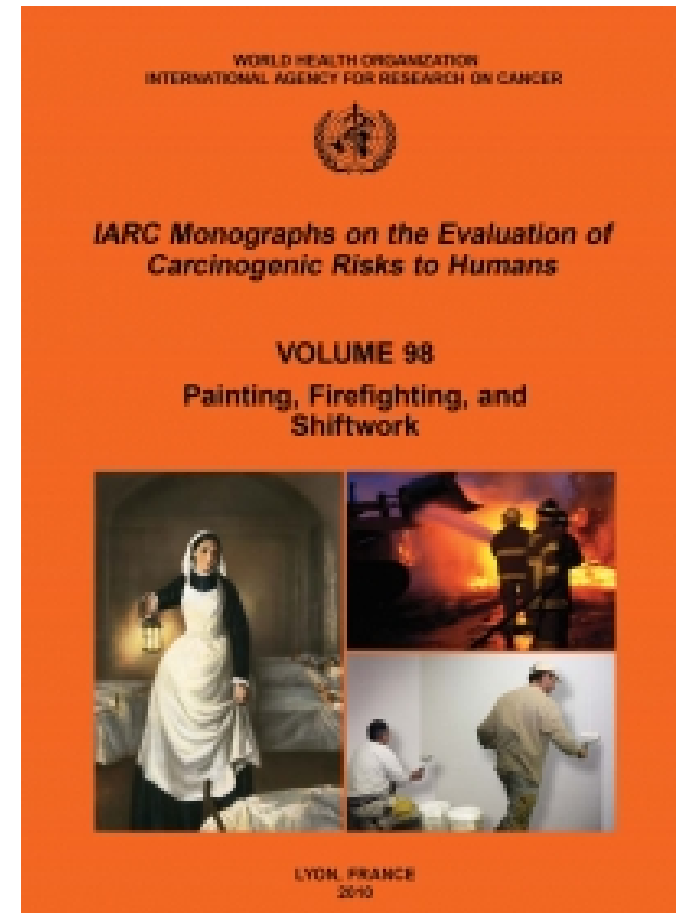


# Health Effects



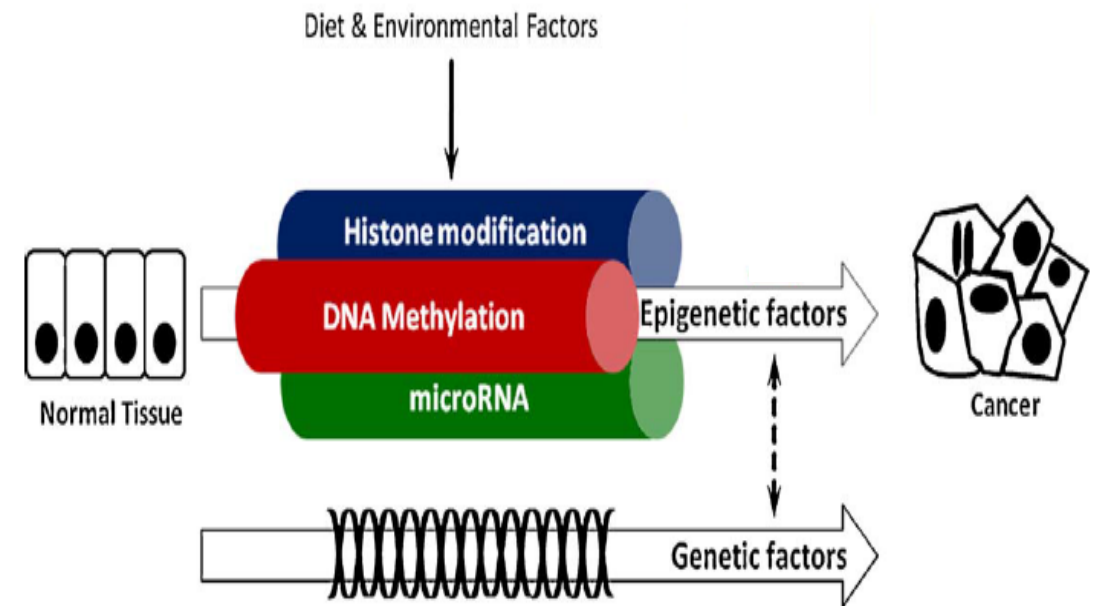
# Presumptive Legislation

- Identification of cellular mechanisms will support presumptive legislation
- Need to provide scientific support for moving from *possibly carcinogenic to humans (2B)* to *probably carcinogenic to humans (2A)* or *carcinogenic to humans (1)*



# Epigenetic Changes

- Change in gene expression without changes in DNA sequence
- Profound roles in carcinogenesis
- DNA hypermethylation silences tumor suppressor genes
- microRNA: small molecules that control gene expression
  - Can act as oncogenes or tumor suppressor genes



Link et al. Biochem Pharmacol 2010;80:1771-92.

# DNA Methylation Pathway Analysis

Disease annotation	p-value	# genes	Hub genes
Abdominal cancer	5.1e-18	88	STAT3, TP63, TP73, FOXO1, PML, DAXX, RUNX2, INSR, PCNA
Colon tumor	5.9e-09	44	STAT3, TP63, TP73, FOXO1, DAXX, RUNX2, INSR, PCNA
Skin cancer	2.9e-07	51	STAT3, TP63, PML, DAXX, RUNX2, INSR
Lung tumor	6.6e-07	49	INSR, PCNA, STAT3, TP63, TP73

# MicroRNA Results

miRNA Name	Incumbents vs. new recruits*			New recruits at 2 yrs vs. baseline**			Role in cancer	Select cancer associations
	FC	95% CI		FC	95% CI			
miR-1260a***	<b>0.55</b>	0.43	0.71	<b>0.66</b>	0.47	0.91	Tumor suppressor	Brain (glioblastoma)
miR-548h-5p	<b>0.59</b>	0.51	0.69	0.83	0.50	1.16	Tumor suppressor	Cervical and lung
miR-145-5p***	<b>0.44</b>	0.32	0.61	<b>0.61</b>	0.45	0.82	Tumor suppressor	Prostate
miR-4516	<b>0.56</b>	0.48	0.65	0.81	0.56	1.16	Tumor suppressor	Apoptosis of keratinocytes
miR-331-3p	<b>0.60</b>	0.52	0.70	1.05	0.77	1.44	Tumor suppressor	Prostate & colorectal
miR-181a-5p	<b>0.62</b>	0.53	0.72	1.03	0.83	1.27	Tumor suppressor	Lung (Non-small cell)
miR-5010-3p***	<b>1.59</b>	1.41	1.81	<b>1.79</b>	1.32	2.42	Unknown	
miR-374a-5p	<b>1.72</b>	1.40	2.13	1.31	0.94	1.83	Oncogene	Esophageal & gastric
miR-486-3p***	<b>3.35</b>	2.59	4.33	<b>4.95</b>	3.14	7.81	Oncogene	Colorectal

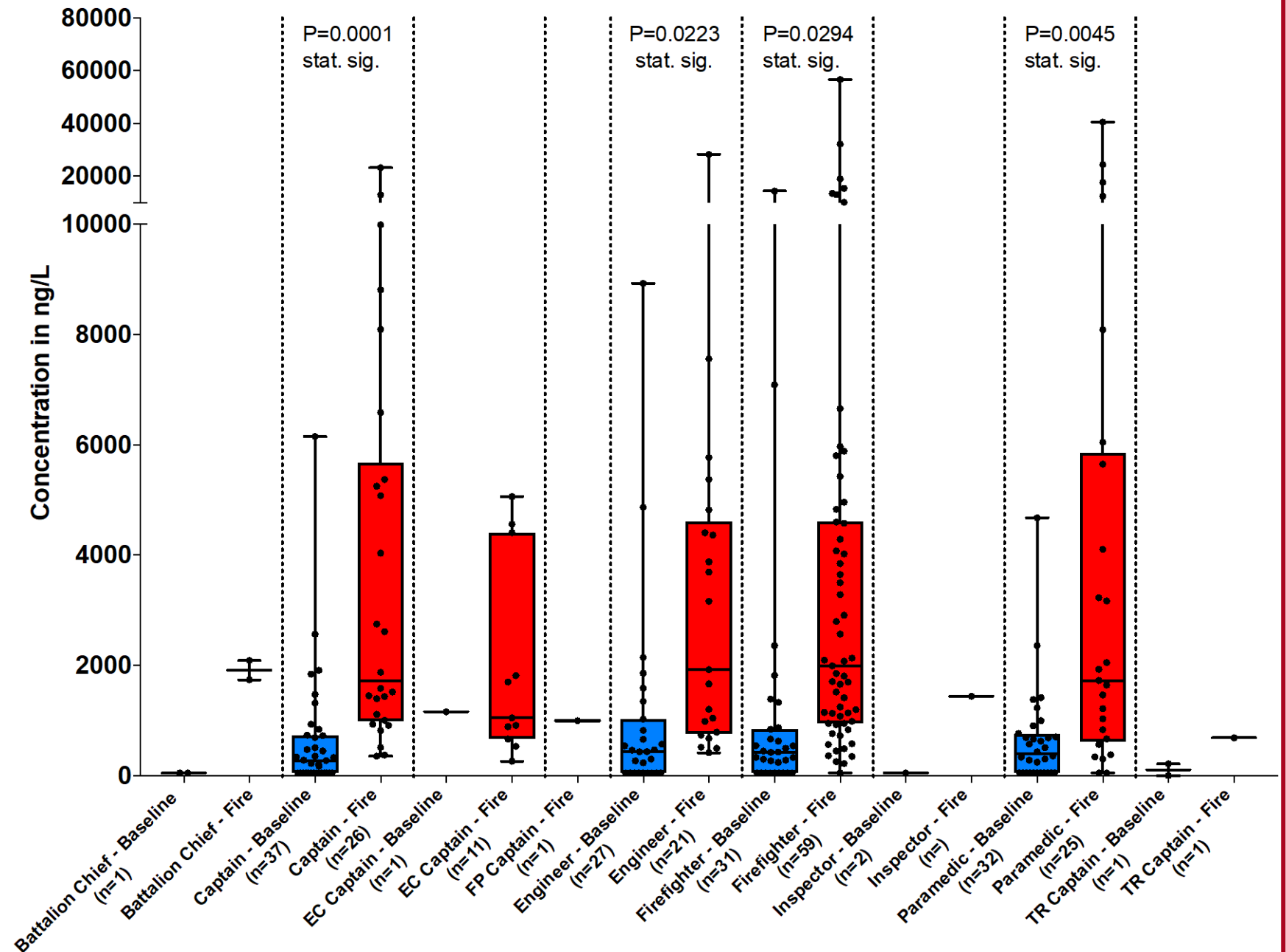
\*Fold changes of incumbents (n=52) compared to new recruits (n=45), adjusted for age, obesity and ethnicity, male non-smokers only (Jeong et al., *J Occup Environ Med.* 2018;60(5):469-474); \*\*Also adjusted for batch effects; \*\*\*Markers also significant in longitudinal analysis of new recruits after adjustment.

# Fireground Exposures

# Inhalation and Dermal Exposure



# Firefighter urinary PAH (1-naphthol) levels before (blue) and after (red) structural fires



# Interventions

# TFD Interventions



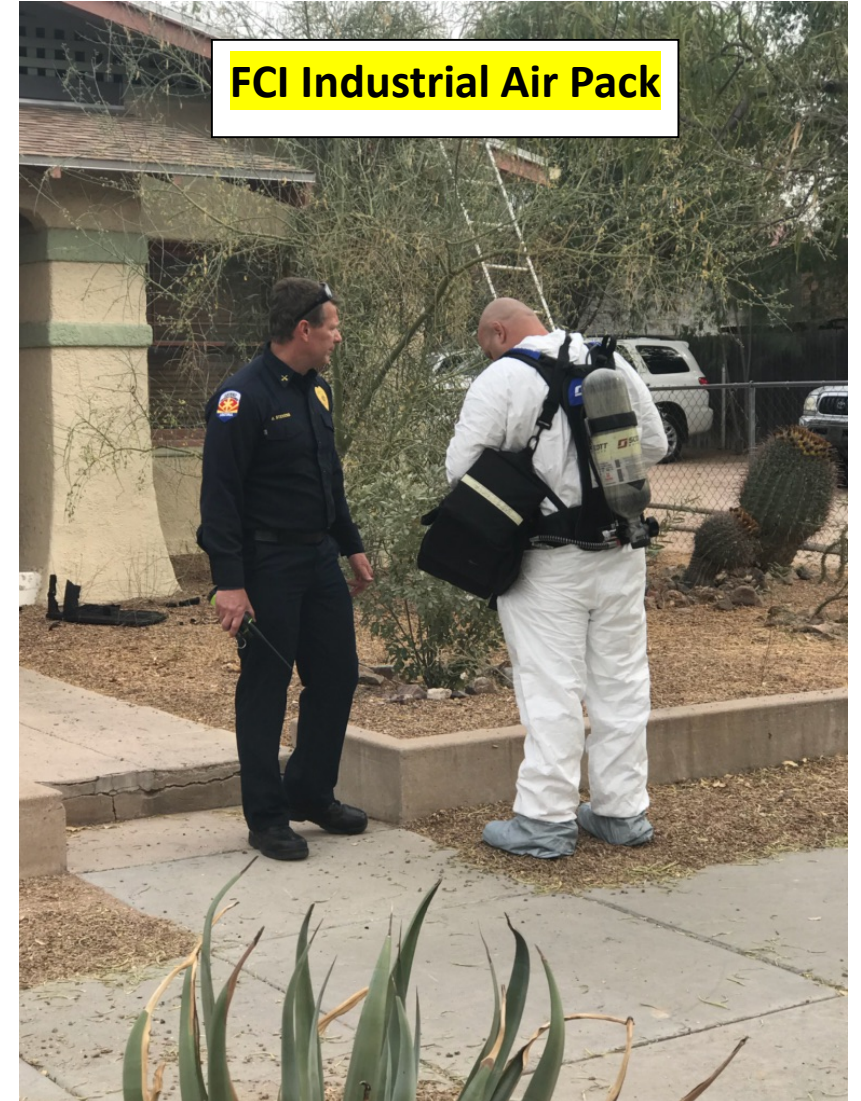
## **Plan: Evaluate**

1. “Engineers on Air” Intervention
2. Wash Down
3. Clean Cab

## **Additional Interventions**

1. Fire Cause SOP
2. Rehab placement and no running vehicle when possible

# Inhalation Exposure Reduction

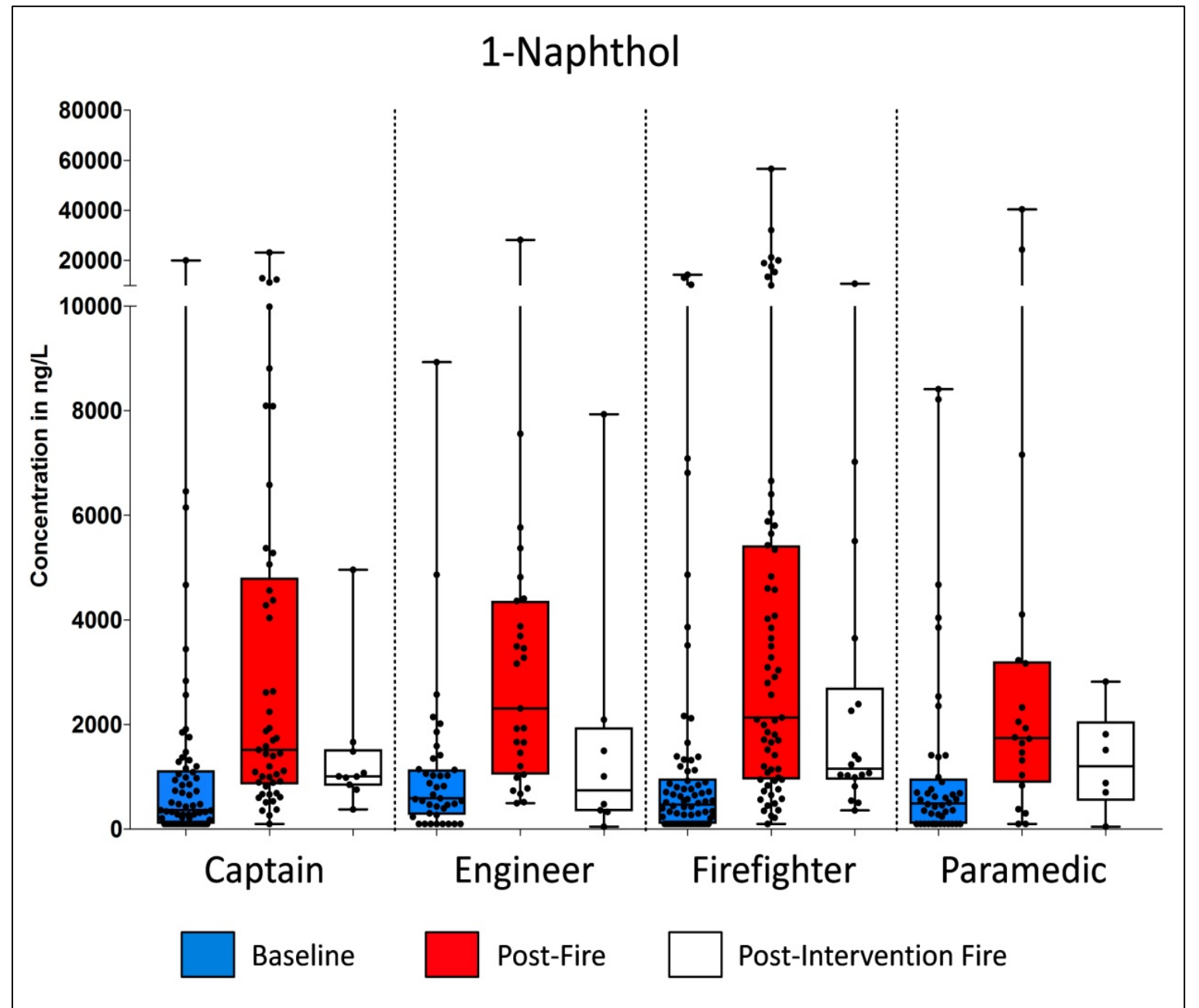


# Dermal Exposure Reduction

- Wet-soap decon gear on-scene
- Use wipes to clean skin
- Bag or transport turnouts and gear (fire hose, etc.) outside of the apparatus cab
- Shower as soon as possible
- Launder hoods and turn-out gear



# Preliminary post- intervention results (urinary PAHs)



# Overhaul Study

- TFD wore no respiratory protection and PFD wore APRs
  - CC16 and SP-A are serum pneumoproteins which spill into the blood with lung inflammation
  - FEV<sub>1</sub>: forced expiratory volume in one second
  - FVC: forced vital capacity
- PFD had poorer respiratory outcomes despite APR use

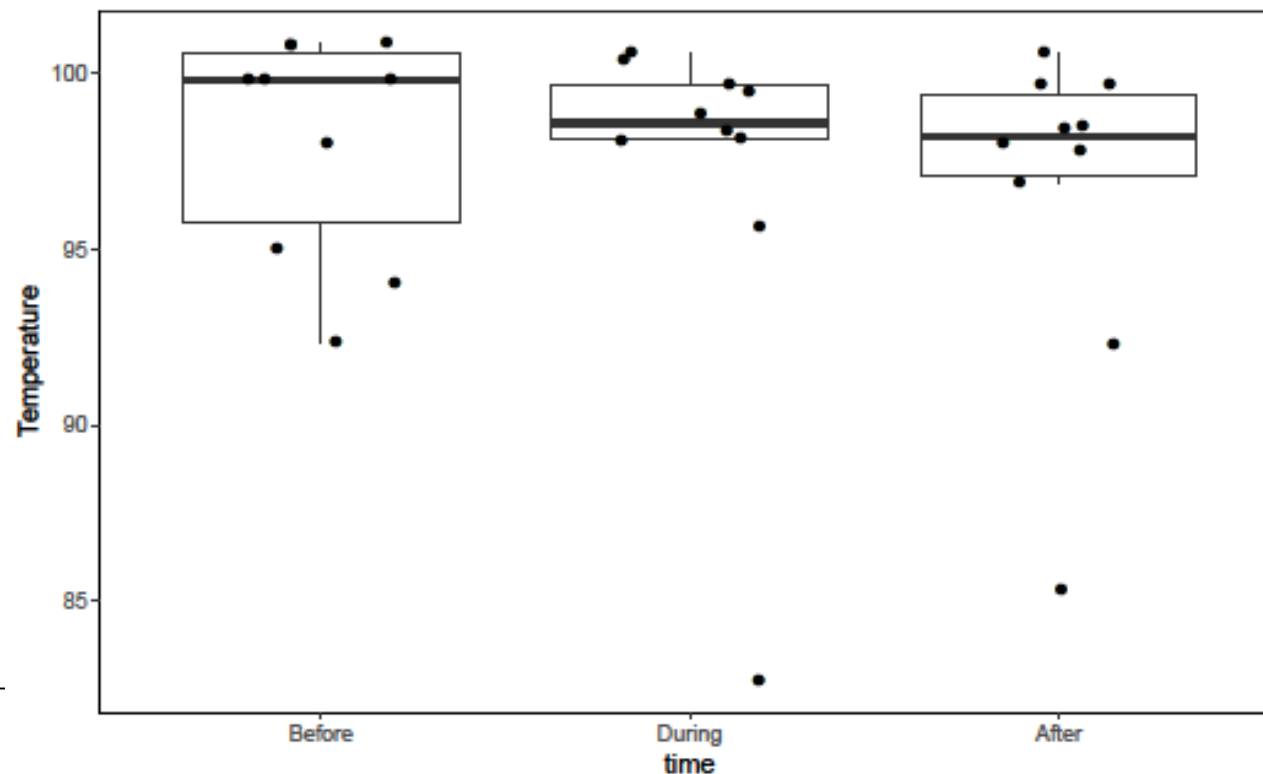
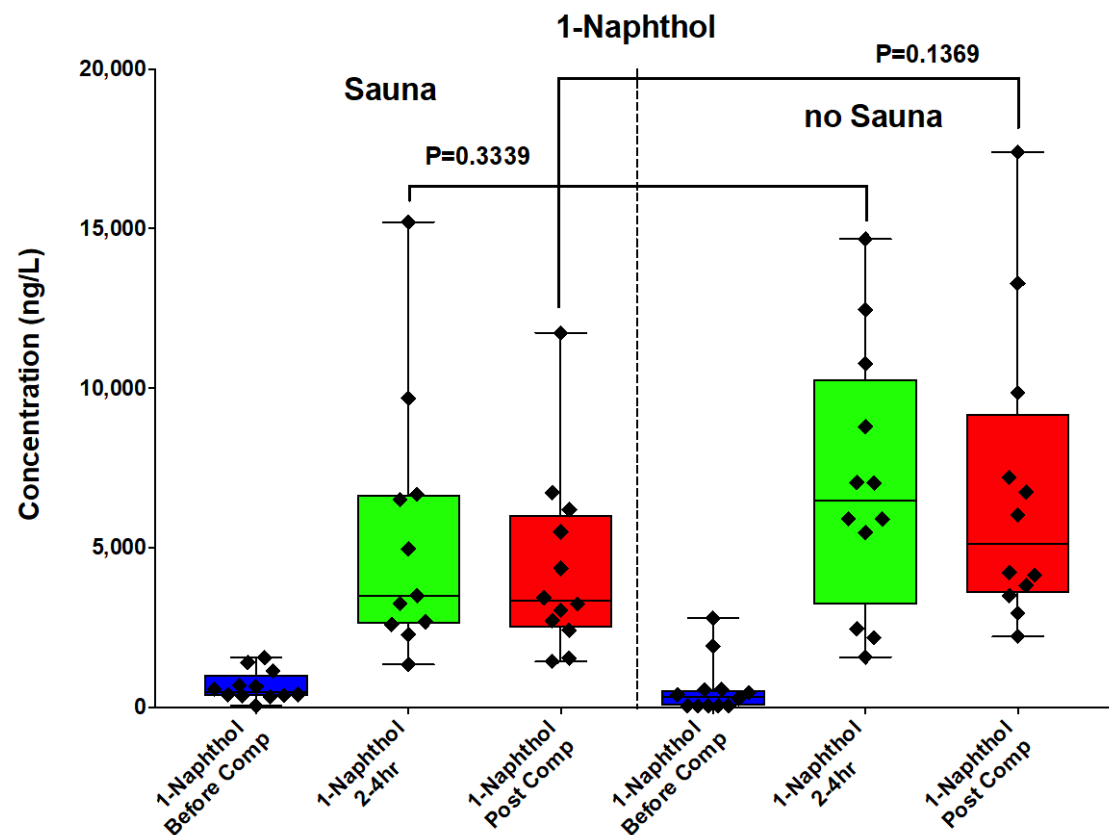
Group	n	CC16	SP-A	n	FVC (L)	FEV <sub>1</sub> (L)
TFD	25	8.9±3.5	287±144	19	5.42±0.72	4.10±0.62
TFD-OH	25	<b>12.3±3.6</b>	306±157	19	5.36±0.73	3.94±0.65
PFD	26	9.6±3.5	250±117	26	5.44±0.68	4.22±0.51
PFD-OH	26	<b>14.6±5.2</b>	<b>334±141</b>	26	<b>5.29±0.74</b>	<b>4.09±0.56</b>

Burgess JL et al. *J Occup Environ Med.* 2001;43:467-473.



# Sauna Study (preliminary)

- Partnership with Scottsdale Fire Department
- Two training evolutions & rehab followed by shower
- Half (n=12) of the firefighters had infrared sauna for 20 minutes then shower

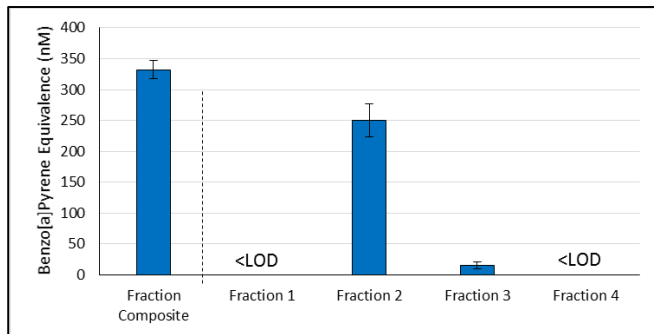


# *In vitro* Testing

## Background/Aim

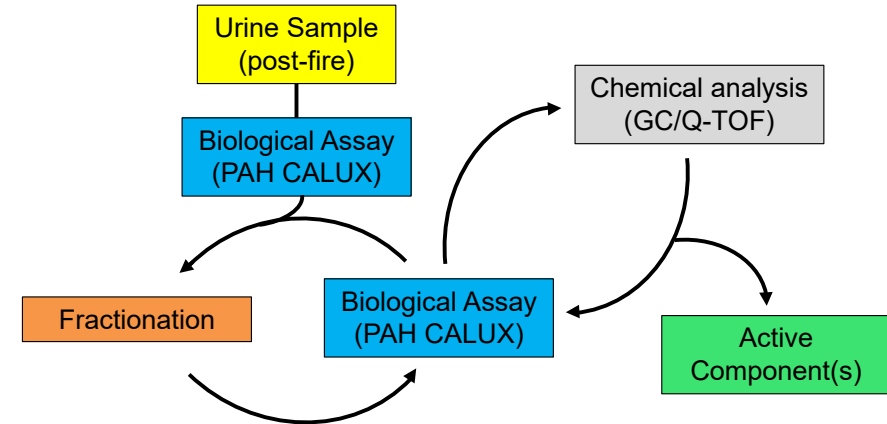
- Greater *in vitro* PAH CALUX assay response in post-fire urine (biomarker of effect)
- The responsible compounds for the bioassay response are unknown
- Aim: Identify compounds responsible for the bioassay response post-fire

## Fractionation is Ongoing

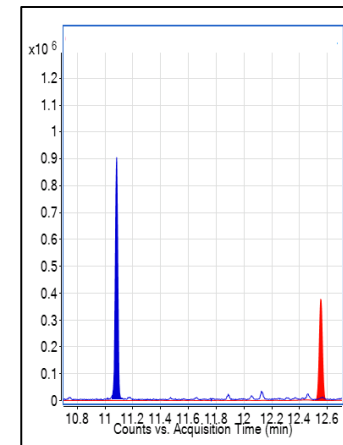


- Fractionation of samples to separate out active compounds

## Approach: Effect Directed Analysis



## Going Forward



- Continued fractionation of samples
- Fractions will be tested at to give insight into the compounds responsible for bioassay response

# Additional Studies

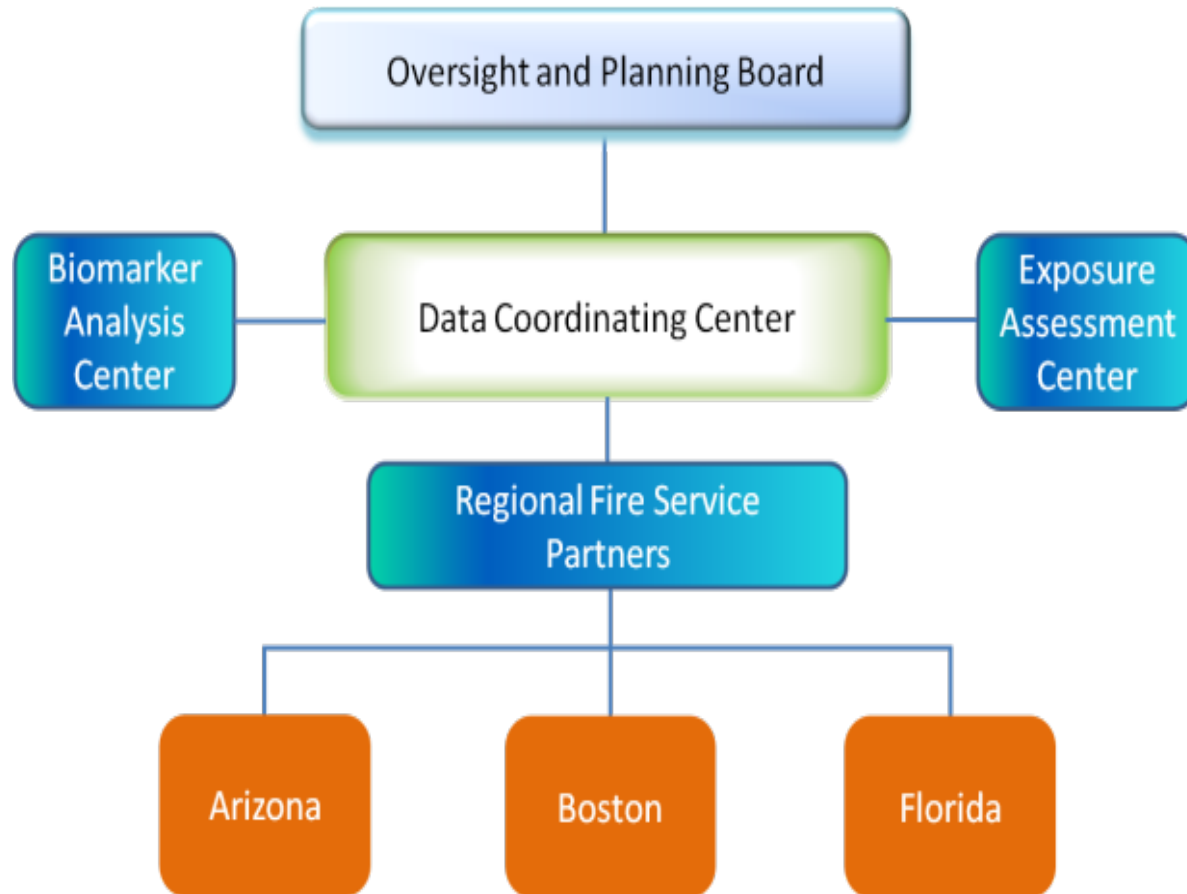
# Fire Fighter Cancer Cohort Study (FFCCS)

## **Goal:**

Establish a large prospective  
multicenter study focused on  
carcinogenic exposures and effects

Funding: FEMA AFG EMW-2015-FP-00213

# FFCCS Framework (Initial)



## Initial Partners

University of Arizona

University of Miami

NIOSH

FPRF

Dongguk University (Korea)

IFSI

NDRI

Boston Fire Department /Local 718

Elephant Head Volunteer Fire Dept.

Firefighter Cancer Support Network

Helmet Peak Volunteer Fire Department

IAFC/NFPA Metro Chiefs

International Association of Fire Fighters

National Fallen Firefighters Foundation

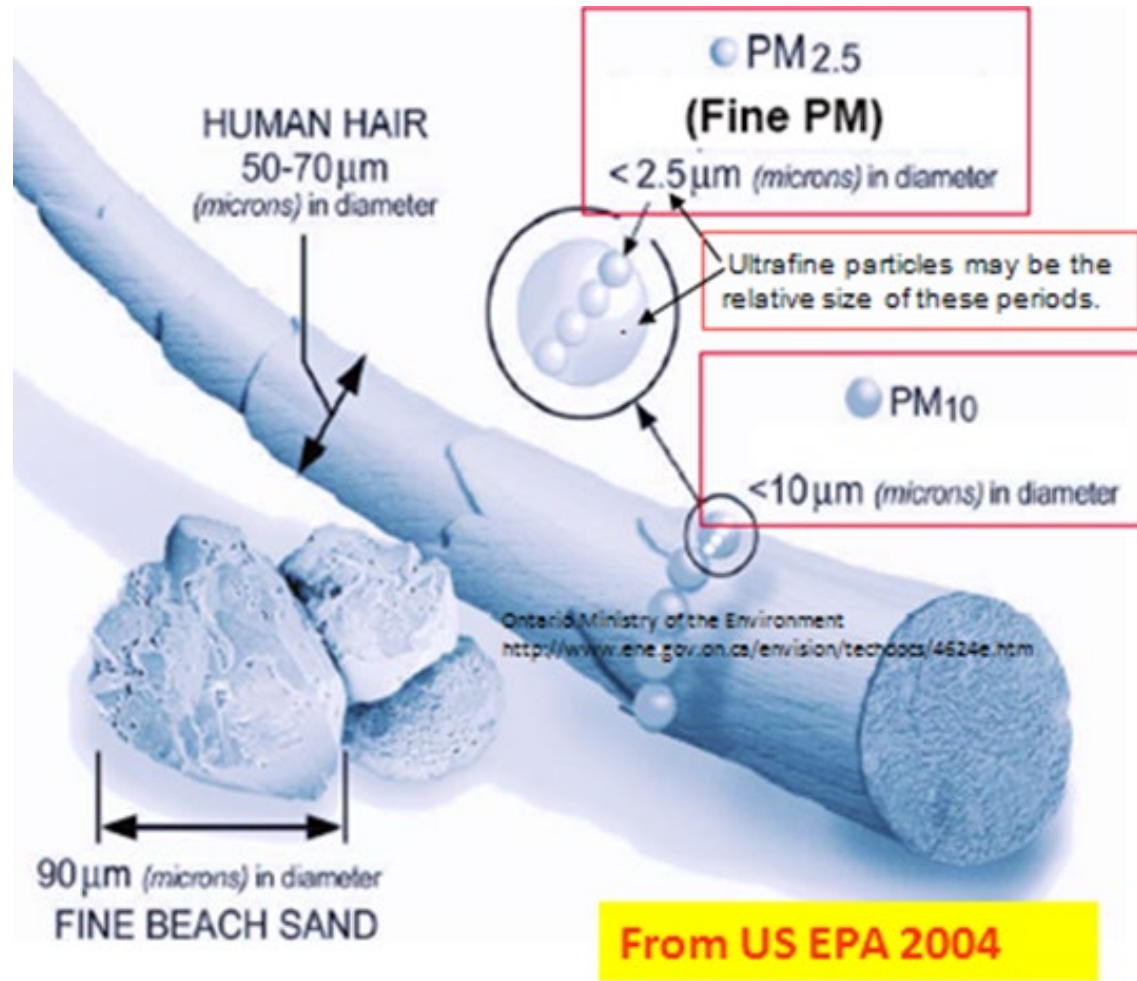
National Volunteer Fire Council

Palm Beach County Fire Rescue/Local 2928

Tucson Fire Department/Local 479

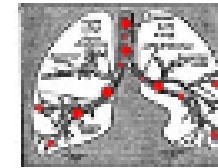
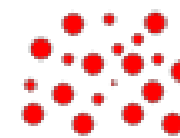
WellAmerica

# Boston University: What are Ultrafine Particles (UFP) and Health Concerns?

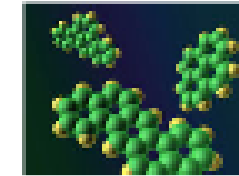


## Why are the smallest particles more proatherogenic ?

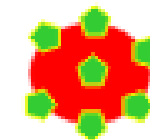
Greater particle number and lung retention



Greater content of prooxidant compounds



Greater bioavailability of reactive compounds



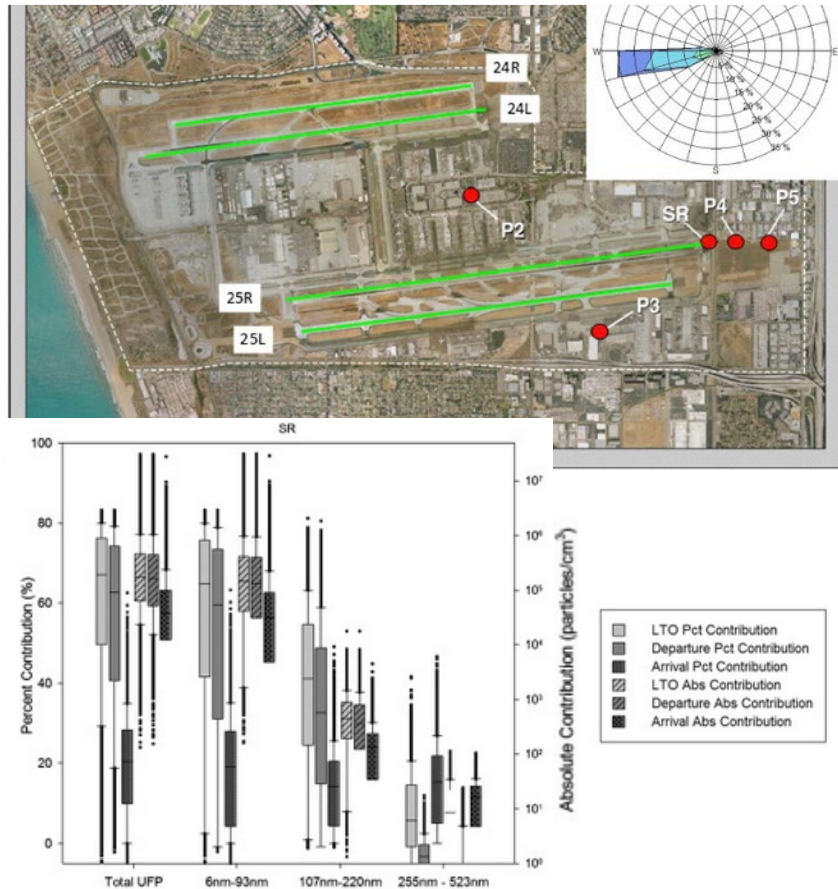
Surface-to-mass ratio

(Araujo & Nel. Particle and Fiber Toxicology. 2009)

- **Airplanes and vehicles are primary sources of exposure to ultrafine particles (UFP).** (Levy et al. 2014; Hudda et al. 2017)
- **Growing body of literature indicates associations between increased UFP exposure and adverse cardiovascular health.** (Lane et al. 2016; Ostro et al. 2015; Downward et al. 2018; Corlin et al. 2018)
- **Acute UFP exposures have been associated with increased oxidative stress and DNA methylation** (Mostafavi et al. 2018), **but there are currently few cohort studies on long-term UFP exposure and lung cancer.** (Weichenthal et al. 2017)

# Ultrafine Particle (UFP) at Los Angeles International Airport

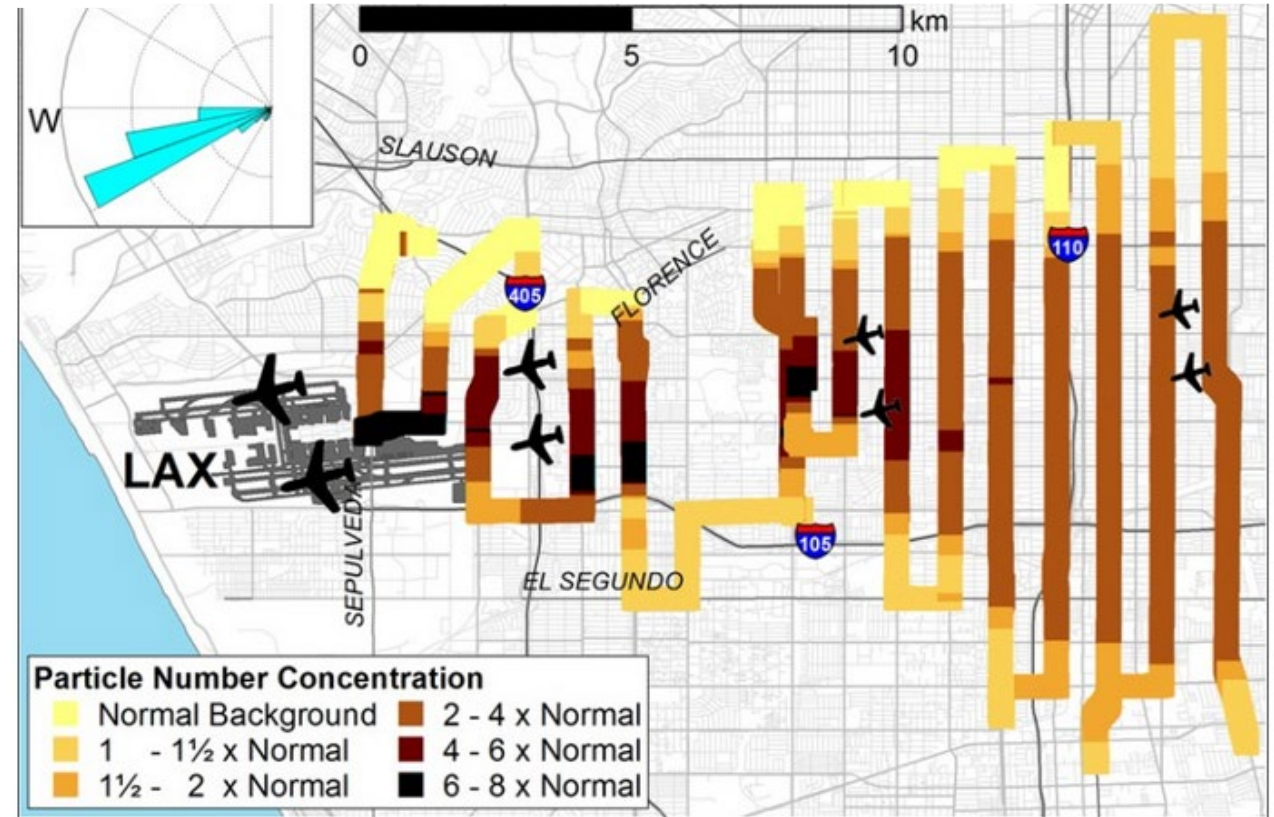
## Airport Measures



(Hsu et al. Science of the Total Environment. 2014)

- At the end of a major departure runway, Landing and takeoff contributed a median of 150,000 particles/cm<sup>3</sup>. Many contribution estimates exceeded 1,000,000 particles/cm<sup>3</sup>, far in excess of UFP concentrations typically for roadway traffic.


## Community Measures



(Hudda et al. Environmental Science & Technology. 2014)

- Areas underneath arrival flight paths observed an increased amount of UFP measured as particle number concentration up to 10 miles from the airport.

# Persistent Chemical Contaminants

- Per- and polyfluoroalkyl substances (PFAS) are found in smoke from fires, turnout gear, and many Class B firefighter foams
- Legacy PFAS exposure in the general population has been associated with testicular, kidney, prostate, and ovarian cancers and non-Hodgkin lymphoma, as well as respiratory disease and reproductive toxicity
- We previously found  PFOS and PFHxS levels in firefighter's blood in Arizona
- Opportunity: use the FFCCS to measure PFAS exposures and toxic effects in firefighters



<http://sanfrancisco.cbslocal.com/video/3580561-crews-clean-up-firefighting-foam-that-spilled-from-airport-hangar-in-santa-clara/>

# Firefighter PFAS Studies

PFAS Species*†	Arizona firefighters (n=40) serum geometric mean (95% CI) µg/L	NHANES adults (n=221) serum geometric mean (95% CI) µg/L
PFOS	<b>13.21 (11.58, 15.07)</b>	<b>9.64 (8.74, 10.64)</b>
PFOA	3.38 (2.95, 3.88)	3.00 (2.78, 3.24)
PFHxS	<b>3.02 (2.64, 3.48)</b>	<b>1.54 (1.38, 1.71)</b>
PFNA	0.93 (0.82, 1.06)	1.35 (1.24, 1.46)
PFDeA	0.26 (0.22, 0.30)	0.30 (0.27, 0.33)
PFUA	0.12 (0.10, 0.14)	0.20 (0.17, 0.23)

- PFOA and PFNA serum levels were also associated with reduction in our firefighter's forced vital capacity (FVC) over time, with increased concentrations associated with a significantly more rapid decline.

- Elevated PFOS and PFHxS serum concentrations were also observed among Australian firefighters, with a significant dose-response effect with years of exposure to AFFF (Rotander et al., 2015).
- In Finland serum PFAS concentrations increased after three AFFF training sessions, with PFHxS and PFOS demonstrating the largest increases (Laitinen et al., 2014).
- Other studies of US firefighters have reported elevated PFHxS (Jin et al., 2011) and PFDeA (Dobraca et al., 2015).

# Cancer Screening

- Colorectal cancer mortality ↑ 31% and first incidence ↑ 28% in firefighters\*
- Opportunity: Use the FFCCS to test predictive ability of blood miRNA tests for polyps and cancer
- Opportunity: Use the FFCCS to test messaging interventions to increase screening rates



<http://www.womens-health-advice.com/polyps/colon.html>

\*Daniels et al. *Occup Environ Med* 2014;71:388-397.

# Additional Grants and Proposals

## Funded

- FFCCS Expansion proposal (FEMA)
  - WUI, fire investigators, trainers and volunteers
- Serum per- and polyfluoroalkyl substances (PFAS) (IAFF)
- Serum PFAS and epigenetic analysis (NIEHS)

## Submitted

- Firefighter colorectal cancer (CRC) proposal (NCI, to be resubmitted)
- Longitudinal analysis of epigenetic changes (NIOSH)
- Social media messaging for CRC screening (NCI)
- PFAS exposure and toxicity evaluation (FEMA)
- Reproductive outcomes in male firefighters (FEMA)

# Questions?

