

Health Impacts of California Wildfire PM_{2.5} Across the Lifespan



California Air Resources Board Research Seminar June 7, 2024

Lisa A. Miller PhD

Professor
UC Davis School of Veterinary Medicine

Associate Director of Research
California National Primate Research Center

UCDAVIS
CALIFORNIA NATIONAL
PRIMATE RESEARCH CENTER

 **UCDAVIS**
VETERINARY MEDICINE

 **NATIONAL
PRIMATE
RESEARCH
CENTERS**
Causes | Preventions | Treatments | Cures

UCDAVIS

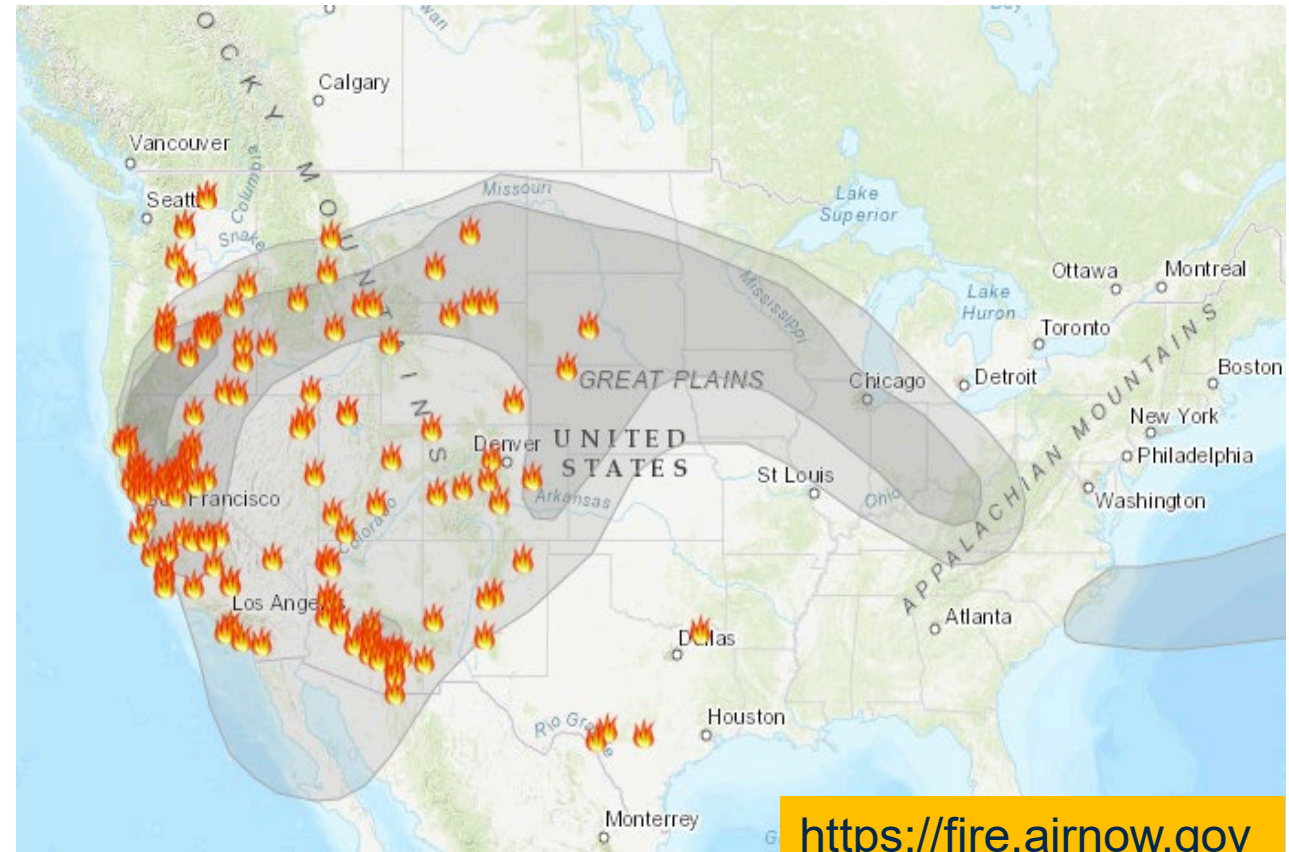
Health Impacts of California Wildfire PM_{2.5} Across the Lifespan

Agreement Number 19RD005 Completed April 19, 2024

The objective of this study is to determine the long-term health impact of wildfire smoke exposure during neonatal development

The Problem with Wildfires-part 1

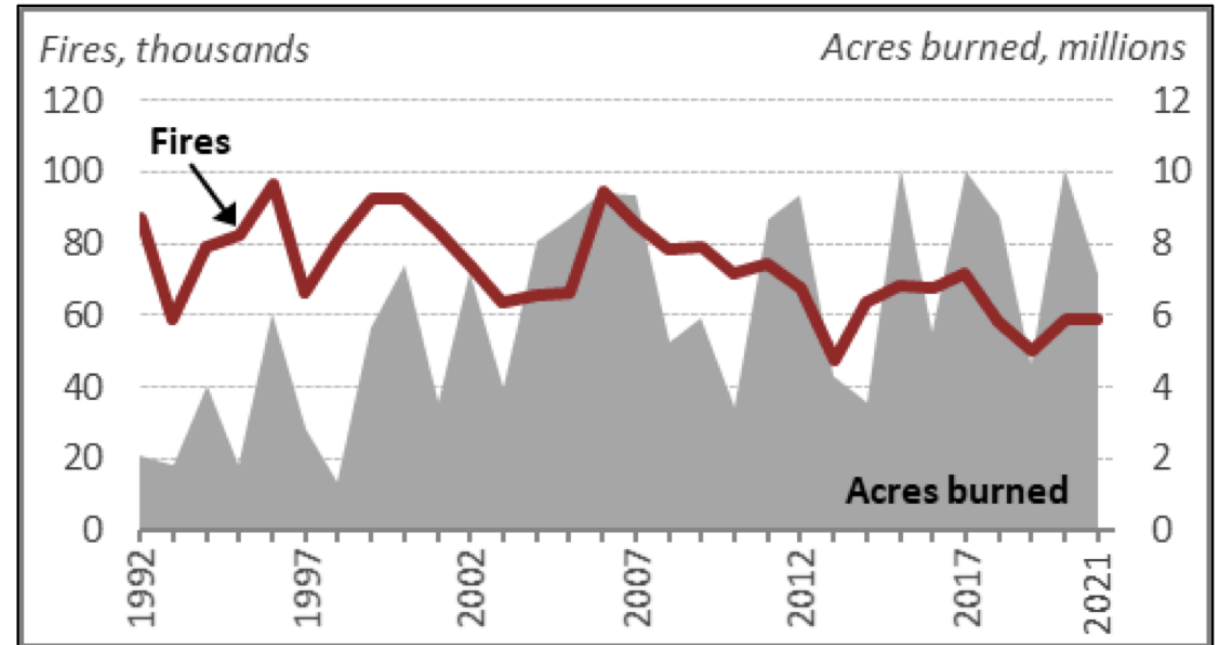
- Wildfires are recognized by the US Environmental Protection Agency as a significant source of air pollution
- Recent wildfires have created half of the air pollution in the western US
- Major pollutants of concerns during a wildfire events are carbon monoxide, ozone, and particulate matter



Extreme Wildfire Events are Increasing

Nationwide data compiled by the National Interagency Coordination Center (NICCC) indicate that the number of annual wildfires has remained relatively steady while the number of acres affected annually has generally increased

Figure 1. Annual Wildfires and Acres Burned, 1992-2021



Source: NICCC Wildland Fire Summary and Statistics annual reports.

Note: Data reflect wildland fires and acres burned nationwide, including wildland fires on federal and nonfederal lands.

Health Risks from Wildfire Events

- Direct physical risks from wildfires (e.g. burns, heat-related illness) and mental health issues in firefighters and residents
- Wildfire smoke can cause eye irritations, increased respiratory events including ER visits and hospitalizations
- Cardiovascular events following wildfire events have been inconsistent

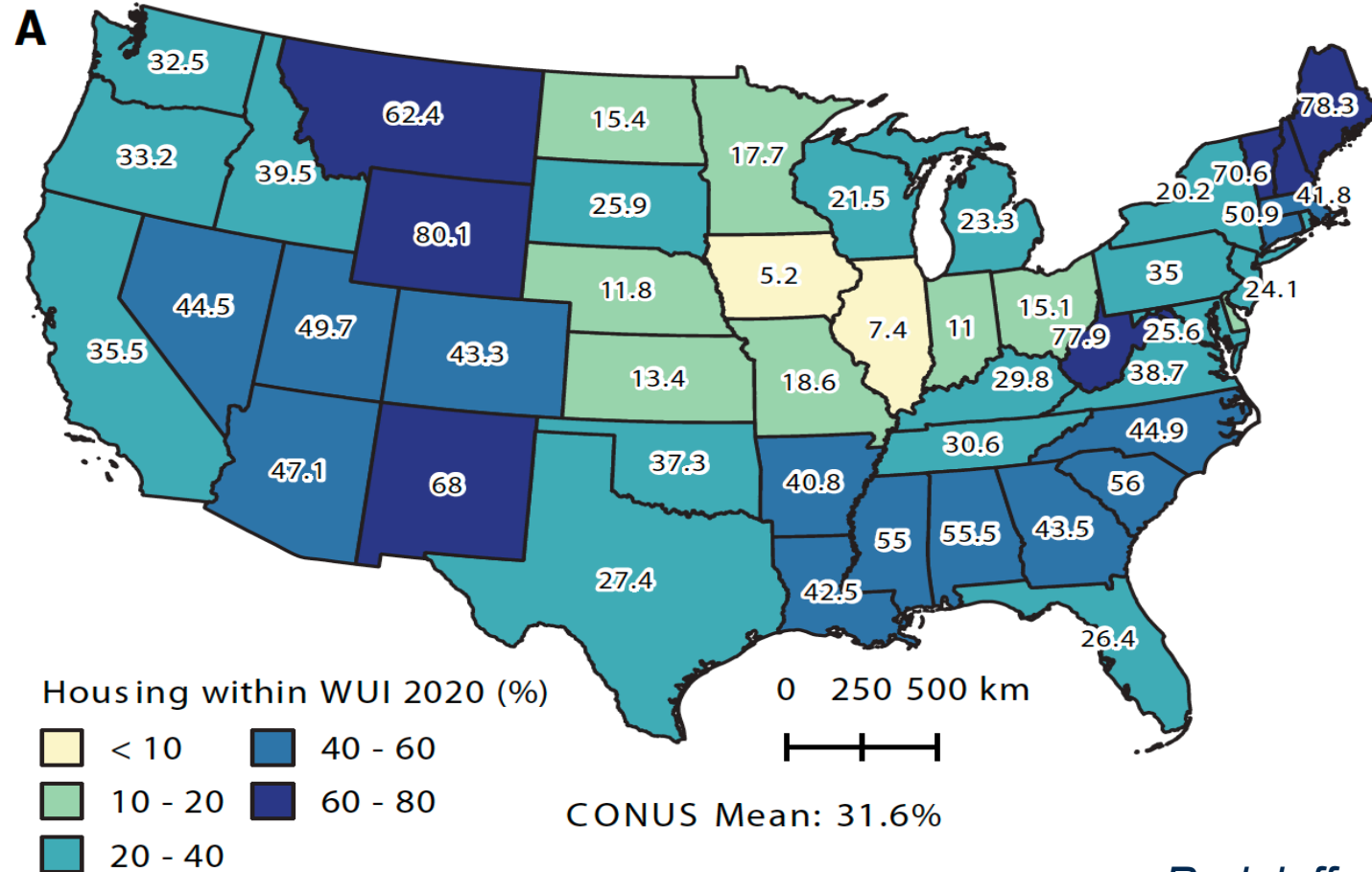


The Problem with Wildfires-part 2

- **Wildland Urban Interface (WUI)** – where wildland vegetation and houses are in close proximity
- During a wildfire event both biomass and man-made materials undergo combustion
- Toxic smoke plumes can be carried hundreds of miles away from site

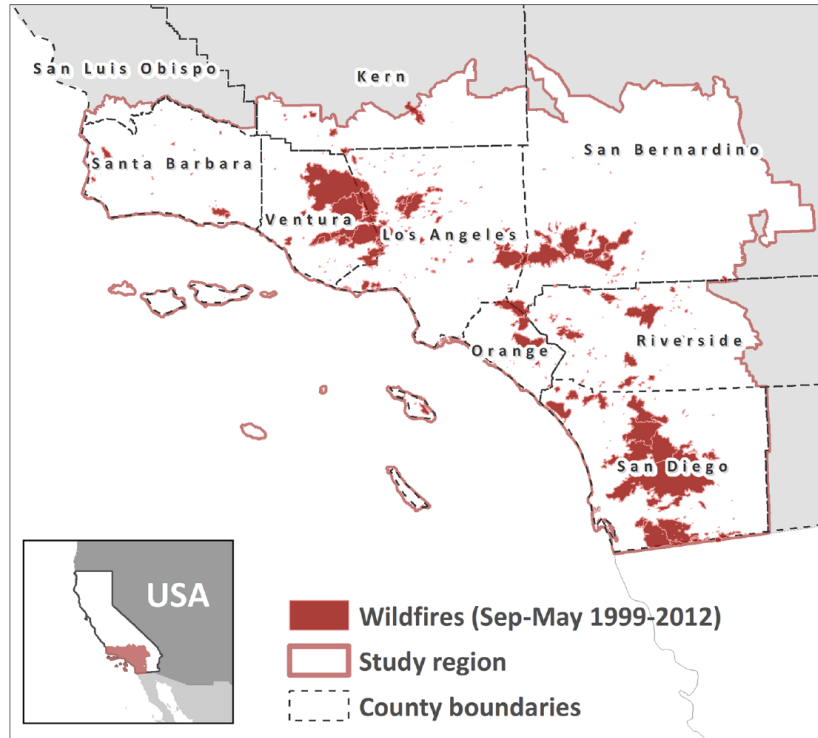


Rising Wildfire Risk to US Homes

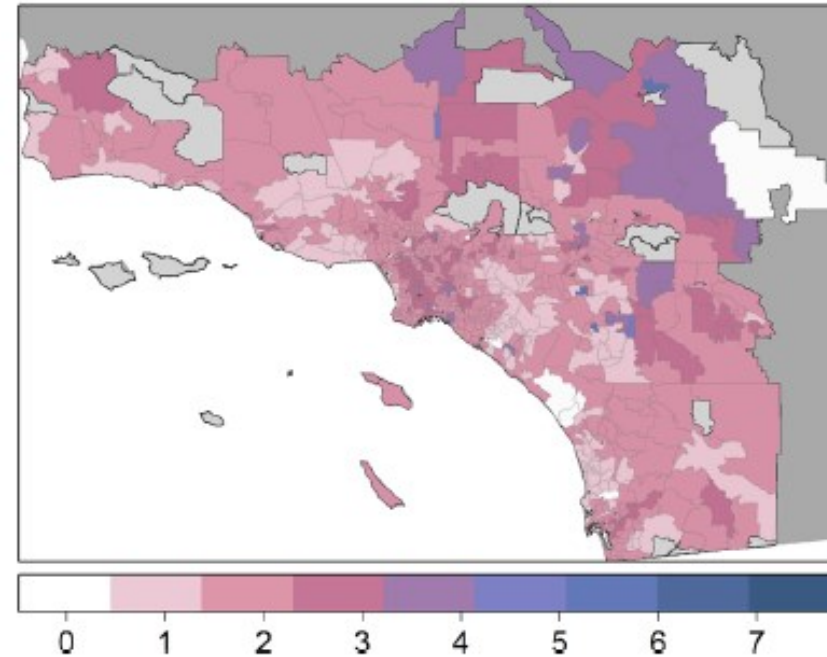


Radeloff, et. al. Science 2023

Evidence for Differential Toxicity of Wildfire Smoke



Mean Rate of Respiratory Admissions - 1999-2012



Wildfire Smoke Impacts Respiratory Health More than Fine Particles From Other Sources

Aguilera, et. a. Nature Comm 2021

Effects of Prescribed Fire versus 2015 California Wildfire on Systemic Immunity

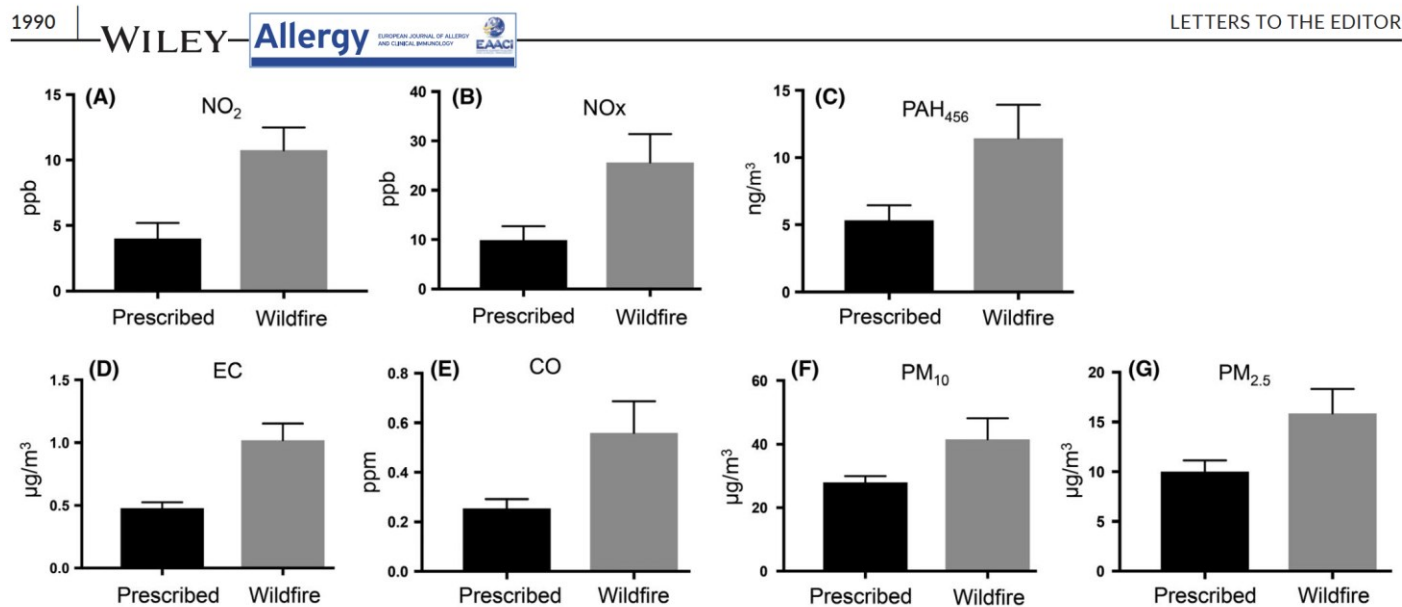


FIGURE 1 Average levels of pollutants during the wildfire and prescribed fire. When comparing prescribed vs wildfire, $P < 0.0001$ for each pollutant shown

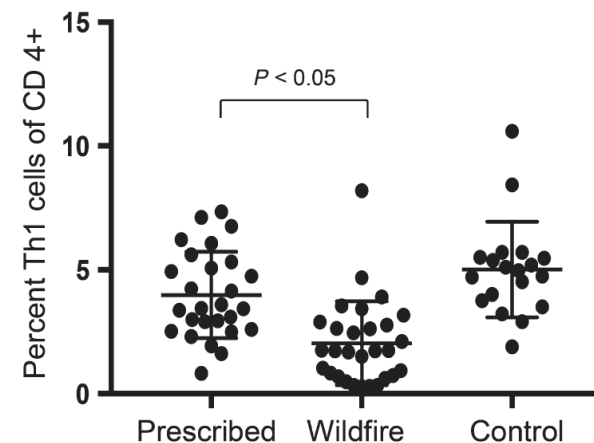


FIGURE 2 Th1 Cell percentage of CD 4+ cells for children 90 d after being exposed to a prescribed fire, wildfire, or no exposure (1-way ANOVA, $P < 0.0001$)

Prunicki, et. al. Allergy 2019

Can exposure to wildfire smoke result in long-term health outcomes in susceptible populations?



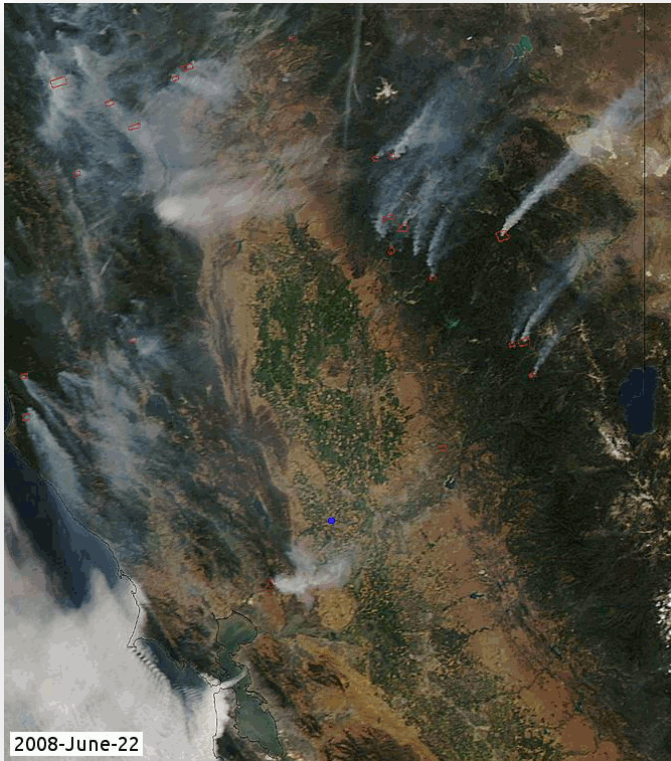
Weed Elementary School, Weed, CA 2014

Wildfire Smoke Susceptible Populations

- Children < 18 years of age
- Older adults
- Pregnant people
- People with pre-existing health conditions
- Outdoor workers

UC Davis has experienced multiple acute air quality events over the past 15 years

Humboldt/Trinity
County Fires 2008



MODIS satellite images
<http://modis.gsfc.nasa.gov/>

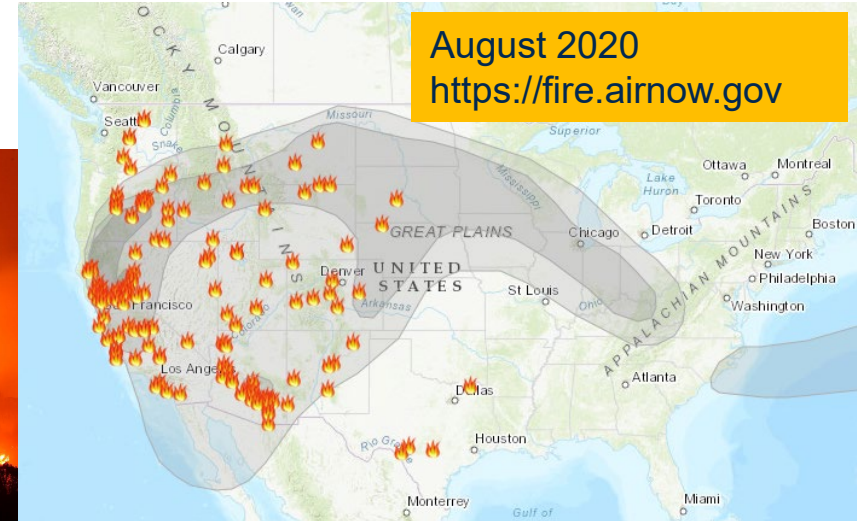
Camp Fires 2019



November 8, 2018
Paradise, CA

November 15, 2018
UC Davis Aggie Stadium
(~100 miles away)

August Complex Fires 2020



August 2020
<https://fire.airnow.gov>



September 2020
San Francisco, CA

California National Primate Research Center



~2500 rhesus macaques live outdoors as breeding groups in half acre field cages



~ 600 infants born March-July



NIA supported geriatric animals

Wildfires Coinciding with Birth Seasons = Natural Experiments

- Rhesus macaques have a predictable natural breeding season; pregnant in fall, birth in the spring
- Wildfire smoke events have overlapped with infancy (first year of life) and pregnancy

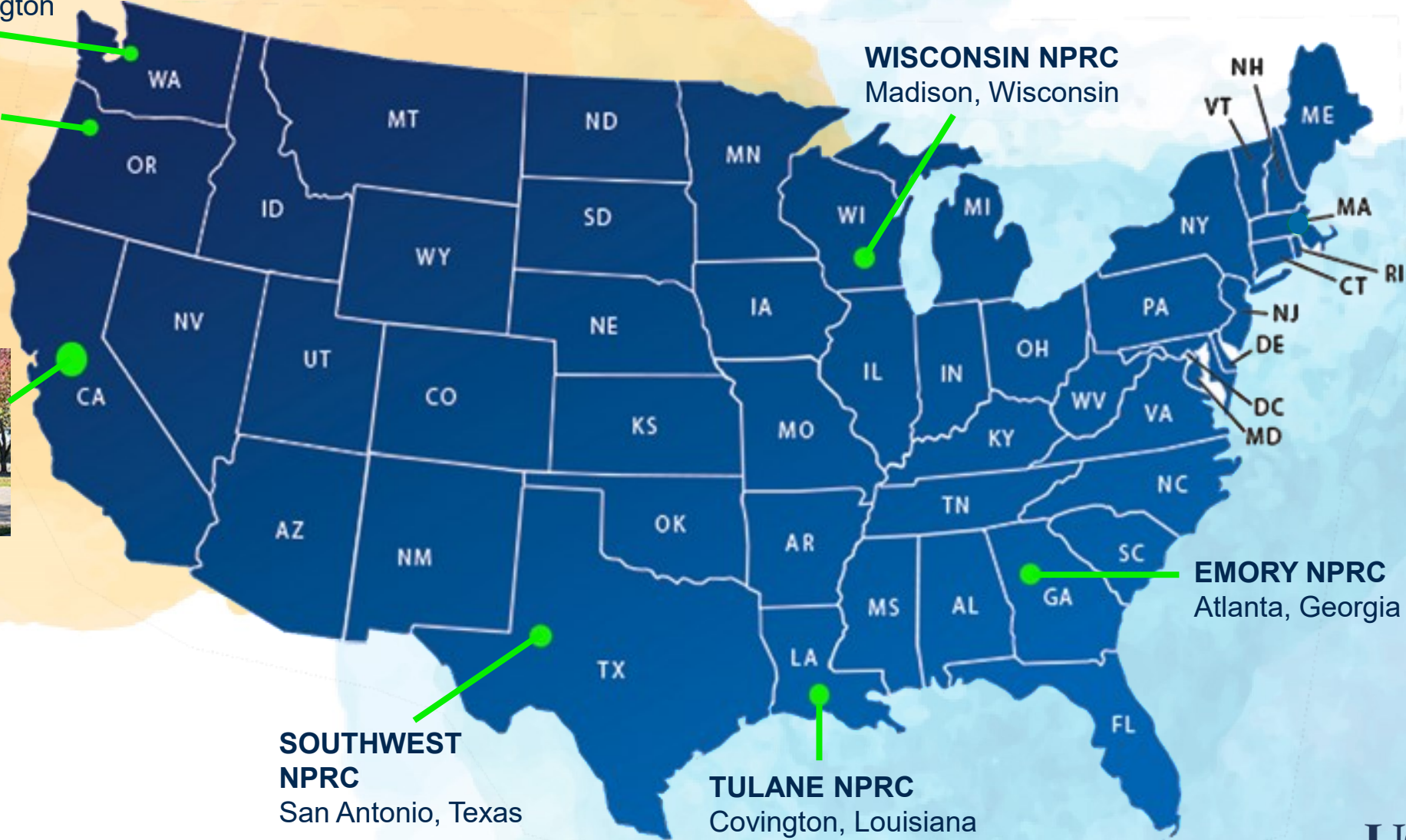


NIH National Primate Research Centers

WASHINGTON NPRC
Seattle, Washington

OREGON NPRC
Beaverton, Oregon

WISCONSIN NPRC
Madison, Wisconsin



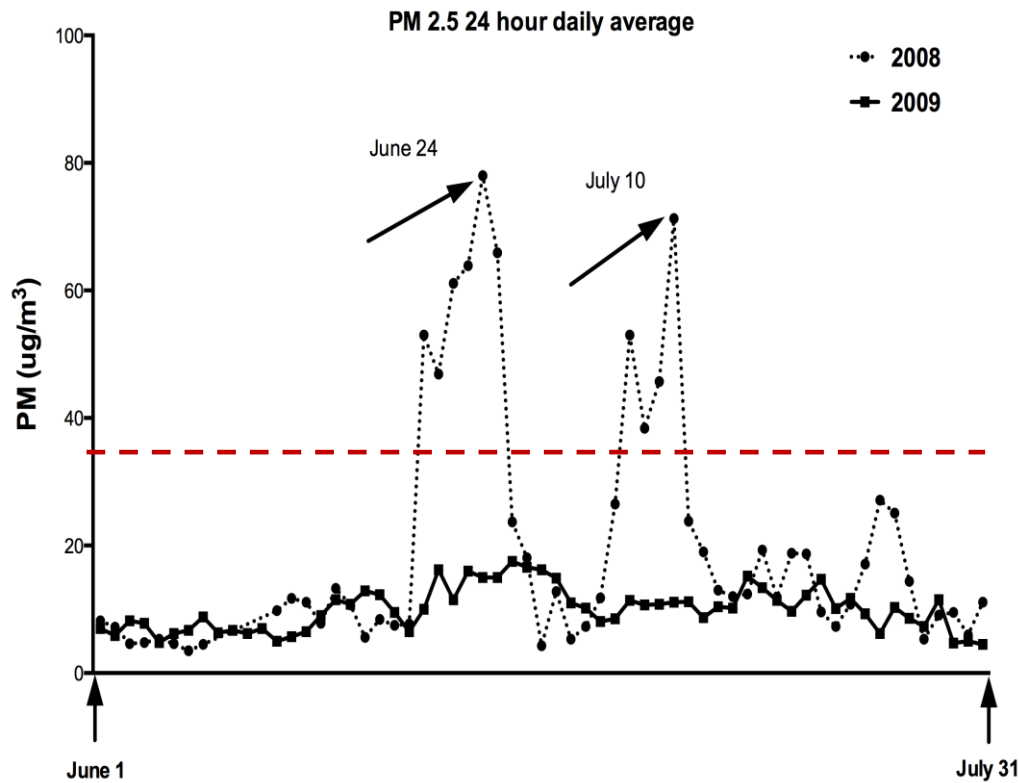
CALIFORNIA NPRC
Davis, California

EMORY NPRC
Atlanta, Georgia

SOUTHWEST NPRC
San Antonio, Texas

TULANE NPRC
Covington, Louisiana

Can exposure to wildfire smoke result in long-term health outcomes in a susceptible population?



NAAQS standard 35 ug/m³ per 24 hour period

- Studied animals that were infants and living outdoors during the 2008 Trinity/Humboldt wildfires
- Number of acres and structural loss were less than 2018 Camp Fire and 2020 August Complex fires
- Animals evaluated in adolescence and adulthood

Research Agreement Objectives

Specific Objective 1: Measure cumulative exposure to particles <2.5 micrometer in diameter (PM_{2.5}) and ozone (O₃) for 11 year-old CNPRC monkeys housed outdoors during and subsequent to the 2008 Humboldt and Trinity County summer wildfire events.

Specific Objective 2: Determine if wildfire smoke exposure can result in persistent dysregulation of immune function in 11 year-old CNPRC monkeys housed outdoors during and subsequent to the 2008 Humboldt and Trinity County summer wildfire events.

Specific Objective 3: Determine if parameters of respiratory health including lung volume and remodeling have been persistently compromised with wildfire smoke exposure in 11 year-old CNPRC monkeys housed outdoors during and subsequent to the 2008 Humboldt and Trinity County summer wildfire events.

Specific Objective 4: Assess whether parameters of respiratory function correlate with activity levels in 11 year-old CNPRC monkeys housed outdoors during and subsequent to the 2008 Humboldt and Trinity County summer wildfire events.

Effect of Wildfire Smoke Exposure on Measures of Health Across the Lifespan



2009 age-matched controls

Effect of Wildfire Smoke Exposure on Measures of Health Across the Lifespan: Data Summary

Infant



0-12 months

- Exposure event



Juvenile



3 years

- Hyporesponsive immune cells
- Smaller lungs
- Stiffer lungs (females)



Adult

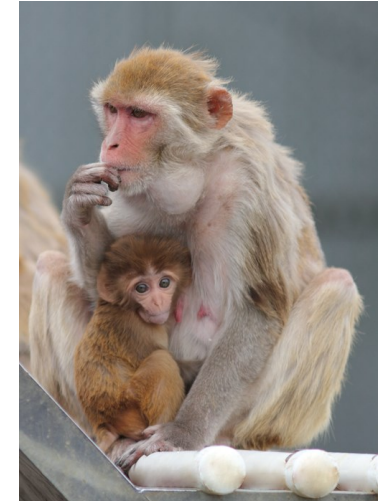


8 years

- Hyperresponsive immune cells
- Smaller lungs
- Lung remodeling consistent with restrictive airways

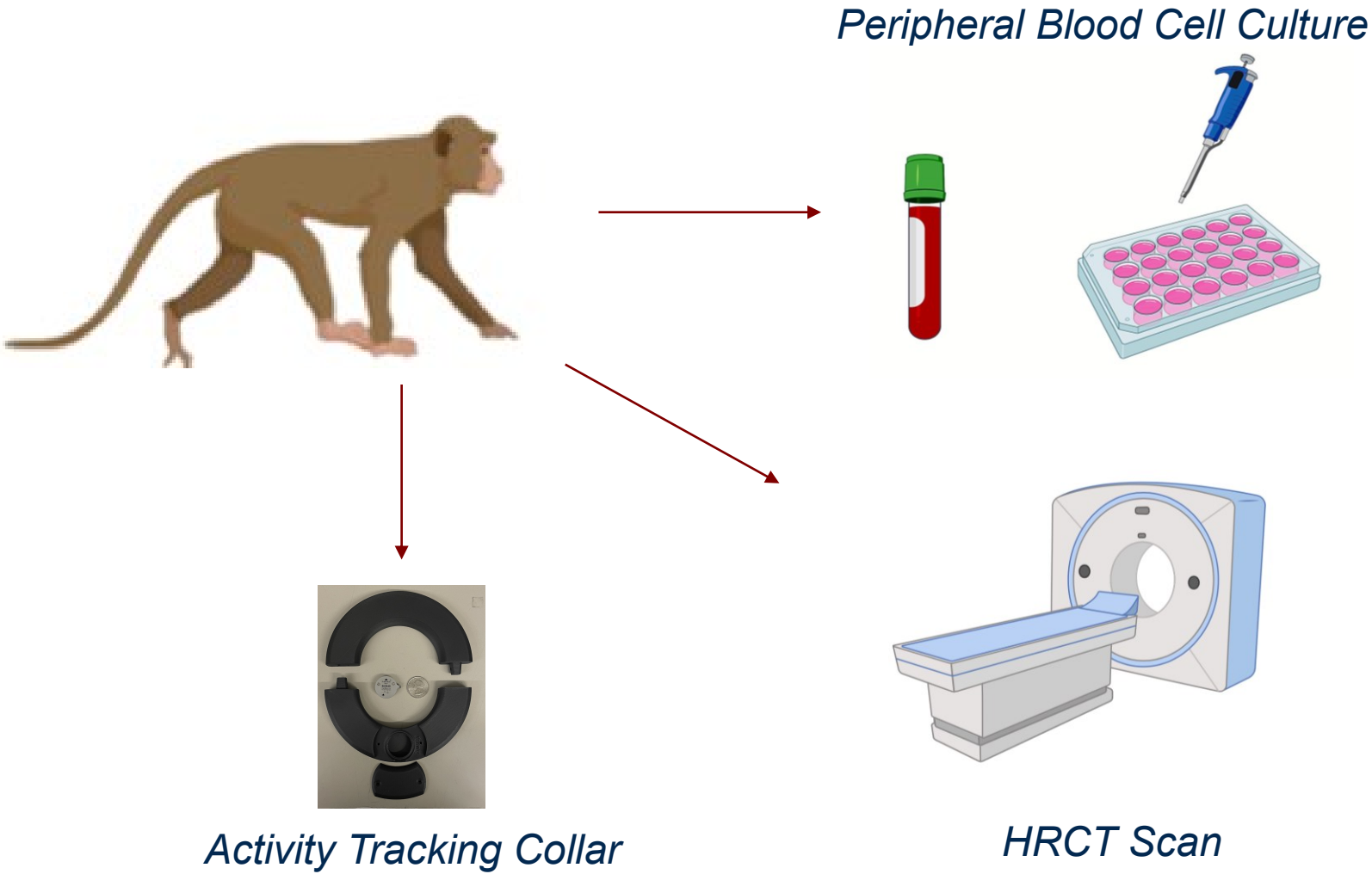


Adult

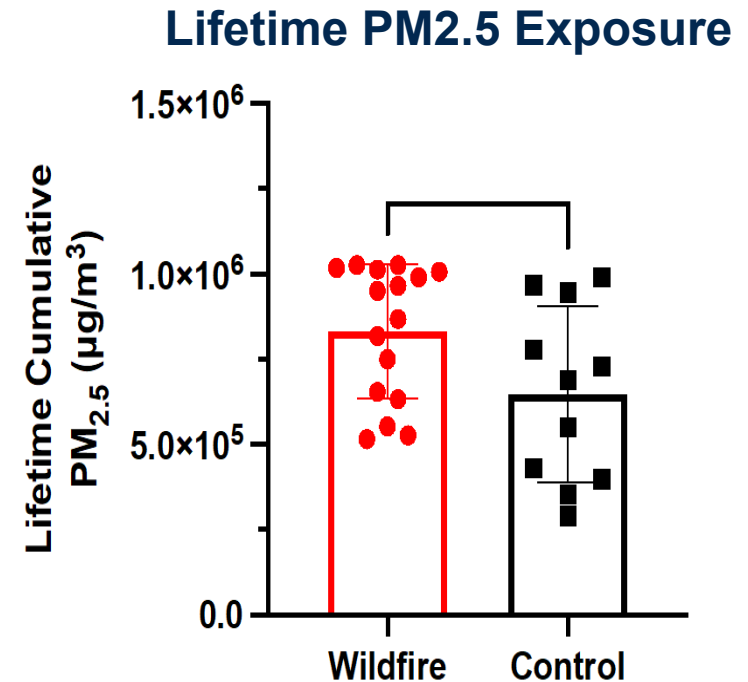
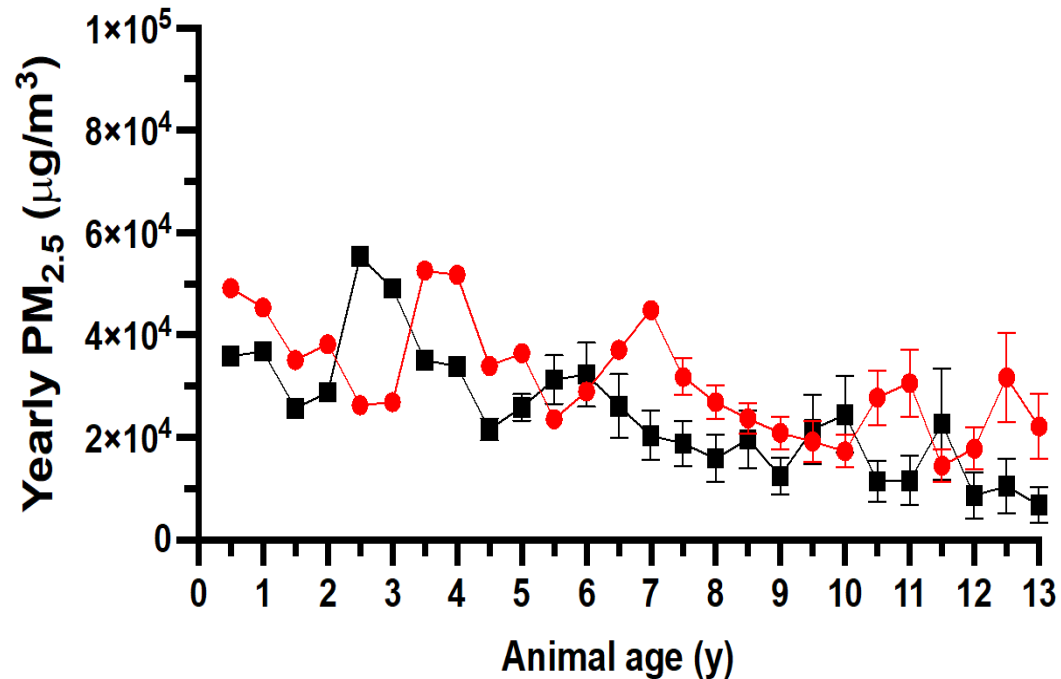


13 years

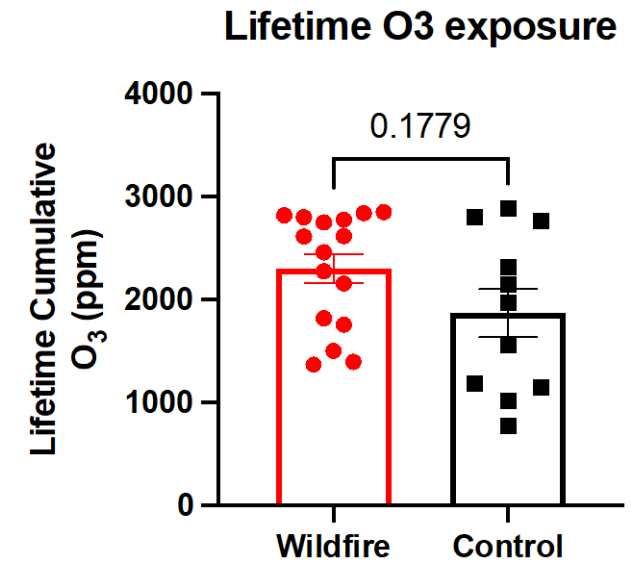
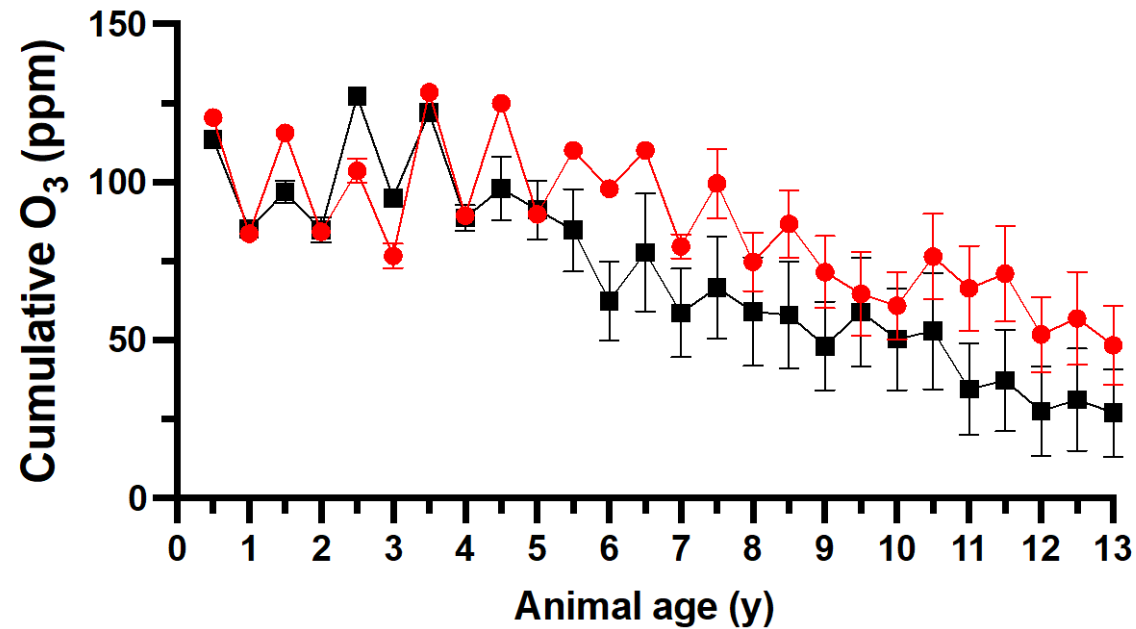
Overall Approach for Measures of Health in 13 Year Old Adult Monkeys



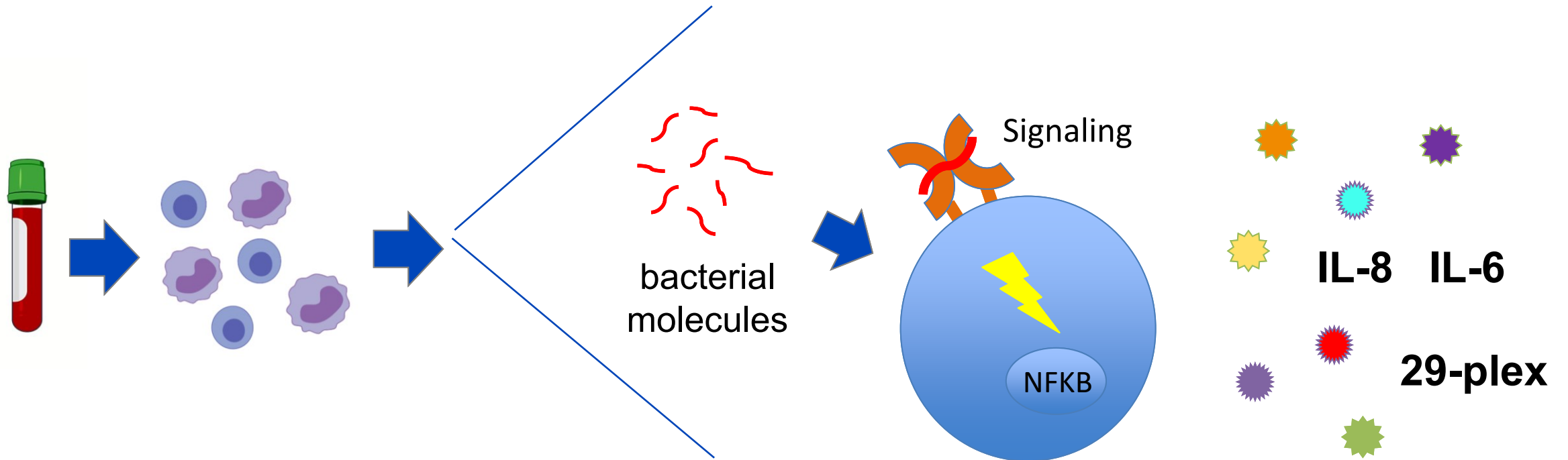
Objective 1: Cumulative Exposure to Particles <2.5 Micrometer in Diameter (PM_{2.5})



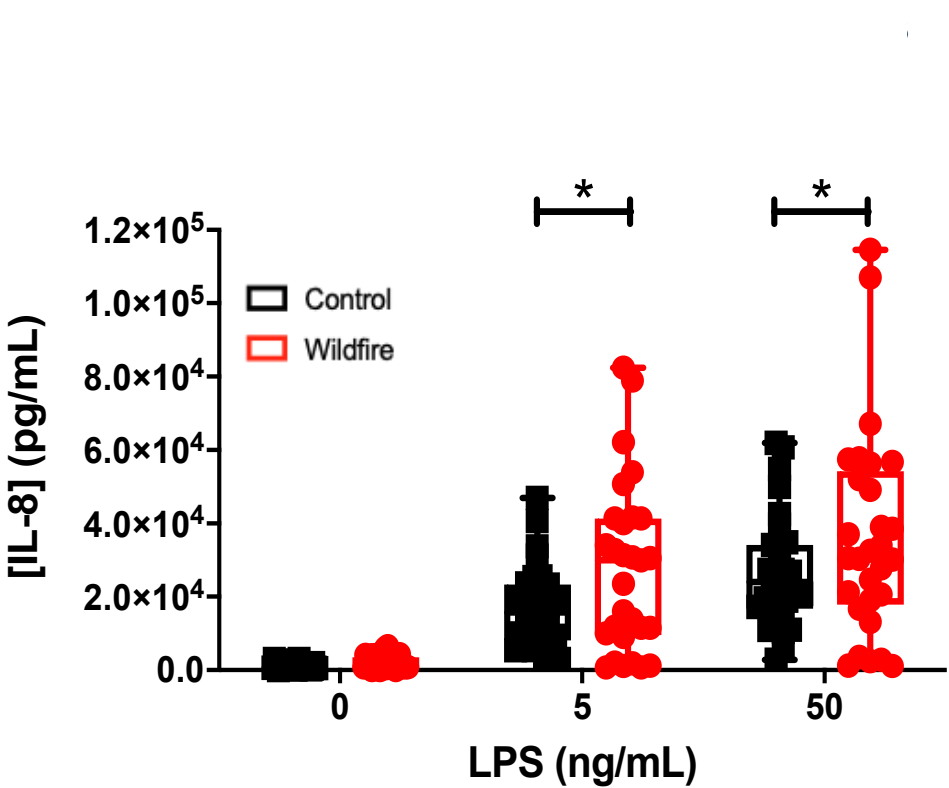
Objective 1: Cumulative Exposure to Ozone (O₃)



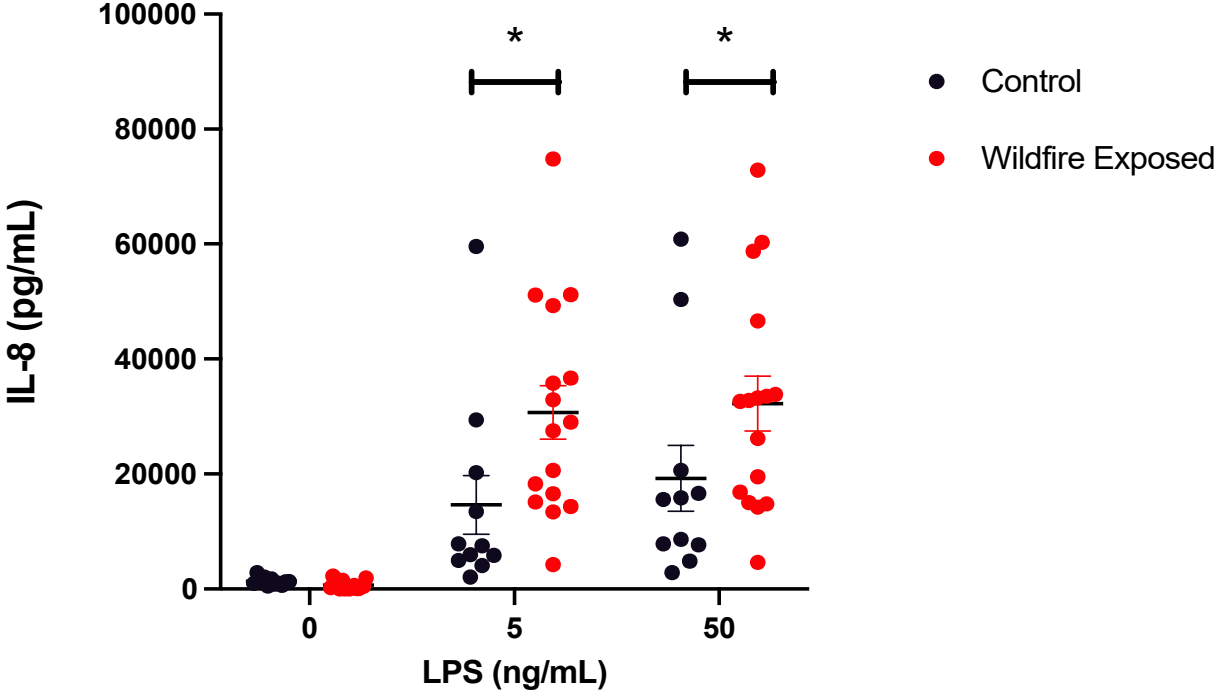
Objective 2: Effects of Early Life Wildfire Smoke Exposure on Immune Function in Adults



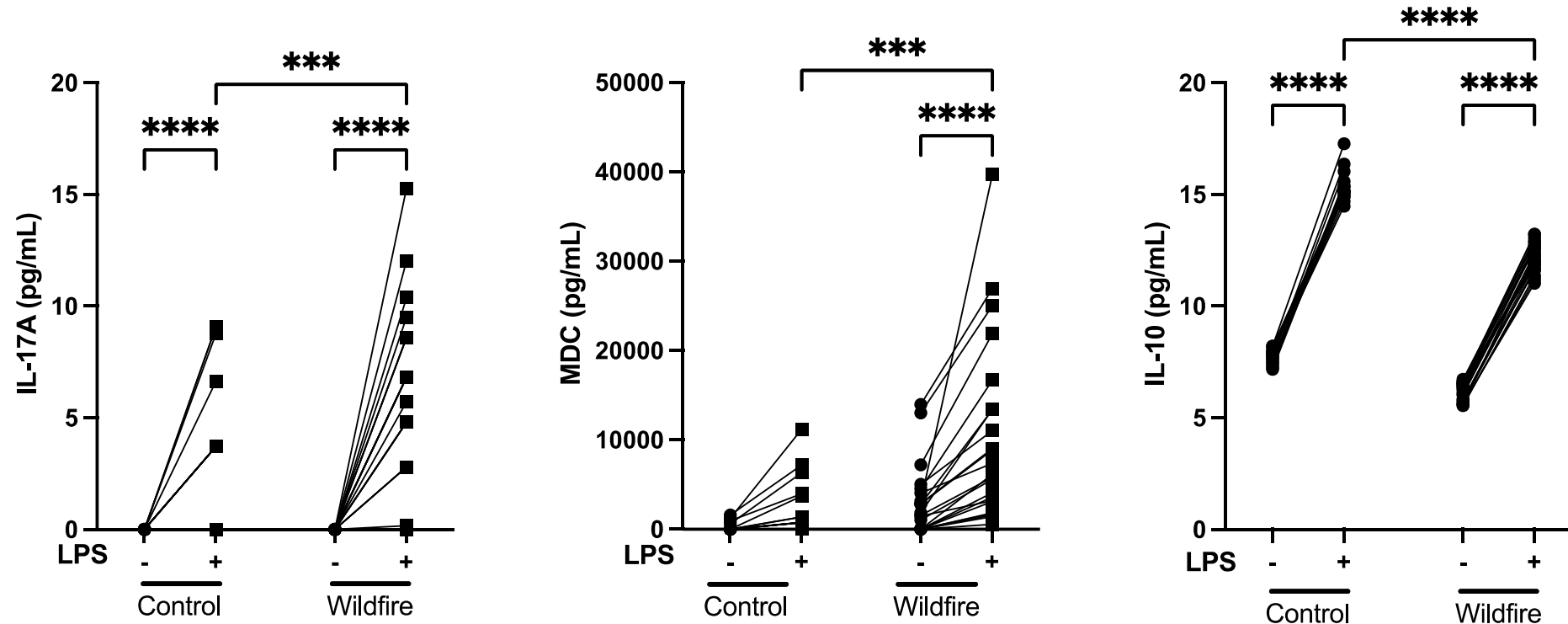
Wildfire Smoke Exposure is Associated with Immune Dysregulation in Adult Monkeys



13 year old female rhesus monkeys

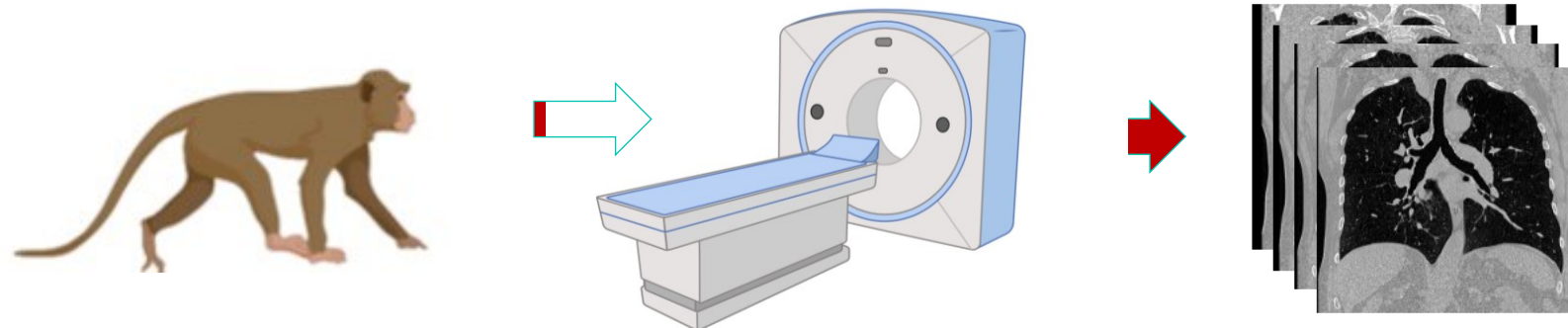


Wildfire Smoke Exposure is Associated with Immune Dysregulation in Adult Monkeys



- Enhanced secretion of cytokines involved in chronic inflammation (IL-17, Macrophage Derived Chemokine)
- Reduced secretion of an anti-inflammatory chemokine (IL-10)

Objective 3: Effects of Early Life Wildfire Smoke Exposure on Respiratory Health in Adults



CT Scan

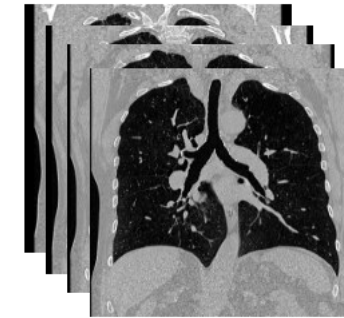
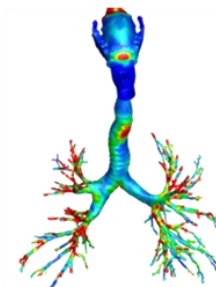
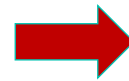


Image Acquisition



Structural Segmentation



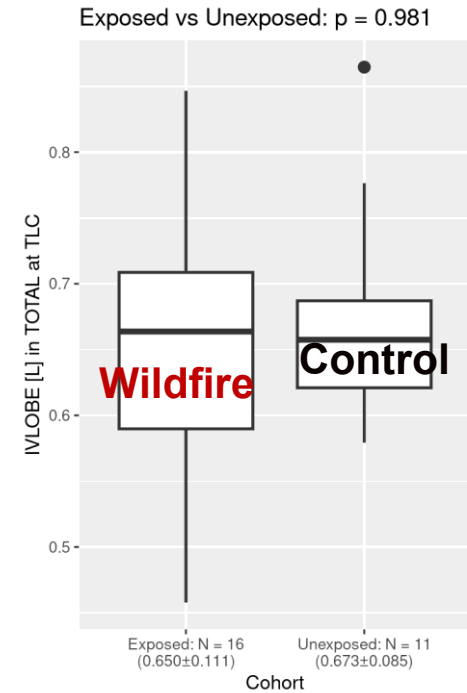
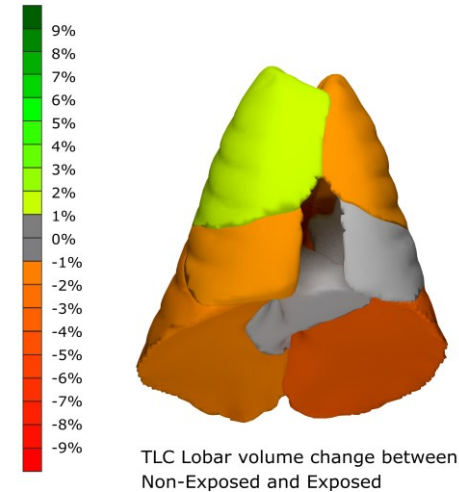
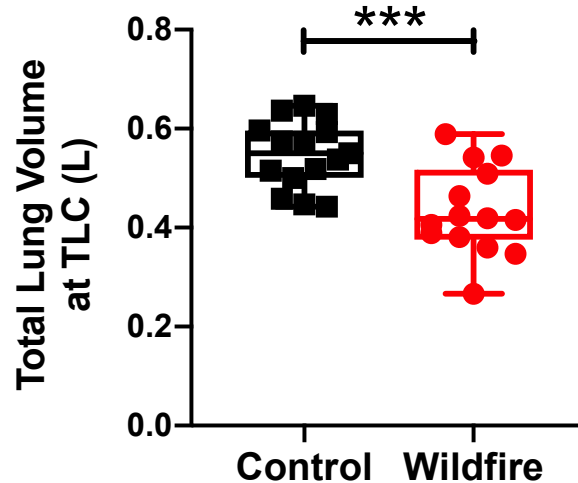
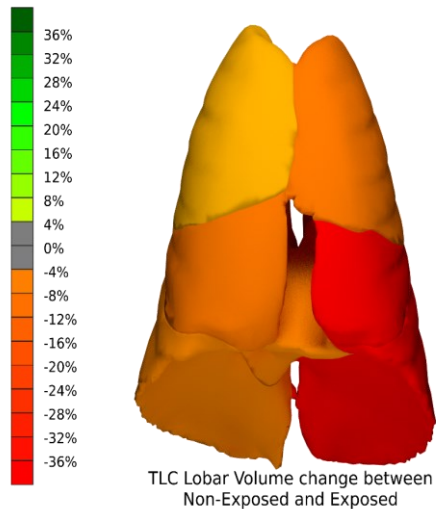
Flow Simulation



Reduced Lung Volumes with Wildfire Smoke Exposure Normalized at 13 Years of Age

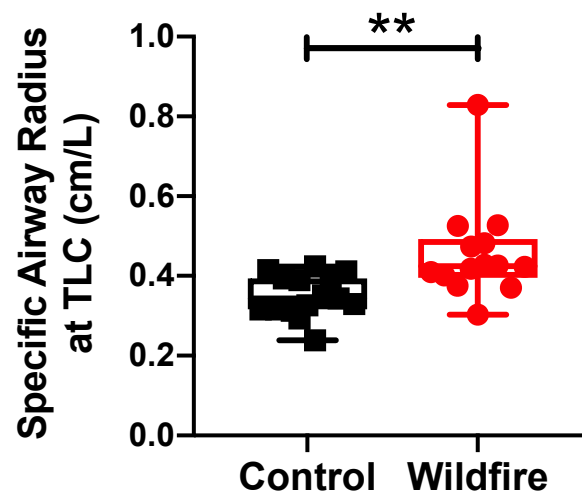
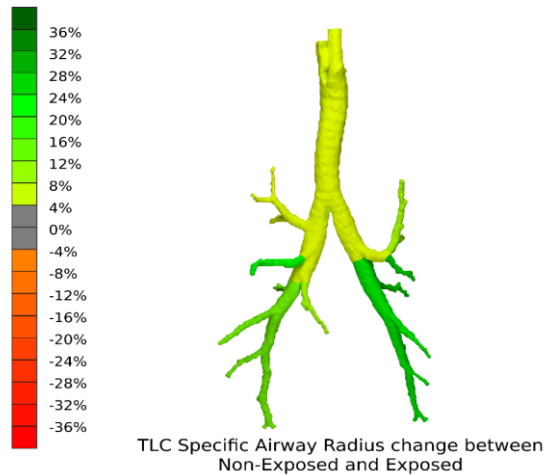
8 year old female rhesus monkeys

13 year old female rhesus monkeys

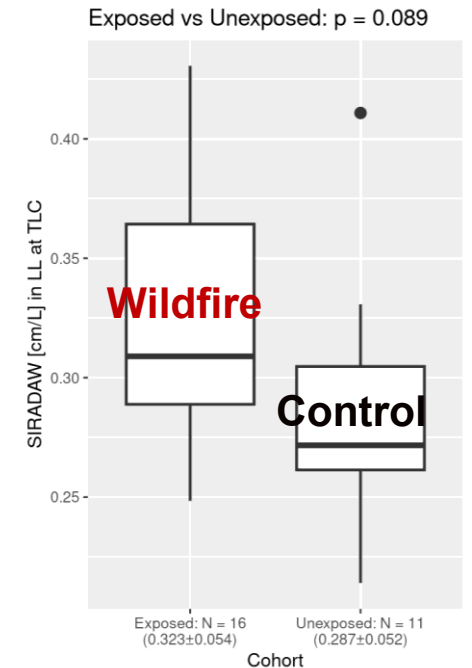
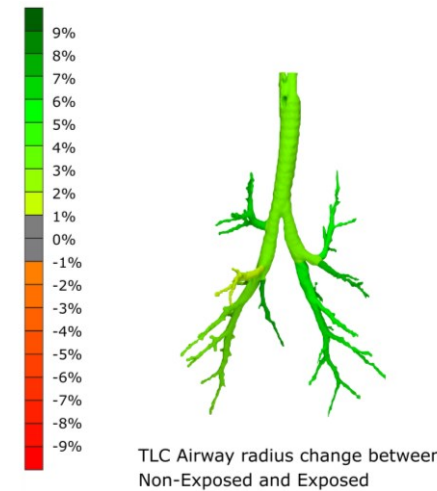


Trend in Larger Airway Radius with Wildfire Smoke Exposure at 13 Years of Age

8 year old female rhesus monkeys



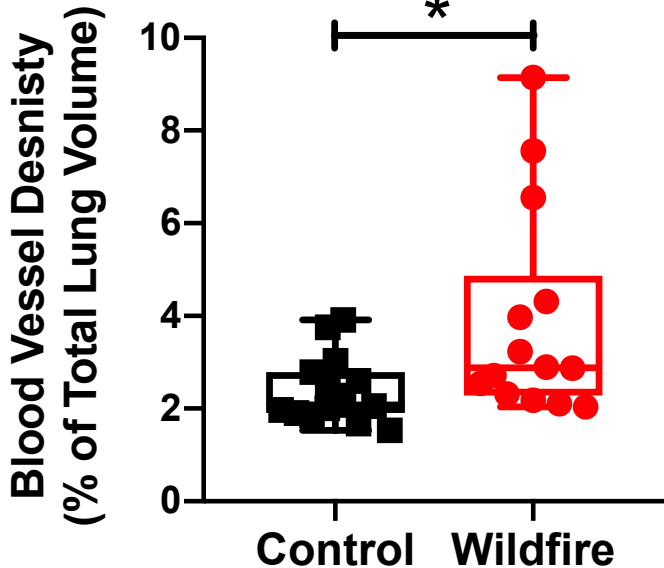
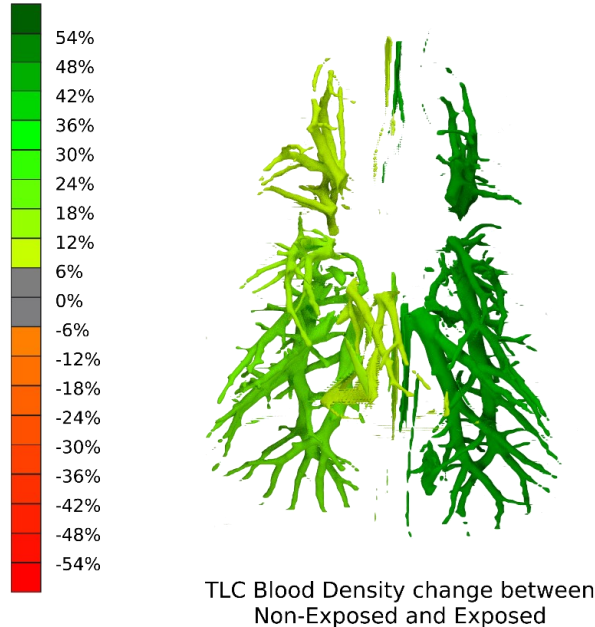
13 year old female rhesus monkeys



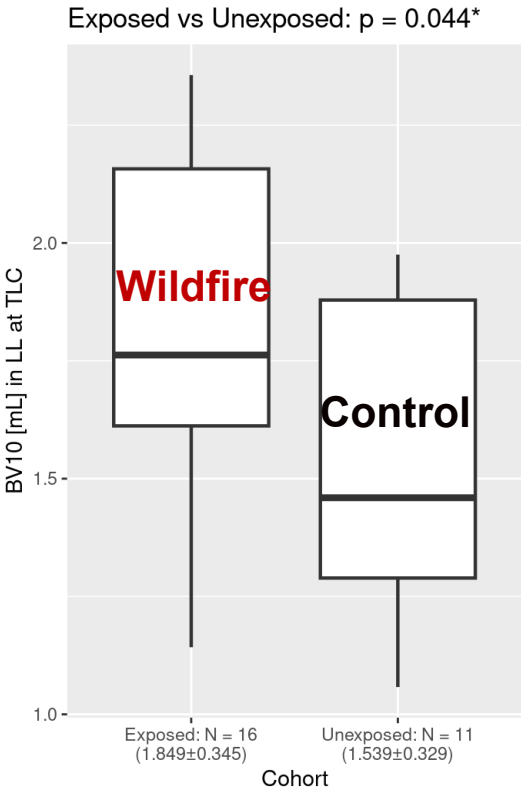
FLUIDDA

Wildfire Smoke Exposure is Associated with Increased Lung Blood Vessel Density in Adult Monkeys

8 year old female rhesus monkeys



13 year old female rhesus monkeys

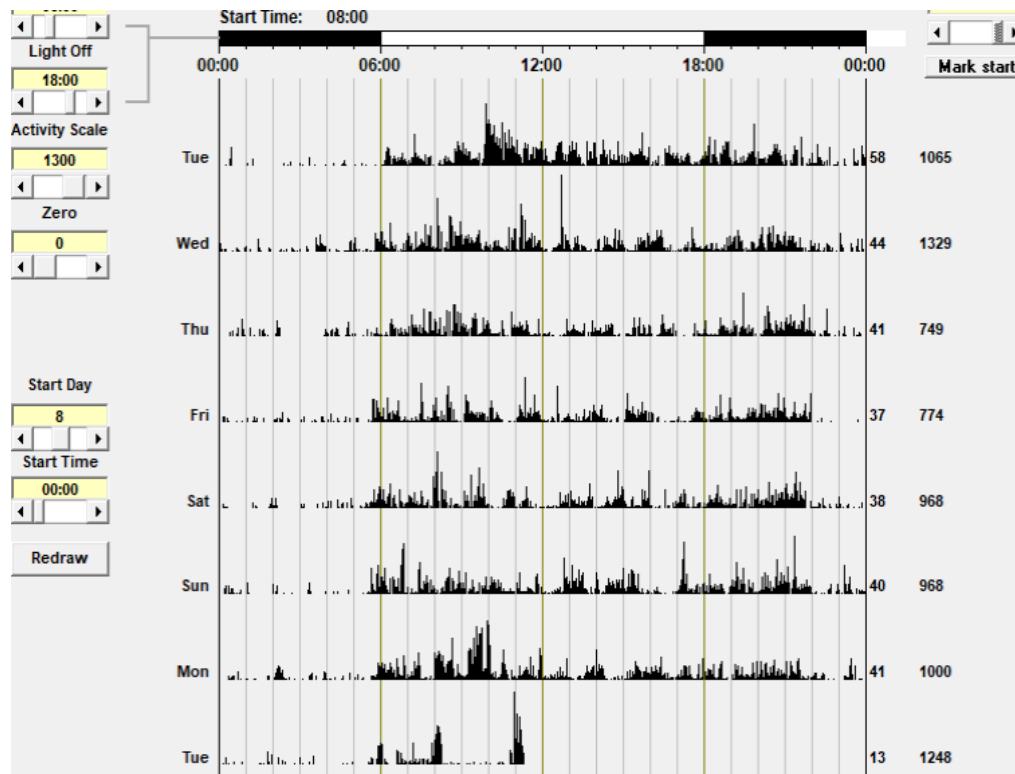


Objective 4: Effects of Early Life Wildfire Smoke Exposure on Physical Activity in Adults

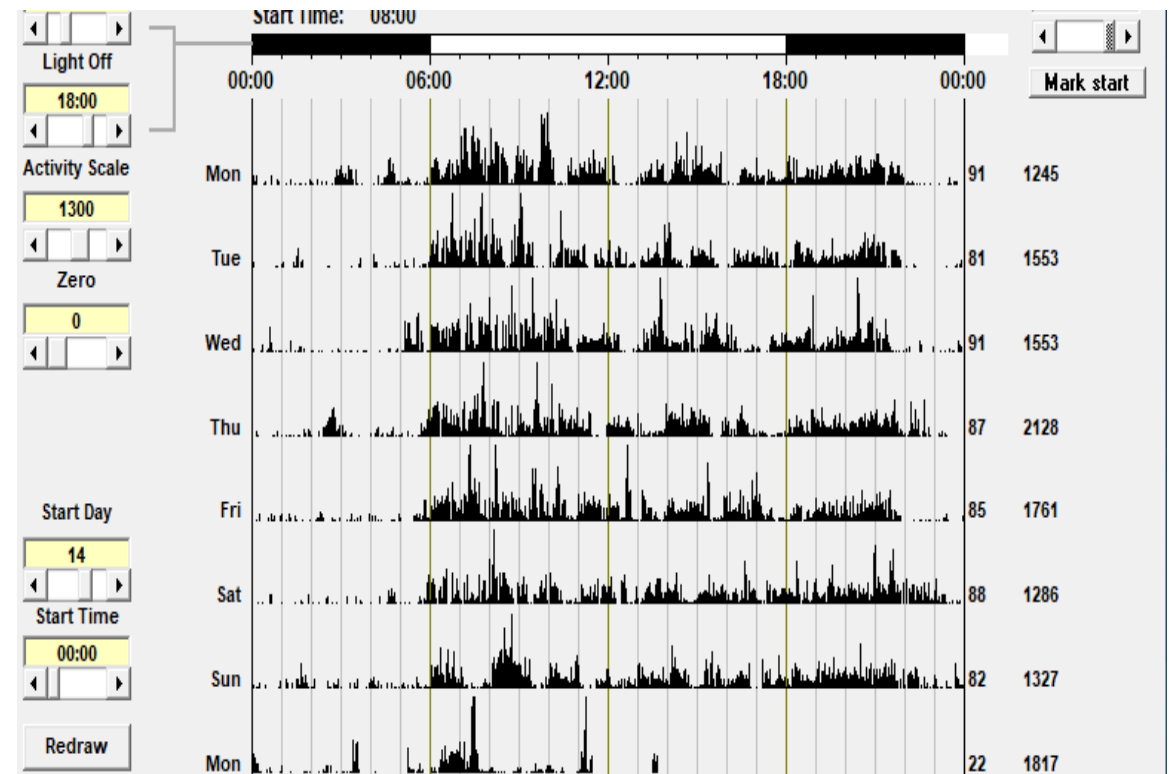


Wildfire Smoke Exposure Is Associated with Increased Activity in Adult Monkeys

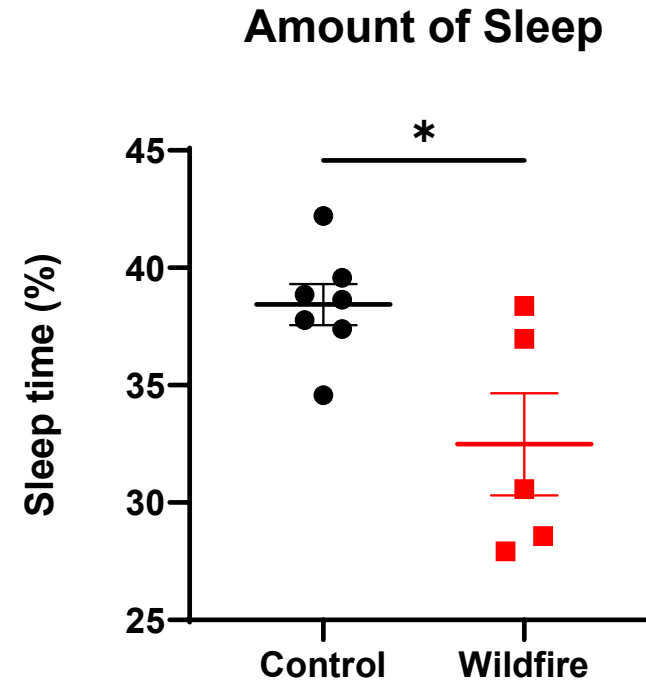
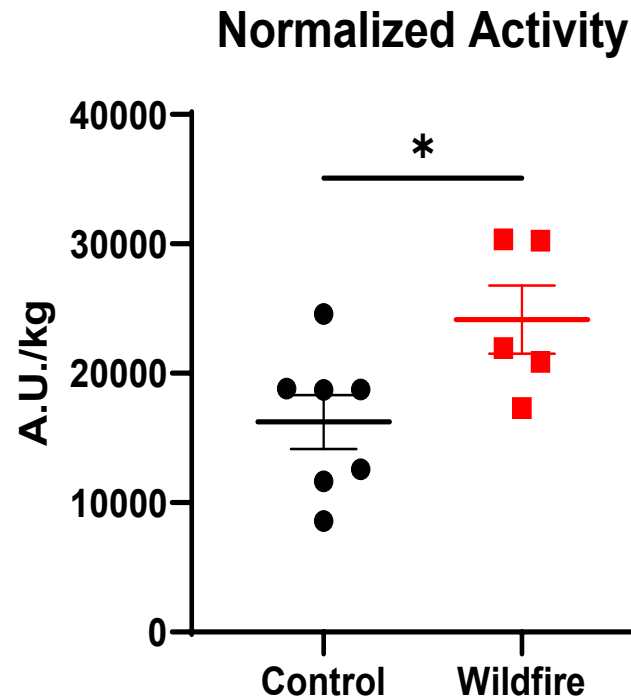
Control



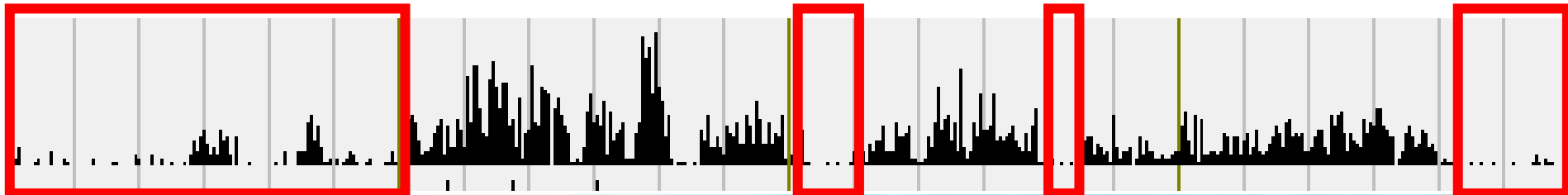
Wildfire



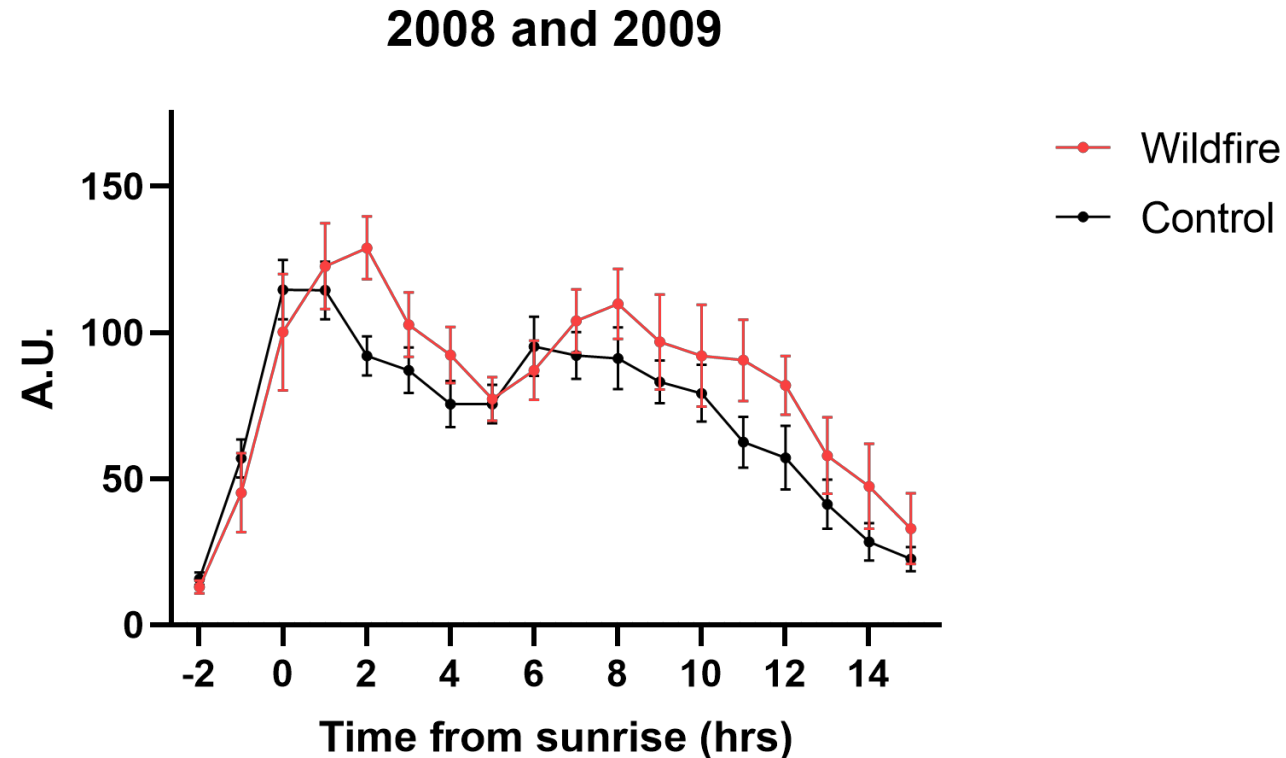
Wildfire Smoke Exposure is Associated with Sleep Disturbances in Adult Monkeys



Sleep



Early Life Exposure to Wildfire Smoke is Associated with Delayed Peak Activity



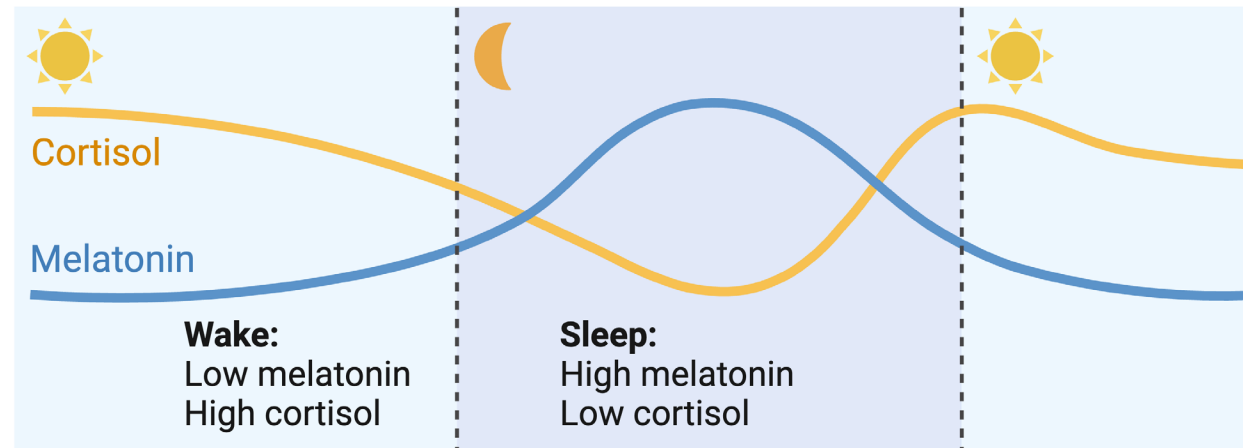
Peak activity levels shift to the right (later in the day)

Potential Mechanisms for Effects of Air Pollution on Sleep Disturbances?

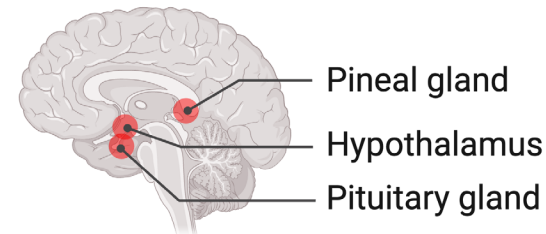


Circadian rhythm is part of the body's **internal clock**; it follows a 24-hour schedule and regulates the sleep-wake cycle.

During the 24-hour cycle, our hormone levels fluctuate in response to light, particularly **melatonin** and **cortisol**.



Regions of the brain that regulate the circadian rhythm include **pineal gland, hypothalamus** and **pituitary gland**.



Biobehavioral Assessment (BBA) program at California National Primate Research Center

Biobehavioral Assessment (BBA) program at California National Primate Research Center is designed to characterize behavioral and physiological responsiveness in young animals.

The assessment is performed annually on a subset of infant primates.

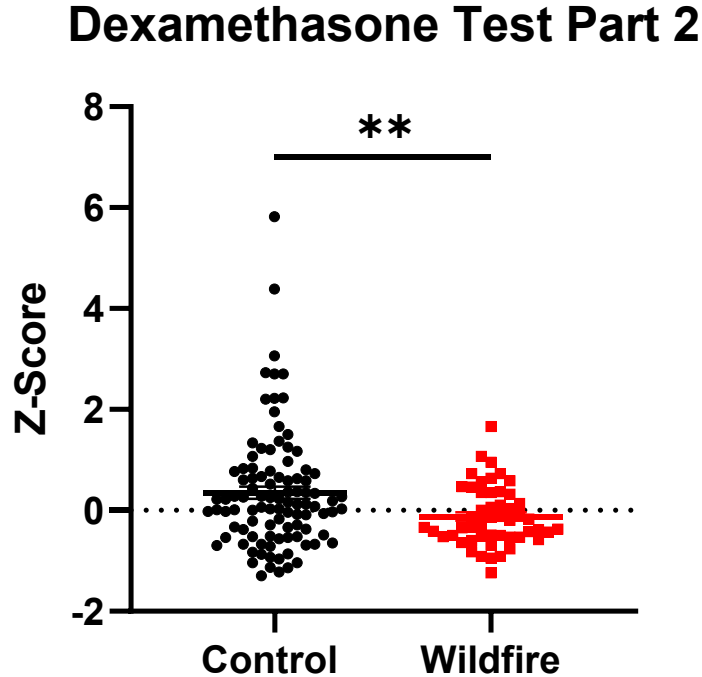
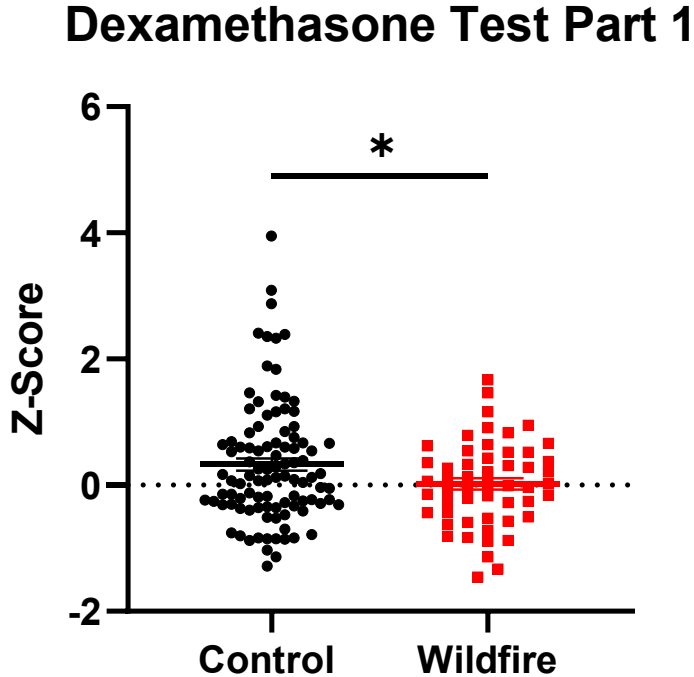
Blood is sampled to assess infants' responses to separation and relocation.

Dexamethasone suppression test measures cortisol regulation.

Cortisol is the primary stress hormone evaluated.

A cohort of infant monkeys have been evaluated annually since 2001

Dysregulated Cortisol Levels Observed After Wildfire Smoke Exposure



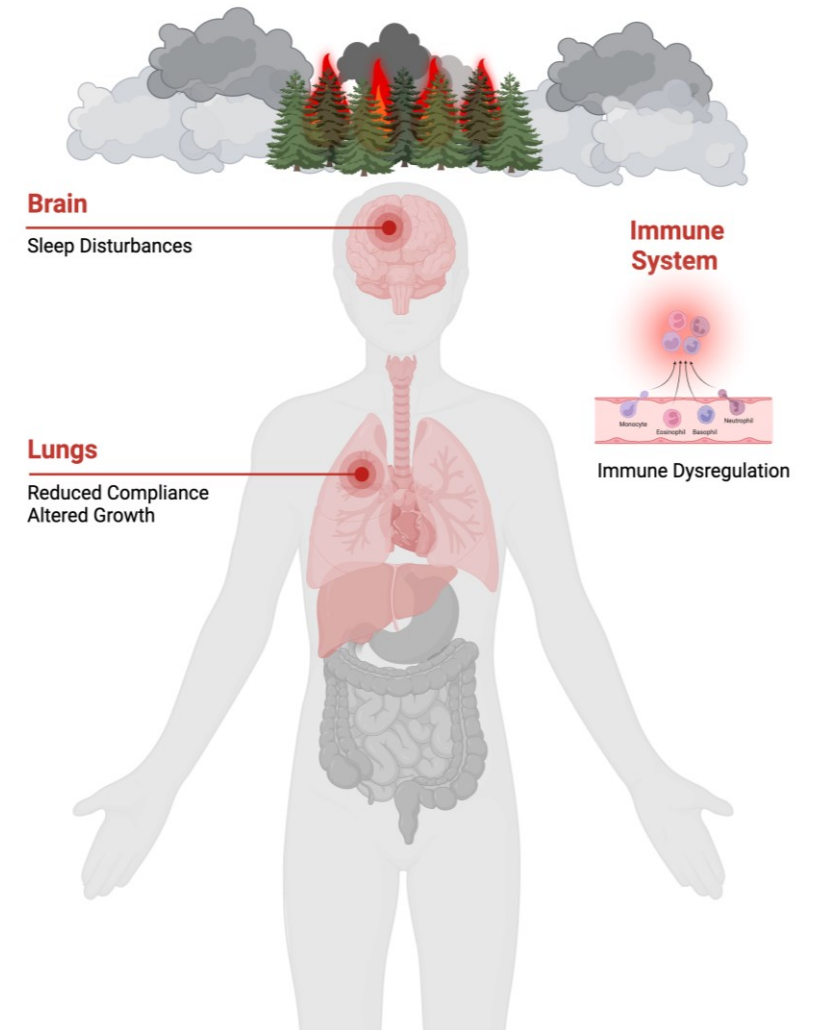
Dexamethasone suppression test measures cortisol regulation and is performed routinely by the behavioral unit at CNPRC and collected shortly after the wildfire in 2008/2009.

Cortisol levels in serum were dysregulated in the wildfire smoke exposed group compared to the control shortly after the wildfire

Summary

Early life ambient wildfire smoke PM_{2.5} exposure in rhesus macaque monkeys is associated with:

- Dysregulation of host pathogen immune responses
- Increased pulmonary blood vessel density and a trend toward a larger airway radius
- Evidence of sleep disturbances and altered cortisol responses
- Suggests increased susceptibility to infectious disease, lung pathology, and other chronic health conditions in adult human populations who have experienced comparable exposures



Take Home Messages

An acute ambient wildfire smoke event can elicit adverse health effects in a susceptible population that persist with age

Important points to note when considering translation of our findings to the human population:

Animals in this study were housed outdoors throughout the exposure event

Normal growth and development of nonhuman primates is accelerated relative to humans

Acknowledgements

Miller Lab

Dorothy You
Alexa Rindy
Diwash Shrestha
Chloe Chou
Chris Royer
Ross Allen
Taylor Westmont
Noah Siegel
Krista Thongphanh
Jed Bassein
Noah Marx



CNPRC

Alice Tarantal
Kent Pinkerton

UCDAVIS
CALIFORNIA NATIONAL
PRIMATE RESEARCH CENTER

 **UCDAVIS**
VETERINARY MEDICINE

 NATIONAL
PRIMATE
RESEARCH
CENTERS
Causes | Preventions | Treatments | Cures

California Air Resources Board, NIH P51OD11107