The LSU Superfund Research Center

Dr. Stephania Cormier, Center Director and Project 1 Lead

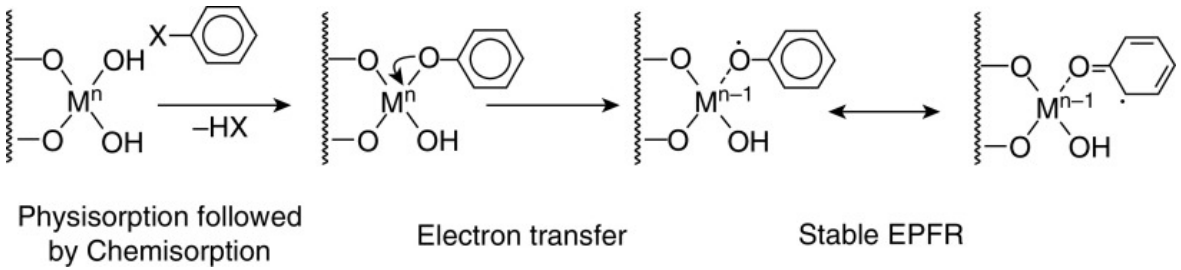
Dr. Tammy Dugas, Project 2 Lead and Training Core Director

Dr. Jennifer Richmond-Bryant, Project 3 Lead

National Institute of Environmental Health Sciences
Your Environment. Your Health.

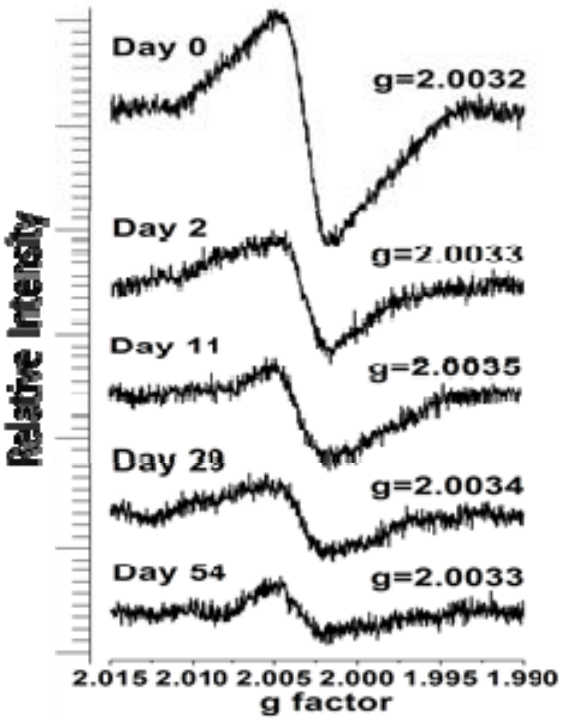
National Institute of Environmental Health Sciences
Superfund Research Program

Environmentally Persistent Free Radicals (EPFRs)



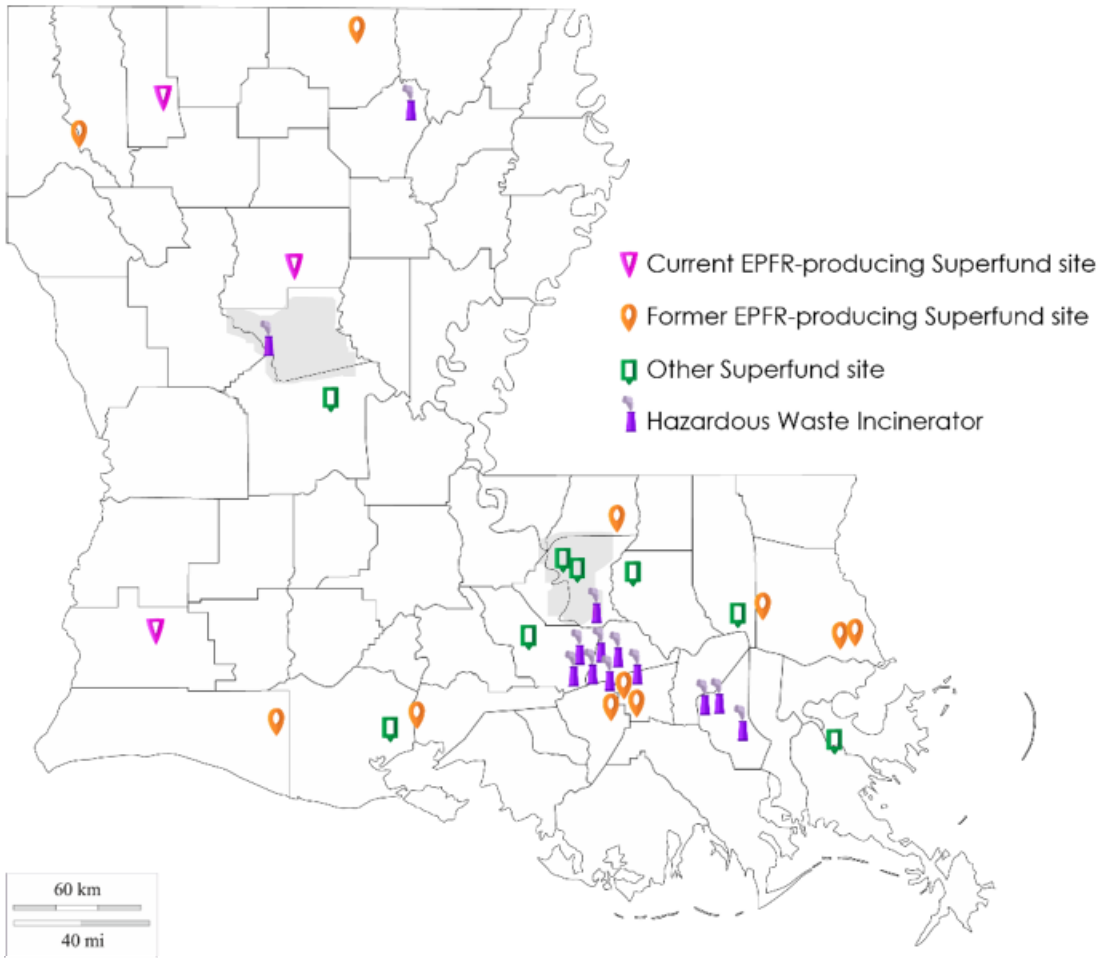
Mechanism of formation of a phenoxyl-type EPFR on a metal (M) oxide surface (Lomnicki et al 2008, Sly et al, 2019)

- EPFRs are pollutant particle systems that can be formed during combustion
- EPFRs are produced during thermal treatment (TT) of organic materials commonly found at Superfund sites
  - 30% of Superfund sites use TT to dispose of their waste (excludes groundwater)
- EPFRs are an understudied contaminant with the potential to impact human health



EPFRs on airborne PM near an industrialized Superfund site exhibit a slow decay (>54d) Gehling et al. 2013

Environmentally Persistent Free Radicals (EPFRs)

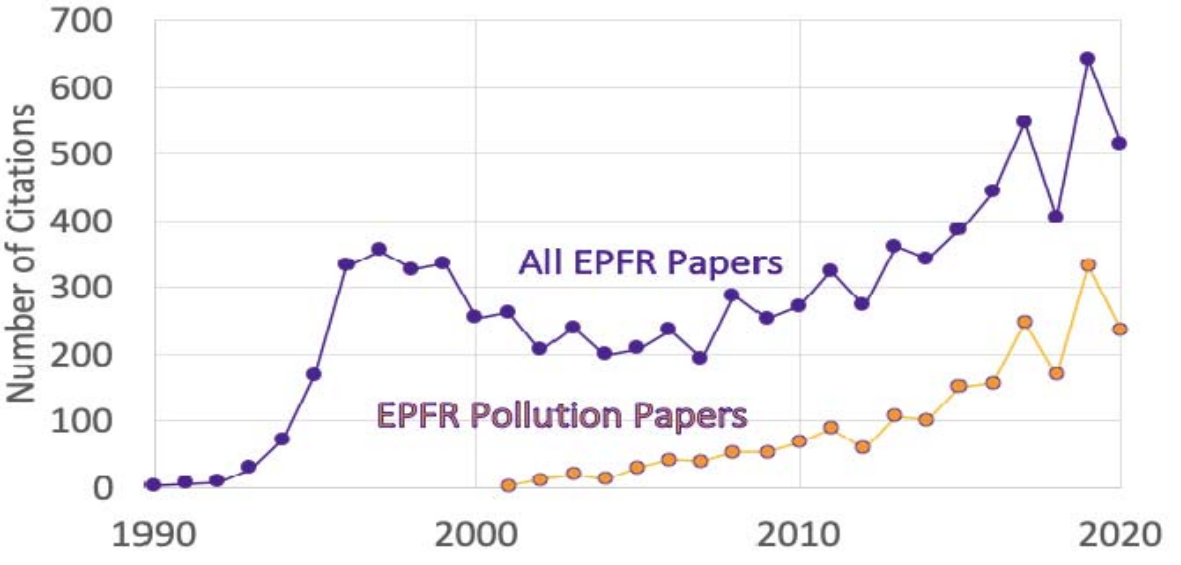


Growth of EPFRs as an Area of Study

Studies Published around the World

- 435 - China
- 180 - USA
- 42 - Australia
- 40 - Germany
- 36 - India
- 33 - Spain
- 26 - South Korea
- 26 - France
- 24 - Japan
- 10 - England

Sum of the LSU SRP EPFR Citations per Year



07 June 2018
Issue 509

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Source: Vejerano, E., Rao, G., Khachatryan, L., Cormier, S., Lomnicki, S. (2018) Environmentally Persistent Free Radicals: Insights on a New Class of Pollutants. *Environmental Science and Technology*. 52(5): 2468-2481.

Contact:
vejerano@mailbox.sc.edu

Read more about:

European Commission

Science for Environment Policy

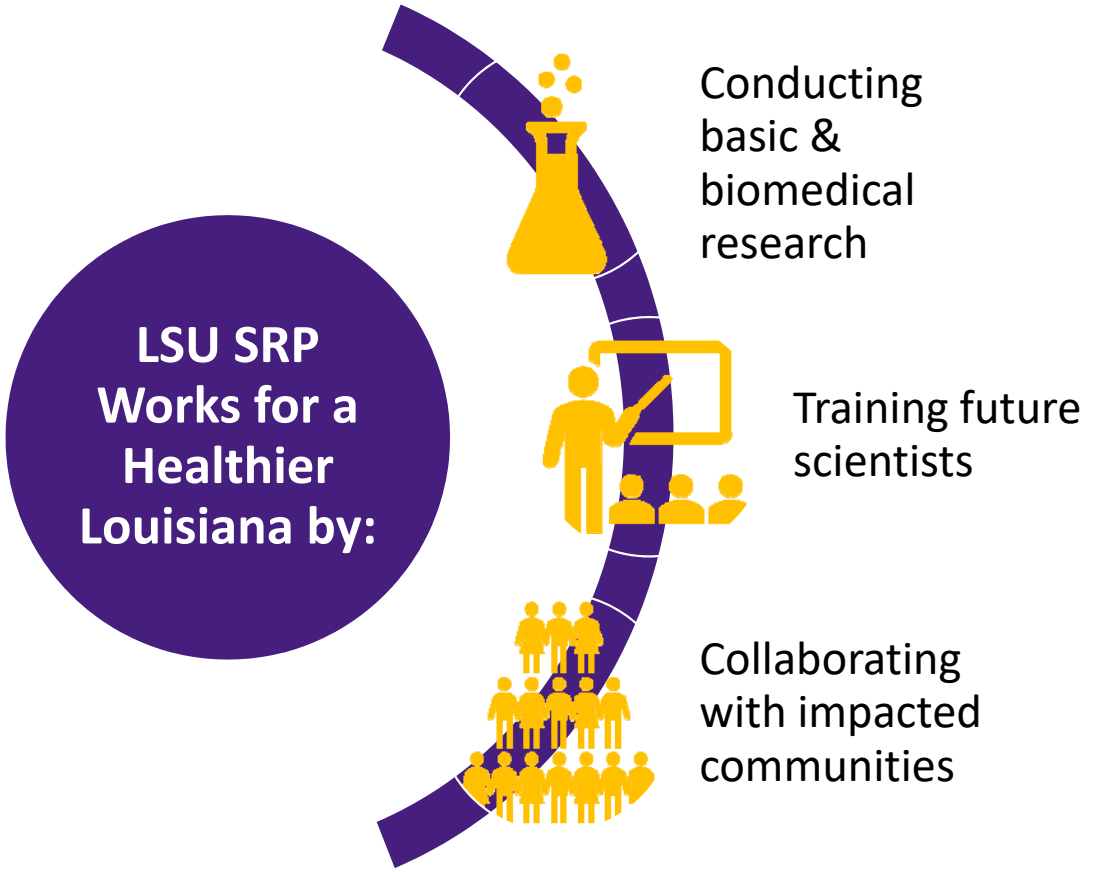
Environmentally persistent free radicals: what do we know about this newly recognised class of pollutants? *(continued)*

Research to date has found that EPFRs are present in the environment at levels which are high enough to cause health issues, as implied by animal and human cell studies. Studies conducted in Germany[4], Saudi Arabia and the US have provided figures of around 10^{16} to 10^{17} free radicals per gram of atmospheric PM. The EPFR content of PM will vary by location, depending on local combustion emissions; the review's researchers predict that concentrations will be higher in Beijing and New Delhi than in London and Paris, for instance.

Research suggests that EPFRs may also potentially form during incineration on some engineered nanomaterials (ENMs) with similar properties to metals — such as fullerenes (balls, 'cages' or tubes of carbon atoms), carbon nanotubes and nano-silica. This possibility remains hypothetical and is based upon known concepts and principles of chemistry and physics, rather than direct evidence. Nonetheless, this concern deserves more research, given that products containing ENMs, on the consumer market, continue to rise and that many of these will be incinerated and emitted into the atmosphere.

LSU SRP – Advancing Science, Promoting Health

- LSU SRP researchers are studying environmentally persistent free radicals (**EPFRs**), pollutants associated with the remediation of hazardous waste sites
- The goals of our research are to:
  - Clarify the pulmonary & cardiovascular effects of inhaling EPFRs (**Projects 1 & 2**)
  - Understand community exposure (**Project 3**)
  - Understand how EPFRs are formed and develop methods to destroy them (**Projects 4 & 5**)



External Advisory Committee

Administrative Core

Director: Stephania Cormier
Deputy Director: Phillip Sprunger
RT Coordinator: Jen Irving

Internal Advisory Committee

Community Engagement Core*

Margaret Reams

Research Experience & Training Coordination Core

Tammy Dugas

Data Management & Analysis Core

Donald Mercante

Inhalation Toxicology Core

Alexandra Noel

Materials Core

Lavrent Khachatryan

Environmental Science & Engineering Projects

Molecular Structure & Decay of EPFRs

Phillip Sprunger

Activation, Sensing & Prevention of Formation of EPFRs

Slawo Lomnicki

Community Exposure to EPFRs

Jen Richmond-Bryant

Biomedical Research Projects

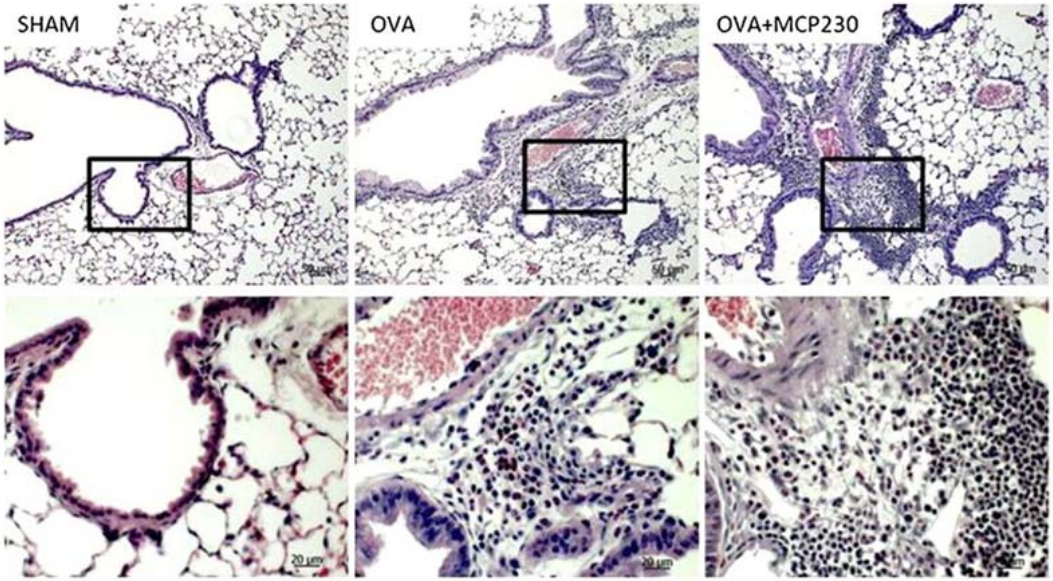
EPFRs & Cardiovascular Dysfunction

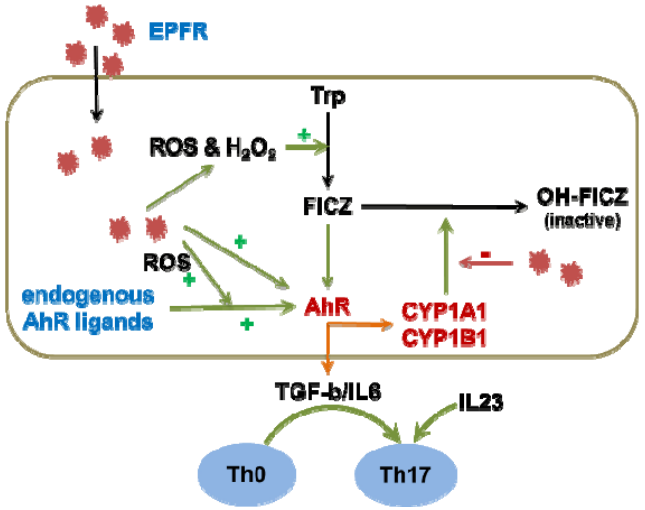
Tammy Dugas

EPFRs & Pulmonary Dysfunction

Stephania Cormier

Project 1 – EPFRs Alter Pulmonary Immunologic Homeostasis





Steroid insensitive asthma

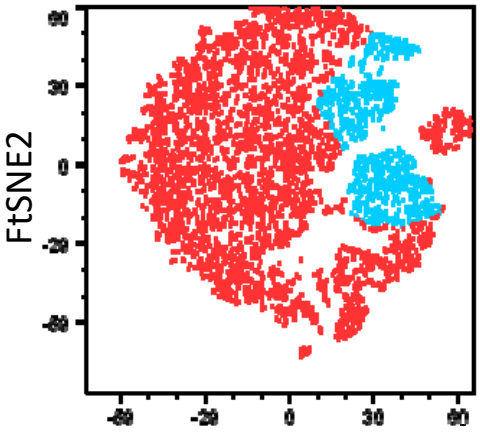
Cormier

Project 1 – EPFRs Alter Pulmonary Immunologic Homeostasis

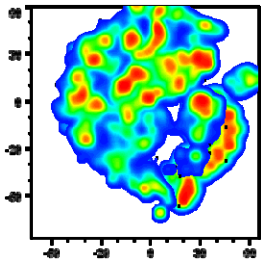
- **Hypothesis**: EPFRs modulate AhR signaling leading to a pleiotropic response that alters both immunologic and P450 function

- **Aims**
  1. Determine the role of AhR activation in AECs in the induction of EPFR-induced Th17 responses.
  2. Define mechanisms by which EPFRs alter the interaction and function between P450s and their redox partners.
  3. Demonstrate a link between EPFR exposure and poor respiratory health in children. Neutrophil/Th17 mediated?

Project 1 - EPFRs Alter Pulmonary Immunologic Homeostasis

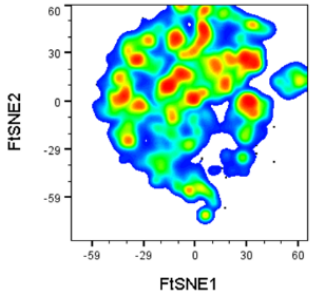


Sample Name	Subset Name
concat_1.fcs	cyp1a1+
concat_1.fcs	Ungated

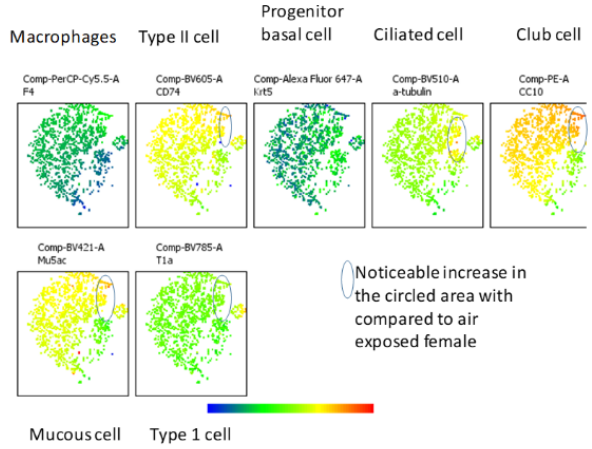


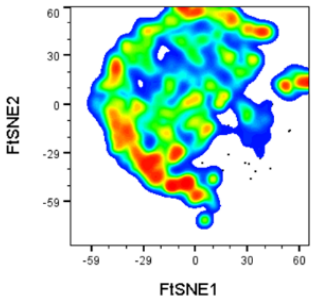
Cyp1a1 expression (AhR activation):

- Difference between females and males
- Club, ciliated, mucous, and Type II cells

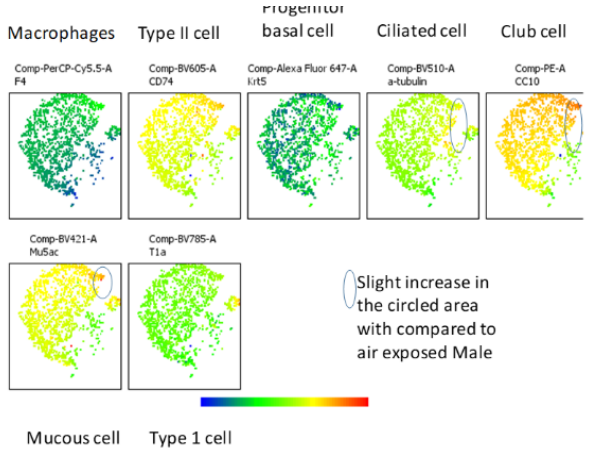


MCP 230 Exposure Female



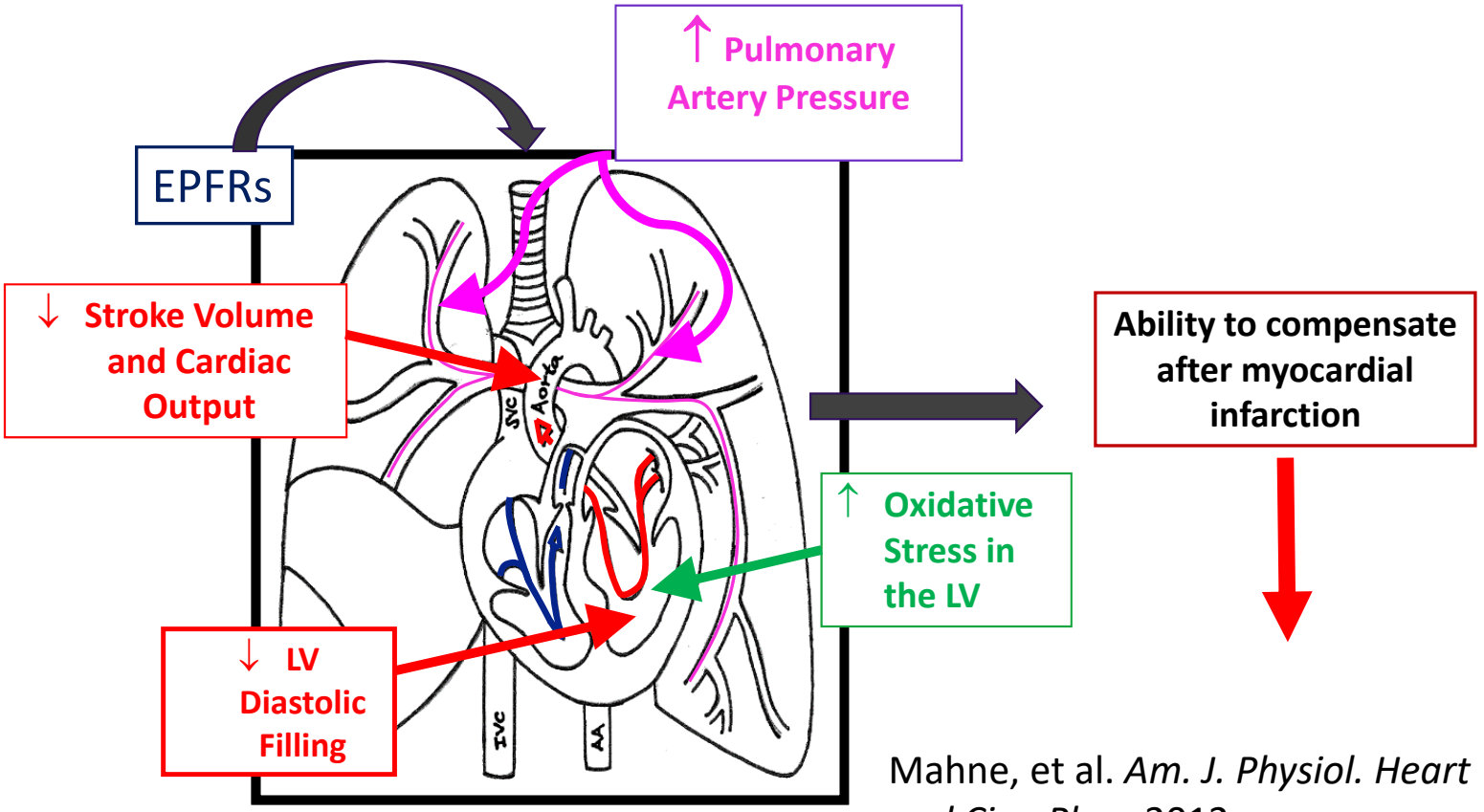


MCP 230 Exposure Male



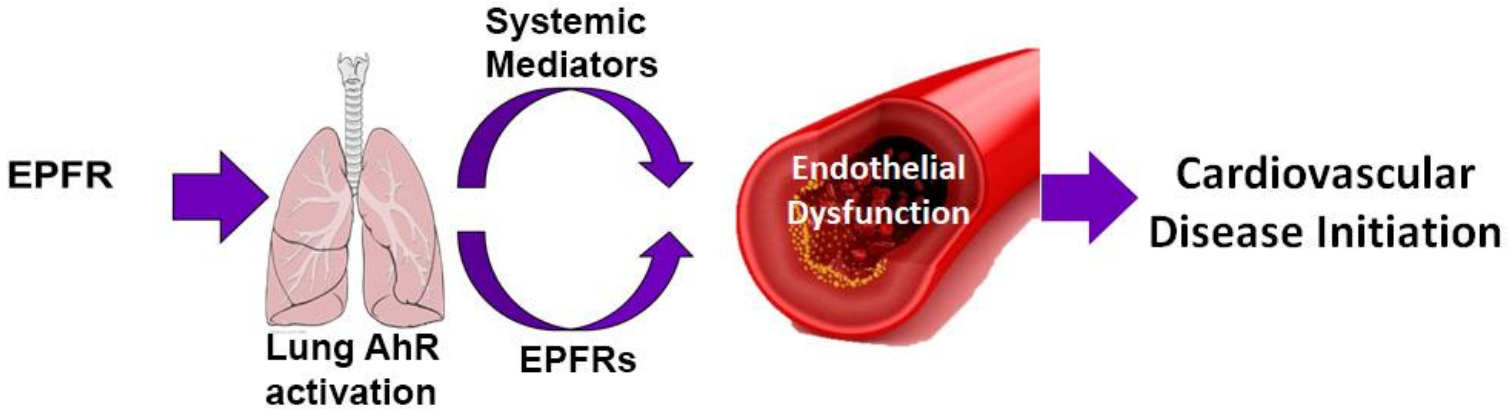
Project 2 – Assessing Cardiovascular Risks of Exposure

Dr. Kurt Varner
LSU Health Sciences Center



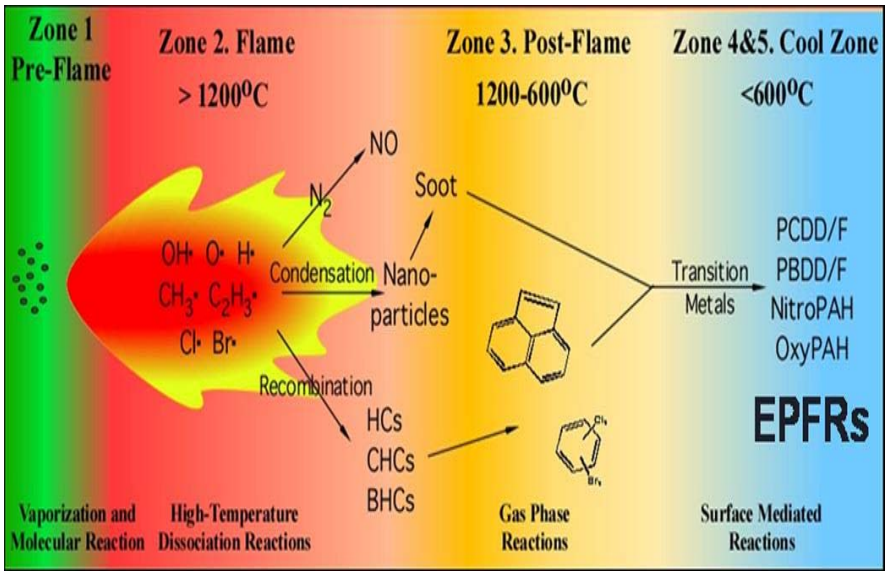
Mahne, et al. *Am. J. Physiol. Heart and Circ. Phys.* 2012.

Project 2 – Central Hypothesis



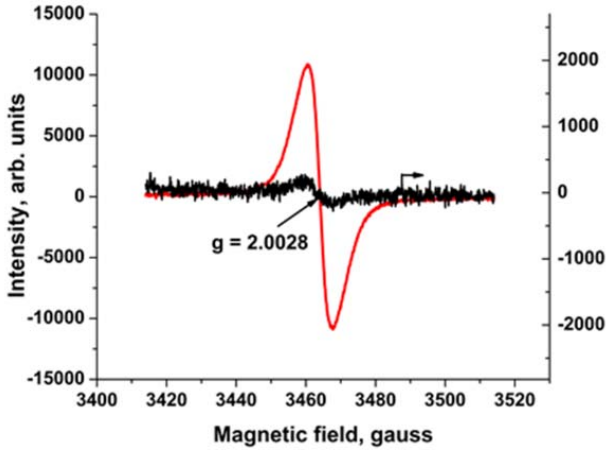
- **Aim 1.** ***Working hypothesis:*** AhR activation in the lung results in EPFR-induced cardiac dysfunction via increased pulmonary vascular resistance.
- **Aim 2.** ***Working hypothesis:*** Lung epithelial AhR activation culminates in vascular dysfunction.
- **Aim 3.** ***Working hypothesis:*** Small molecules (oxidized lipids) released from the lung into the systemic circulation induce cardiovascular dysfunction.

Interfacing with our Materials Core to Arrive at Environmentally-Relevant EPFRs and their Controls



Combustion system for generating EPFRs:

Collect particles in differing zones results in particles of high and low EPFR content!



EPR analysis:

EPFR Lo -**1.5×10^{16}** spins/g

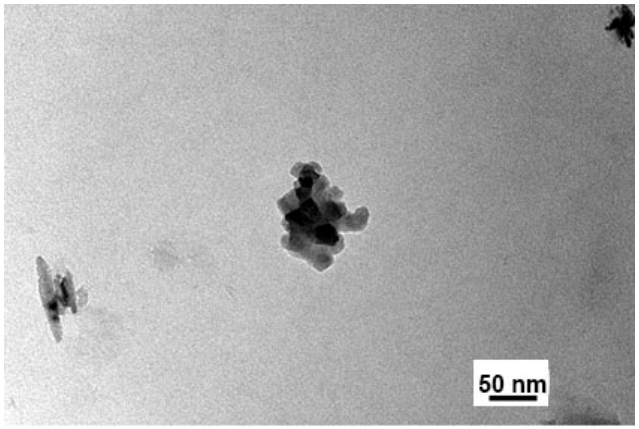
EPFR Hi -**1.0×10^{18}** spins/g

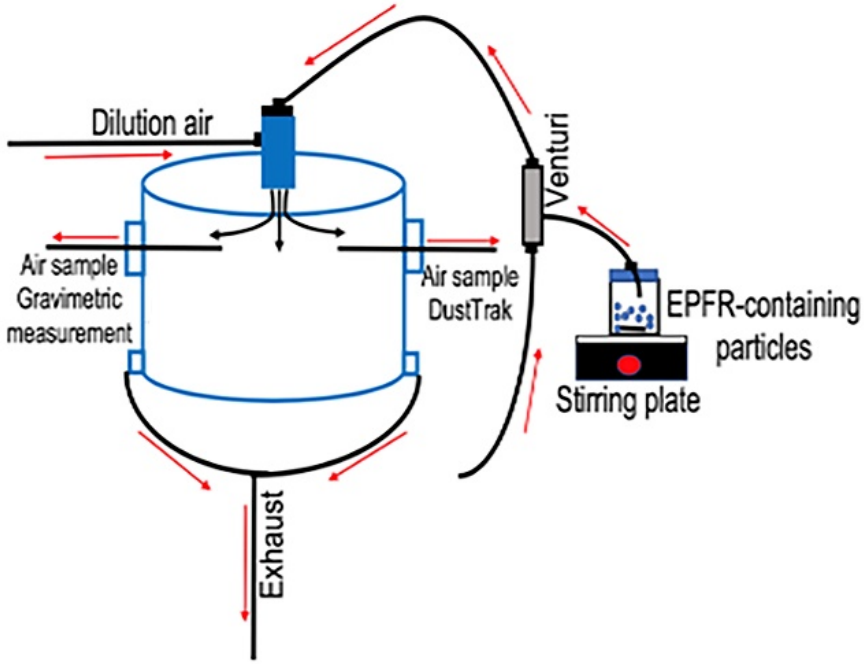
Khachatryan

Interfacing with our Inhalation Toxicology Core to Ensure Environmentally-Relevant Exposures

Provides the facilities, expertise and training to conduct *in vivo* and *in vitro* EPFR-aerosol inhalation studies, as well as lung function testing in mice.

SEM analysis revealed particles are 50-200 nm.

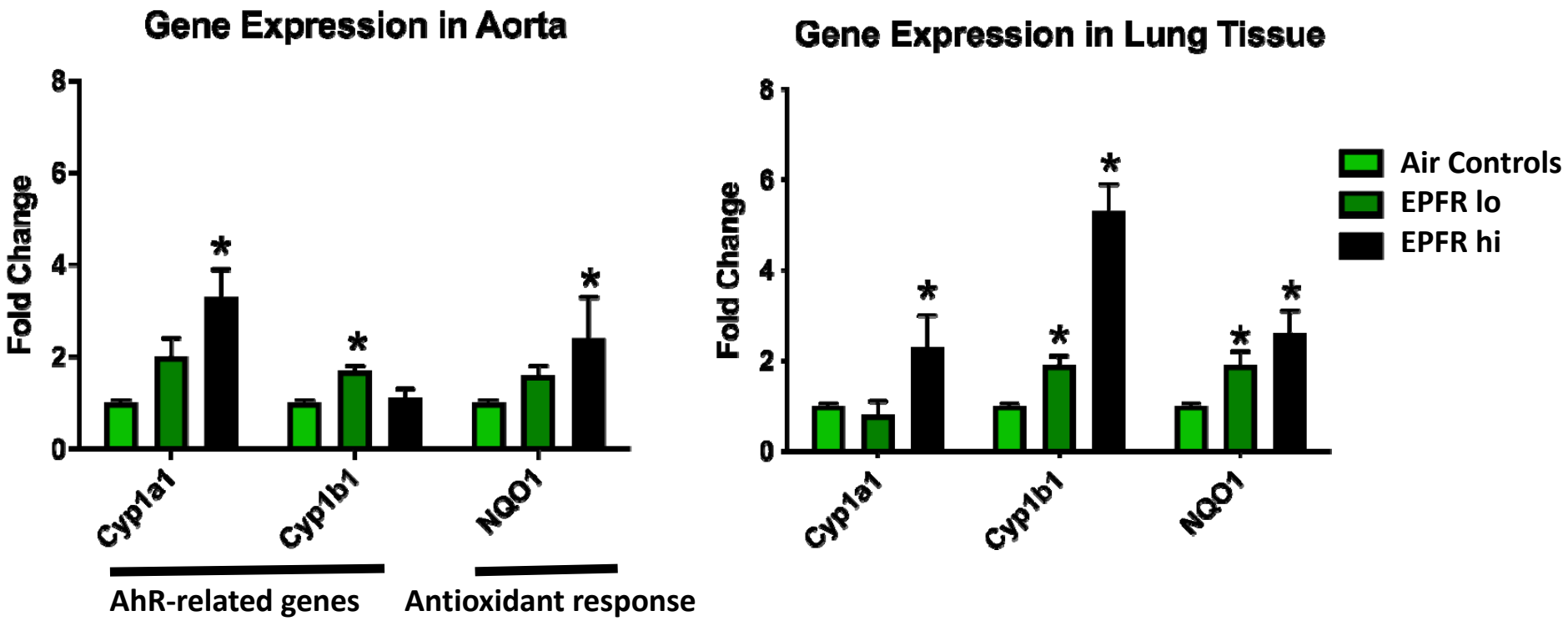




Mice exposed by whole-body inhalation in 18-L chamber

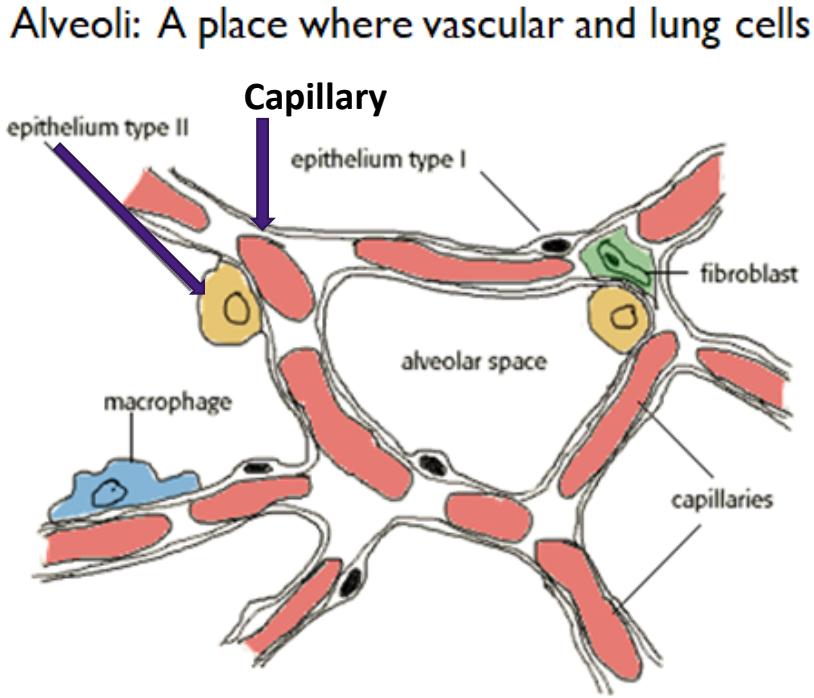
Noël

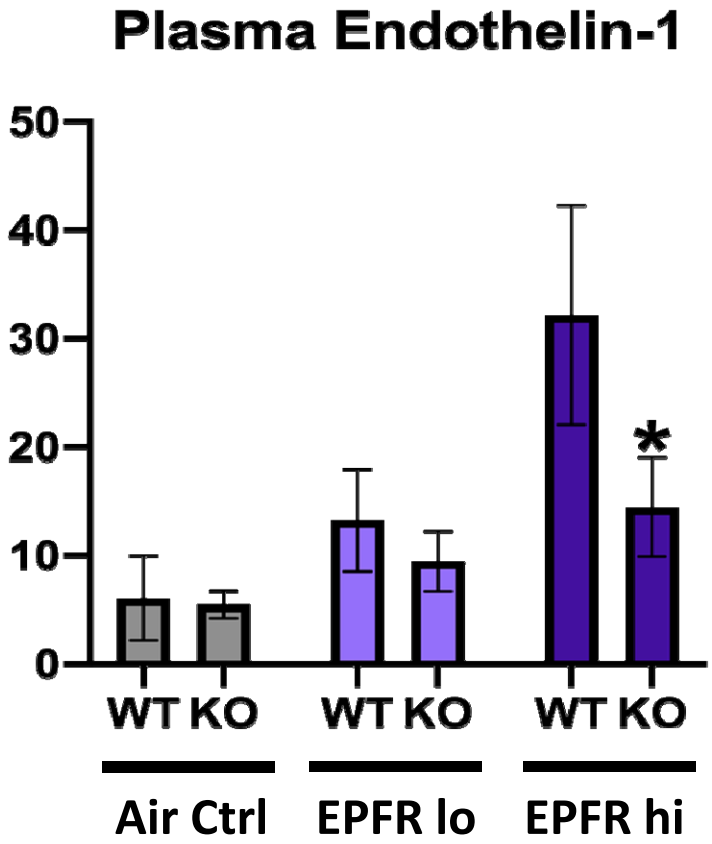
1 Day Exposure to EPFRs Dose-Dependently Elevates AhR and Oxidative Stress Related Genes



Dugas

1-3 Day EPFR Exposure Induces EPFR-Dependent Vascular Dysfunction that is Absent in Mice Deficient in Alveolar Epithelial AhR



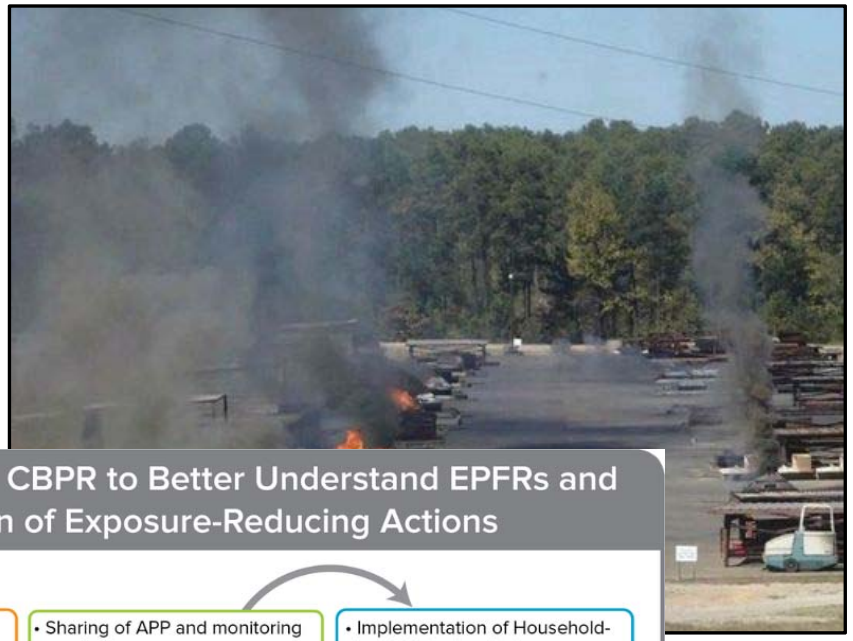


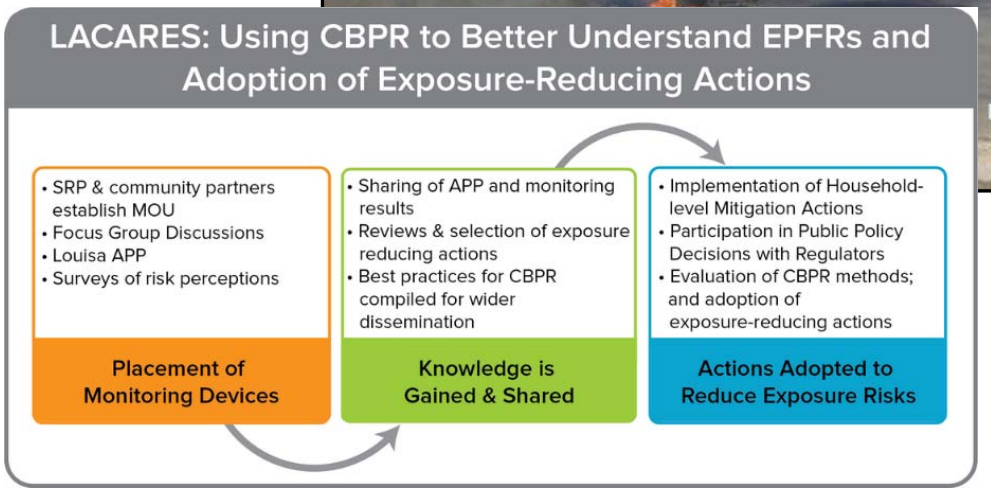
Forming Partnerships through our Community Engagement Core

LA Clean Air Research Engagement for Superfund (LaCARES)

- Goal – partner with communities to support collective & individual actions to reduce exposure
- Focus on Colfax, Louisiana, where the community sought our help to characterize air pollutants
- Community-engaged air pollutant monitoring program
- Translation of findings to residents

Reams





Project 3 – Community-Engaged EPFR Exposure Assessment

Hypothesis: EPFRs are produced in measurable quantities in PM during TT, so that outdoor and in-home exposure to EPFRs increases with decreasing downwind distance from the source

Aims:

1. Determine if partnering with the Colfax community on plans for assessing exposure to air pollutants from hazardous waste thermal treatment (TT) emissions will promote community empowerment and engagement

2. Characterize Colfax residents' exposures to environmentally persistent free radicals (EPFRs) in speciated PM by size distribution, influence of wind speed and direction downwind of the TT facility, and correlations with detonation-related noise

3. Characterize in-home concentrations of EPFRs and additional chemical and non-chemical stressors among Colfax study participants

Richmond-Bryant

Growing Partnerships through our Community Engagement Core

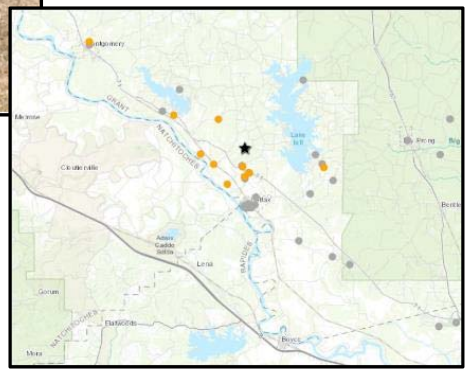
- Bi-weekly and quarterly meetings bring together the CEC with community partners in Colfax
- Meeting the community where they are to:
  - Introduce our work to Colfax residents
  - Establish connections between researchers and community members for data gathering
- Environmental health literacy activities
  - Support Superfund community's participation in site decisions
  - Update Louisiana Citizens' Guide to Environmental Engagement
  - Develop new course on Community-Engaged Research Methods in partnership with Southern University

The CEC's 1st External Advisory Board Meeting was held remotely on July 13, 2020.

Project 3 – Community-Engaged EPFR Exposure Assessment

- Public comments submitted to the LDEQ on July 27, 2018 were analyzed
- Oral history interviews
- Data extracted included:
  - Self-reported observations of smoke, noise, vibration, damage to homes
  - Self-reported health issues including thyroid, skin, respiratory, heart, and gastrointestinal problems
  - Names and addresses of those contributing comments

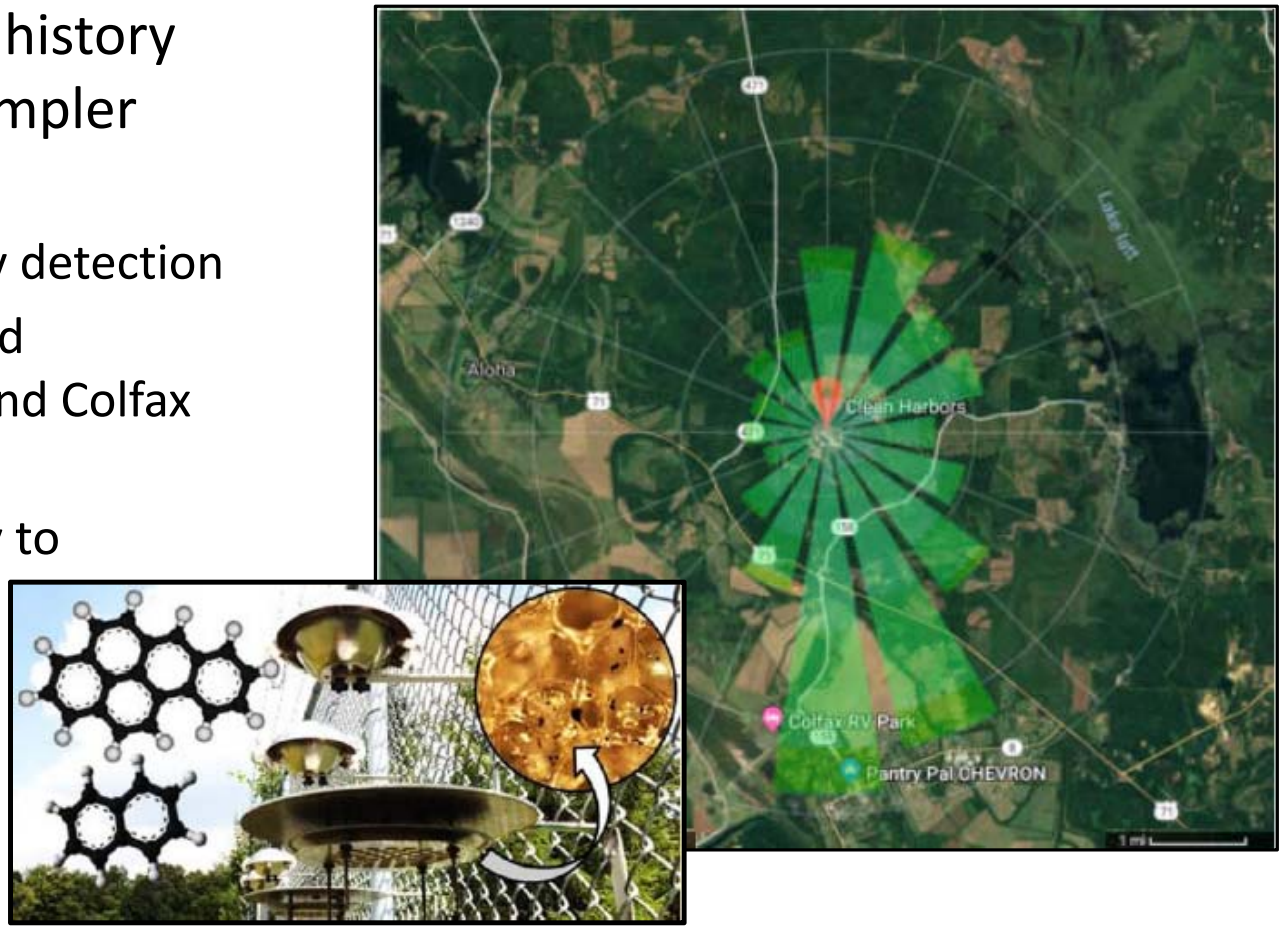
"…one thing that really struck me and it was just mind boggling is so many people with thyroid problems. Everybody has thyroid problems." – Rebecca Lonidier, resident of The Rock



"I've seen the smoke heard the bombings… but I also can see the smoke from down where I live (~10 mi from the facility)" – Grant Parish Police Juror Cephas Bowie and Colfax resident

Project 3 – Community-Engaged EPFR Exposure Assessment

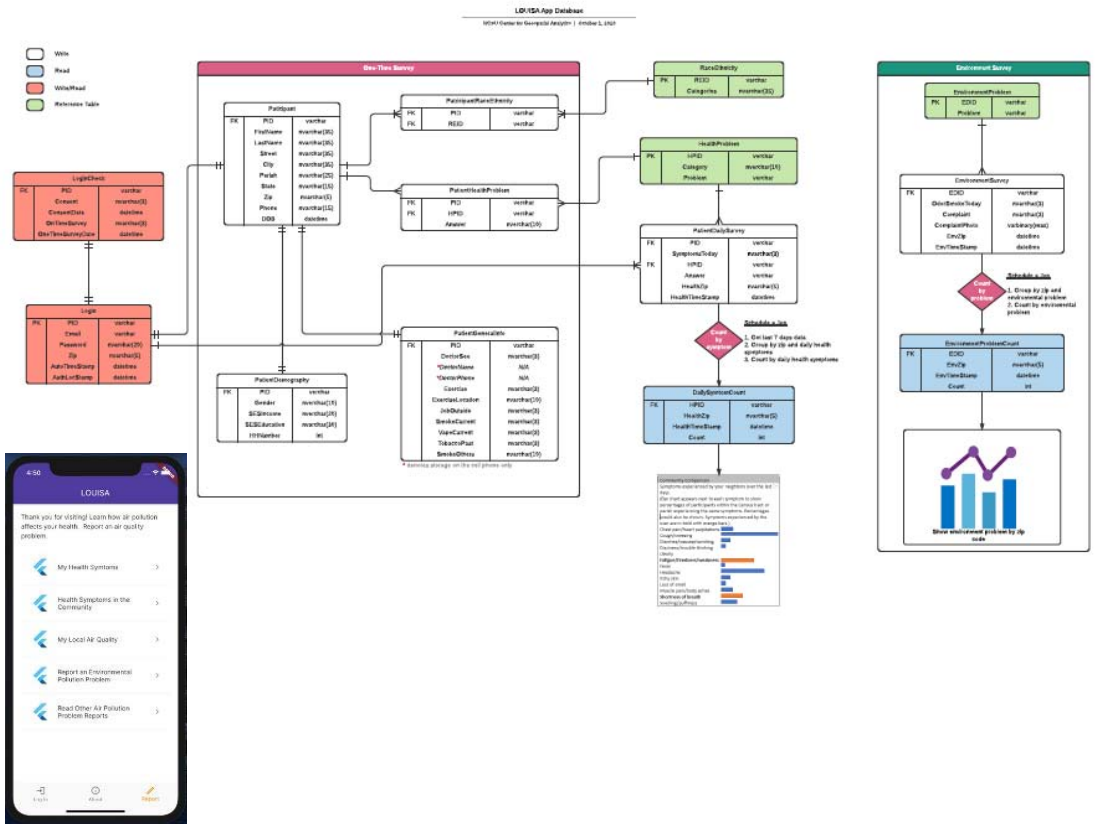
- Mapping comments and oral history interview findings informs sampler deployment
  - $PM_{2.5}$ monitors for high quality detection
  - Low-cost sensors corrected and distributed around The Rock and Colfax to report $PM_{2.5}$ to residents
  - Passive sampler in dense array to capture composition and size distribution



Eng et al. Environ Sci Technol Lett. 2014;1:77-81.

DMAC – Data Management and Storage

- Configuring a server with up to 100 TB of storage to support all Projects and Cores
- Building database through Globus Endpoint
- Set up Sharepoint site for secure data transfer
- Attended University of Louisville DMAC conference on big data
- Data being developed into a curated collection
- Back-end support for the CEC's mobile application in development

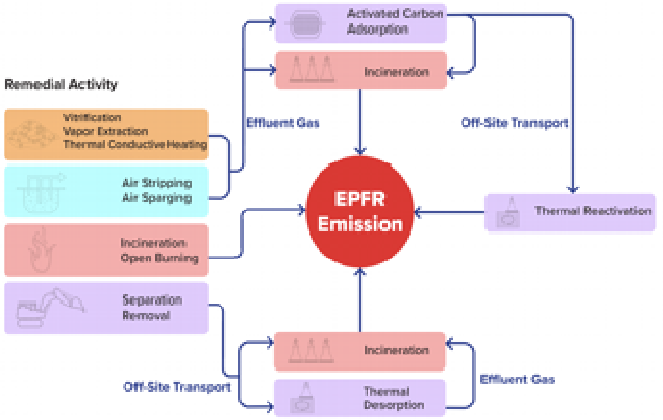


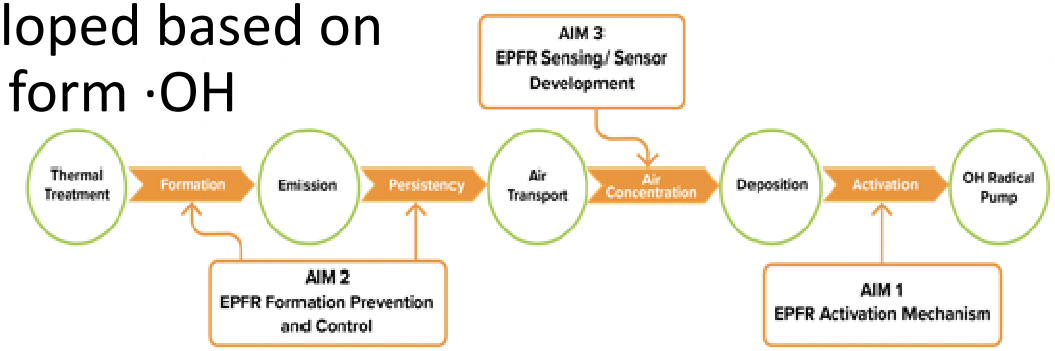
Mercante

Project 4 – Discovering New Methods to Deactivate EPFRs

Aims:

1. Hydrolysis and abstraction of a proton from EPFRs activates ·OH generation by the EPFR redox cycle (·OH pump)
2. EPFR formation during TT of Superfund site materials can be prevented by deactivation of metal centers and controlled by terminating EPFR redox cycling
3. Field EPFR sensors can be developed based on the EPFR oxidative potential to form ·OH



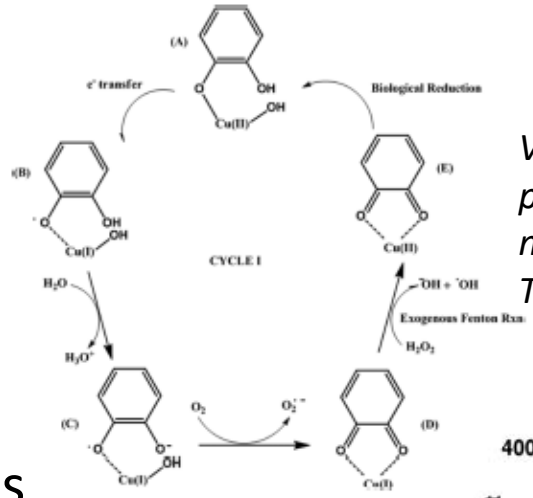


Lomnicki

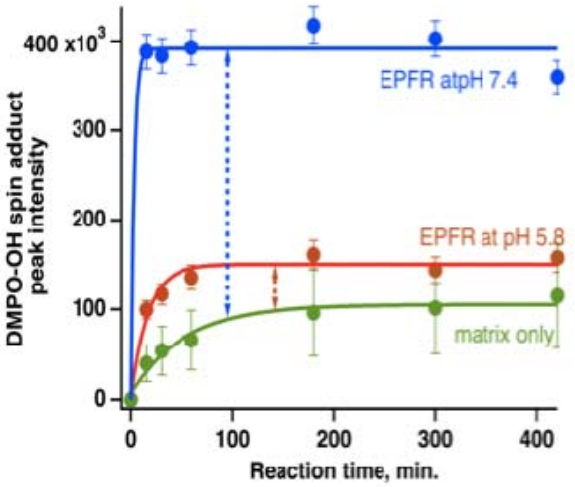
Project 4 – Discovering New Methods to Deactivate EPFRs

Aim 1

- Hydrolysis and abstraction of a proton from EPFRs activates ·OH generation by the EPFR redox cycle (·OH pump)
  - Previous research shows that removal of a proton from EPFRs is needed to start a reaction cycle
  - We are testing how reaction rates and EPFR intensity are affected by environmental conditions, such as acidity



Vejerano et al. Environmentally persistent free radicals: Insights on a new class of pollutants. Environ. Sci. Technol. 2018;52:2468-2481.



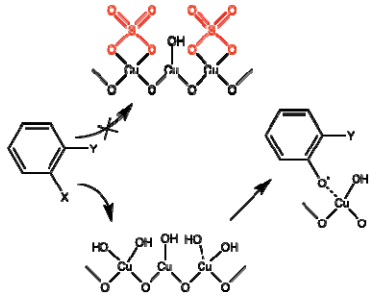
Project 4 – Discovering New Methods to Deactivate EPFRs

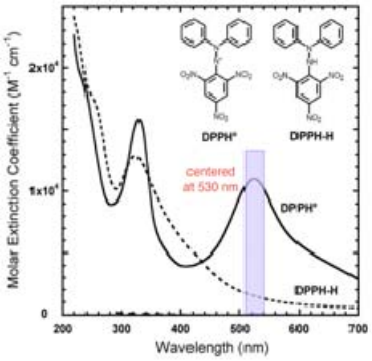
Aim 2

- Testing the ability of compounds to suppress EPFR formation
- Introduction of compounds can be done at the EPFR creation stage or in the cool zone of thermal treatment

Aim 3

- Visual sensing based on reactions of EPFR-generated •OH with litmus-like probe based on color

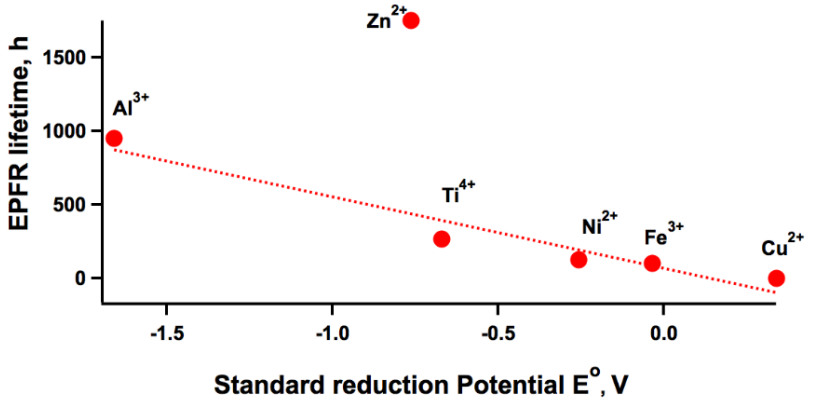




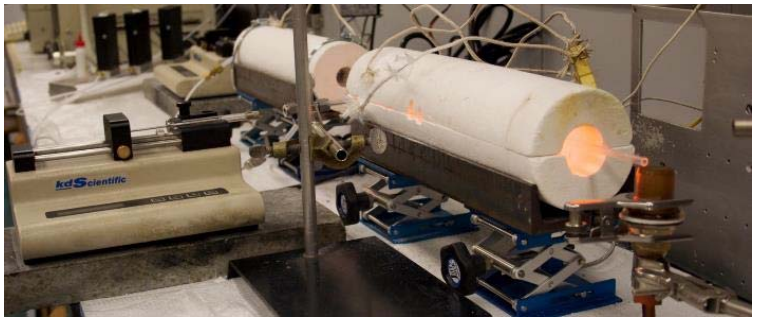
A semi-quantitative phone-app EPFR sensor **for communities** will compare a paper strip sensor's color change to predefined colors

Supporting Our Exploratory Laboratory Work through Our Materials Core

- Generating real combustion particles for lab testing
  - Control over composition
  - Using different metals and precursors
  - Environmentally-relevant
- Analysis of field and laboratory samples
- Developing field detection devices



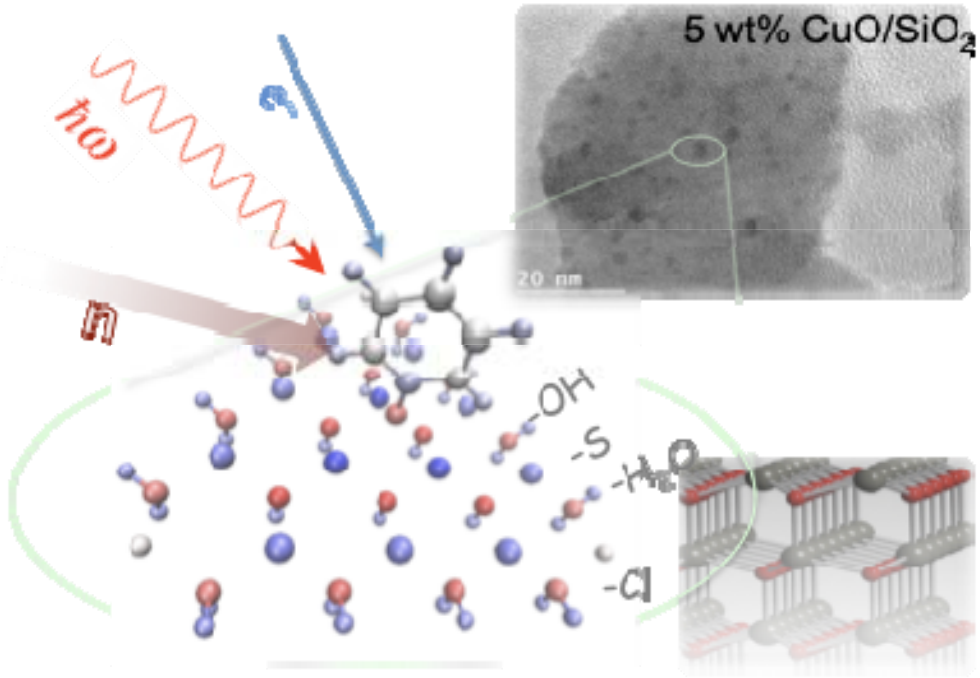
Metals affect EPFR lifetime and yield



Khachatryan

Project 5 – Microstructural Pathway of EPFR Formation and Decay Mechanisms

- Understand EPFR's molecular structure
- Study processes responsible for EPFR formation and decay
- Design effective approaches for limiting EPFR production
- Develop neutralization schemes once EPFRs are formed
  - **Reducing their dangerous health effects!**



Sprunger

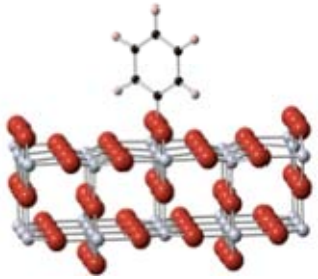
Project 5 – Microstructural Pathway of EPFR Formation and Decay Mechanisms

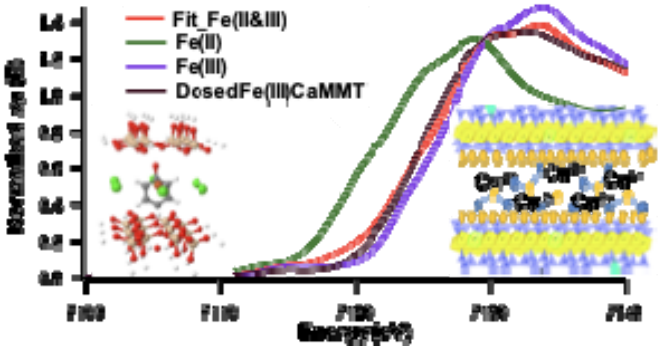
Aims:

1. Develop a fundamental understanding of electron transfer within organic molecule–inorganic redox center mechanisms that result in EPFR formation

2. Determine EPFR degradation pathways

3. Determine EPFR formation and *destabilization* similarities and differences

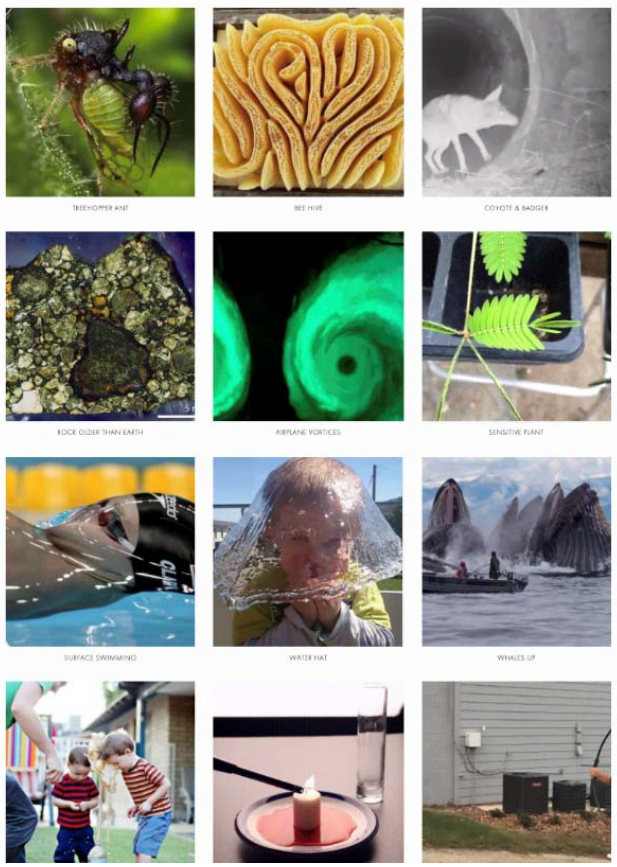




Training Leaders with our RETCC

- Training in research practices (10 hours)
  - Responsible conduct of research
  - Intellectual property
  - Rigor and reproducibility in data collection and analysis
  - Environmental communication and EJ
- Lead discussions in a journal club (10 hours)
- Annotation project
  - Trainees annotated a peer-reviewed paper to make it understandable at a 9th-grade level
  - Will be submitted to an electronic database used by LA science teachers

Dugas



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