The Duke University Superfund Research Center

Developmental Co-Exposures:
Mechanisms, Outcomes, and Remediation

Director: Heather M. Stapleton, PhD
Deputy Director: Richard DiGiulio, PhD

Duke SUPERFUND Research Center

Early Life Exposures | Later Life Consequences

Center Focus

Our Research: Early Life Exposures & Later Life Consequences

Engaging North Carolinians to Prevent or Mitigate Exposure and Lead Healthier Lives

Project 1: Characterizes prenatal exposure to PAHs, Pb and Cd, identifies Pb sources, and examines associations with neurodevelopment in childhood

Project 2: Uses the rat and zebrafish models to investigate neurodevelopmental and behavioral impacts of PAH and metal co-exposures

Project 3: Investigates impacts of PAH and metal co-exposures on mitochondrial neurotoxicity and cell fate & programming

Project 4: Examines the role of early life reprogramming in resistance to contaminant mixtures from Superfund sites and assess later life consequences

Project 5: Precision bioremediation to degrade PAHs while simultaneously minimizing the mobilization of metals

Overarching Themes

- Human Co-Exposure Assessment
- Mechanisms of Toxicity & Neurodevelopment
- Human & Ecological Impacts
- Risk Reduction & Treatments

PROJECT 1. Prenatal Exposures to PAHs and Metals in an Impacted Community: Assessing Neurodevelopmental Impacts and Tracing Metal Sources

NEW!

PI: Heather Stapleton

Co-I: Kate Hoffman

Co-I: Heileen Hsu-Kim

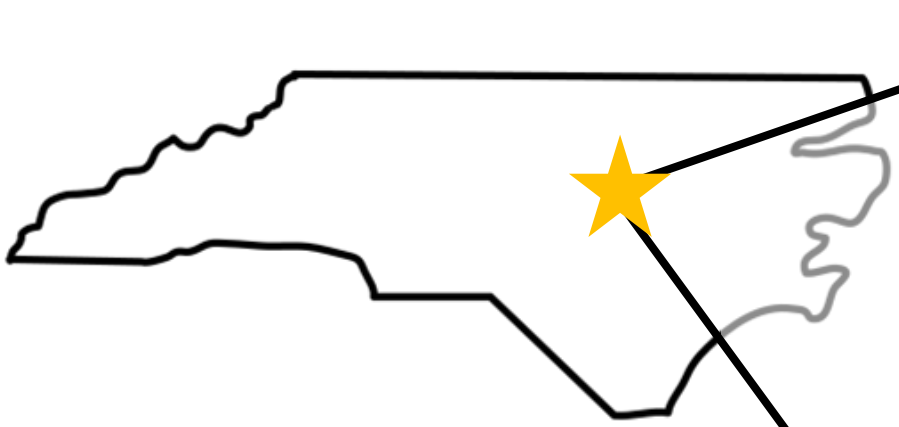
Co-I: Avner Vengosh

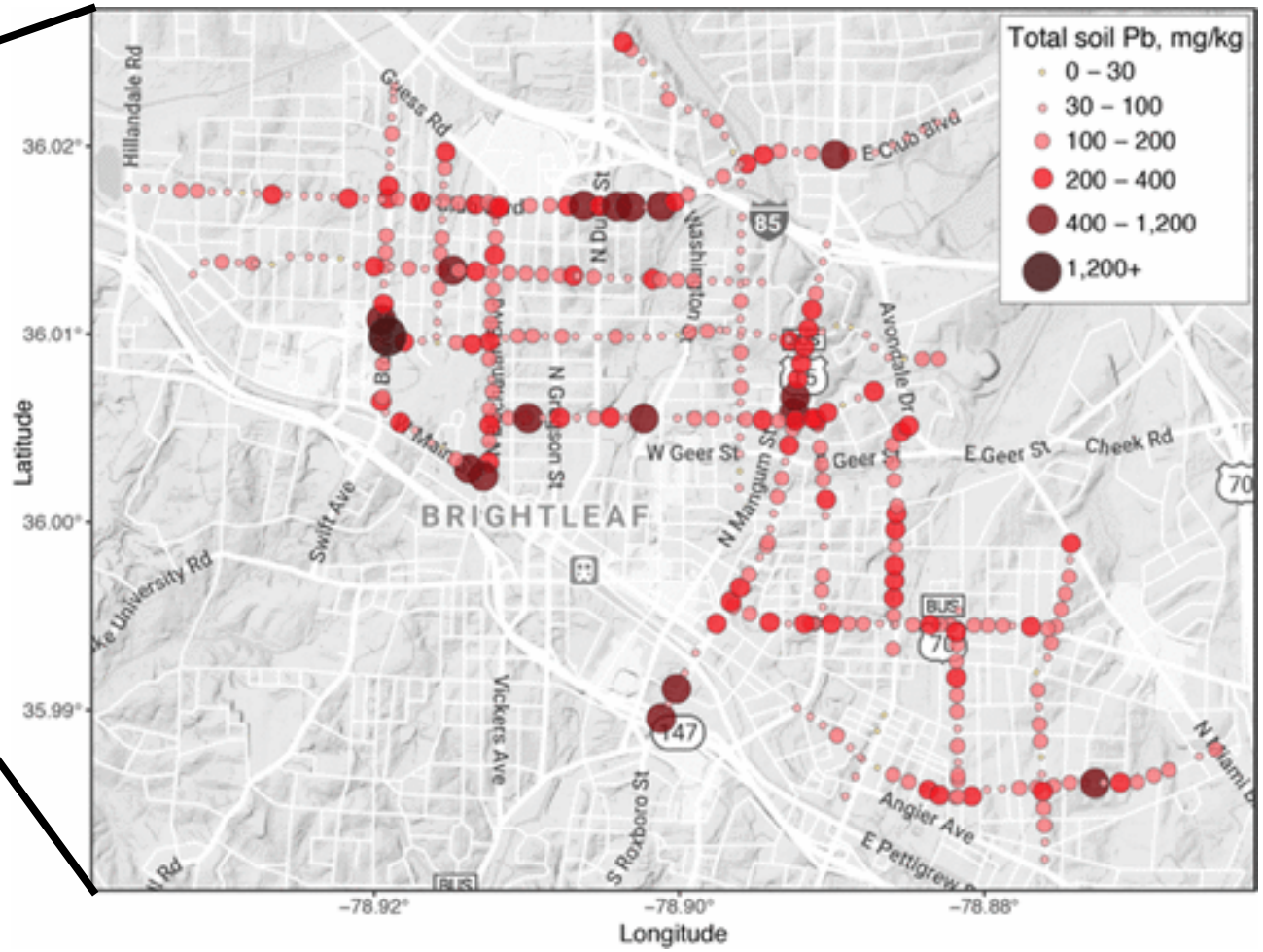
Duke SUPERFUND Research Center

Early Life Exposures | Later Life Consequences

Kate Hoffman, PhD
Assistant Professor
Nicholas School of the Environment
Duke University, NC.

Lead Research Conducted in Durham, NC





Source: Wade et al., 2021

Assess prenatal co-exposures to PAHs and metals	Evaluate relationship between prenatal exposures and neurodevelopment	Assess sources and bioaccessability of lead in the home environment

HOPE 1000 Pregnancy Cohort

Prenatal exposures

Blood samples →

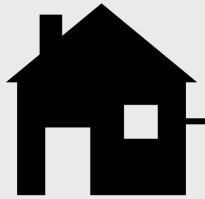
Silicone wristbands →

Metals

PAHs & other organics

Neurodevelopmental assessments

Home visits for study participants

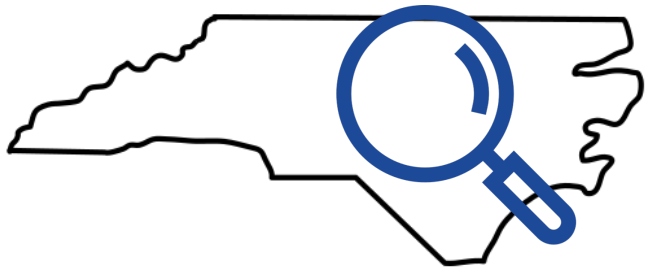


House dust, tap water and soil

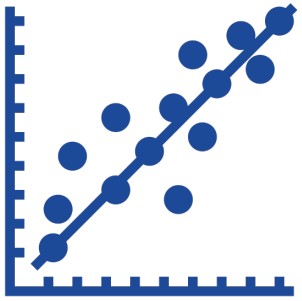
Metals

PAHs & other organics

Geospatial analysis of exposure patterns in Durham, NC

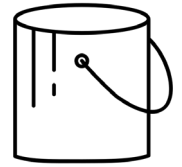


Statistical analysis of associations between prenatal exposures and neurodevelopment



Isotopic analysis of relative sources of lead in home environment

leaded gasoline



lead paint

Our Study Population: Project HOPE 1000

Children's Health & Discovery Initiative
At Duke University

*A Longitudinal Study of 1000 Mothers and Infants to Understand **H**ealth **O**utcomes Related to **P**regnancy and Early Life **E**xposures*

The first 1000 days establishes:

- Health trajectory
- Growth trajectory
- Neurodevelopment

Long-term records follow-up

- Electronic Health Records
- Vital statistics
- Educational data
- Medicaid
- Social Services

Collect biospecimens

- Maternal samples:
  - Each trimester
  - Delivery
  - Post-partum
- Infant samples:
  - Delivery
  - 2-, 4- or 6-mo.
  - 12-mo. and 24-mo

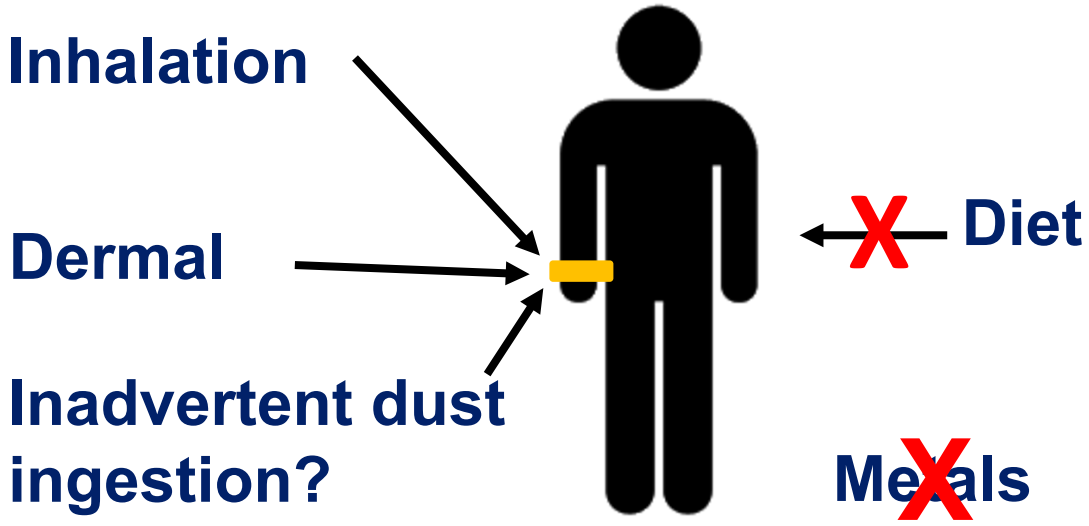
Capture environmental exposures

- One week each trimester

Why Use Silicone Wristbands?

- Wearable samplers
- Integrate average exposure over time
- Overcomes some limitations of urine and blood sampling
- Levels measured on wristbands are positively correlated with levels in blood and urine for many SVOCs

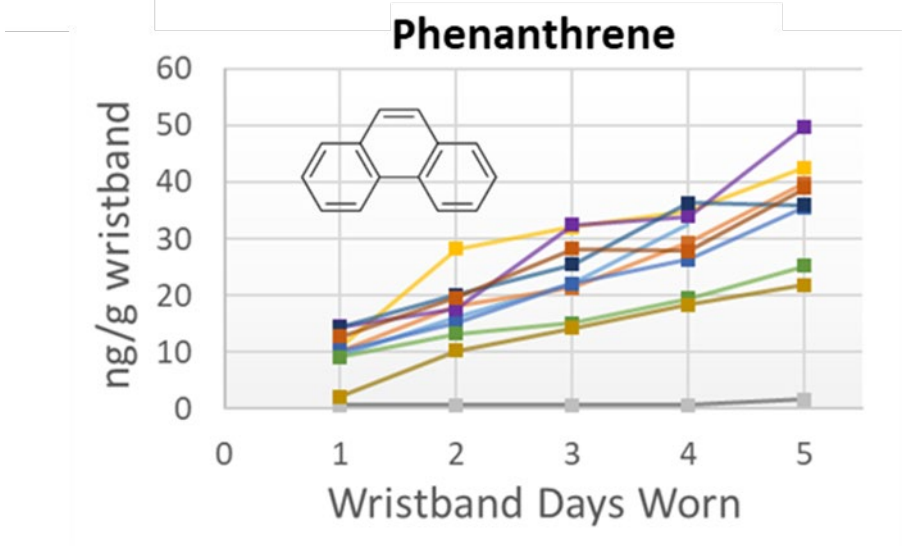
Exposure Routes

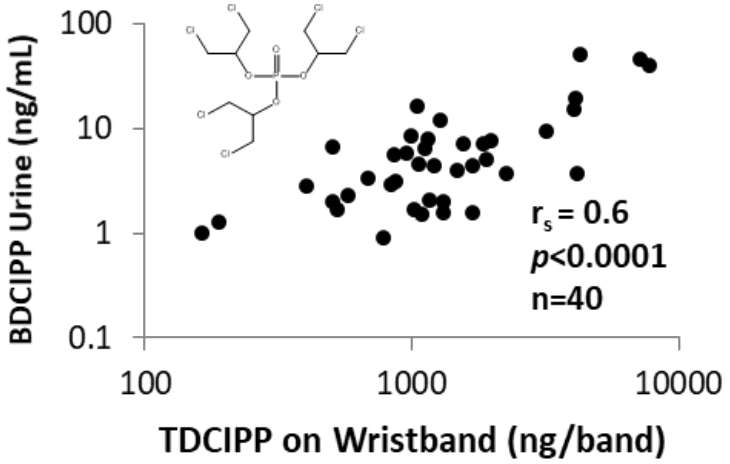


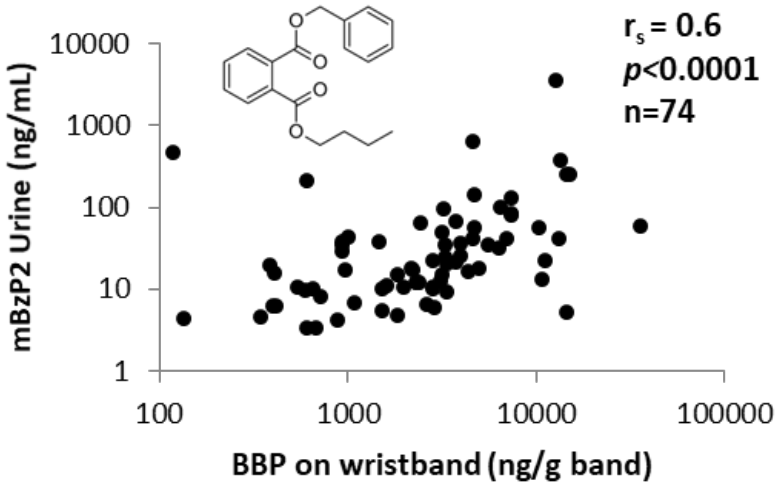
Hammel et al. 2016; 2018; Levasseur et al. 2021; Wise et al. 2021

Measuring Exposure Using Silicone Wristbands

Chemical Class	# of chemicals in class	Detection Frequency (%)
PAHs	21	97
BFRs	29	98
PCBs	10	76
Pesticides	9	98
Phthalates	10	100
OPEs	22	100
PFAS*	36	55
Phenols	8	100





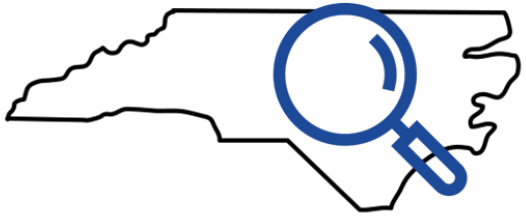


Evaluating Early Indicators of Neurodevelopment

- The Owlet Smart Sock records oxygen saturation, infant's heart rate and movement at a 2-second resolution.

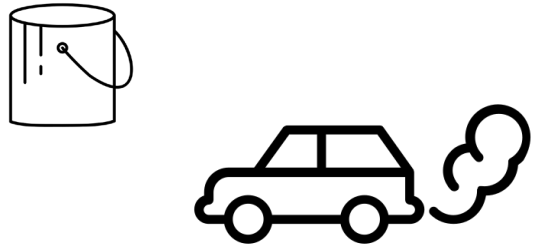
- Disordered sleep is associated with hyperactivity, impaired attention, cognitive function, and behavior problems.

Project 1: Overarching Goals and Highlights



Geospatial analysis of exposure patterns in Durham, NC using silicone wristbands and blood samples to identify impacted communities

Statistical analysis of associations between prenatal exposures and neurodevelopment using novel approaches



Unique approach with isotopic analysis to trace the relative sources of lead and cadmium in Durham, NC

Project 4: Ecological impacts, adaptation, & fitness costs

PI: Nishad Jayasundara

Co-I: Richard Di Giulio

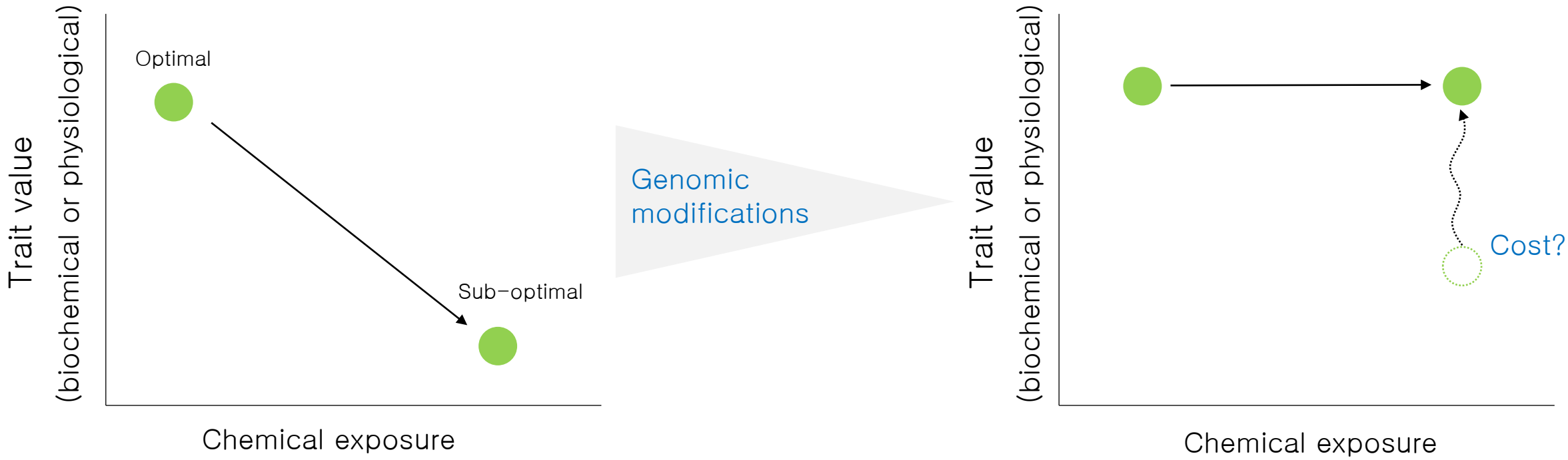
Nishad Jayasundara, PhD
Assistant Professor
Nicholas School of the Environment
Duke University, NC.

Duke SUPERFUND Research Center

Early Life Exposures | Later Life Consequences

Overall premise

- To uncover mechanisms of evolved resistance to chemical pollutants and determine costs

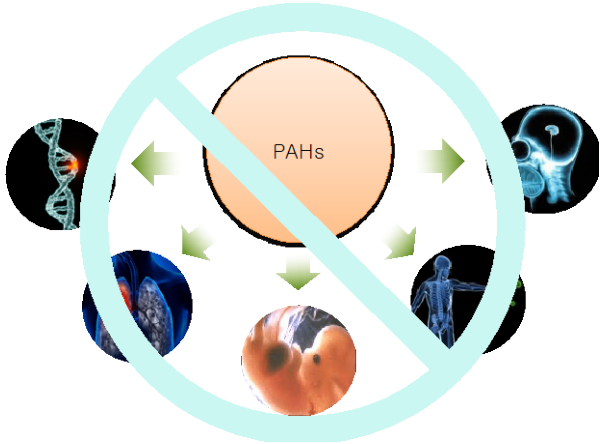


Goals:

- To understand processes driving evolution
- To inform adverse health (human and animal) outcomes of chronic chemical exposure and
- To determine ecological consequences (risks) of long-term pollution exposure

PAH resistant killifish in the Elizabeth River

A population of killifish in the Elizabeth River are resistant to polycyclic aromatic hydrocarbon toxicity



http://www2.dnr.cornell.edu/cek7/nyfish/Cyprinodontidae/mummichog.html

Resisting PAH toxicity since early-mid 1900s

Elizabeth River fish are resistant to cardiotoxicity of PAHs

Fish embryos from the clean reference site

Unexposed

Exposed

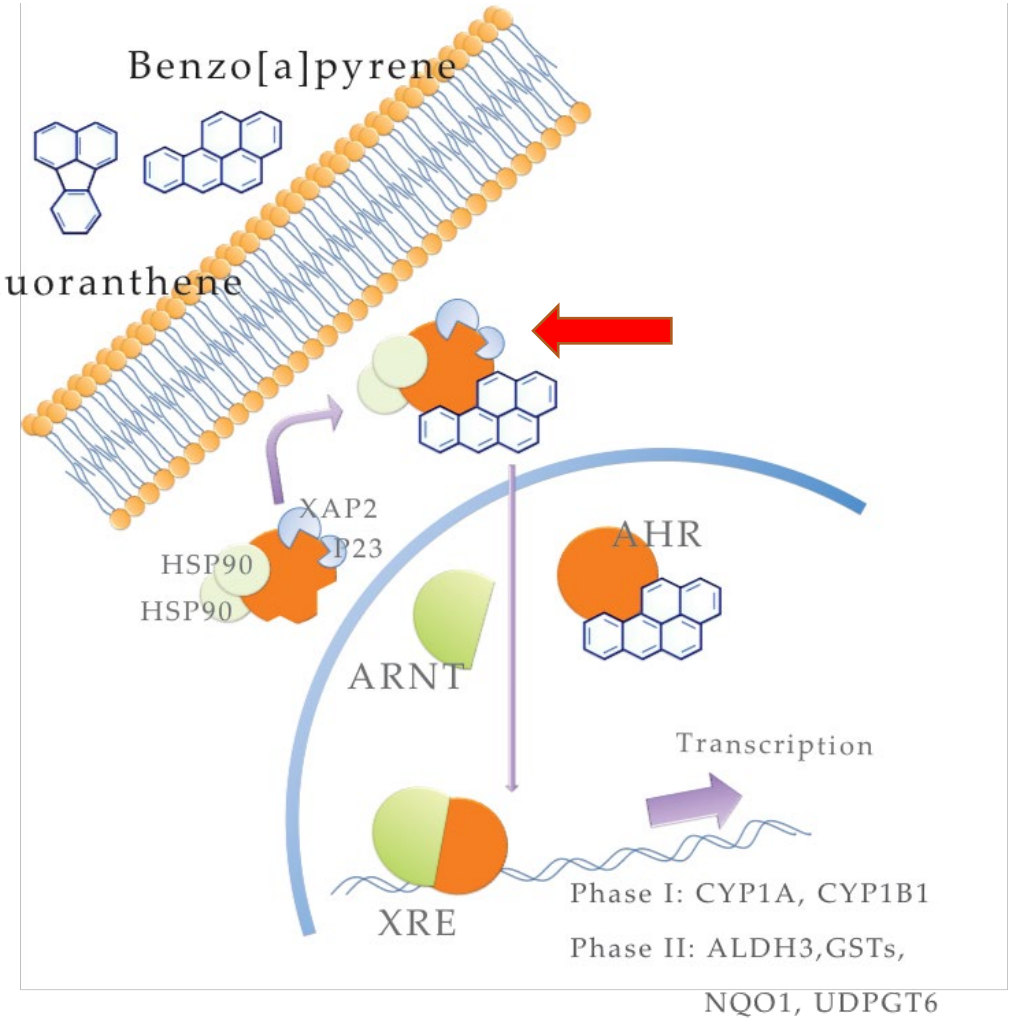
Resistant embryos
from a highly contaminated site
(120,000 ng/g)

Unexposed

Exposed

3% of the sediment extract

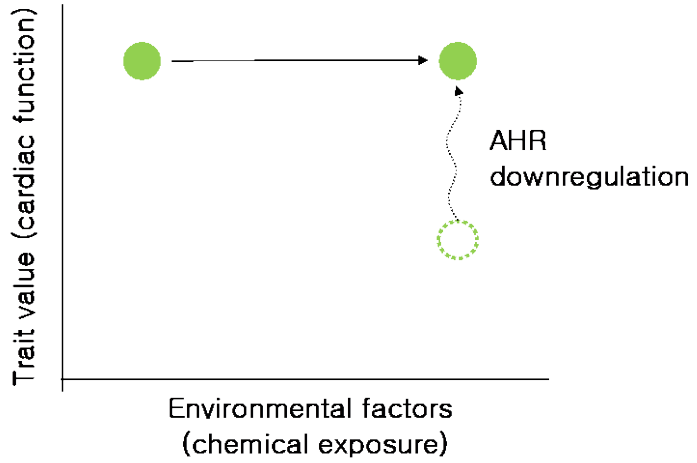
Mechanisms of resistance? – altered aryl hydrocarbon receptor



Reduced AHR activity in fish from the Elizabeth river
(Clark et al 2013)

A chimeric form of AHR in the killifish genome
(*Reid et al 2016, and Osterberg et al, 2018*)

Down regulation of AHR rescues cardiotoxicity
(*Jayasundara et al 2015*)



Our focus for 2022–2027

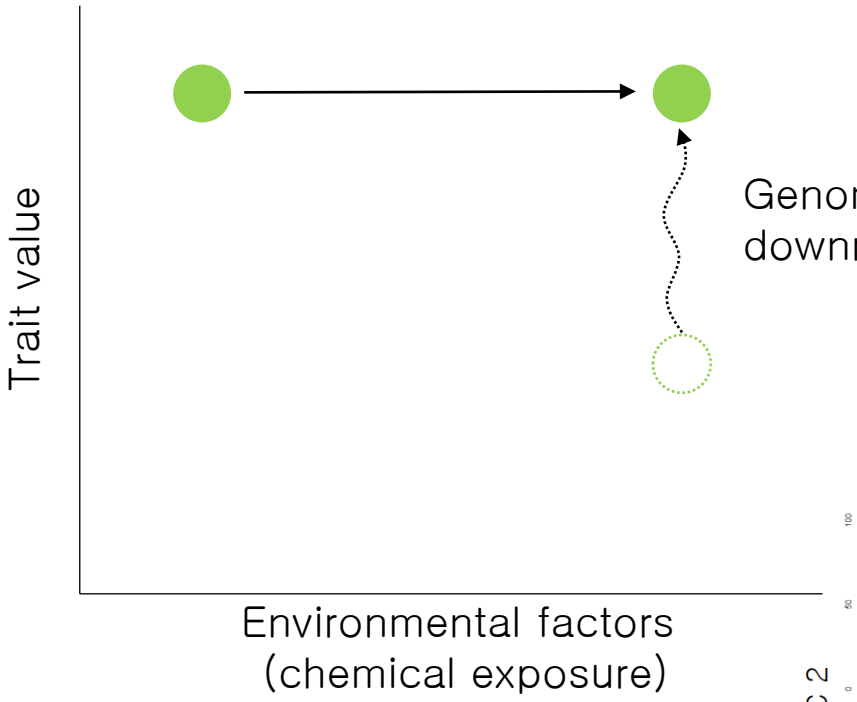
Neurobehavioral and bioenergetic consequences of evolving resistance to polycyclic aromatic hydrocarbons

- in fish collected from PAH contaminated, PAH + metal contaminated, and clean sites.

- in a multi-stressor environment (Pb, Cd, temperature, hypoxia)

- And the role of non-genomic processes in PAH resistance

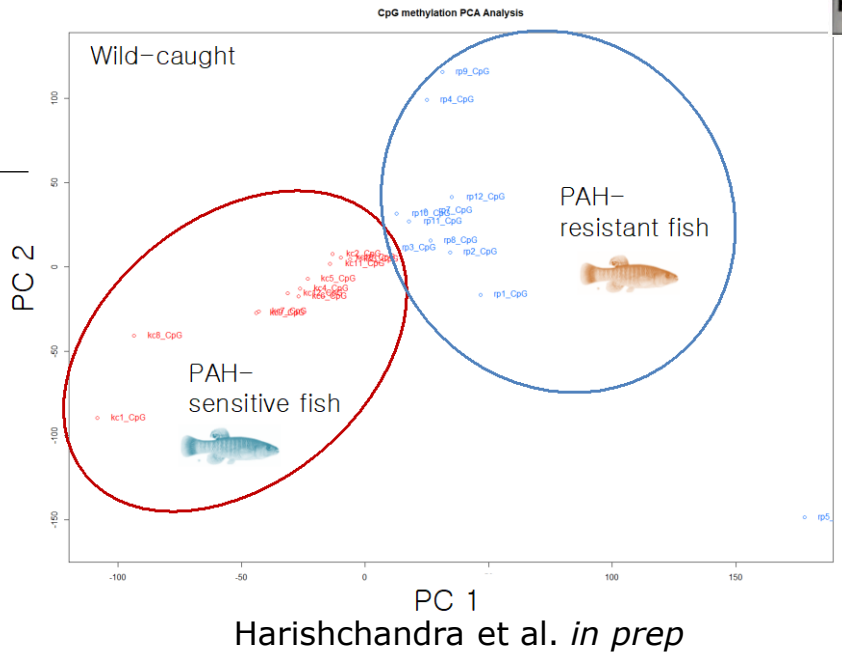
A complex biology underlying rapid adaptation associated with cascading effects/costs !



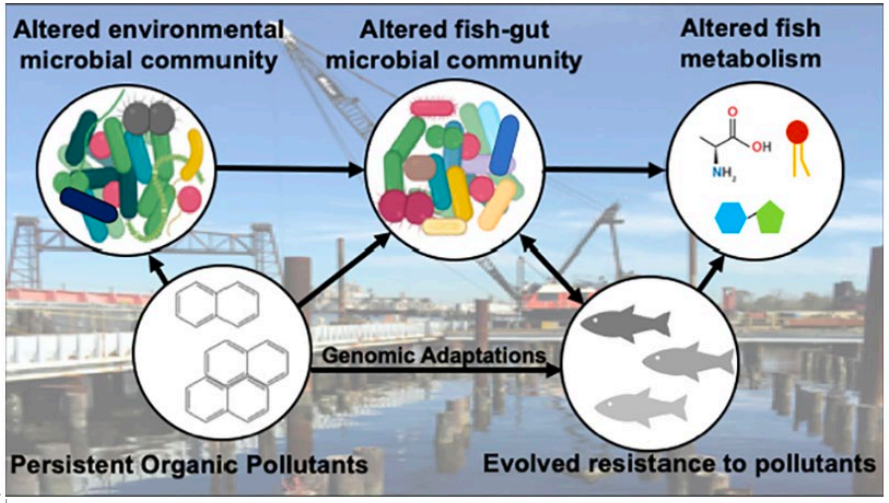
Genomic (AHR downregulation)

Microbiome

Epigenetics



Harishchandra et al. *in prep*



Redfern et al. 2021

Emily Green (ITEHP PhD student)

Dr. Prabha Ranasinghe

Creating germ free fish to conduct Killifish gut microbiome transplant studies

Ecological effect directed analysis for community engagement and risk assessment

- Determining mitochondrial and larval behavioral outcomes of exposure to chemical mixtures

Environmental samples (Elizabeth River, Ellerbe Creek, Navassa, samples from other superfund centers, dust sample extracts?)

Database of Toxicity outcomes and chemical composition

Multivariate mixed models determining/predicting mixture toxicity (e.g., Babich et al, 2021 Sci Reports)

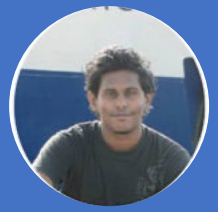
Data teaching tool for community engagement on river/water pollution (e.g., Maine middle school water health project)

Thermal tolerance studies

Dr. Lindsay Jaspers

- Differential resistance to PAHs is associated with distinct metabolic thermal phenotypes

Transcriptome, & Methylation studies



Akila Harishchandra (PhD candidate – UMaine)

- Distinct global methylation patterns in PAH resistant fish compared to clean site fish

Metal levels and toxicity responses in ER killifish

Samantha Murphy (ITEHP)

- Pescara fish in the ER are exposed to high levels of Pb and accumulate them

Microbiome research

Dr. Prabha Ranasinghe
Emily Green (ITEHP)

- BaP toxicity (neuro and mitochondrial) is dependent on the gut microbiome in zebrafish and PAH-adapted killifish

Melissa Chernick, MS

- Environmental monitoring with fish embryos and ecological effect directed analysis

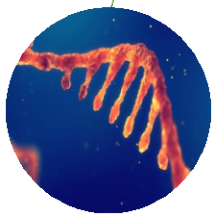
Prof Rich Di Giulio

- Co-PI
- Assistant Director of the Duke Superfund Center.

Project 5

Gut microbiome

Genome

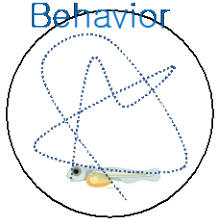


Methylation

Project 3

Project 3/ACC

Bioenergetics & Behavior



Project 2/ACC

Final Outcomes

Project 1,2,3 - phylogenetic comparisons

Ecological effect directed analyses (community engagement)

Center collaborations

DMAC and RTC

Thank you

Duke UNIVERSITY | SUPERFUND Research Center

early life exposures, later life consequences

NIH National Institute of Environmental Health Sciences

Superfund Research Program

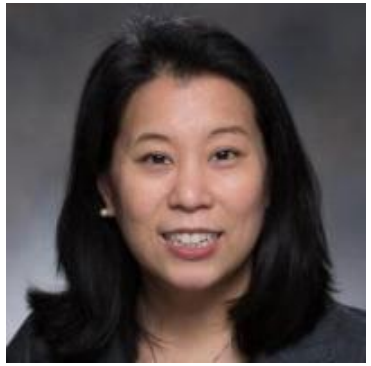
National Institutes of Environmental Health Awards – Duke Superfund Research Center Project 4
P42-ES010356
2022-2027

Project 5: Microencapsulation Delivery Vehicles for the Implementation of Precision Bioremediation at PAH-Contaminated Superfund Sites

PI: Claudia Gunsch

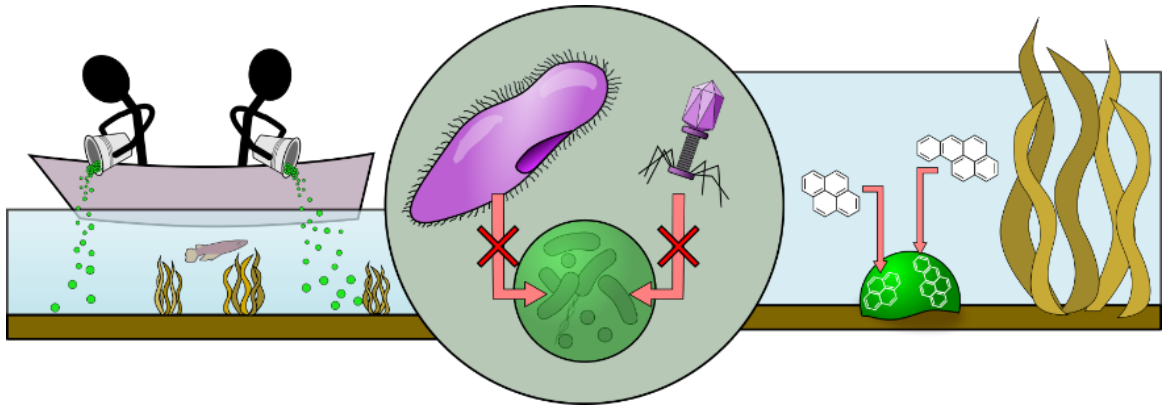
Co-I: Heileen (Helen) Hsu-Kim,

Co-I: Mark Wiesner

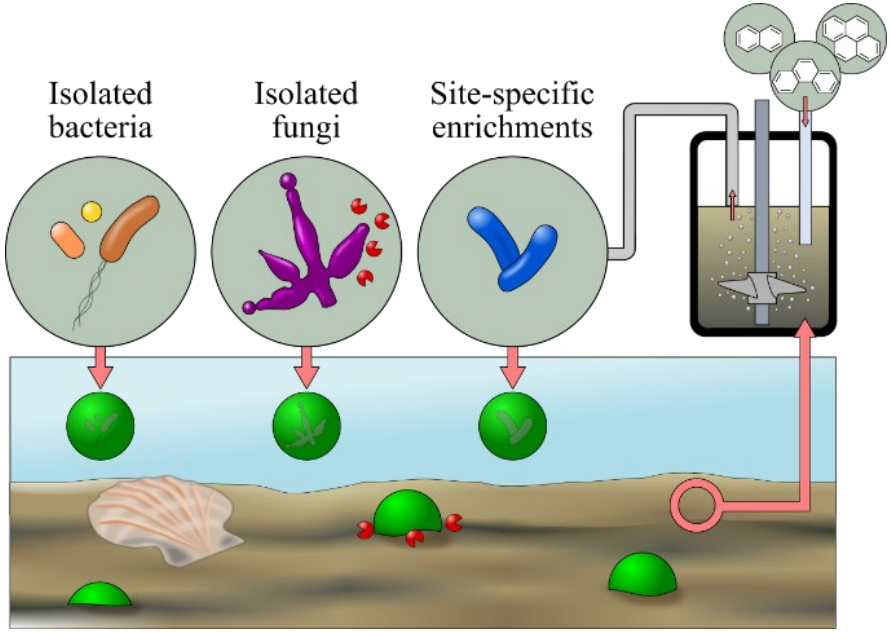


Heileen Hsu-Kim, PhD
Professor
Pratt School of Engineering
Duke University, NC.

Overarching goal: To develop microbial encapsulation delivery vehicles to implement precision bioremediation of contaminated soil and sediment

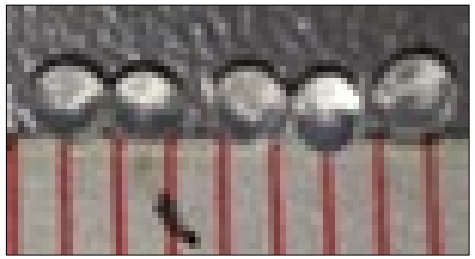


- Target delivery of key microbial strains to sites of concern
- Increase fitness of these strains
- Enhance contaminant bioaccessibility with these strains
- Understanding impacts of co-contaminants



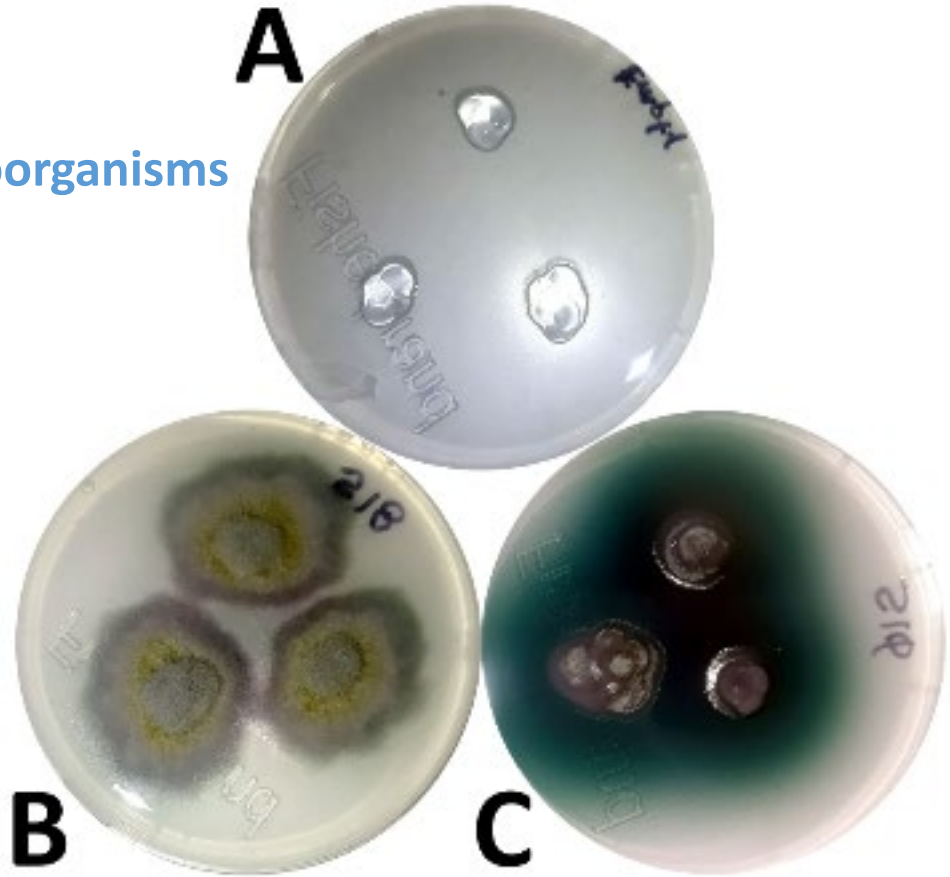
Extracellular laccase production by alginate microcapsules with:

alginate microcapsules



1mm

No microorganisms

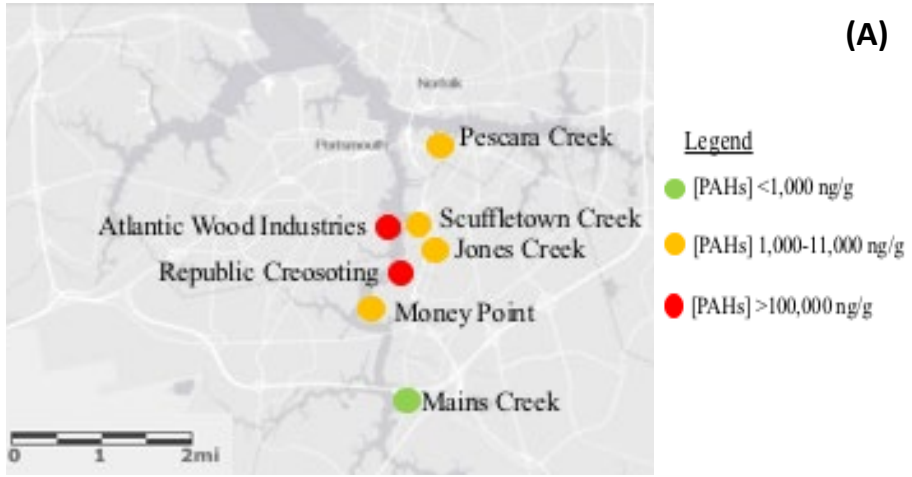


filamentous fungal isolate *Septoriella* sp. str. S18

fungi *Cladosporium* sp. str. S10

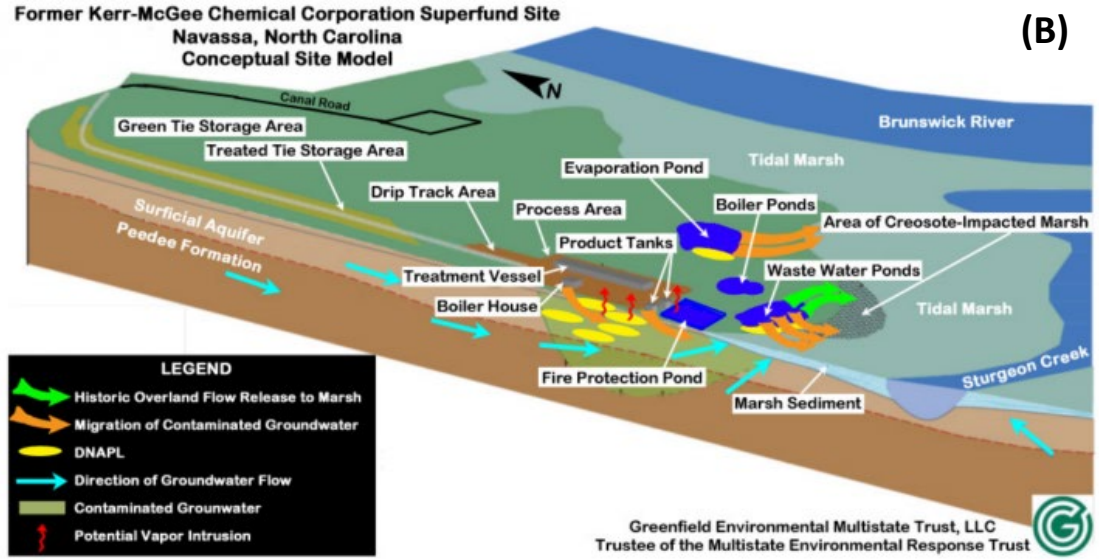
Co-contaminants at creosote-impacted sites

Elizabeth River Estuary



Republic & Pescara:
Pb, Zn, Cu = 50 – 400 μg g^{-1}

Kerr-McGee Superfund Site

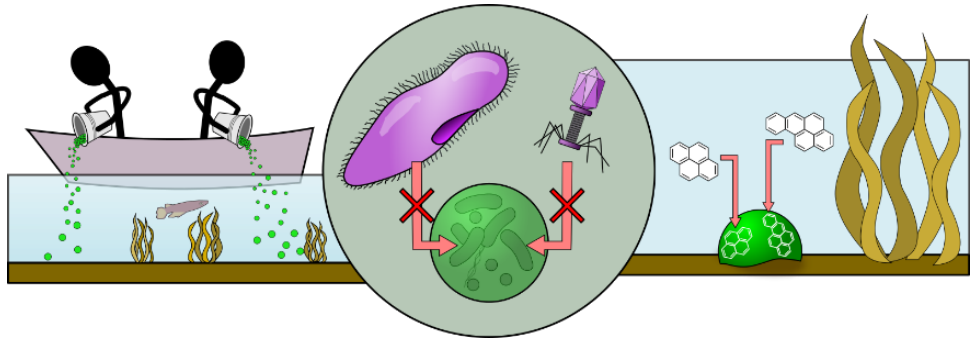


Marsh sediments:
[PAHs] = 1-10^4 μg g^{-1}
[Hg] = 0.1-0.5 μg g^{-1}

Project 5
Microbial encapsulation delivery vehicles for precision bioremediation

Specific Aims:

1. Optimize microcapsule synthesis for delivery and application for bioaugmentation
2. Develop site-specific encapsulated microbial consortia of PAH degraders and compare to pure cultures for PAH degradation
3. Investigate unintended impacts of encapsulated bioaugmentation



Duke SUPERFUND Research Center

Early Life Exposures | Later Life Consequences

Project 1: Characterizes prenatal exposure to PAHs, Pb and Cd, identifies Pb sources, and examines associations with neurodevelopment in childhood

Project 2: Uses the rat and zebrafish models to investigate neurodevelopmental and behavioral impacts of PAH and metal co-exposures

Project 3: Investigates impacts of PAH and metal co-exposures on mitochondrial neurotoxicity and cell fate & programming

Project 4: Examines the role of early life reprogramming in resistance to contaminant mixtures from Superfund sites and assess later life consequences

Project 5: Precision bioremediation to degrade PAHs while simultaneously minimizing the mobilization of metals

Overarching Themes

- Human Co-Exposure Assessment
- Mechanisms of Toxicity & Neurodevelopment
- Human & Ecological Impacts
- Risk Reduction & Treatments