Duke UNIVERSITY | SUPERFUND Research Center

early life exposures, later life consequences

NIH National Institute of Environmental Health Sciences

Superfund Research Program

NIH National Institute of Environmental Health Sciences
Superfund Research Program

Duke UNIVERSITY | SUPERFUND Research Center

early life exposures, later life consequences

Four Funding Cycles

2000 – 2005: Superfund Chemicals Impact on Reproduction and Development

2005 – 2009: Superfund Chemicals Impact on Development

2011 – 2017: Developmental Toxicants: Mechanisms, Consequences and Remediation

2017 – 2022: Developmental Exposures: Mechanisms, Consequences and Remediation

Duke Superfund Research Center

"early life exposures, later life consequences"

(DOHaD: Developmental Origins of Health and Disease)

Duke UNIVERSITY | SUPERFUND Research Center

early life exposures, later life consequences

Five Research Projects

Three Biomedical
Two Non-biomedical

Six Research Support Cores

Project 1: Developmental neurotoxicants:

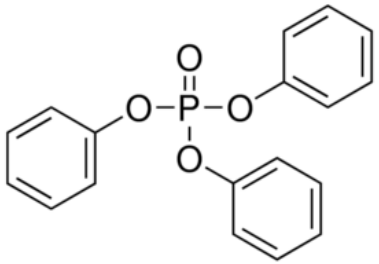
Sensitization, Consequences, and Mechanisms

PIs: Ted Slotkin, Ed Levin, Fred Seidler

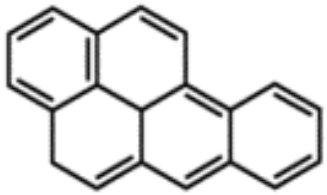
Questions:

What happens to the brain when it is exposed to a chemical during development?

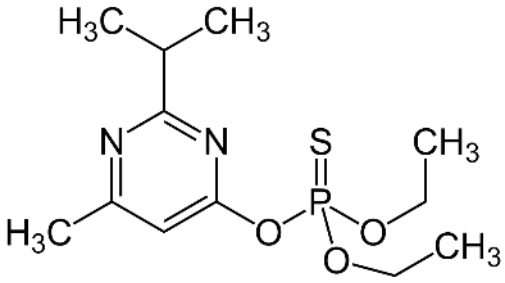
Do different chemicals that act by different mechanisms converge on the same pathways?



Triphenyl Phosphate



Benzo[a]pyrene

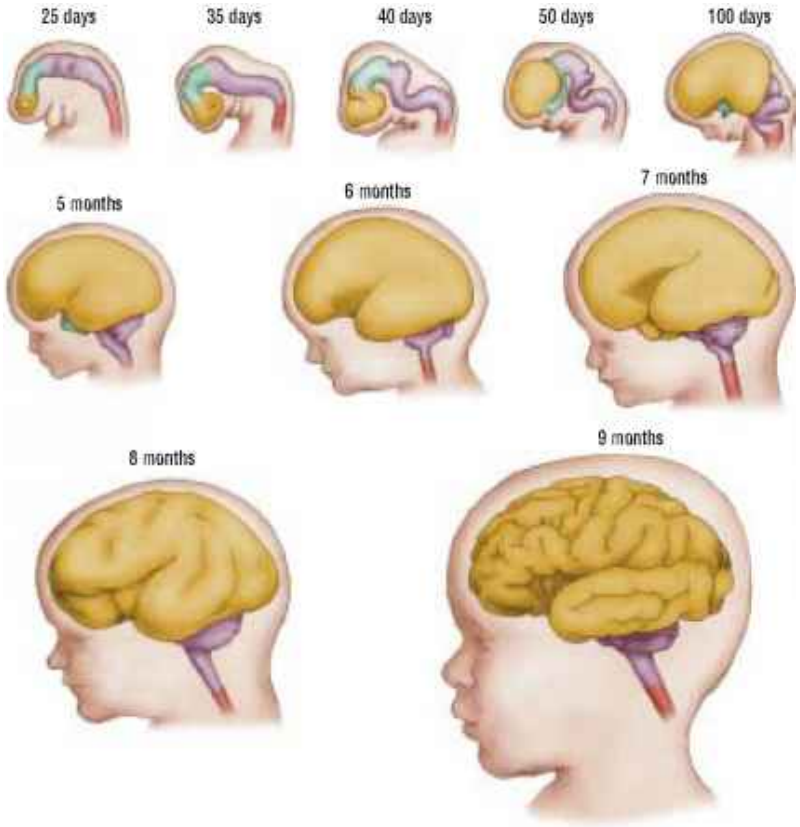


Diazinon

Project 1: Developmental neurotoxicants

Questions:

- How does brain development change because of chemical exposures?
- How do those changes lead to behavioral problems?
- What therapies may help?
- To what extent can we study these processes in simpler organisms?



Project 2: ALTERING THE BALANCE OF ADIPOGENIC AND OSTEOGENIC REGULATORY PATHWAYS FROM EARLY LIFE EXPOSURE TO ENVIRONMENTAL CHEMICALS

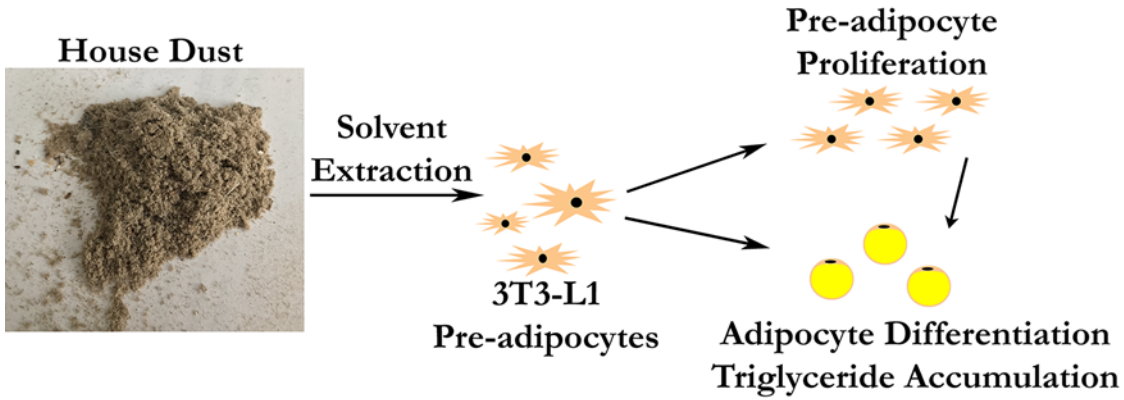
PIs: Heather Stapleton, Seth Kullman, Lee Ferguson

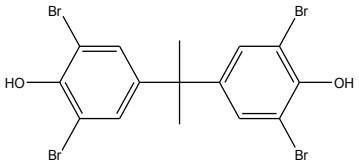
Examining pathways through which environmental chemicals might perturb the development of fat cells.

WHY?

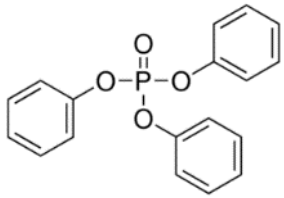
- ~40% of the US population now obese, ~20% of adolescents; increasing health care burden
- Caloric intake, activity, genetics insufficient to account for magnitude/speed of trend
- Increasing data on pharmaceuticals and other environmental chemicals as metabolic disruptors

Project 2: How do indoor chemicals and mixtures (house dust) alter the development of fat cells

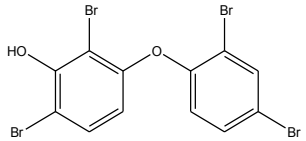




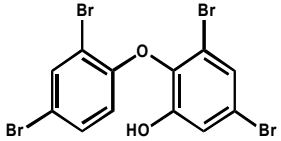
Tetrabromobisphenol A



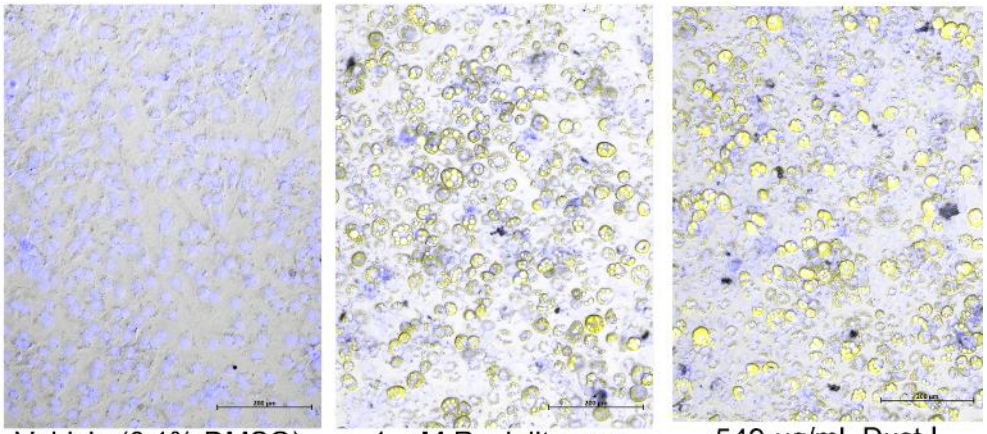
Triphenyl Phosphate



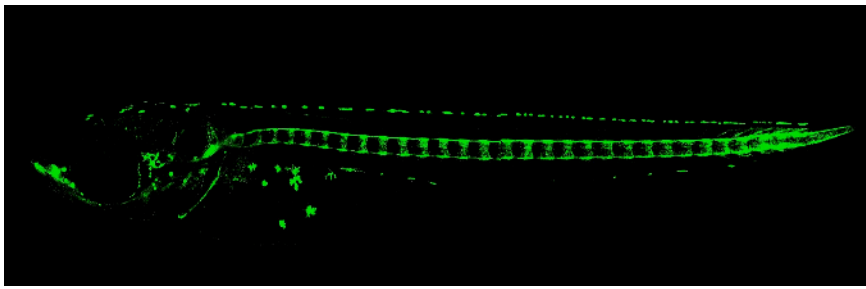
3-OH-BDE-47



6-OH-BDE-47



Vehicle (0.1% DMSO) 1 μM Rosiglitazone 549 μg/mL Dust I

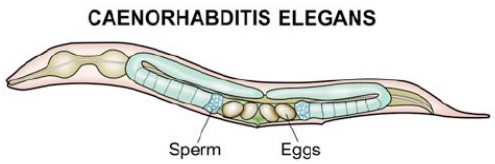


Project 3: Persistent mitochondrial and epigenetic effects of early-life toxicant exposure

PIs: Joel Meyer, Susan Murphy

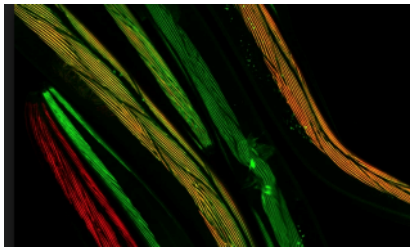
Exposing *C. elegans* to "mitotoxicant" chemicals and measuring effects in their great-grand progeny.

Benzo[a]pyrene, arsenic, mercury, pentachlorophenol, triphenylphosphate, diazinon, Superfund (creosote) mixture

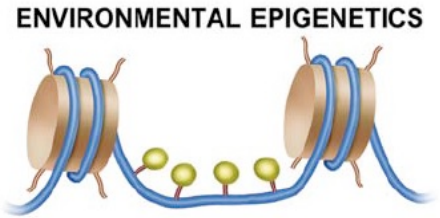


Chemical exposure

No chemical exposure for 2 generations (only 8 days)



Mitochondrial function

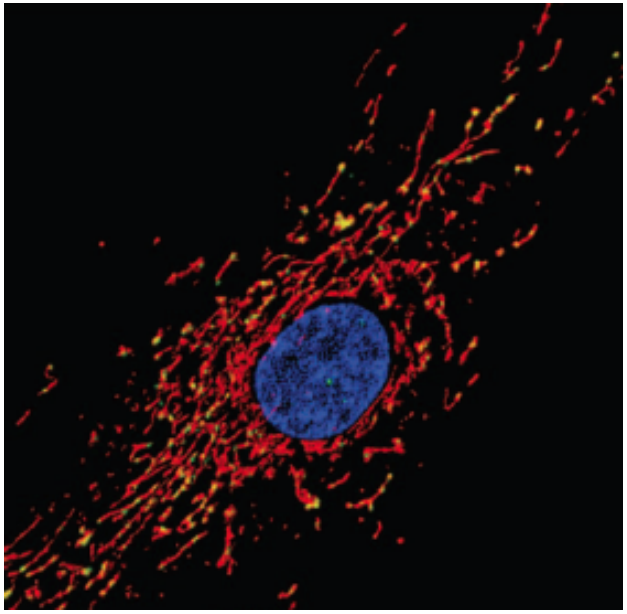


Project 3: Role of genetic differences in sensitivity

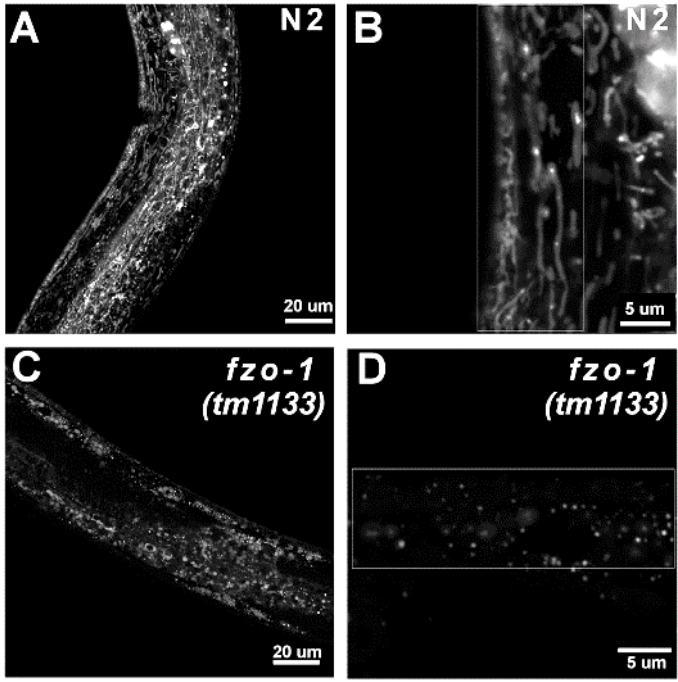
Human disease genes involved in mitochondrial dynamics.

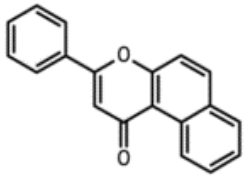
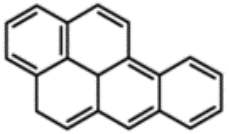
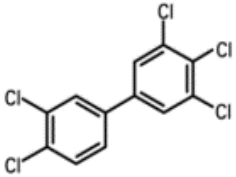
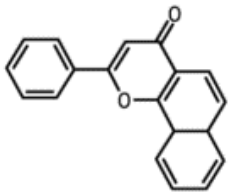
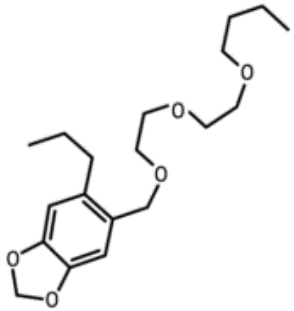
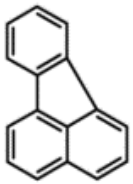
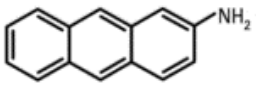
Human Gene	Estimated Disease Incidence	Human Disease	Function
MFN2	~1/7500	Charcot-Marie Tooth Neuropathy type 2A	Outer membrane fusion
OPA1	~1/10,000-1/30,000 (Lenaers et al., 2012)	Dominant Optic Atrophy	Inner membrane fusion
DRP1	Very rare (a few known cases) (Mishra and Chan, 2016)	Neuro-degeneration and early death	Fission
PARK2	~1/6000	Parkinson's Disease	Mitophagy
PINK1	~1/60,000	Parkinson's Disease	Mitophagy

UNITED MITOCHONDRIAL DISEASE FOUNDATION.
HOPE. ENERGY. LIFE.



Nuclear DNA
Mitochondria
Mitochondrial DNA



Project 4: Mechanisms and Consequences of Evolved Adaptation to Environmental Pollution

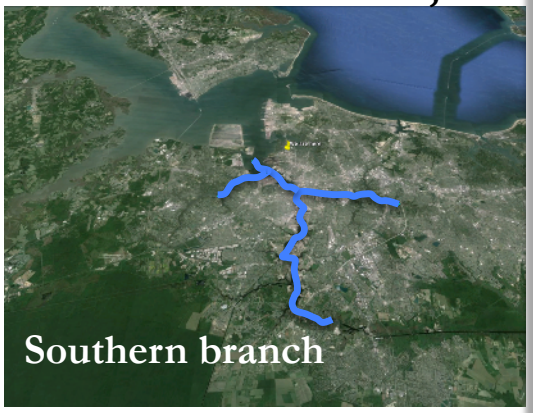
PI – Di Giulio, Co-PI- Hinton

Trainees - Jordan Kozal and Casey Lindberg

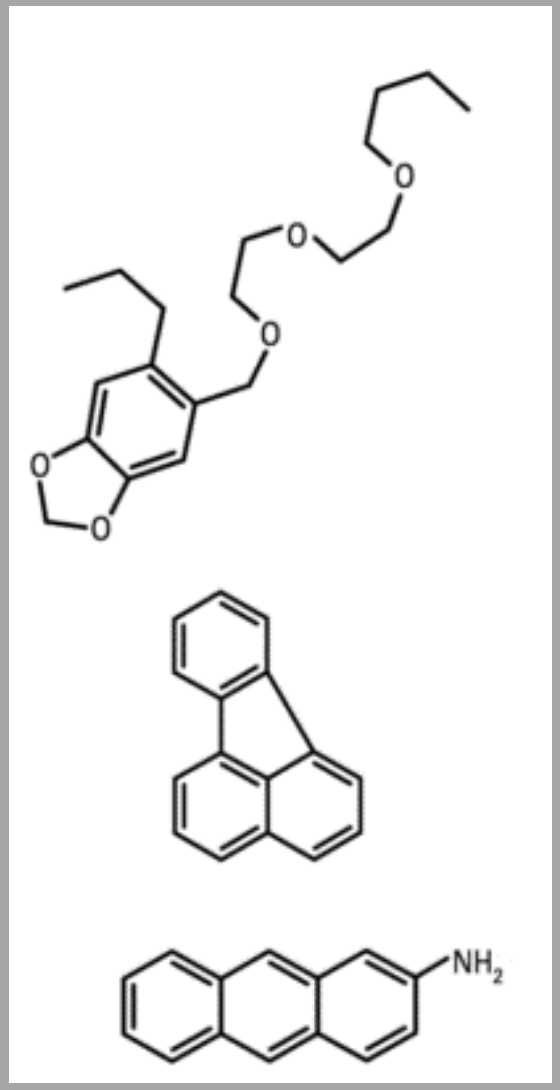
- The phenomenon pollution driving evolution has implications for environmental health and management in terms of genetic diversity, organisms' abilities to adapt to environmental changes such as warming, and understanding future risks posed by contamination.
- Linking effects of specific chemicals and mixtures to cardiovascular and nervous systems, yields great relevance to human and ecological health.

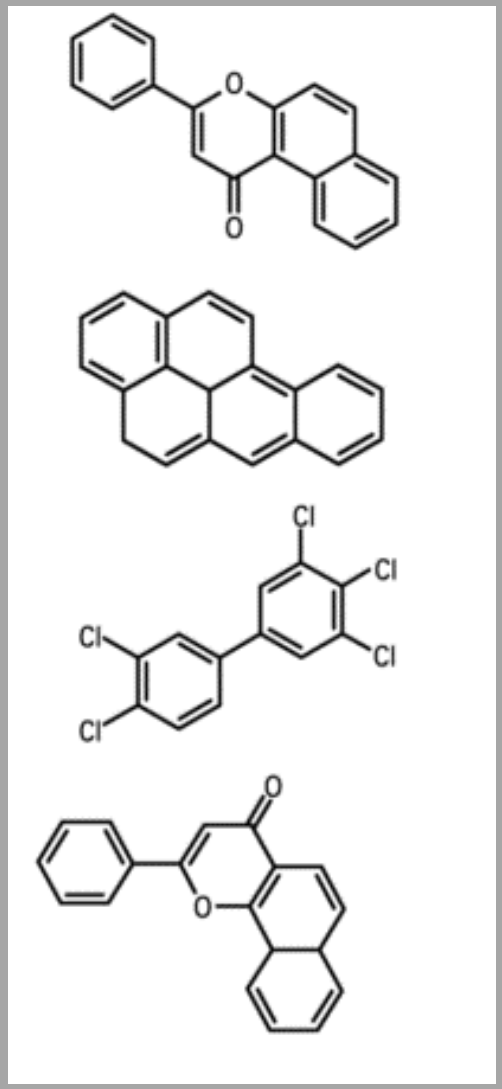
Polycyclic Aromatic Hydrocarbons (PAHs)

The Elizabeth River, VA



Atlantic Wood Industries





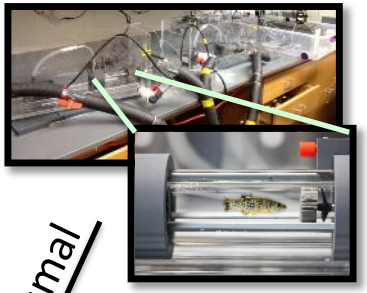
The Elizabeth River, VA

Atlantic Wood Industries

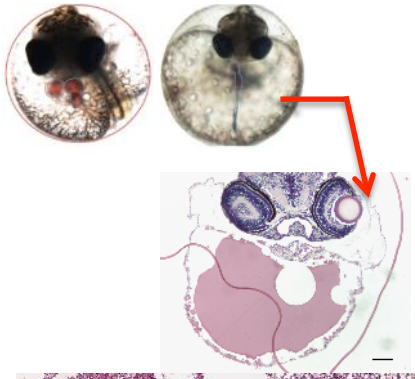
Fish collections

Organismal

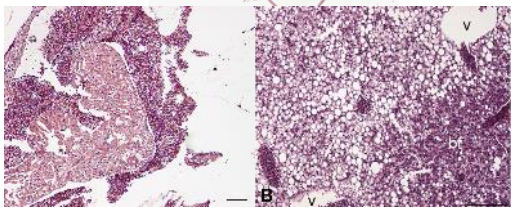
swim tunnel



morphology



Organ/Tissue

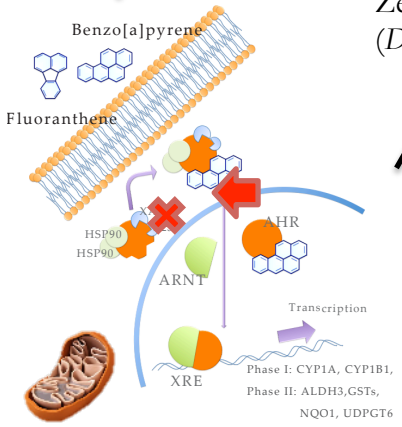


Atlantic killifish
(*Fundulus heteroclitus*)

PAH
resistance

ERSE

Molecular



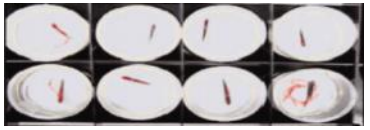
Cellular

Bioenergetics:
Extracellular
flux analyzer

Zebrafish
(*Danio rerio*)

Behavioral

Neurotoxicity

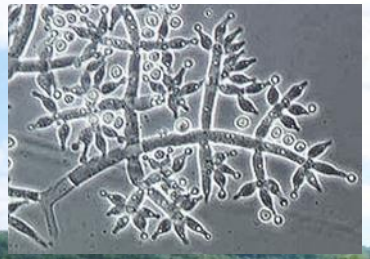


Project 5: Engineering the Physico-Chemical Environment to Enhance Polycyclic Aromatic Hydrocarbon (PAH) Bioremediation

PIs: Gunsch, Hsu-Kim, Wiesner and Vilgalys
Trainees: Volkoff, Bippus, Rodriguez and Crittenden

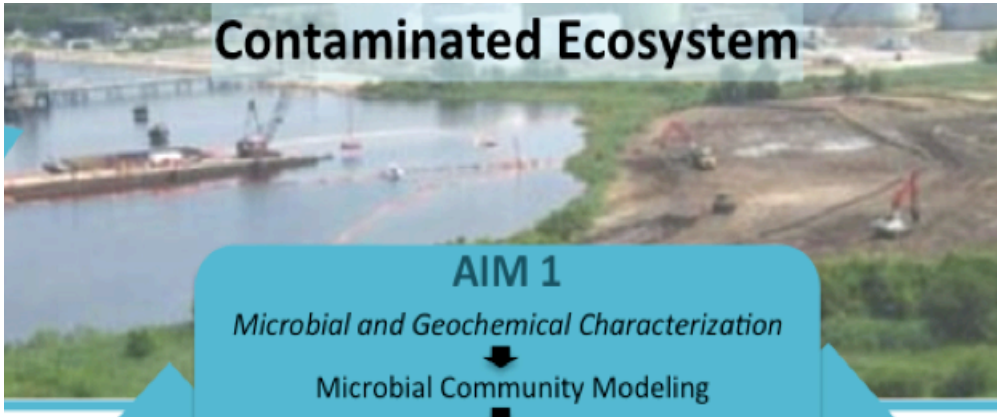
Challenge: Low PAH bioavailability to bacteria

Fungi: An Underused Resource in Bioremediation



Trichoderma harzanium

How can we improve fungal-bacterial cooperation for enhancing PAH biodegradation?


Contaminated Ecosystem
AIM 1
Microbial and Geochemical Characterization
Microbial Community Modeling
Microbial Association Network Construction
AIM 2
Organic Amendment selection
Fungal-Bacterial Biofilm stimulation
Enhanced Contaminant Degradation
Microbial Remediation Strategy Design
Composite Organic Amendment
AIM 3
Composite Material Selection
In Situ remediation Application Evaluation
Ecological Impact assessment
Composite Amendment Design

Research Support Cores

Administrative Core

Director: Richard Di Giulio; Deputy Director: Heather Stapleton

Training Core PI: Joel Meyer

Neurobehavioral Toxicity Core PI: Edward Levin

Analytical Chemistry Core PI: Lee Ferguson

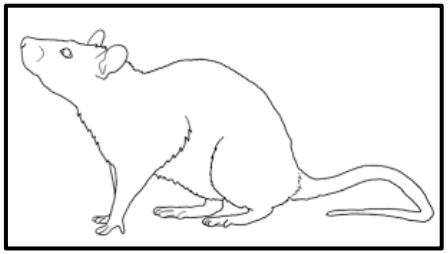
Community Engagement Core PI: Elizabeth Shapiro-Garza

Research Translation Core PI: Charlotte Clark

Neurobehavioral toxicity core

Principal Investigator: Edward Levin

Goal: To provide assessments of neurobehavioral impairments resulting from developmental toxicant exposure



Behavioral tests to assess:

Activity
Emotional Health
Learning
Cognition

Analytical Chemistry Core
PI: Lee Ferguson, Co-PIs: Heather Stapleton & Helen Hsu-Kim

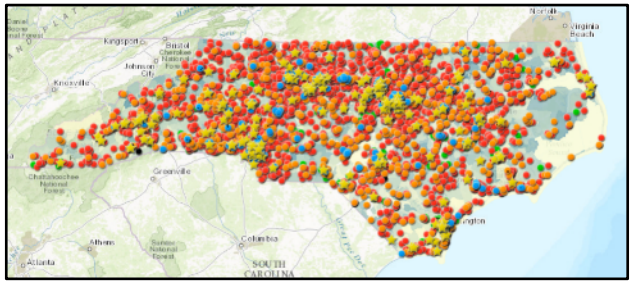
Goal: Provide routine analysis of organic and inorganic contaminants on a routine basis to investigators in support of the SRC research projects.

Examples of services by the ACC –

- Quantify hormones in biological tissues.
- Analysis of flame retardants and emerging contaminants (GenX) in environmental and biological samples.
- Analysis of PAHs (polycyclic aromatic hydrocarbons) in sediment, water and fish tissues.
- Analysis of trace metals in sediment, water and tissues.

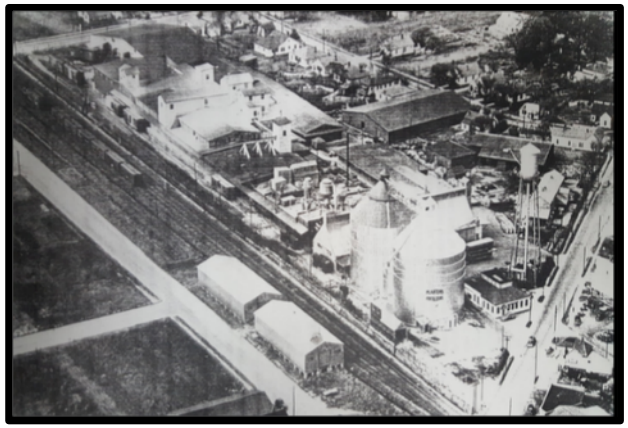
Community Engagement Core
PI: Dr. Elizabeth Shapiro-Garza

GIS Mapping Tool

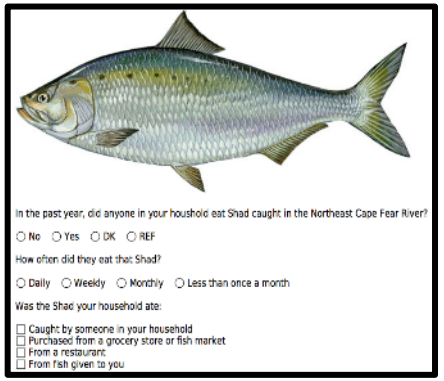


Core Projects:

Community Gardens
Communities near former industrial sites
Subsistence fish consumers



Former Planter's Oil Mill Site, Rocky Mount, NC



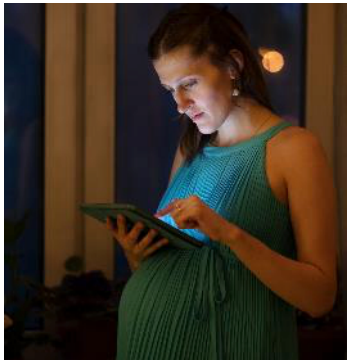
Research Translation Core
PI: Charlotte Clark

PI-initiated Research Translation

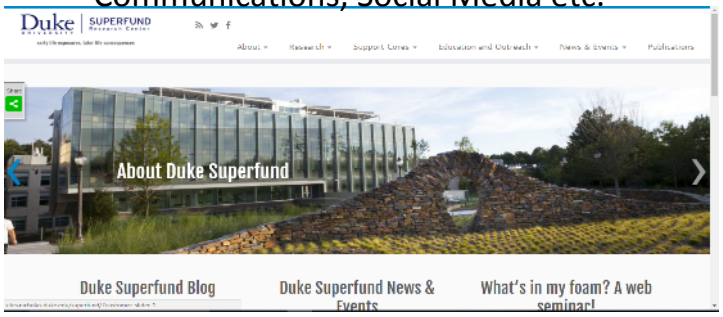
Center-wide Formal Training

Trainee Communication Skills

On-line networks – children's health



Communications, Social Media etc.



Stakeholder, Partnership Engagement

Finally: To the NIEHS Superfund Research Program

THANKS!!!!!

Dr. William Suk

Dr. Heather Henry