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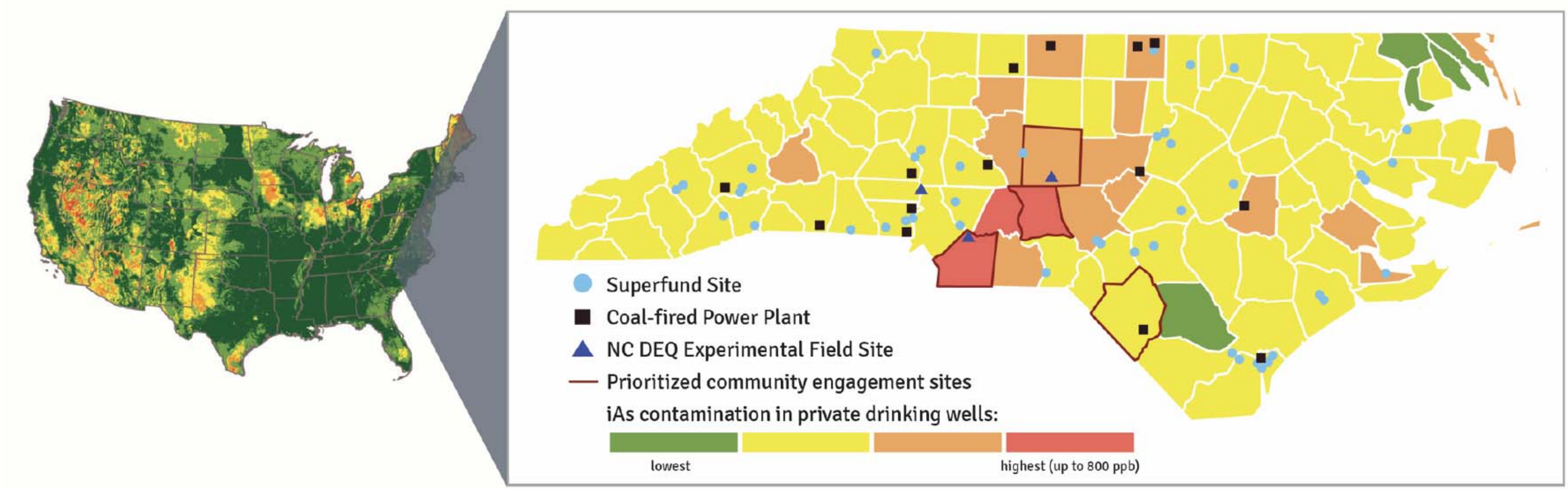

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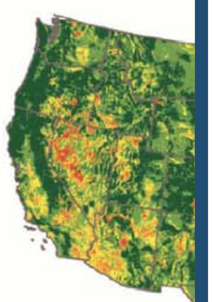

UNC-SRP theme

Identifying novel methods to reduce iAs exposure and elucidating mechanisms underlying iAs-induced metabolic dysfunction with a vision for disease prevention.

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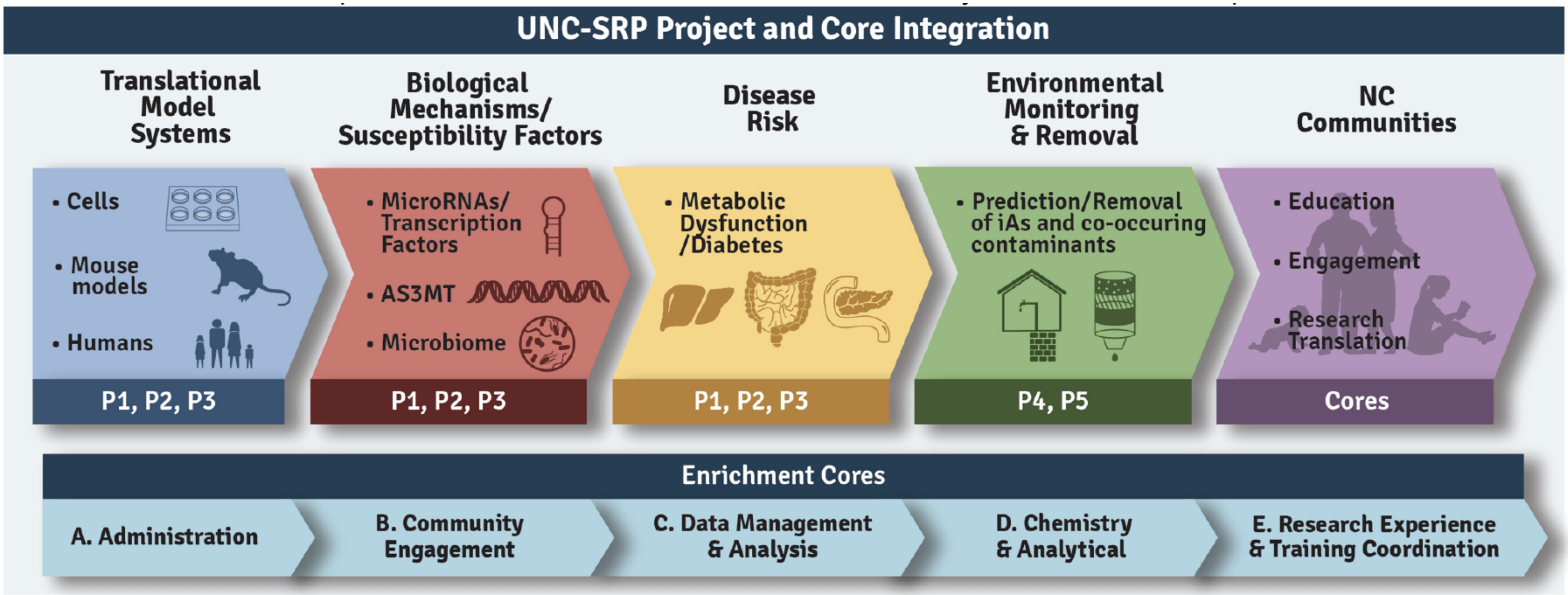
Our mission

Develop new solutions for iAs reduction and disease prevention through mechanistic and translational research.



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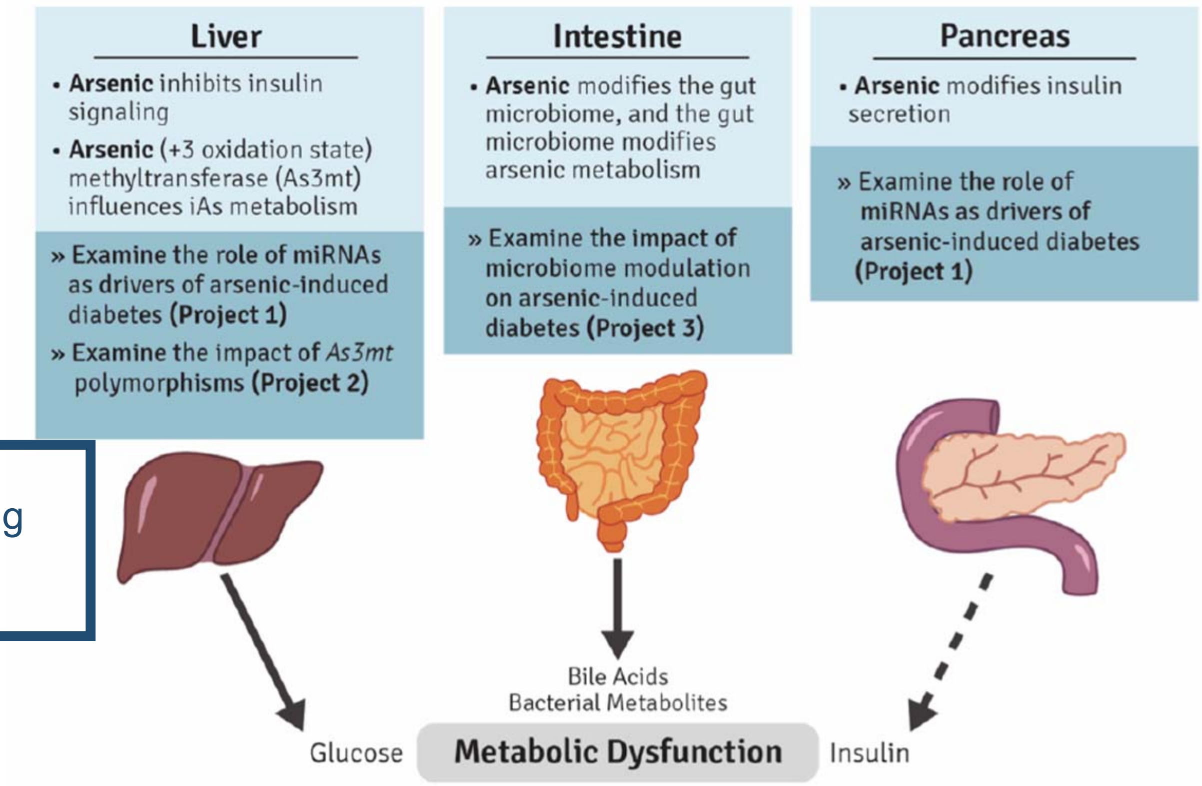


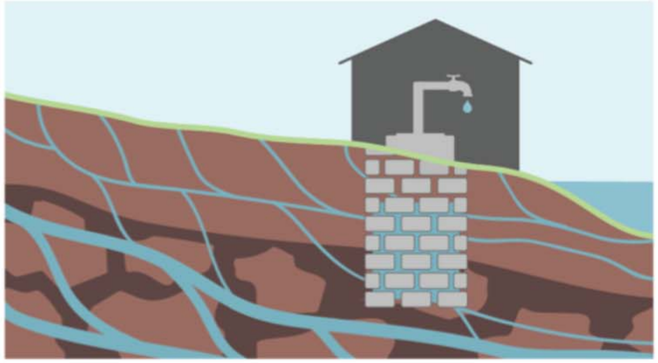
Insulin secretion from pancreas

Insulin signaling in liver

Prediction

- iAs contamination in wells is linked to the presence of chemical oxidants

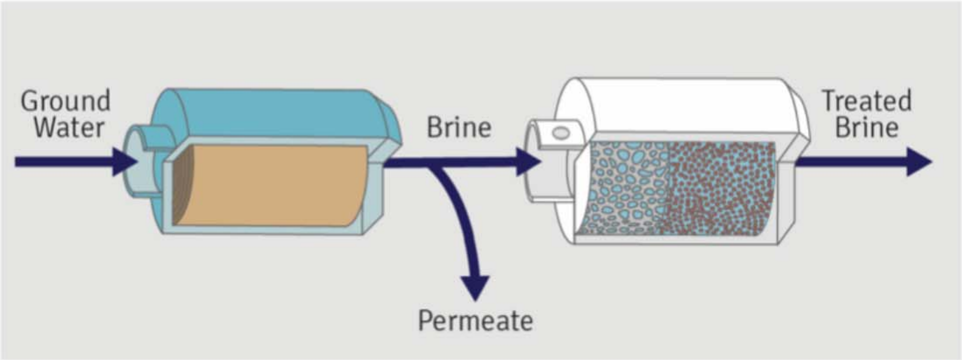
» Identify geochemical methods to predict high levels of iAs contamination using **(Project 4)**



Removal

- iAs and other contaminants co-occur in drinking water from private wells

» Test effectiveness of an integrated membrane-sorbent system to remove iAs and co-occurring contaminants **(Project 5)**



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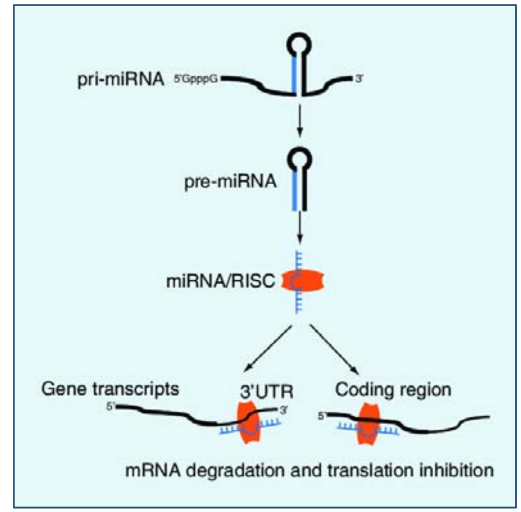
P1: Molecular Drivers of Arsenic-Induced Diabetes

P. Sethupathy

M. Styblo

L.M. Del Razo
R. Fry
G. Garcia-Vargas
M. Kanke
F. Zou



Aim 1. Do **miRNAs** control iAs-associated diabetes phenotypes in mice and in beta cells?

Aim 2. What are the **transcription factors** driving iAs-induced diabetes in cells?

Aim 3. Are circulating non-coding RNAs **biomarkers** of iAs-associated diabetes?

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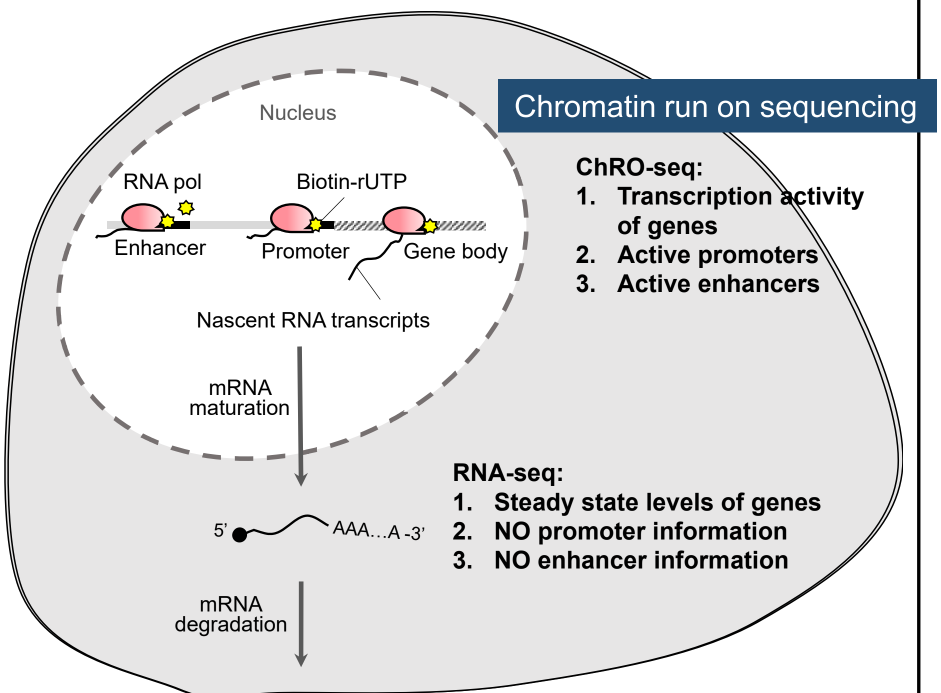
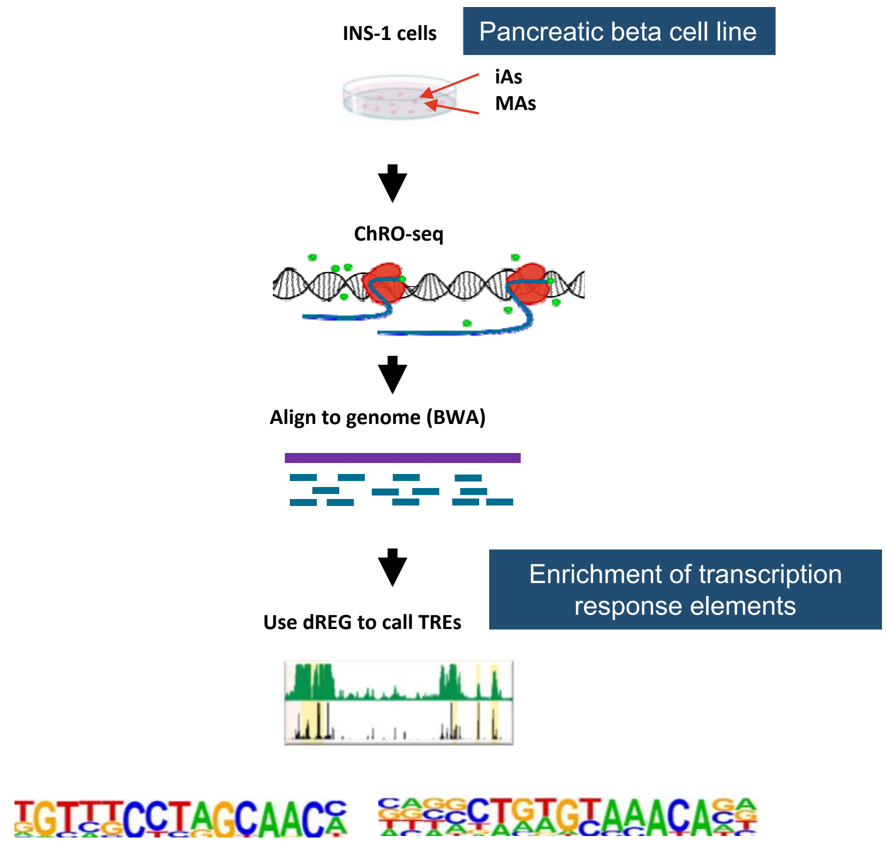
Kieran Koch-Laskowski

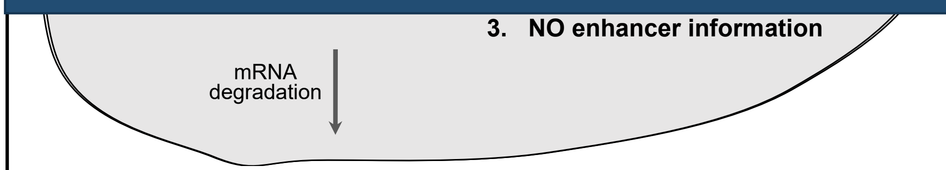
Understand the effects of arsenic on transcriptional regulation in cells relevant to metabolic dysfunction.

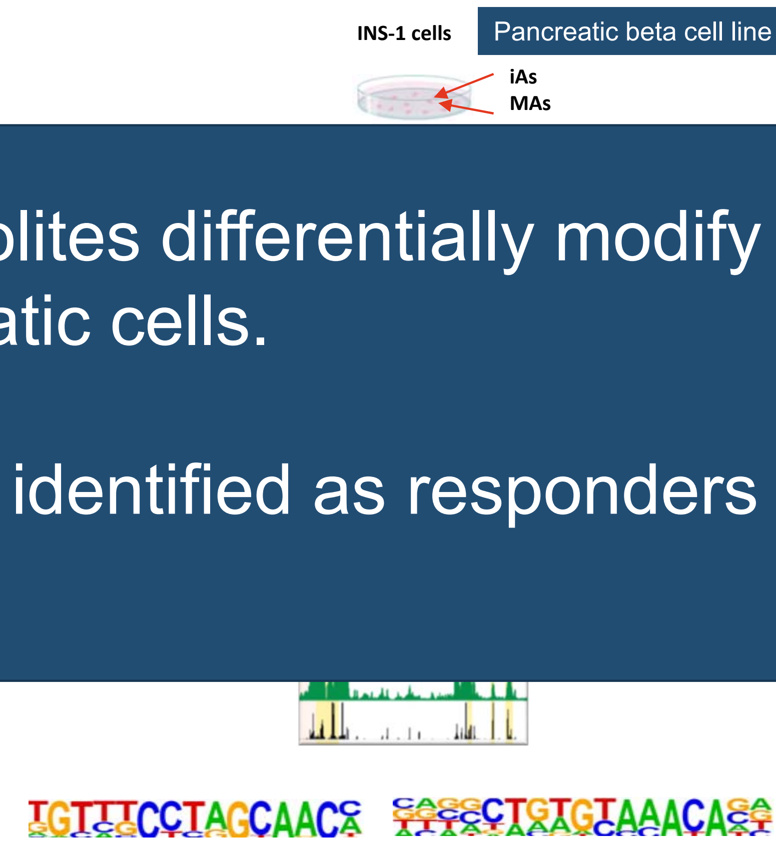




Kieran Koch-Laskowski

Understand the effects of arsenic on transcriptional regulation in cells relevant to metabolic dysfunction.





- ❖ Inorganic arsenic and its metabolites differentially modify the transcriptional activity in pancreatic cells.
- ❖ Several transcription factors are identified as responders to arsenic and its metabolites.

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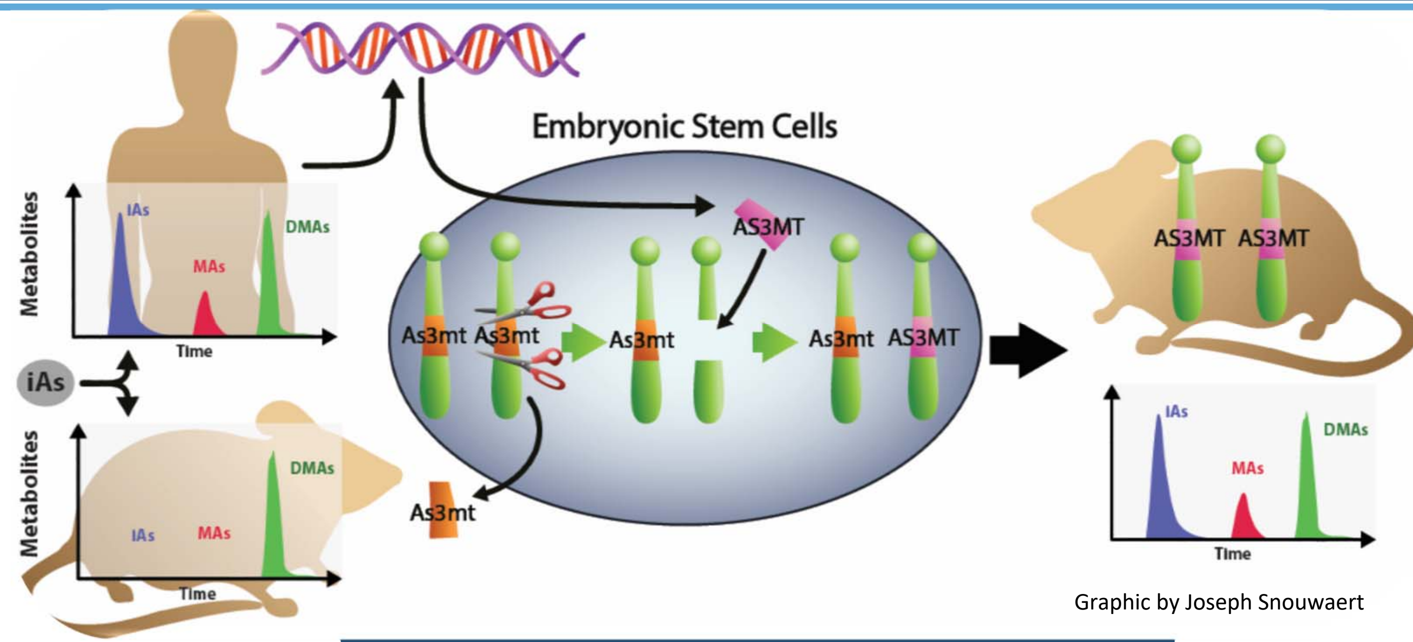

Graphic by Joseph Snouwaert

Mouse gene encoding arsenic methyltransferase was replaced with the orthologous human gene.

Styblo, Koller develop novel humanized mouse model with implications for studying arsenic exposure in humans

Koller et al. 2020 EHP Vol 128; 8

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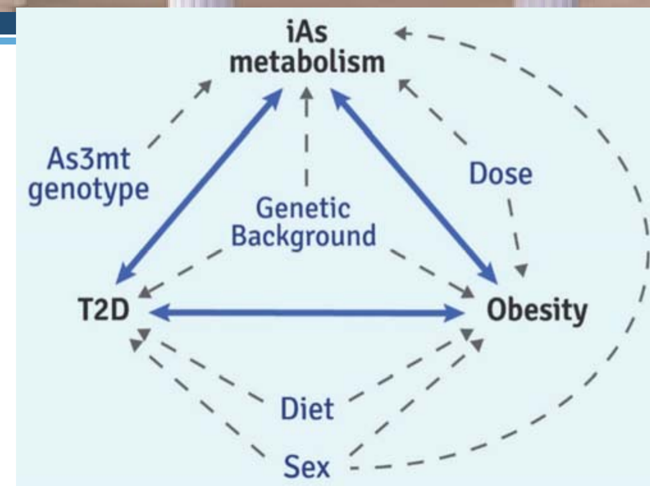
P2: Arsenic – Obesity – Diabetes Interactions

F. Pardo-Manuel de Villena

R. Fry
P. Hock
M. Styblo
J. Xenakis
F. Zou



Aim 1. How do As3mt genotype, genetic background, and obesity **interact** and influence **iAs metabolism**?

Aim 2. What are the roles of As3mt genotype, genetic background, and obesity in iAs-associated **diabetic phenotypes**?

Aim 3. What are the **molecular signatures** of iAs-associated T2D in obese or non-obese mice with varied iAs metabolism?

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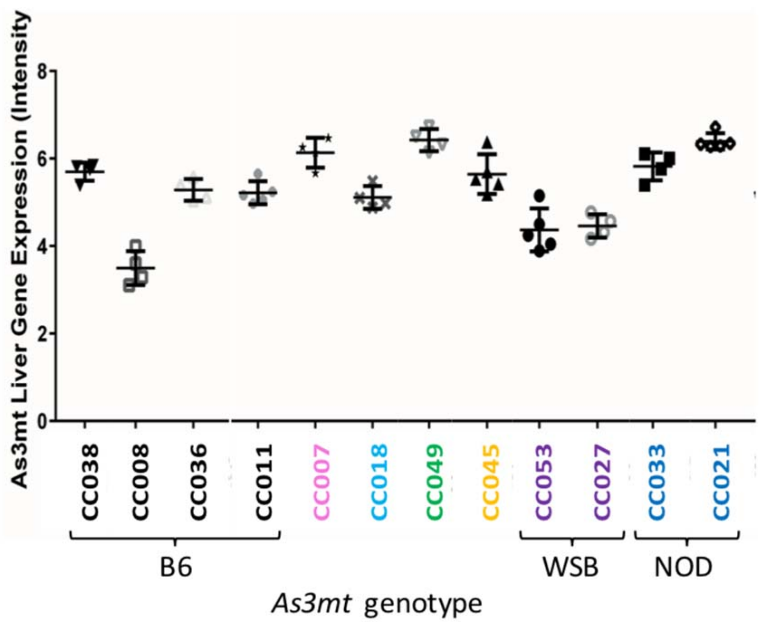
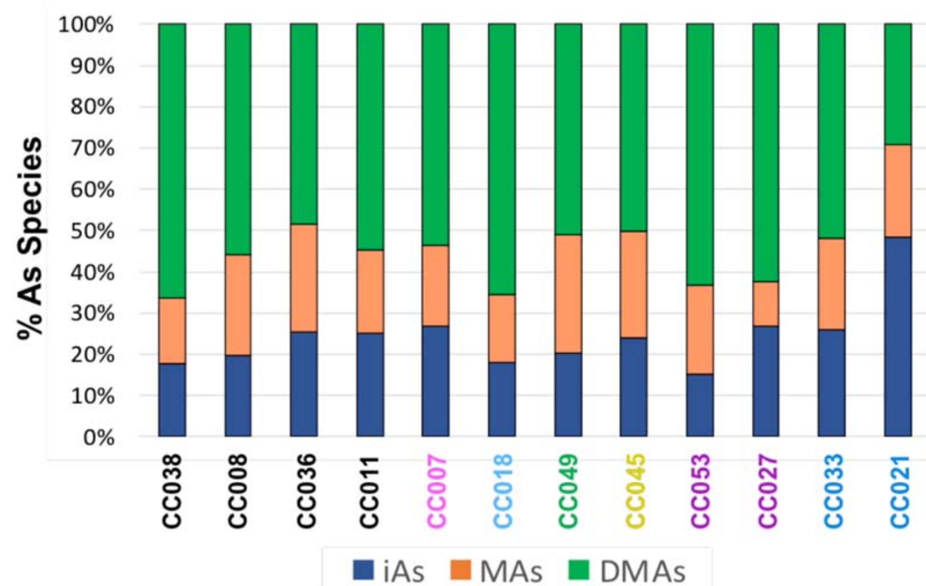
As3mt expression in livers



Arsenic species in livers (50 ppm)



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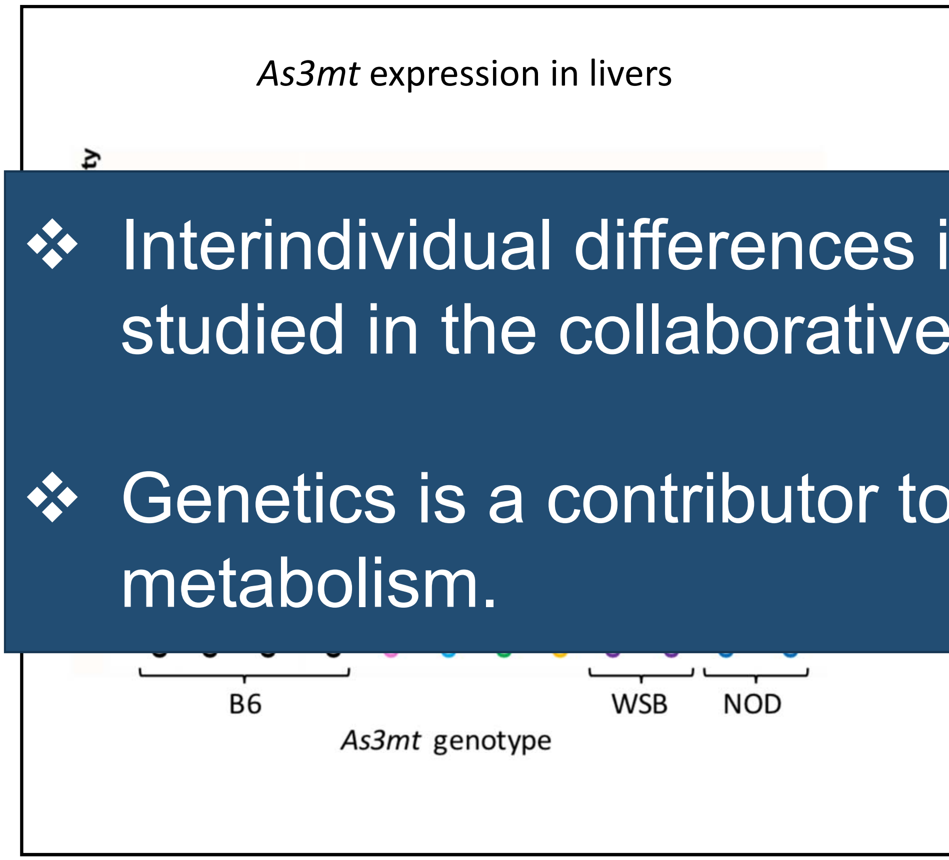

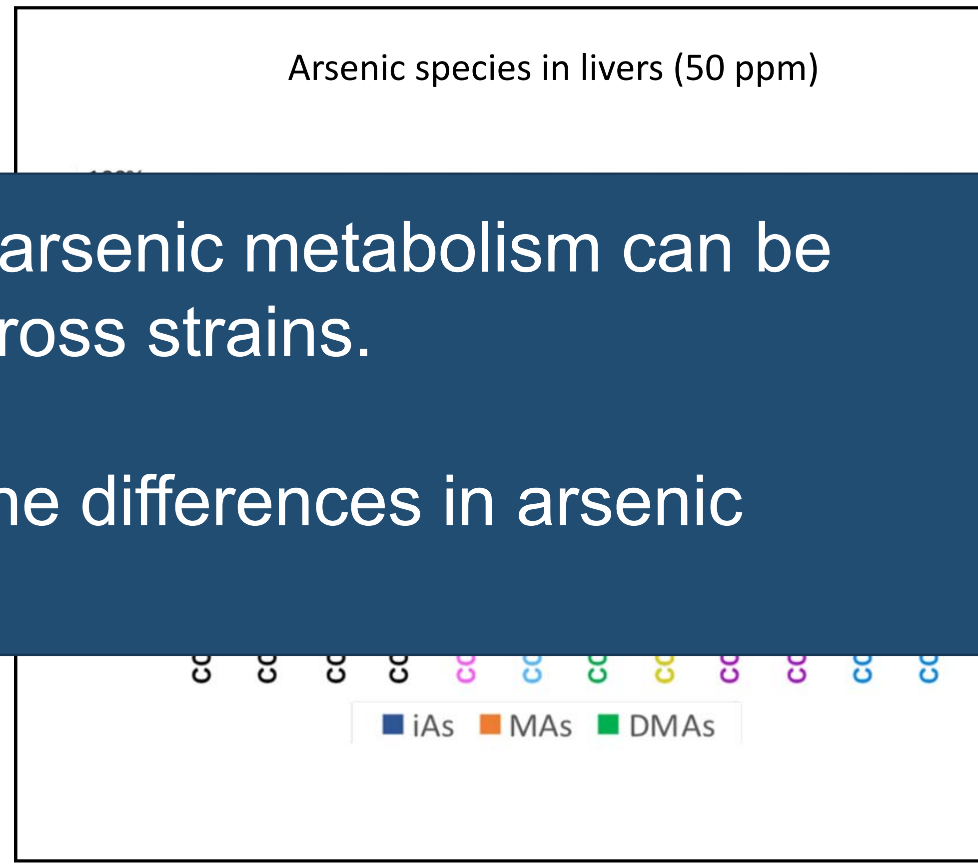

- Interindividual differences in arsenic metabolism can be studied in the collaborative cross strains.
- Genetics is a contributor to the differences in arsenic metabolism.

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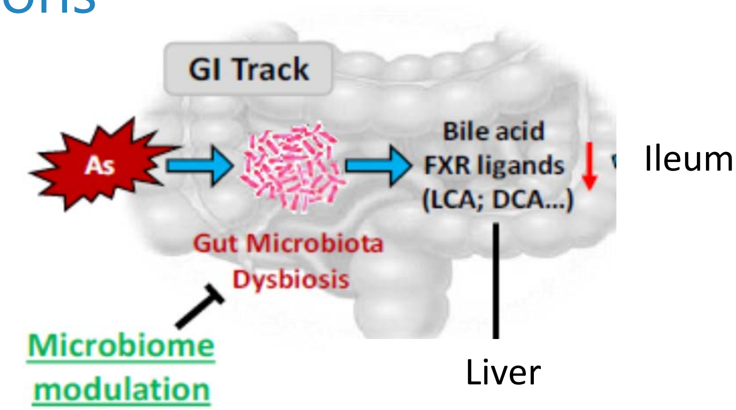
P3: Gut Microbiome-Arsenic-Diabetes Interactions

K. Lu

L. Chi
Y. Lai
C. Liu
T. McDermott
R. Sartor
M. Styblo
F. Zou



Aim 1. What is the link between the **gut microbiota** and iAs-impaired bile acid metabolism?

Aim 2. Does the gut microbiome inhibit the **Farnesoid X receptor** and exacerbate diabetes?

Aim 3. Can gut microbiome **manipulation** restore Farnesoid X receptor activation?

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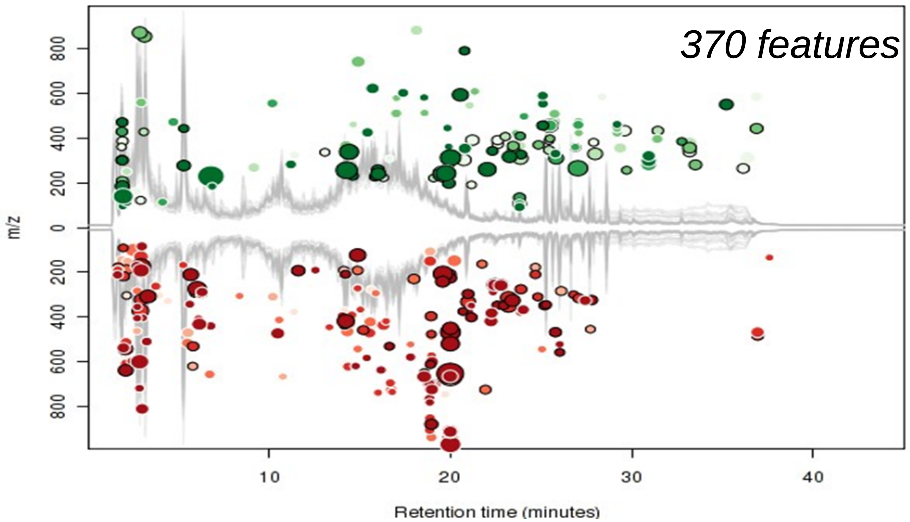
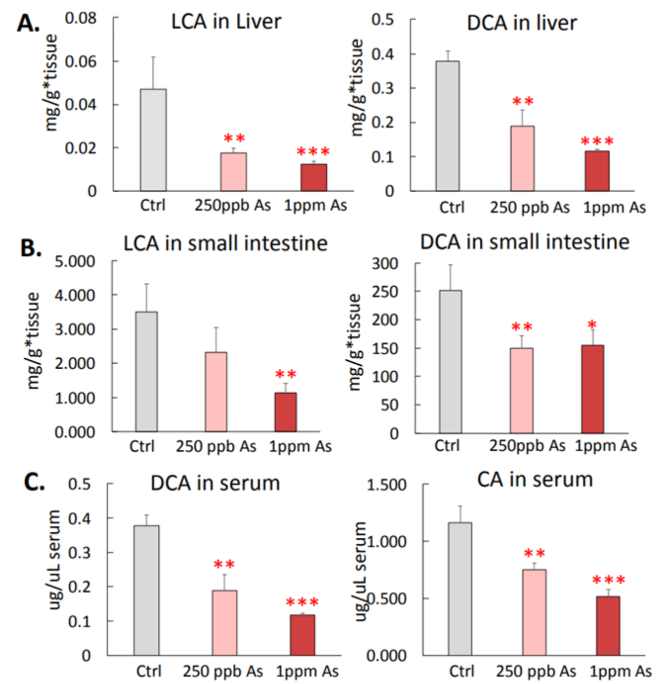
Metabolomic profiling of fecal samples C57Bl/6 mice (10 ppm)



Lu et al, Environ Health Perspective. 2014, 122(3):284-91

Lithocholic acid, cholic acid, deoxycholic acid



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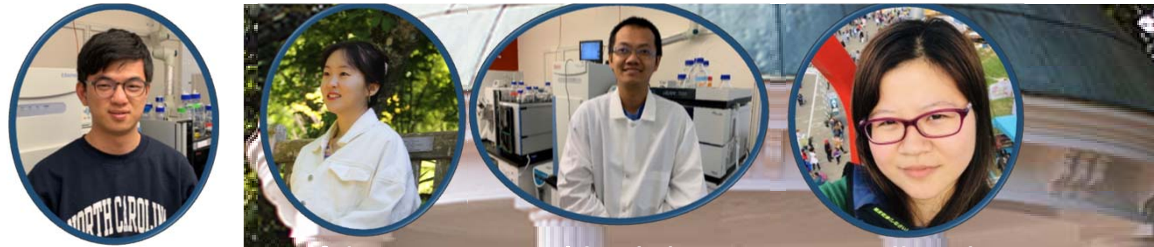
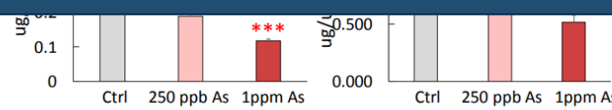


Metabolomic profiling of fecal samples
C57Bl/6 mice (10 ppm)

Lithocholic acid, cholic acid, deoxycholic acid

- ❖ Arsenic impacts the gut microbiome and metabolite profiles.
- ❖ Arsenic decreases bile acids in tissue and serum, highlighting the impact of changes in the gut microbiome.

Lu et al, Environ Health Perspective. 2014, 122(3):284-91



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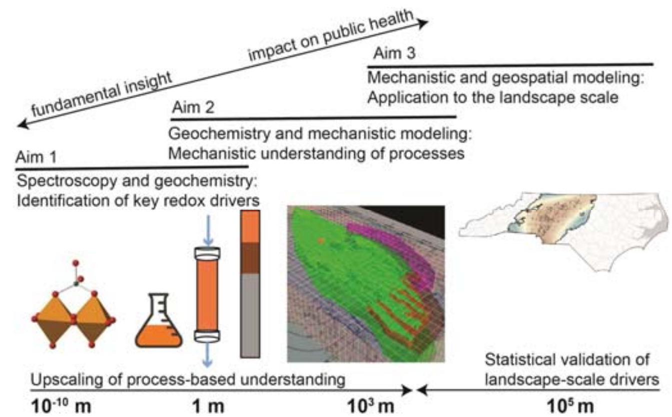
P4: Geochemical Predictors of iAs Contamination

O. Duckworth

R. Austin
C. Miller
J. Osborne
M. Polizzotto
D. Vinson



Aim 1. What are the **geochemical factors** that influence iAs, V, and Cr movement in ground water?

Aim 2. How does **land management** impact contamination?

Aim 3. How can we best **predict** levels of iAs, V, and Cr in drinking water wells?

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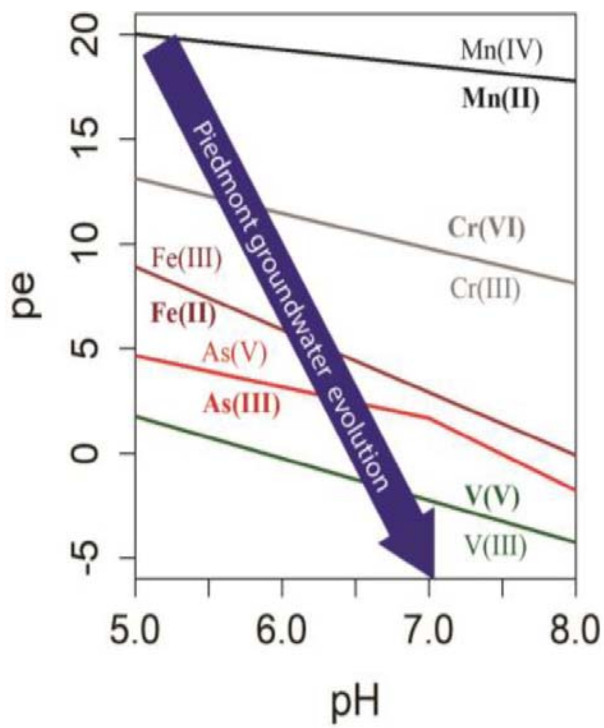
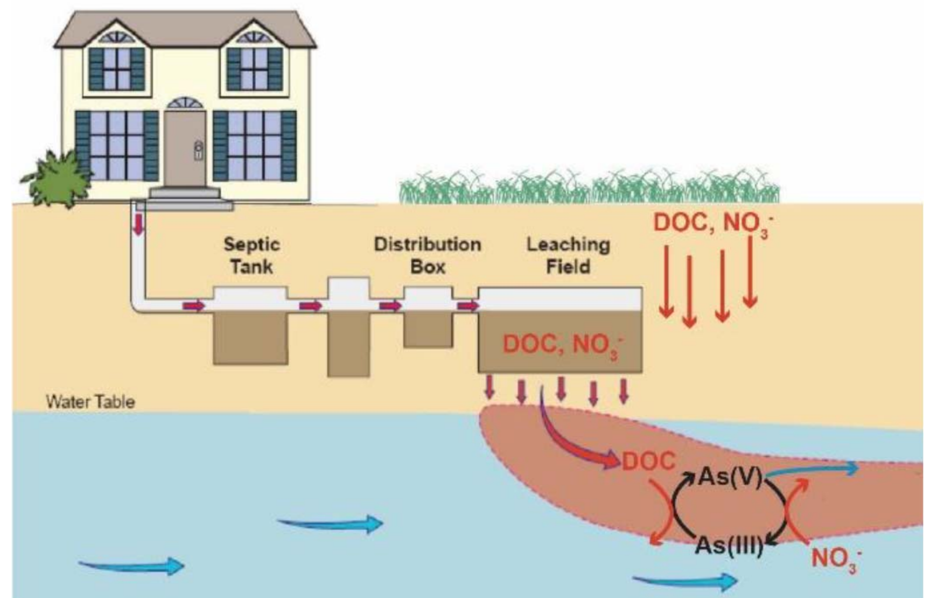
Chelsea Obeidy Fatai Balogun Chris Bowers Hannah Peel

Biogeochemical factors that can influence arsenic and other redox-active contaminants



manganese oxide depletion- arsenic solubility

Land development and management: Nitrate and dissolved organic carbon



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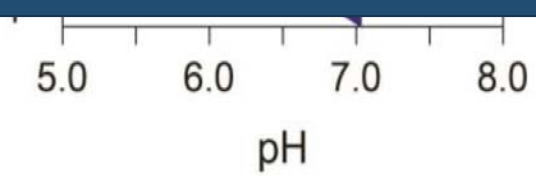
Chelsea Obeidy Fatai Balogun Chris Bowers Hannah Peel

Biogeochemical factors that can influence

Land development and management:

- Arsenic levels depend on local land use factors that enrich for nitrate and dissolved organic compounds fluxes to groundwater.

- Arsenic levels and co-occurring contaminants can be predicted by manganese oxide, of use to well construction in NC.



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O. Duckworth

Owen Duckworth receives the Jackson Soil Chemistry and Mineralogy Award!

Recognized for outstanding contributions in the areas of soil chemistry and mineralogy

(SSSA) Soil Science Society of America

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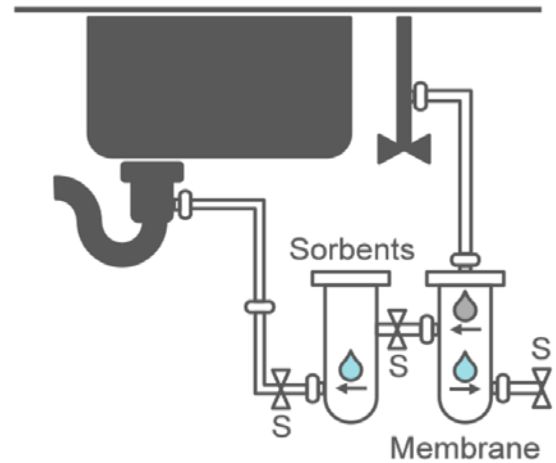
P5: Novel Filtration Devices for Arsenic Reduction

O. Coronell

K. Gray
G. Kim
C. Miller
M. Soukri
H. Zhou



Aim 1. What is the optimal membrane chemistry for removal of iAs and co-occurring contaminants?

Aim 2. What is the optimal sorbent for iAs and co-occurring contaminants removal?

Aim 3. What is the optimal combination of membrane and sorbent for iAs and co-occurring contaminants removal in point use systems?

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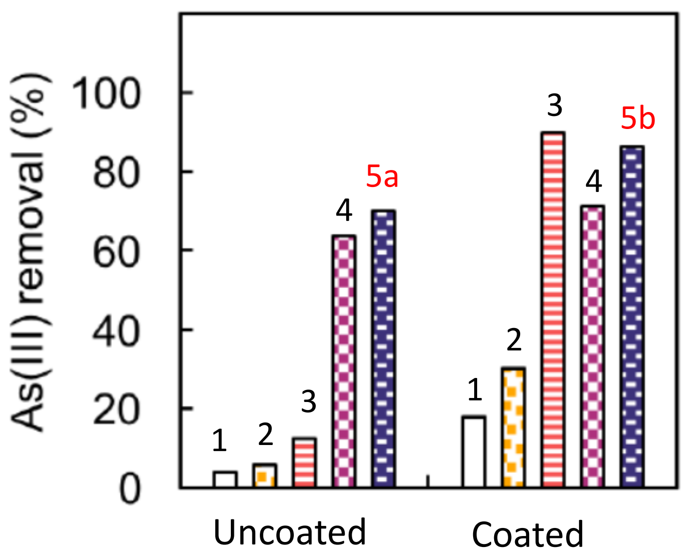
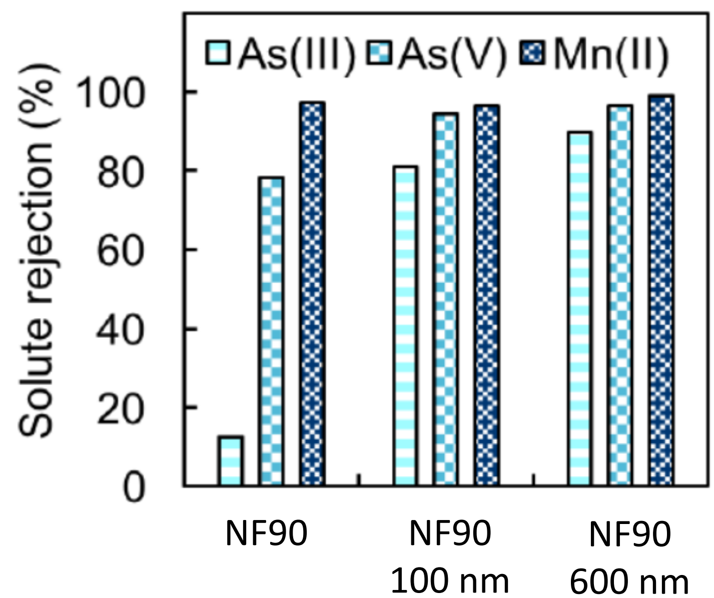
Chris Bowers Mikayla Armstrong Riley Vickers Nick Chew Elizabeth Batianis

Developing optimized membrane filtration systems for arsenic removal



Membranes modified using ion exchange polymer coatings increase arsenic removal



Coating thickness enhances removal

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Chris Bowers Mikayla Armstrong Riley Vickers Nick Chew Elizabeth Batianis

Developing optimized membrane filtration systems for arsenic removal

As(III) As(V) Mn(II)

- ❖ Membranes can be optimized for small inorganic solute removal.
- ❖ These membranes offer a removal strategy for arsenic in at risk areas in NC.

Uncoated Coated

NF90 NF90 100 nm NF90 600 nm

Membranes modified using ion exchange polymer coatings increase arsenic removal

Coating thickness enhances removal

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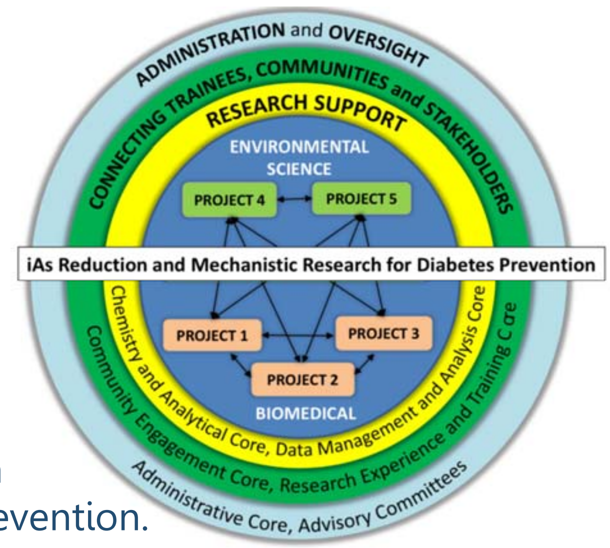
Cass Miller and Orlando Coronell receive computing award from the NSF

“Molecular dynamics simulations of water and solute transport through crosslinked aromatic polyamide reverse osmosis membranes”

Core A: Administration

R. Fry

Z. Gleason
F. Pardo-Manuel de Villena
M. Rodgers
L. Smeester
K. Smith
M. Styblo
W. Vizuete
S. Yelton



Aim 1. Integrate, coordinate, and monitor UNC-SRP interdisciplinary research activities focused on iAs reduction and metabolic disease/diabetes prevention.

Aim 2. Convene advisory groups to provide critical guidance on UNC-SRP activities.

Aim 3. Develop effective research translation and communication strategies for UNC-SRP stakeholders related to iAs reduction and disease prevention.

Aim 4. Provide training and career development opportunities for graduate students and post-doctoral fellows that foster integration across the Biomedical and Environmental Science research areas.

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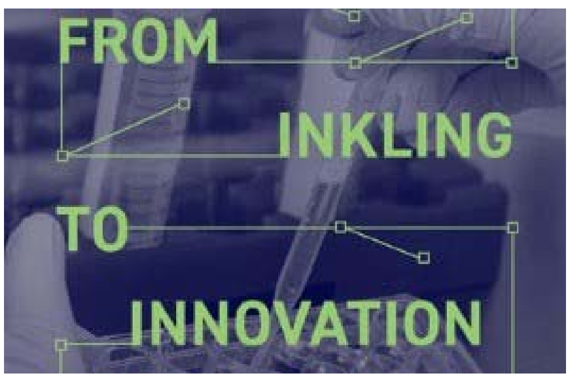
Communicating within SRP

- UNC SRP
- NIEHS
- Other SRPs

Partnerships with Government Agencies*



Technology Transfer

- UNC Office of Technology Commercialization

Information Dissemination to other End-Users

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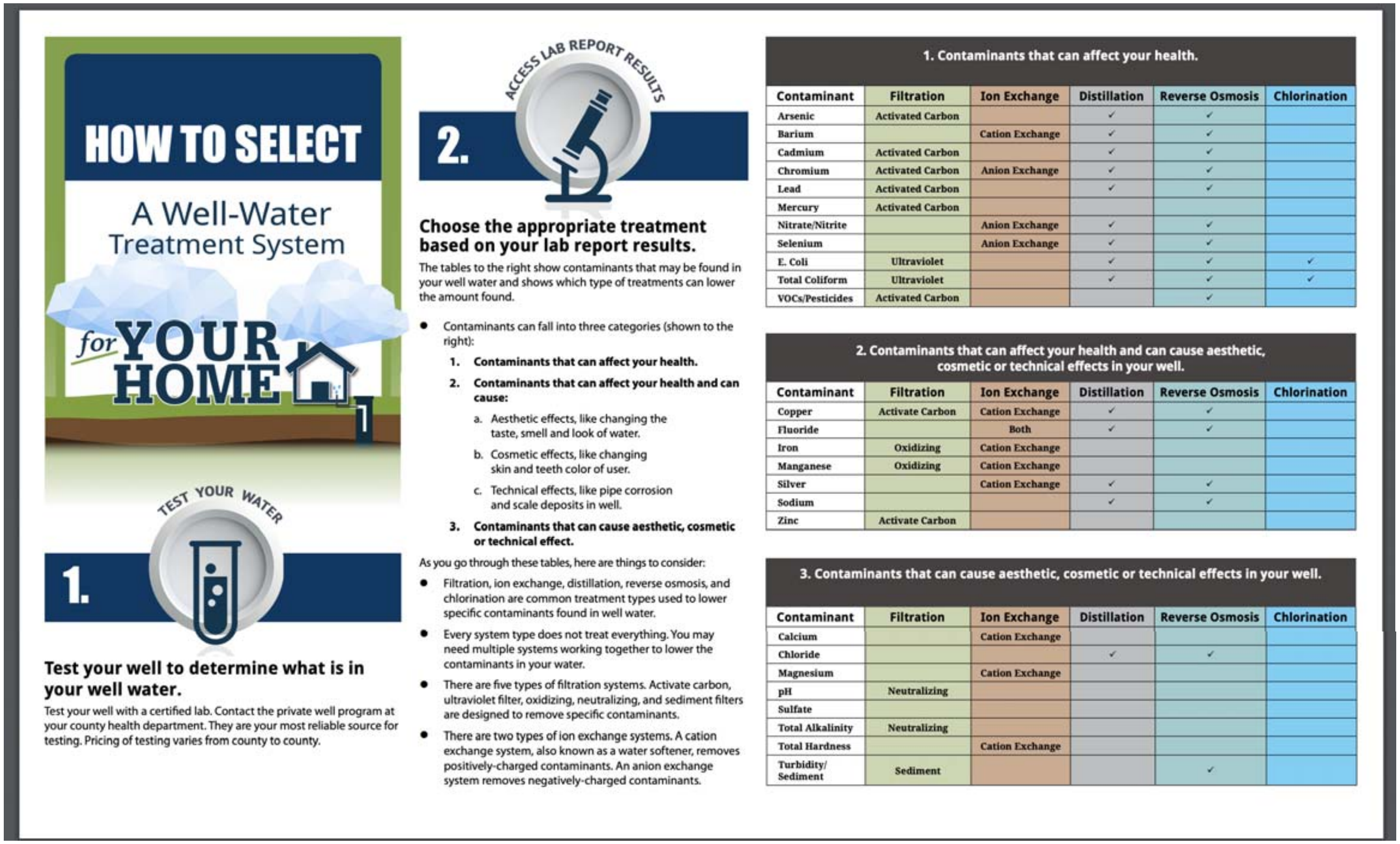

HOW TO SELECT

A Well-Water Treatment System

for YOUR HOME

TEST YOUR WATER

1.

Test your well to determine what is in your well water.

Test your well with a certified lab. Contact the private well program at your county health department. They are your most reliable source for testing. Pricing of testing varies from county to county.

ACCESS LAB REPORT RESULTS

2.

Choose the appropriate treatment based on your lab report results.

The tables to the right show contaminants that may be found in your well water and shows which type of treatments can lower the amount found.

- Contaminants can fall into three categories (shown to the right):
  1. **Contaminants that can affect your health.**
  2. **Contaminants that can affect your health and can cause:**
     a. Aesthetic effects, like changing the taste, smell and look of water.
     b. Cosmetic effects, like changing skin and teeth color of user.
     c. Technical effects, like pipe corrosion and scale deposits in well.
  3. **Contaminants that can cause aesthetic, cosmetic or technical effect.**

As you go through these tables, here are things to consider:

- Filtration, ion exchange, distillation, reverse osmosis, and chlorination are common treatment types used to lower specific contaminants found in well water.
- Every system type does not treat everything. You may need multiple systems working together to lower the contaminants in your water.
- There are five types of filtration systems. Activate carbon, ultraviolet filter, oxidizing, neutralizing, and sediment filters are designed to remove specific contaminants.
- There are two types of ion exchange systems. A cation exchange system, also known as a water softener, removes positively-charged contaminants. An anion exchange system removes negatively-charged contaminants.

1. Contaminants that can affect your health.

Contaminant	Filtration	Ion Exchange	Distillation	Reverse Osmosis	Chlorination
Arsenic	Activated Carbon		✓	✓	
Barium		Cation Exchange	✓	✓	
Cadmium	Activated Carbon		✓	✓	
Chromium	Activated Carbon	Anion Exchange	✓	✓	
Lead	Activated Carbon		✓	✓	
Mercury	Activated Carbon				
Nitrate/Nitrite		Anion Exchange	✓	✓	
Selenium		Anion Exchange	✓	✓	
E. Coli	Ultraviolet		✓	✓	✓
Total Coliform	Ultraviolet		✓	✓	✓
VOCs/Pesticides	Activated Carbon			✓	

2. Contaminants that can affect your health and can cause aesthetic, cosmetic or technical effects in your well.

Contaminant	Filtration	Ion Exchange	Distillation	Reverse Osmosis	Chlorination
Copper	Activate Carbon	Cation Exchange	✓	✓	
Fluoride		Both	✓	✓	
Iron	Oxidizing	Cation Exchange			
Manganese	Oxidizing	Cation Exchange			
Silver		Cation Exchange	✓	✓	
Sodium			✓	✓	
Zinc	Activate Carbon				

3. Contaminants that can cause aesthetic, cosmetic or technical effects in your well.

Contaminant	Filtration	Ion Exchange	Distillation	Reverse Osmosis	Chlorination
Calcium		Cation Exchange			
Chloride			✓	✓	
Magnesium		Cation Exchange			
pH	Neutralizing				
Sulfate					
Total Alkalinity	Neutralizing				
Total Hardness		Cation Exchange			
Turbidity/ Sediment	Sediment			✓	

NC DEPARTMENT OF HEALTH AND HUMAN SERVICES

Online guide to help well owners determine the best well water treatment option for specific contaminants

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Examining relationships between locations of Superfund sites in the US and demographic variables

Eric Brown

Understanding the impact of arsenic exposure on the health of pregnant women

Liyah Clark

Identifying hot spots of concern for arsenic exposure in NC

Lauren Eaves

Working with at risk communities in NC

Amaree Gardner

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Core B: Community Engagement

K. Gray

A. George

S. Yelton

Aim 1. Facilitate dialogue among UNC-SRP investigators (P1-P5) and key NC stakeholders about SRP research and its implications for reducing exposure to iAs in well water.

Aim 2. Enhance understanding of iAs exposures in high-risk communities and implement local strategies to prevent or reduce harmful exposures.

Aim 3: Inform the development of local and state policies that prevent or reduce iAs exposure in private wells used for drinking water.

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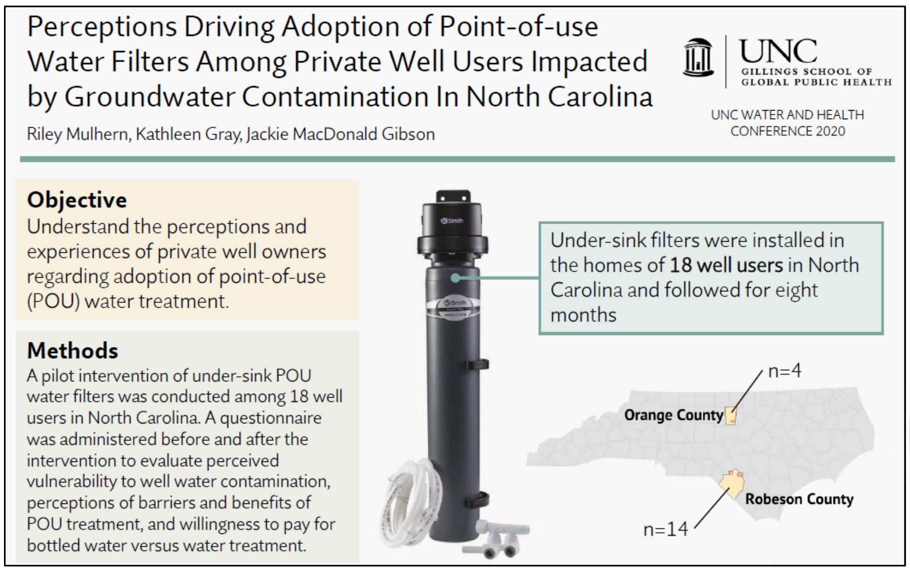
Provides key information to community partners and key stakeholders related to levels of contaminants in their private drinking wells that may be linked to metabolic dysfunction

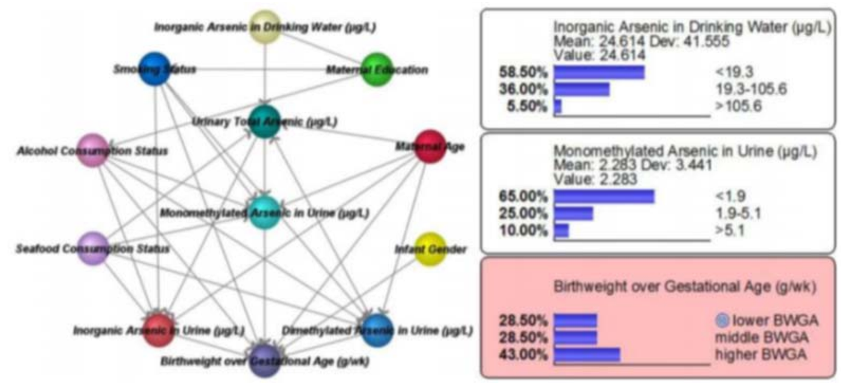


Co-leading a well water working group of key stakeholders across NC focused on improving well testing and remediation of contaminated wells.

Core C: Data Management & Analysis

S. Ahalt J. Rager F. Zou

K. Robasky
H. Zhou



Aim 1. Develop the UNC-SRP-wide comprehensive Data Management Plan to include high quality data generation and systems that foster sharing and interoperability.

Aim 2. Facilitate UNC-SRP Project-specific research activities by implementing state-of-the-art bioinformatic and biostatistical methods.

Aim 3. Integrate UNC-SRP data across Projects to understand risks of iAs exposure and mechanisms underlying iAs-associated metabolic dysfunction/diabetes.

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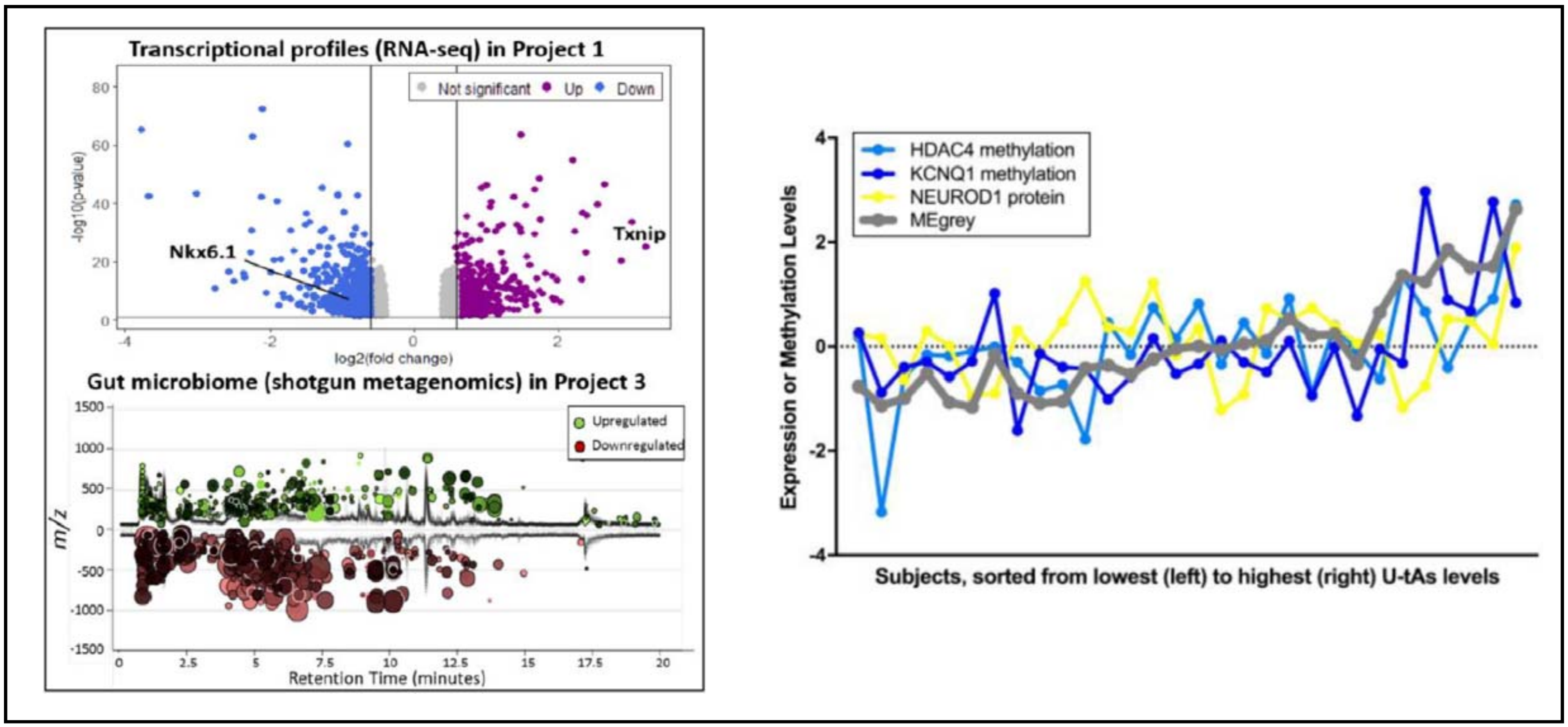
Providing key analysis support for the projects to identify novel mechanisms underlying arsenic-induced metabolic dysfunction.



- ❖ Optimized data sharing
- ❖ Sophisticated analytics
  - ❖ DNA seq
  - ❖ RNA seq
  - ❖ Metabolomic analysis
  - ❖ Mixtures modeling
  - ❖ Data dimension reduction

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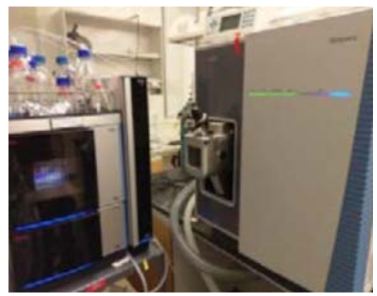
Core D: Chemistry and Analytical

K. Lu

W. Bodnar

P. Cable

C. Liu



Aim 1. Develop and implement analytical methodologies, with a focus on separation, detection and quantitation of metals and their metabolites/species.

Aim 2. Examine toxicant-induced gut microbiome perturbation and metabolic disruption through metagenomics and metabolomics.

Aim 3. Provide consultation to Biomedical and Environmental Science Projects and a supportive environment for graduate student and postdoctoral training on state-of-the-art analytical equipment.

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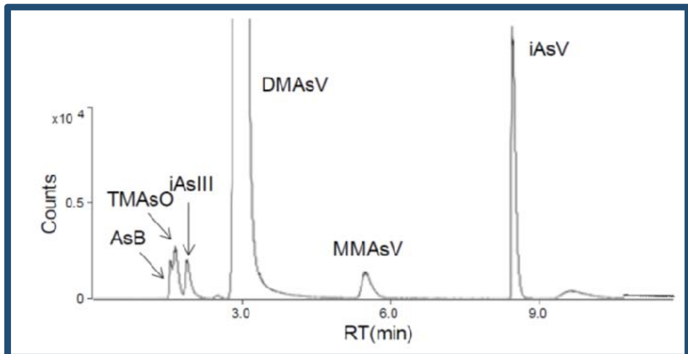
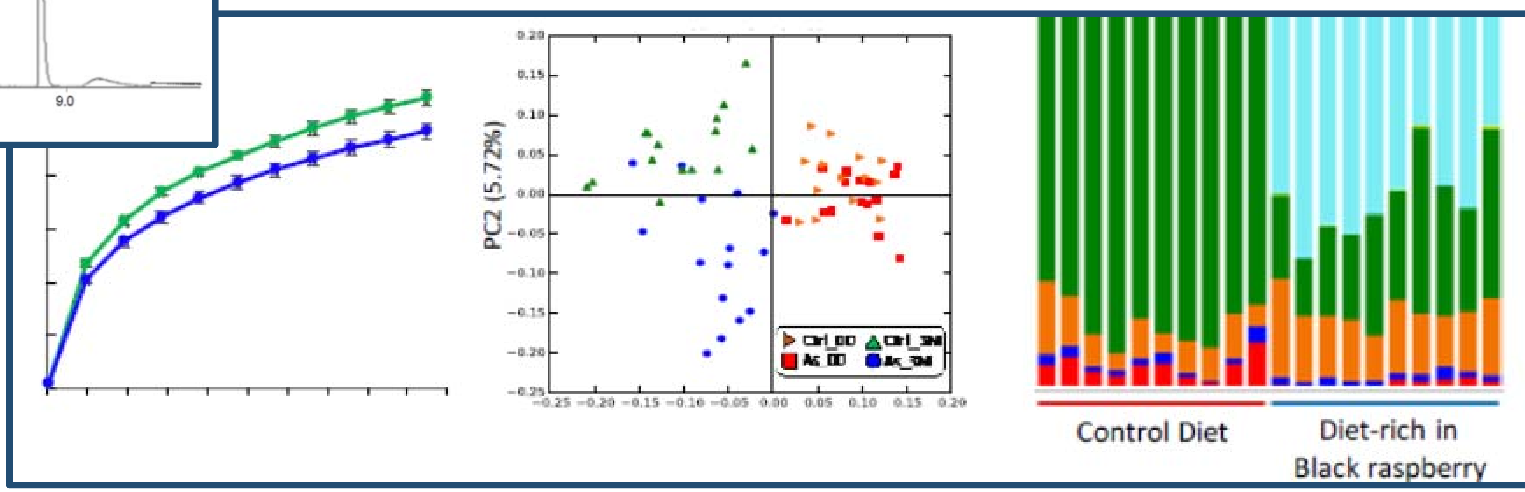
Assessment of the arsenic and its metabolites and co-occurring contaminants to inform how these factors are tied to metabolic dysfunction



- ❖ Assessment of iAs and its metabolites in water and biosamples
- ❖ Expanded analysis for co-occurring contaminants



Core E: Research Experience & Training Coordination

I. Jaspers

M. Rebuli

Z. Gleason

J. Rager

E. Martin wins SRP Karen Wetterhahn Award (Gwen Collman, left)

Aim 1. Enrich **professional career development** and growth of UNC-SRP trainees.

Aim 2. Promote **cohesive approaches** that connect biomedical research, environmental sciences and engineering, and public health.

Aim 3. Foster **outreach** opportunities for trainees to hone skills in community engagement and research translation.

Aim 4. Coordinate opportunities for trainees to obtain skills in 21st century **data analysis methods** through partnership with the data management and analysis core (DMAC).

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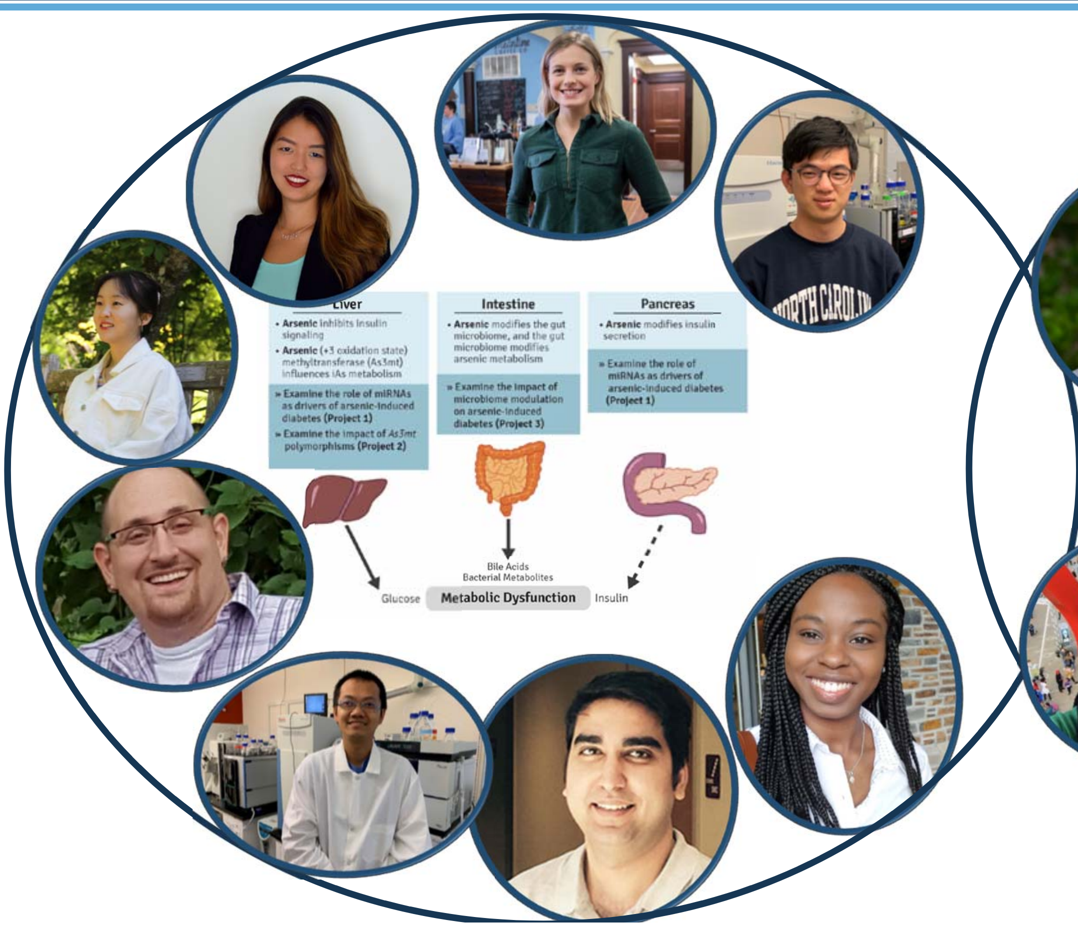

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https://sph.unc.edu/srp/

@UNC_SRP