Dartmouth Toxic Metals
Superfund Research Program

Sources and Protracted Effects of Early Life Exposure to Arsenic and Mercury

Bruce A. Stanton, Ph.D.
Director

Mary Lou Guerinot, Ph.D.
Associate Director

GEISEL SCHOOL OF MEDICINE AT DARTMOUTH

http://www.dartmouth.edu/~toxmetal/

Dartmouth Superfund Program

- The Dartmouth Superfund Research Program uses an interdisciplinary approach to investigate the ways in which arsenic and mercury in the environment affect ecosystems and human health.

- Our research is highly relevant to the mission of the SRP because **arsenic and mercury are two of the top three environmental chemicals of concern regarding human health in the US**.

- Work with our stakeholders to: (1) Reduce exposure to arsenic in well water, rice and rice products, and (2) Reduce exposure to mercury (eating low mercury fish and reduce coal burning emissions of mercury).

Arsenic Uptake, Transport and Storage in Plants

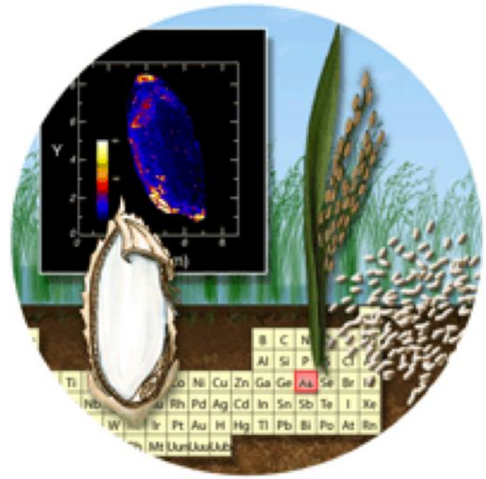
Project Leader:

Mary Lou Guerinot Ph.D.

Associate Director, Toxic Metals Superfund Research Program

Professor, Biological Sciences

Dartmouth College



Project Co-Leader:

David E. Salt Ph.D.

Professor and 6th Century Chair, University of Aberdeen

PERSPECTIVE

doi:10.1038/nature11909

Using membrane transporters to improve crops for sustainable food production

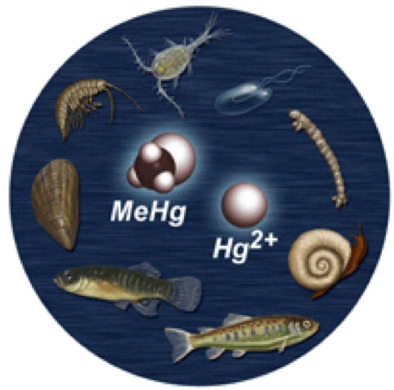
Julian I. Schroeder[1], Emmanuel Delhaize[2], Wolf B. Frommer[3], Mary Lou Guerinot[4], Maria J. Harrison[5], Luis Herrera-Estrella[6], Tomoaki Horie[7], Leon V. Kochian[8], Rana Munns[2,9], Naoko K. Nishizawa[10], Yi-Fang Tsay[11] & Dale Sanders[12]

http://www.ncbi.nlm.nih.gov/pubmed/23636397

Methylmercury Production and Fate in Response to Multiple Environmental Factors

Project Leader:

Celia Y. Chen, Ph.D.
Research Professor
Department of Biological Sciences
Dartmouth College



Project Co-Leaders:

Robert Mason, Ph.D.
Professor of Marine Sciences, University of Connecticut

Nicholas S. Fisher, Ph.D.
Distinguished Professor & Director, Consortium for Inter-Disciplinary Environmental Research, Stony Brook University

OPEN ACCESS Freely available online PLOS ONE

Experimental and Natural Warming Elevates Mercury Concentrations in Estuarine Fish

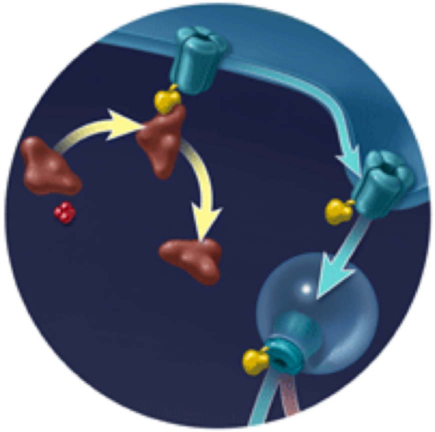
Jennifer A. Dijkstra[1]*, Kate L. Buckman[2], Darren Ward[3], David W. Evans[4], Michele Dionne[1], Celia Y. Chen[2]

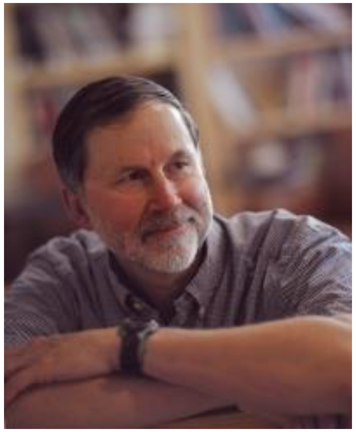
http://www.ncbi.nlm.nih.gov/pubmed/23554891

Arsenic and Innate Immune Function of the Lung

Project Leader:

Bruce A. Stanton, Ph.D.
Director, Toxic Metals
Superfund Research Program
Professor, Department of Microbiology and Immunology
Andrew C. Vail Professor
Geisel School of Medicine at Dartmouth





Other Research Team Members:

Tom Hampton, M.S.

Approaches to Limiting Human Exposure to Arsenic. The Arsenic Prevention and Control Consortium.

Current Environmental Health Reports, in press, 2015

Arsenic Epidemiology, Biomarkers and Exposure Assessment of Metals

Project Leader:
Margaret R. Karagas, Ph.D.

James W. Squires Professor
Professor and Chair
Department of Epidemiology
Geisel School of Medicine at Dartmouth

Project Co-Leaders: Zhigang Li Ph.D., Lisa Chasan-Taber Sc.D., Emily Baker M.D.
Consultants: Susan Korrick Ph.D. (Harvard University), Yu Chen Ph.D. (New York University)

ehp ENVIRONMENTAL HEALTH PERSPECTIVES
http://www.ehponline.org

Blood Pressure Changes in Relation to Arsenic Exposure in a U.S. Pregnancy Cohort

Shohreh F. Farzan, Yu Chen, Fen Wu, Jieying Jiang, Mengling Liu, Emily Baker, Susan A. Korrick, Margaret R. Karagas

http://dx.doi.org/10.1289/ehp.1408472

Received: 25 March 2014
Accepted: 18 March 2015
Advance Publication: 20 March 2015

http://www.ncbi.nlm.nih.gov/pubmed/25793356

Dartmouth Superfund Program Cores

- **Trace Element Analysis Core**: Brian Jackson, Ph.D.

TECHNICAL NOTE

View Article Online
View Journal

CrossMark
click for updates

Cite this: DOI: 10.1039/c5ja00049a

Fast ion chromatography-ICP-QQQ for arsenic speciation

Brian P. Jackson*

- **Training Core**: Bruce Stanton, Ph.D.

  Alan Alda Communication Workshops, Science Writers Workshop, NE Regional SRP Workshop

Dartmouth Works With Alda Center for Communicating Science

Dartmouth Superfund Program Cores

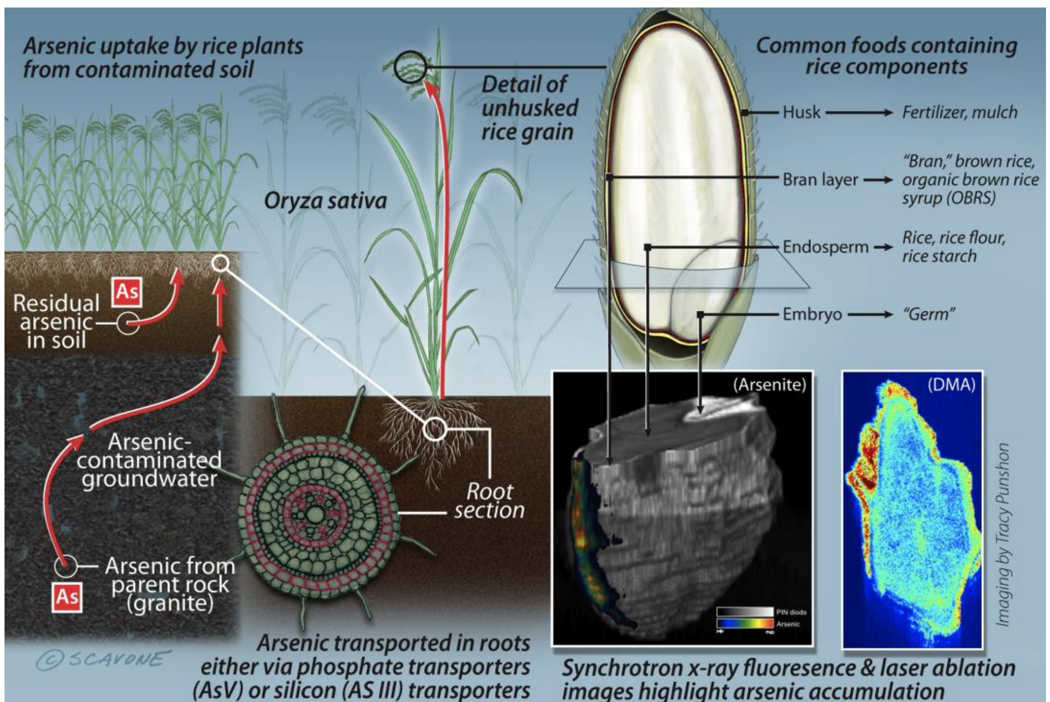
- **Research Translation Core**: Laurie Rardin and Celia Chen, Ph.D.
  Stakeholder outreach on arsenic, mercury and Superfund sites to DES, CDC, ATSDR, EPA and 27 others.
- **Community Engagement Core:** Kathrin Lawlor and Mark Borsuk, Ph.D.
  DES Grant: Private well outreach in 6 NH communities
  EPA Environmental Education Grant: to engage school children and teachers to monitor private wells for arsenic

Solutions to the Problem

Through our research, training, translation and community engagement we will provide relevant information to empower our stakeholders and the communities with whom we engage to make informed decisions to reduce their exposure to arsenic and mercury and, thereby, improve public health.

Project 1: Arsenic Uptake, Transport and Storage in Plants

Project Leader: Mary Lou Guerinot, Ph.D.
Associate Director and Professor of Biological Sciences



Arsenic in Rice

Importance of the problem:

Arsenic, a Class I non-threshold carcinogen, is being found in rice, a staple food eaten by half the world every day

Many rice-based foods are on the market, including infant rice cereals and formula

People with allergies to gluten (Celiac disease) consume many rice-based products

http://www.dartmouth.edu/~toxmetal/arsenic/food.html

- Arsenic occurs naturally in soil and ground water and was used for many years in pesticides.

- Several factors contribute to rice being an efficient accumulator of arsenic relative to other cereals:

-Cultivation in flooded paddies that leads to arsenite [As(III)] mobilization

-Inadvertent uptake and transport of As(III) through the silicon (Si) pathway which is highly efficient in rice

-Inadvertent uptake and transport of arsenate [As(V)] through phosphate transporters

- There are currently no statutory limits for the arsenic content of food sold in the United States and the European Union.

- To protect consumers from excessive exposure, the Codex Alimentarius Commission (FAO/WHO) recommends that the level of arsenic in rice should not exceed 0.2 mg/kg (issued April 2014).

- A study by our SRP group (Project 4) calculated that consumption of 0.56 cup/day of cooked rice was comparable to drinking 1 L/d of 10 µg As/L water, the current US maximum contaminant limit. (Gilbert-Diamond et al. 2011 PNAS 108: 20656)

- To put this number in perspective, US rice consumption averages ~0.5 cup/day, with Asian Americans consuming an average of >2 cups/day.

Consumer Reports
January 2015

The New Rice Rules: 7 Points per Week

We used our new data and analysis to assign a point value to types of rice foods. On average, we recommend getting no more than 7 points per week. Risk analysis is based on weight, so a serving of any food will give children more points than adults.

Products	Serving Size	Child Points [1]	Adult Points [1]
Infant Rice Cereal	¼ cup uncooked	1¼	NA
Rice Cereal, Hot	¼ cup uncooked	8¼	3½
Rice Cereal, Ready to Eat	1 cup	4½	2¼
Rice Drinks	1 cup	4	2
White Basmati [2] or Sushi Rice	¼ cup uncooked	2½	1½
All Other Rice	¼ cup uncooked	5½	3½
Rice Pasta	2 ounces uncooked	7¼	3
Rice Cakes	1 to 3 rice cakes	6¼	2½
Rice Crackers	16 to 18 crackers	2¾	1¼

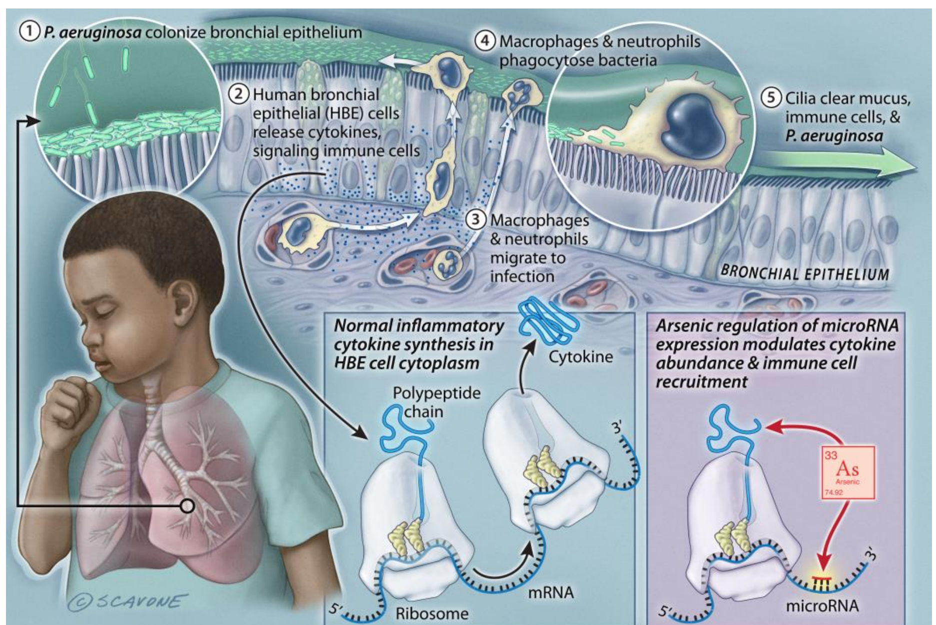
Solutions to the Problem

- Rice cultivars that restrict arsenic accumulation in the grain offer one of the simplest, fastest and most cost effective approaches to solving the problem of arsenic contamination of rice and rice-based products.

- Such cultivars could immediately be used in arsenic-rich soils and can also be used as genetic stock for breeding programs to introduce low grain arsenic traits into agronomically-improved varieties suitable for modern commercial rice production.

Project 3: Arsenic and Innate Immune Function of the Lung

Project Leader: Bruce A. Stanton, Ph.D.
Director and Professor of Microbiology and Immunology

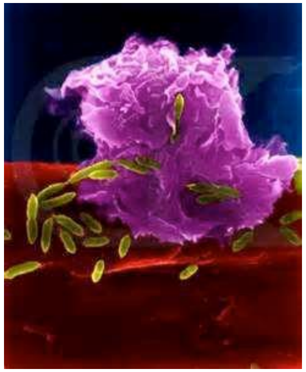


Arsenic and Respiratory Disease

- Arsenic ingestion increases the incidence of respiratory (lung) bacterial and fungal infections.

- Respiratory infections are the third most frequent cause of death worldwide (6.2 million/year-World Health Organization).

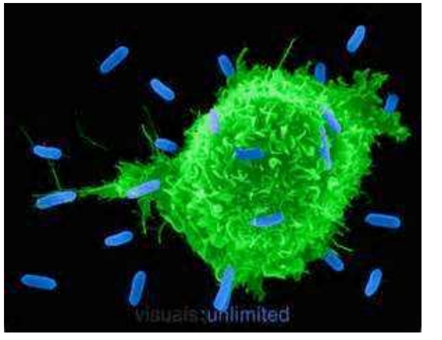
- *In utero* arsenic exposure increases respiratory infections and dysregulates the fetal immune system (Project 4 - Karagas - 2014)



Innate Immunity

- Bacterial infections increase the secretion of interleukins, which recruit macrophages and neutrophils to the lungs

- Macrophages and neutrophils kill bacteria

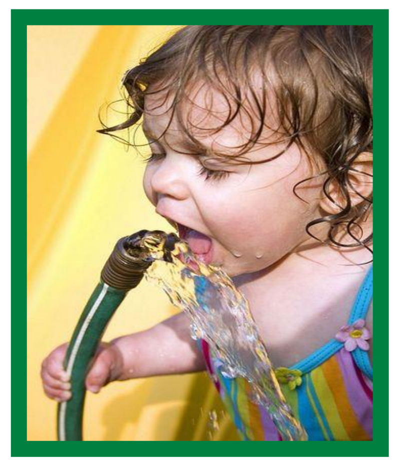


- *Excessive* or *inadequate* cytokine release leads to inappropriate immune cell clearance of bacteria and chronic, irreversible lung damage and death.

- Studies in Project 3 have observed that low levels of arsenic, typical of US exposure, disrupt interleukin secretion and the ability of macrophages to kill bacteria in the lung.

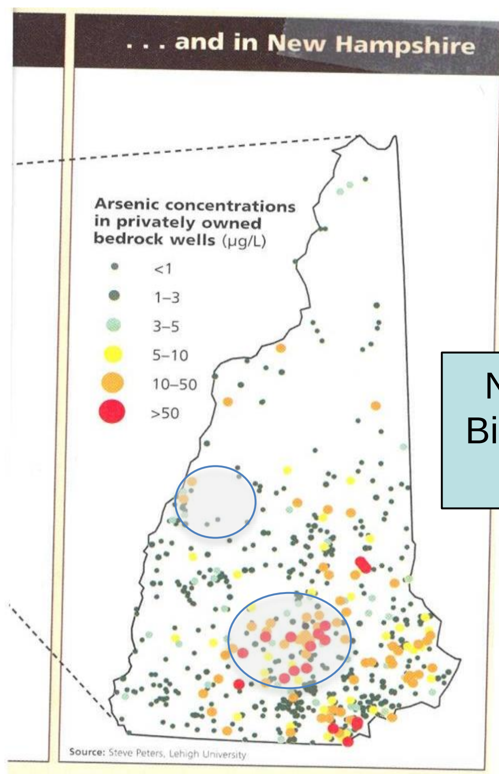
Solutions to the Problem

- Educate and work with state legislators, journalists and public advocacy groups to increase awareness. Project 3 has worked with NH and Maine state legislators to pass bills to inform new home owners of arsenic in well water.
- Work with the FDA to establish regulations for arsenic in food and in well water.



Project 4: Epidemiology, Biomarkers and Exposure Assessment of Metals

Project Leader: Margaret Karagas, Ph.D.
Professor and Chair, Department of Epidemiology



New Hampshire Birth Cohort Study Areas

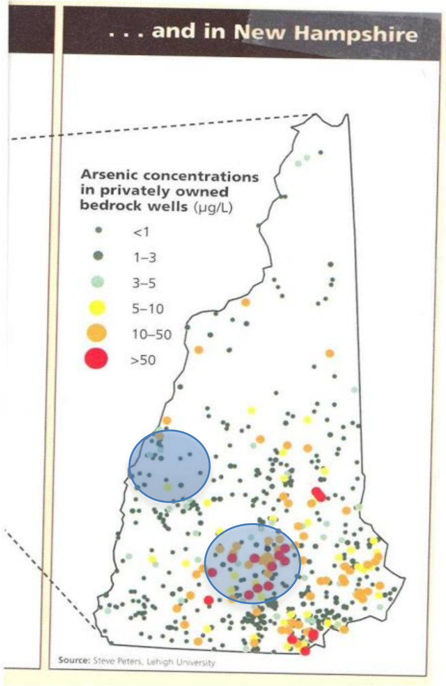
Project 4 Goals

I. To investigate whether higher arsenic exposure influences cardiovascular disease risk factors in pregnant women i.e., alters glucose metabolism, blood pressure and markers of systemic inflammation and vascular endothelial cell dysfunction.

II. To investigate whether in utero arsenic exposure is related to cardiometabolic factors (i.e., glucose metabolism, inflammatory and vascular endothelial cell markers) in the newborn.

The New Hampshire Birth Cohort

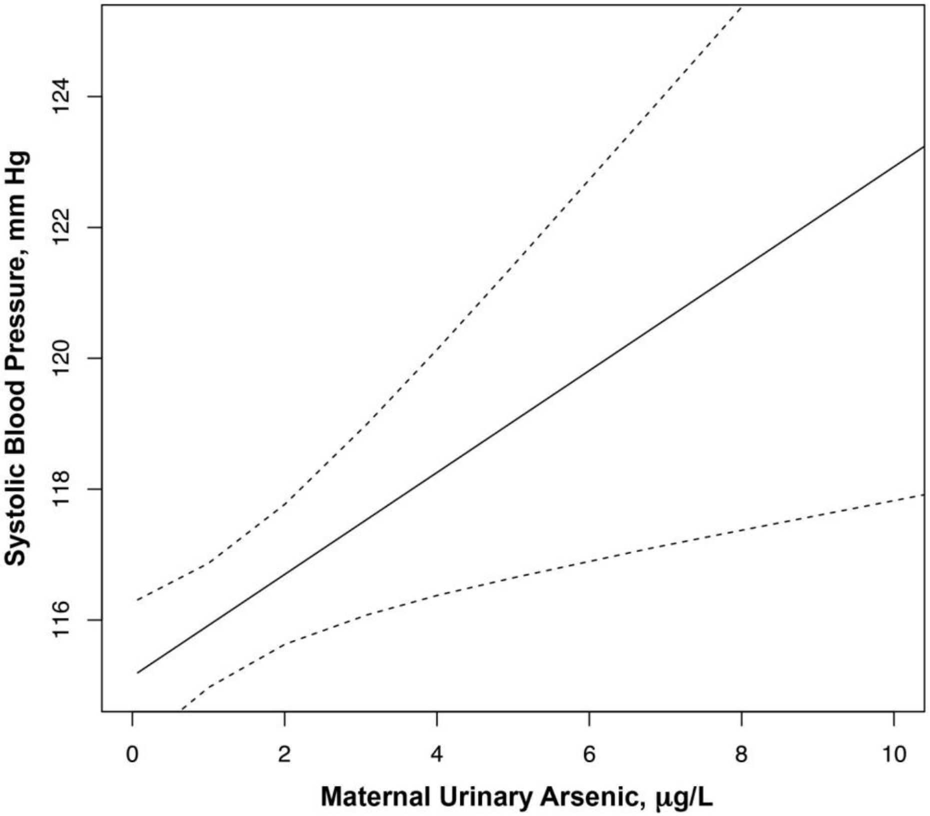
Pregnancy as susceptible window for As exposure



- **Private well users**
- **1,200+ mother-infant pairs**
- **75% response rate**
- **100% urinary arsenic**

Arsenic is Related to Greater BP Increases Over the Course of Pregnancy

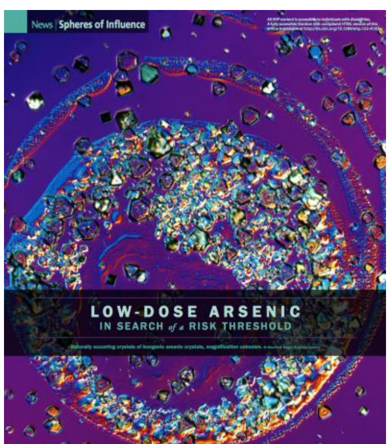
- Over the course of pregnancy, each **10µg/L** increase in urinary As was associated with:
  - **0.31 mmHg** (95% CI: 0.04, 0.57, p = 0.022) greater increase in systolic blood pressure <u>per month</u>
  - **0.28 mmHg** (95% CI: 0.05, 0.52; p=0.018) greater increase in pulse pressure <u>per month</u>



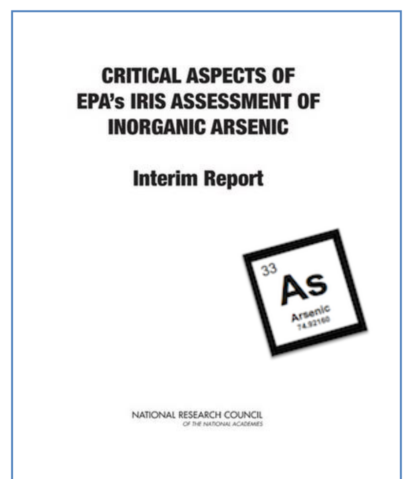
http://www.ncbi.nlm.nih.gov/pubmed/25793356

Solutions to the Problem

- Our work is determining the effects of low level arsenic exposure during pregnancy and contributing to the scientific communication of the health impacts, through:
  - Publications/media releases, including primary research and other reports
  - Participation in lay publications (e.g., Consumer Reports), consensus panels and committees e.g., the NRC committee to evaluate the EPA IRIS
  - Co-leading C-Farr initiative



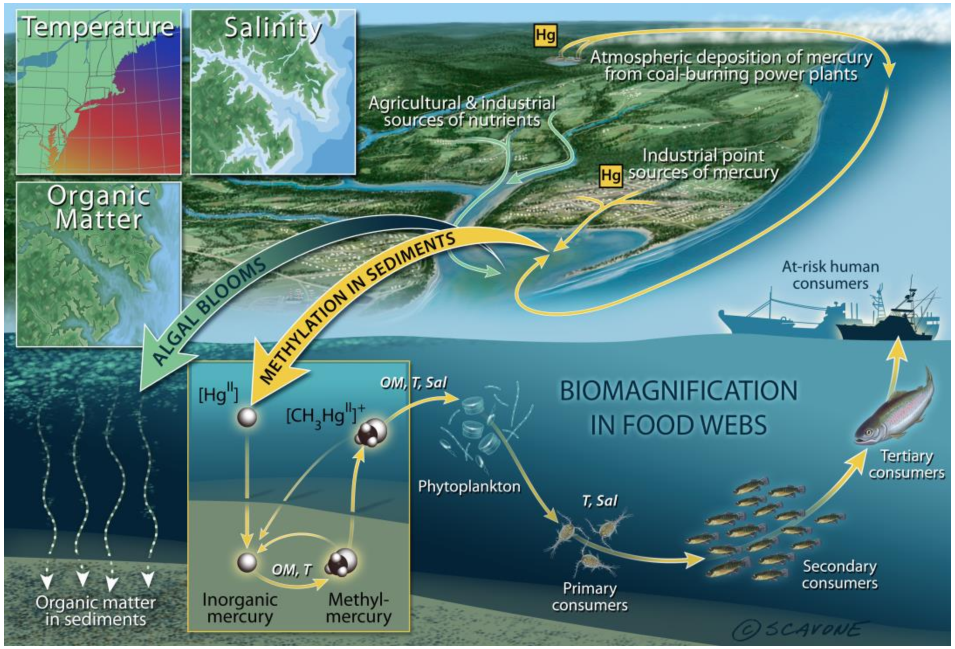

Annals of Internal Medicine
Editorial
Arsenic and Cardiovascular Disease: New Evidence From the United States



Dartmouth Toxic Metals
Superfund Research Program

Project 2: Methylmercury Production and Fate in Response to Multiple Environmental Factors

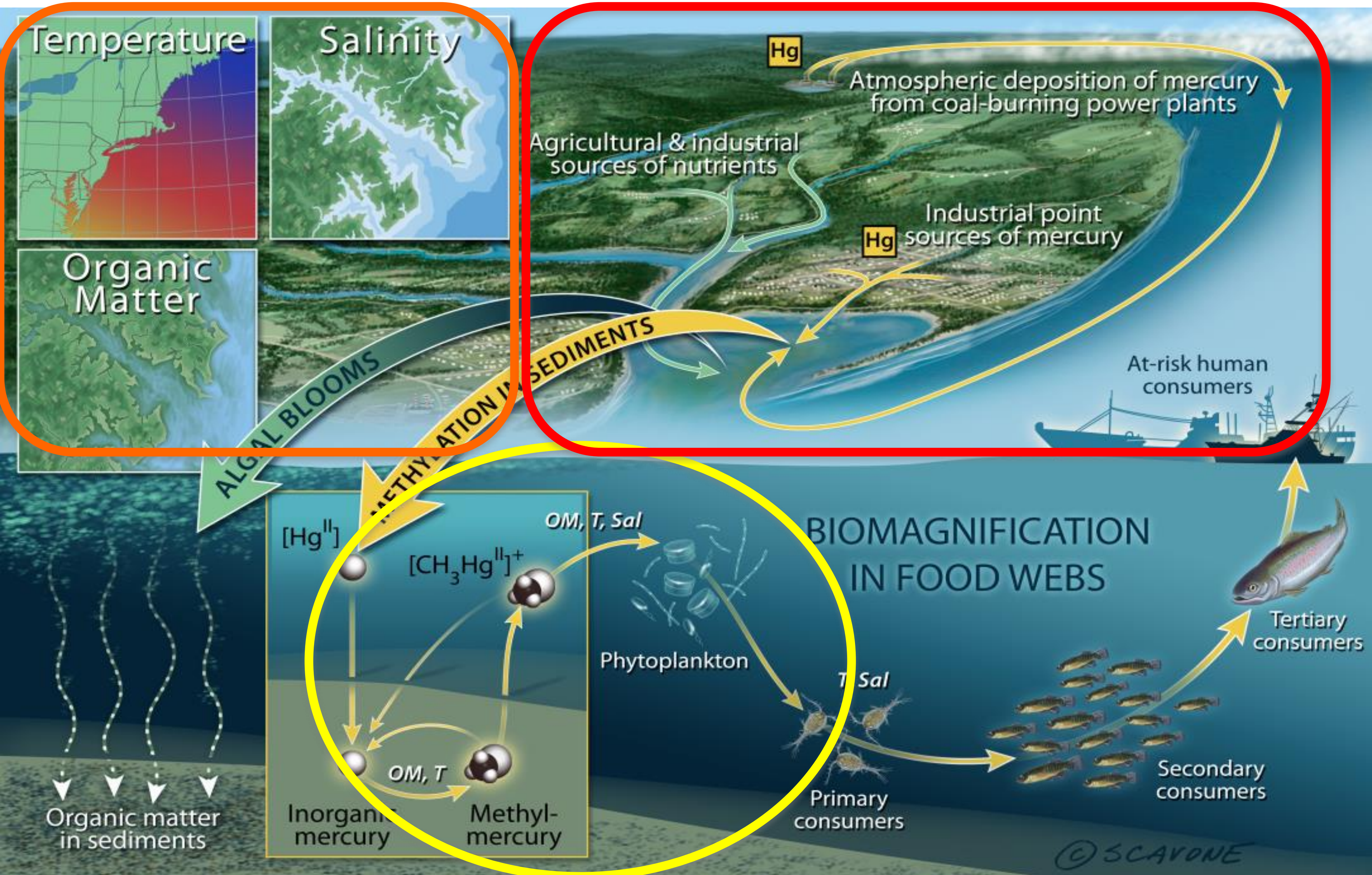
Project Leader: Celia Chen, Ph.D.
Professor of Biological Sciences



Climate Change Effects on Marine Mercury

- *Increased temperatures:*
  - Increased methylation rates and uptake of mercury and methylmercury by biota
- *Increased rainfall, runoff and stream flow:*
  - Increased loading of nutrients and mercury from watershed
  - Increased productivity and biomass dilution
  - Increased carbon flux to sediments and water column
  - Decreases in salinity downstream
- *Sea level rise:*
  - Increased salinity upstream
  - Increased submergence of soils and mercury methylation

Climate Change Effects on Marine Mercury

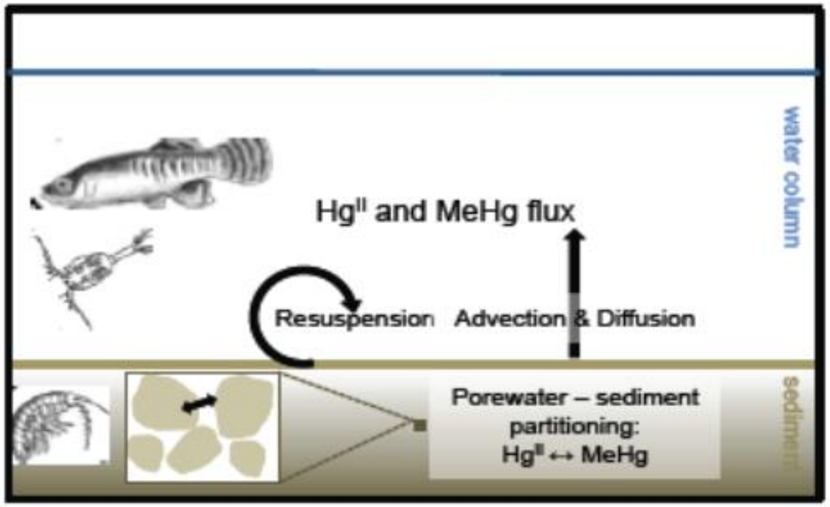


Research Goals

To examine individual and combined effects of three climate-induced factors, temperature, salinity and organic carbon (OC) inputs on:

- Methylmercury production in estuarine sediments and flux to water column

- Bioaccumulation by lower trophic levels of the estuarine food web



Solutions to the Problem

- Global, national, and local policies to reduce mercury emissions and discharges to the atmosphere (e.g., Minimata Treaty, U.S. Mercury Rule, Coastal and Marine Mercury Research Consortium-C-MERC)

- Global policies to evaluate the effectiveness of the Minimata Treaty (UNEP Fate and Transport Partnership)

- Educating the public about the *risks and benefits* of consuming seafood

Dartmouth Toxic Metals
Superfund Research Program

Trace Element Analysis Core

PI: Brian Jackson, Ph.D., Co-I Tracy Punshon, Ph.D.

- **Core service center supporting Dartmouth SRP**

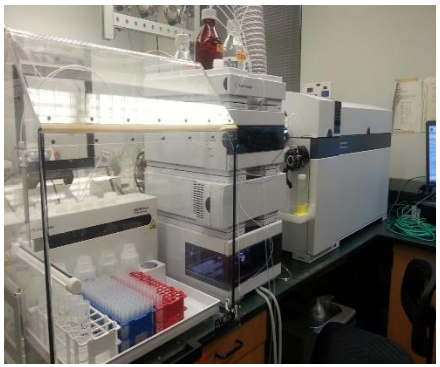
- **Services**
  - Trace metal analysis
  - Mercury speciation
  - Arsenic speciation
  - Method development
    - LC-ICP-MS speciation methods
    - LA-ICP-MS for elemental (bio)imaging

- Training
  - Vivien Taylor;
  2014 KC Donnelly fellowship

Trace Element Analysis Core

<u>State of the art instrumentation</u>

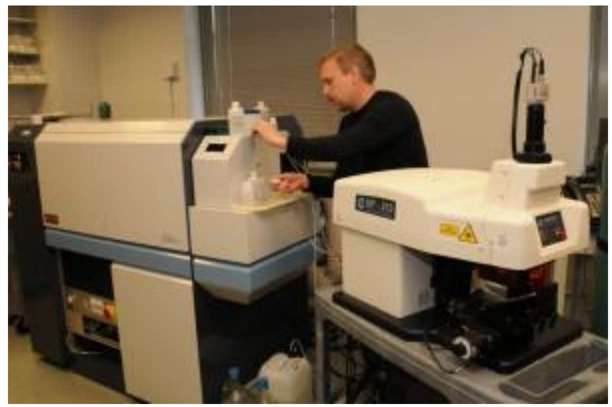
- New reaction Cell triple quad-ICP-MS



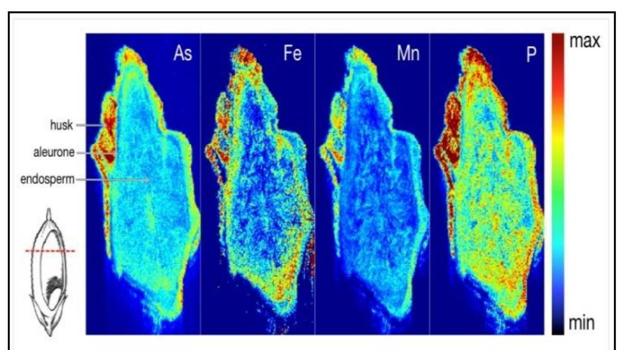
8800 QQQ-ICP-MS
High sensitivity
Low detection limits
(< 5 PPT: parts per trillion for As)

Elemental speciation and bio-imaging

<u>Laser ablation-ICP-MS</u>

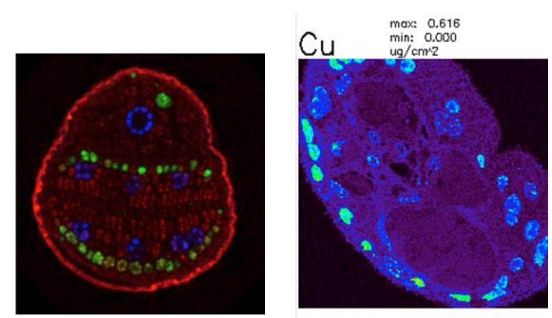


LA-ICP-MS images of arsenic distribution in rice grain



<u>Synchrotron XRF imaging</u>

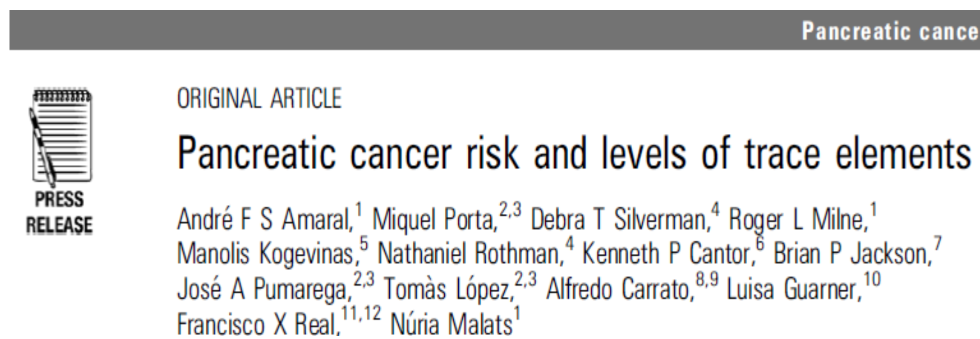
Collaborations with three US synchrotrons: methods for a range of tissue from plants (Arabidopsis seed, left) and animals (Human placenta, right)



Trace Element Analysis Core Collaboration

Analysis of arsenic in GF-foods in support of CEC

Trace metal analysis of toenails
Support for Project 4 and collaboration with:
National Cancer Institute
Spanish National Cancer Research Center



Pancreatic cancer

PRESS RELEASE

ORIGINAL ARTICLE

Pancreatic cancer risk and levels of trace elements

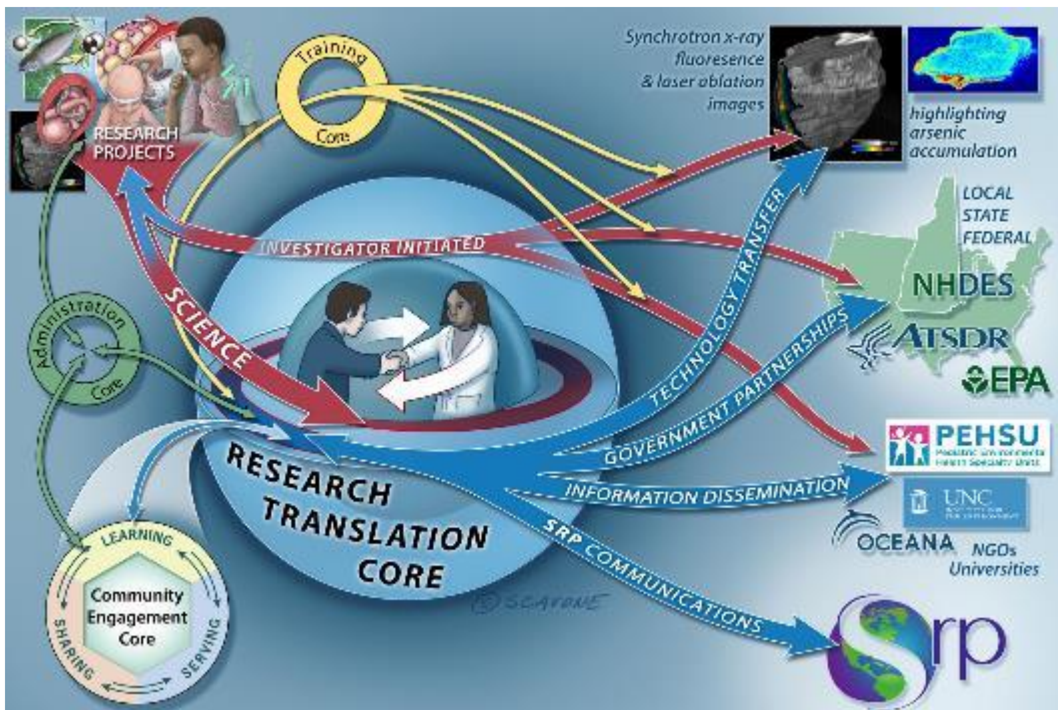
André F S Amaral,[1] Miquel Porta,[2,3] Debra T Silverman,[4] Roger L Milne,[1] Manolis Kogevinas,[5] Nathaniel Rothman,[4] Kenneth P Cantor,[6] Brian P Jackson,[7] José A Pumarega,[2,3] Tomàs López,[2,3] Alfredo Carrato,[8,9] Luisa Guarner,[10] Francisco X Real,[11,12] Núria Malats[1]

Gut; 2011

Research Translation Core

Core Leader: Celia Chen, Ph.D.

Coordinator: Laurie Rardin, M.S.



Research Translation Core Aims

1. Assist U.S. Environmental Protection Agency (EPA) at Superfund sites: Callahan Mine, ME, Berlin, NH, Berry’s Creek, NJ, Penobscot River, ME

2. Share innovative methods: low-level detection, speciation, imaging of metals

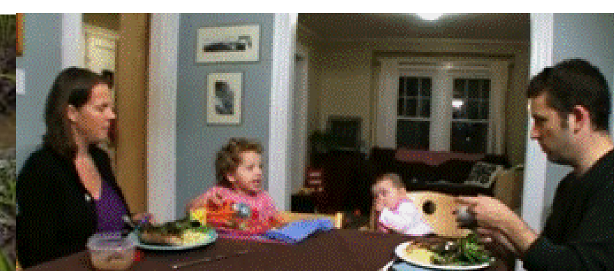
3. Facilitate dialogue between scientists and policy-makers on sources and effects of arsenic exposure

4. Collaborate with the Agency for Toxic Substances and Disease Registry, EPA, New England Pediatric Environmental Health Specialty Unit on risk decisions on Arsenic in food and water and Mercury in fish

5. Provide opportunities for researchers and trainees to communicate research and develop relationships

6. Develop a centralized website on Arsenic and Mercury





Alan Alda Center for Communicating Science

AT STONY BROOK UNIVERSITY

North Atlantic Chapter SETAC

Dartmouth Workshop

Attendees from multiple institutions and agencies throughout New England

NAC-SETAC 2015 Annual Meeting

Communicating Chemical and Environmental Risk

Session on Research Translation and Community Engagement ● collaboration with Brown SRP

NH Arsenic Consortium 2014 Annual Meeting

● 24 stakeholder groups represented

Next Meeting February 2016

Arsenic in Private Wells in NH

Working with our Community Engagement Core to evaluate rate of and barriers to treatment and testing and evaluate interventions.

C-FARR *Collaborative on Food with Arsenic & associated Risk & Regulation*

Bringing together an interdisciplinary group of scientists and policy stakeholders to synthesize the science and identify knowledge gaps relevant to policy on arsenic in food to produce peer reviewed synthesis papers for a special journal issue.

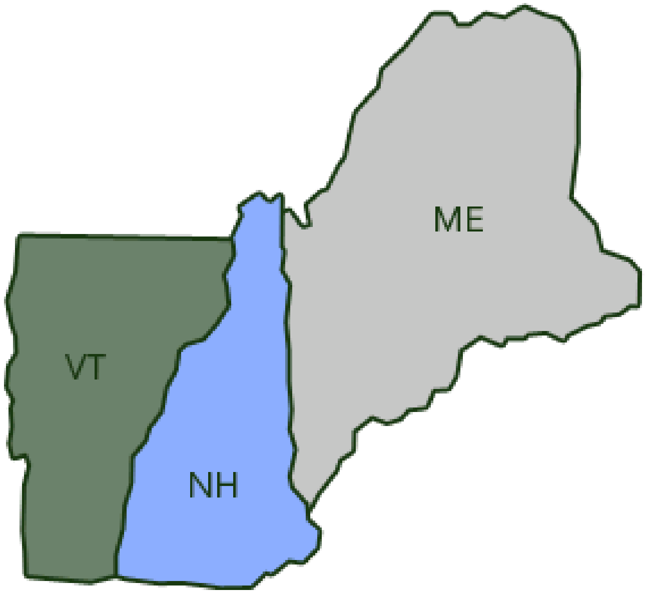
Arsenic in Food and Water Website

The website will allow visitors to understand cumulative arsenic exposure to make informed lifestyle decisions to reduce their exposure to arsenic and improve their long-term health.

Community Engagement Core

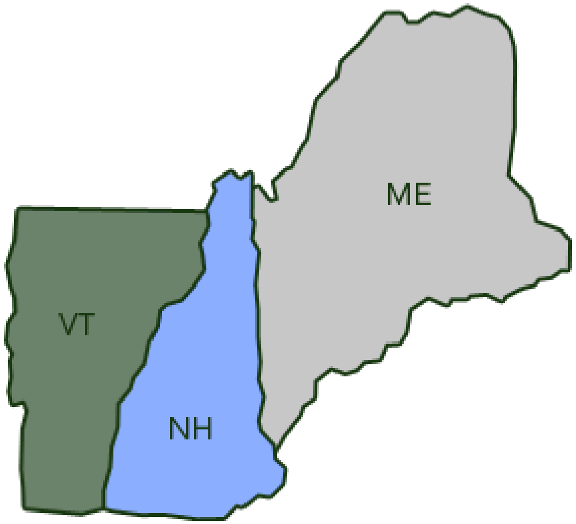
Core Leader: Mark Borsuk, Ph.D.

Coordinator: Kathrin Lawlor, B.A.



Community Engagement Core Aims

Aim 1: To sustain engagement with community partners in Northern New England to better understand and support healthy decision-making

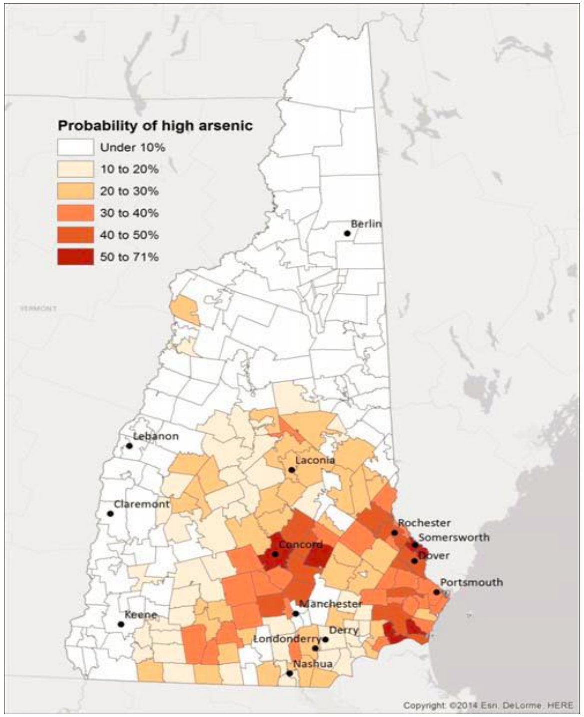


Aim 2: Cultivate opportunities for Dartmouth to serve community partners by providing resources, information, communications, and expertise.

Aim 3: Foster collaborative community-engaged research.

Communities

Arsenic in Private Well Water in NH



Geographic distribution by ZIP code of the probability of arsenic in well water exceeding 10 parts per billion, as estimated by the US Geological Survey model.

Prepared by J. Chipman.

Year One Activities

- Community Focus Groups
- Statewide Survey
- Intervention Selection and Design

Year Two Activities

- Data Storage System for NH Lab Testing Results
- Town Selection Process
- Intervention Planning and Implementation
- Communication Materials Development
- Evaluation
- Toolbox Creation

The Dragonfly Project

- Four High Schools in Vermont and New Hampshire
  - 9 classes total
- Instruction from Trainee Kate Buckman
- Annual Student Symposium at Dartmouth, January 2015.
- Local press coverage of event, including The Valley News, The Berlin Daily Sun, WCAX Channel 3 News

Project Specific RTC and CEC Activities

- **Projects 1, 2 and 4**: C-FARR: Collaborative on Food with Arsenic and Associated Risk and Regulation
- **Project 2**: International mercury policy and Dragonfly Project
- **Project 3**: Arsenic legislation in ME & NH and Arsenic Summit

Stakeholders and Collaborators

- USDA, FDA, EPA, WHO, EFSA (European Food Safety Authority), NH DES, NH DHHS, CT State Legislature, ME State Legislature, Academic Community, California EPA, CT Dept. of Health, US House of Representatives (Rosa DeLauro), USGS, ATSDR, CDC, National Groundwater Association, American Groundwater Trust, Toxics Action Center, Private Water Testing Labs, Water Treatment Companies, Realtors, Local Town Government, Conservation Commissions, Communities in Southeastern NH, and International Mercury Community

- Nick Fisher (SUNY Stony Brook), David Salt (Univ. of Aberdeen), Robert Mason (UCONN), Susan Korrick (Harvard), Yu Chen (NYU)





Dartmouth Toxic Metals
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Sources and Protracted Effects of Early Life Exposure to Arsenic and Mercury

"Working together with the NIEHS, our collaborators and stakeholders, we look forward to continuing to provide cutting edge research to inform policy decisions and community actions that will lead to reduced human exposure to mercury and arsenic and improved public health."

GEISEL
SCHOOL OF
MEDICINE
AT DARTMOUTH

For more information about our program please go to:
http://www.dartmouth.edu/~toxmetal/