UC San Diego
Superfund Research Program

Training Core

Robert Tukey, P.I. (Chem & Biochemistry and Pharmacology)
Michelle Feiock, PM (Pharmacology)

Federal Gov't
- U.S. EPA Reg 9
- CalEPA
- ATSDR
- US Navy
- Mexico EPA (SEMARNAT)

NIEHS

Local Gov't
- City of San Diego
- San Diego Regional Water Quality Board/ Tijuana River Watershed
- 29 Palms Band of Mission Indians

Reproductive Medicine

Mellon
(Mouse Molecular Genetics)
Research Core A

- Neurosciences
- Pharmacology
- Chemistry & Biochemistry

Ellisman, Tsien
Komives
(Multi-Scale Imaging & Proteomics)
Research Core B

Technology Transfer and Intellectual Property Services

Shaw
Technology Transfer

Mellon, Tukey
Training Core

- Reproductive Medicine
- Chem/Biochem
- Pharmacology

Research Translation & Community Engagement Cores

Pezzoli
Al-Delaimy
- Urban Studies & Planning
- Family & Preventative Medicine

Zaslavsky
Spatial Info Integration Lab (Supercomputer Center)

Internal Advisory Committee
Tukey, Karin, Schroeder, Mellon

Research Projects

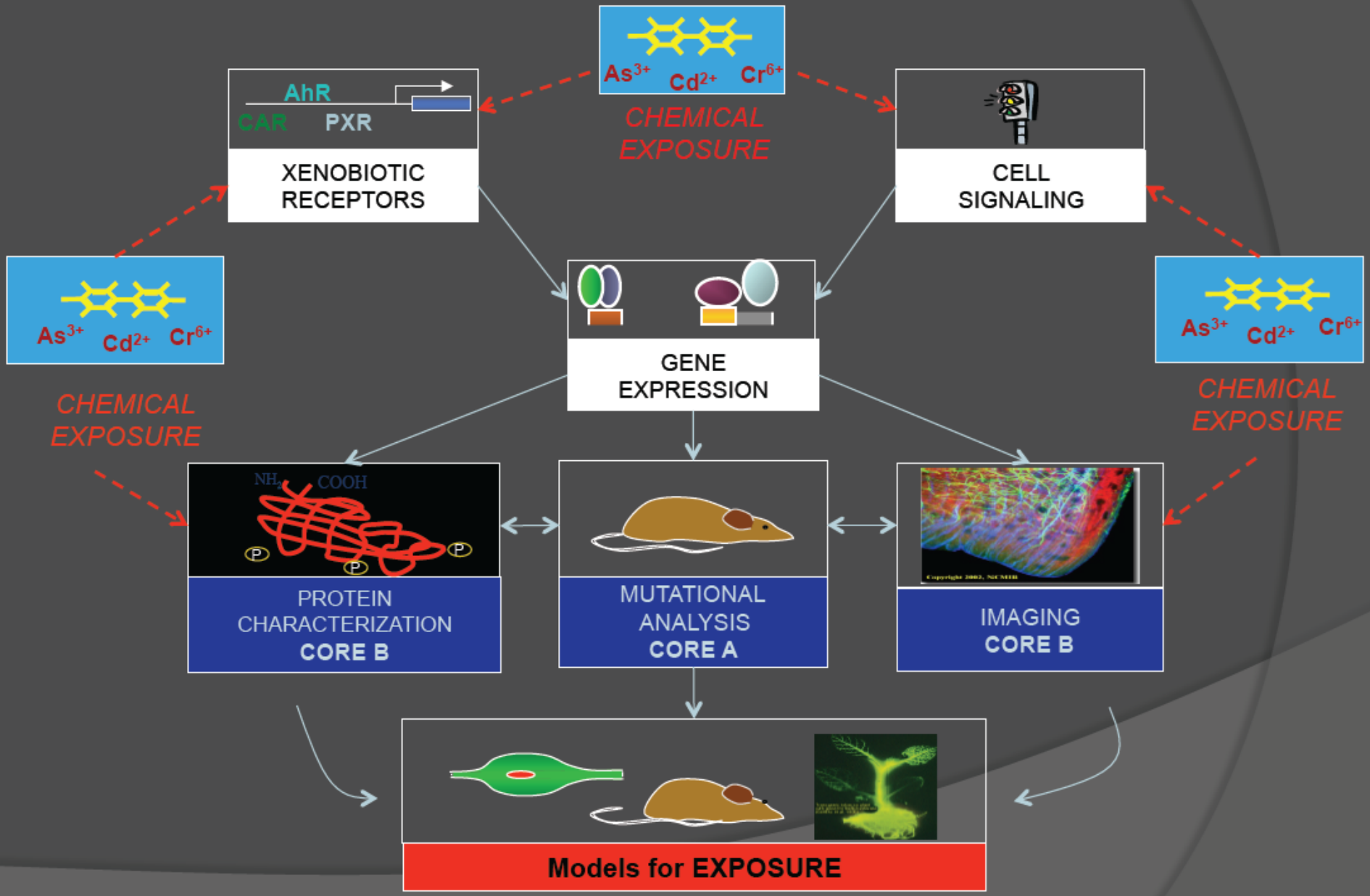
Scripps Research Institute	Salk Institute	Dept Pharmacology (UCSD)	Dept Chemistry Bioch (UCSD)	School of Medicine (UCSD)	Dept Biology (UCSD)
Russell (2)	Evans (3)	Karin (1) Tukey (4) Evans (3)	Tukey (4) Trogler (6)	Seki (5) Brenner (5)	Schroeder (7)

Academic and SRP Partners
- U of Arizona
- Dartmouth
- U of Washington
- U of Oregon
- U of Massachusetts

Research Translation and Community Engagement Partners
- Casa Familiar
- Alter Terra
- 29 Palms Band of Mission Indians
- Industrial Environmental Association
- Wildcoast
- Geosyntec
- Edenspace

External Advisory Committee
- Dr. Eric Johnson
- Dr. Chris Bradfield
- Dr. Max Costa
- Dr. Raina Maier

MOLECULAR MECHANISMS AND MODELS OF EXPOSURE



Detection and Models of Toxicant Exposure

RTC-Pezzoli

COC-Pezzoli

Core A-Mellon

Core B Ellisman & Komives

1-Karin | 2-Russell | 3-Evans | 4-Tukey | 5-Eki Brenner | 6-Trogler | 7-Schroeder

UCSD Superfund Training Core

The primary aim of this Core is to train Ph.D. candidates in the biological, chemical, and molecular sciences as they relate to environmental toxicology, with an emphasis in health, detection, and remediation.

1. Identify students with strong interest in Environmental Health Sciences who have joined labs supported by the Superfund from the variety of allied graduate programs at UC San Diego.
2. Provide training support through Superfund Assistantships to support interdisciplinary Environmental Health Sciences graduate training of three candidates per year.
3. Offer educational opportunities through coursework, the Outreach and Research Translation Cores, guest lecturers, seminars, and meetings that emphasize the unique aspects of the environmental sciences program associated with the Superfund Research Program.
4. Provide travel stipends to attend Superfund national meetings.
5. Provide a strong basis for students to emerge as independent scientists with a broad range of skills and knowledge while maintaining a focus on environmental health sciences.
6. Assure training in ethics and statistics, and the inclusion of under-represented groups in our program.
7. Launch the careers of Ph.D.s in the molecular investigation of toxicology, toxicogenomics, and environmental health sciences.

Trainee List (To Date):

* = Indicates 2013 Current Trainee

Aleman Guillen, Fernando *
Anderson, Craig
Bencheikh-Latmani, Rizlan
Berdy, Sara
Boisson, Aurelien
Bonzo, Jessica
Brace-Sinnokrak, Erin
Butko, Emerald
Butterfield, Cristina
Caputo, Nick
Cavero-Martinez, Santiago
Chen, Alice
Chen, Shu-Juan
Dick, Gregory
Dooley, Colette
Drew, Devin Lee
Gong, Jiming
Hibbs, Ryan
Holzer, Ryan
Jobe, Timothy *
Johnson, Hope
Jonker, Hans
Kim, Juyoun *
Konopnicki, Camille
Lee, David
Li, Tao
Lu, Benson *
Machemer, Daniel
Martin, Victoria
McCarthy, James
Mendoza-Cozatl, David
Miller, Meghan
Noh, Yoon Seok *
Operaña, Theresa
Passino, Melissa
Rodriguez-Gabriel, Miguel
Scott, Michael *
Seneko-Effenberger, Kathy
Shemer, Tamar *
Sonoda, Jun
Sung, Dong Yul
Vashisht, Ajay
Waner, David
Weems, Jessica
Whyte, Jamie *
Witham, Emily
Xie, Qingqing *

Seminar Series

- APR 26, 2013: Mark J. Czaja, Professor, Albert Einstein College of Medicine. "Role of Autophagy in Hepatocyte Metabolism and Survival"
- SEP 26, 2012: David Moore, Professor, Baylor College of Medicine. *Seminar Title: "* CAR : HCC :: ER : BCA"
- MAY 8, 2009: June Medford, Associate Professor, Colorado State Univ. "Biosensors with computer designed input producing detectors for most small molecules using plants."
- MAY 4, 2006: Marie Lynn Miranda, Duke University, Durham, NC. "Using Spatial Analysis to Support Children's Environmental Health Research"
- MAR 10, 2006: Masahiko Negishi, NIEHS. "The Xenosensing Nuclear Receptor CAR-mediated Liver Metabolism and Disease".
- FEB 10, 2005: David A. Schwartz, NIEHS. "Environmental Genomics: A Key to Understanding Human Disease"
- JAN 14, 2005: Sue-Goo Rhee, Chief, Laboratory of Cell Signaling NIH. "Intracellular Messenger Function of Hydrogen Peroxide and Peroxiredoxins"
- JAN 13, 2005: Scott Burchiel, Professor, Univ. New Mexico. "Role of Oxidative Stress by Environmental PAHs in Human Breast Cancer Promotion"
- OCT 7, 2004: Kelvin J. A. Davies, USC. "Protective Roles of the Proteasome and the Lon Protease in Oxidative Stress, Aging, and Disease."
- SEP 20, 2004: Andrei Budanov and Dr. Anna Sablina, Research Fellows, Lerner Research Institute. "p53-modulated sestrins catalyze regeneration of peroxiredoxins" and "Tumor suppressor p53 reduces mutagenesis by stimulating antioxidant defense", respectively.
- AUG 30, 2004: Susan Nowell, Assistant Professor, Roswell Park Cancer Institute. "SULT1A1 genotype and tamoxifen therapy for breast cancer: an exercise in molecular epidemiology".
- AUG 17, 2004: Christoph Moroni, Professor, University of Basel. "PKB/Akt regulation of ARE-dependent cytokine mRNA turnover".
- NOV 7, 2003: Erin Schuetz, Associate Member, St. Jude Children's Research Hospital. *"*Use of Cellular and Animal Models to Test for the Role of Nuclear Hormone Receptors in Environmental Toxicant Signaling*"*
- OCT 1, 2003: Stephen Hecht, Professor, Univ. Minnesota Cancer Center.*"*Cigarette Smoking and Lung Cancer: Chemical Mechanisms and Approaches to Prevention*"*
- AUG 14, 2003: Guri Tzivion, Assistant Professor, Texas A&M Univ., "Intracellular signaling pathways at the junction of cell survival and cell death: Raf, 14-3-3 and MLK"
- APR 10, 2003: Ze'ev A. Ronai, Professor, Mount Sinai School of Medicine, "TRAF2 ubiquitination implications toward stability and diversified IKK/JNK signaling"
- OCT 7, 2002: Samuel Wilson, Deputy Director, NIEHS, "Base Excision Repair in Mammalian Genomic Integrity"
- SEP 23, 2002: Erin Wagner, Deputy Director, Institute of Molecular Pathology, Vienna, Austria, "Functions of Jun and Fos/AP-1 Family Members"
- SEP 12, 2002: Takashi Okamoto, Professor and Chair, Nagoya City University Medical School, "Biological actions of NF κB and its regulation from a viewpoint of newly identified p65-interacting proteins"
- JAN 25, 2002: Nahum Sonenberg, Professor of Biochemistry and Molecular Biology, McGill University, Montreal, Canada, "Signaling to Translation Factors in Control of Cell Growth and Proliferation"
- JUL 25, 2000: Dr. George Thomas, Friedrich Miescher Institute, Basel, "Conditional Deletion of 40S Ribosomal Protein S6 Activities a Novel Cell Cycle Checkpoint"

Coursework

- Statistical Inference (BIOM285) – M. Lawson
- Ethics in Scientific Research (BIOM 219) – J. Trejo and M. Kalichman
- Structural and Quantitative Pharmacology (BIOM230) – T. Handel
- Molecular Pathology of Cancer (BIOM256) – M. Kamps
- Contemporary Topics in the Pharmacological Sciences (BIOM231) – R. Tsien and P. Taylor
- Pharmacogenomics (PHARM/BIOM 235) - O'Connor
- Structural Bioinformatics, Emphasis on Biological Data Representation and Analysis (BIOM201) – P. Bourne
- Enviromental and Molecular Toxicology (Chem 166/266) – R. Tukey
- Modeling Biological Macromolecules (PHAR205) – L. Ten Eyck
- Pharmacologic Analysis of Physiologic Systems (PHAR240) - L. Brunton
- Seminars in Pharmacology (BIOM275A) – M. Simon and J. Trejo
- Seminars in Molecular Pathology (PATH225) – R. Klemke
- Pharmacology and Toxicology (CHEM 118) - R. Tukey
- Molecular Toxicology and Human Health - R. Tukey
- Mass Spectrometry and Contemporary Proteomics (CHEM 283) - E. Komives
- Introduction to Electron Microscopy (NEU 256) – M. Ellisman
- Drug Discovery or Careers in Biomedical Science (BIOM 234) – J. Heller Brown

Superfund Monthly Seminar Series (Program Meetings)

- **---2013---**
- JAN 9- Brenner (Project 5)
- FEB 13- Seki (Project 5)
- MAR 13- Karin (Project 1)
- APR 10- Trogler (Dr. Mike Scott presents) (Project 8)
- MAY 8- Russell (Project 2)
- JUN 12- Evans (Dr. Benson Lu presents) (Project 3)

- **---2012---**
- SEP 12- General Program Meeting
- OCT 10- Tukey (Project 4)
- NOV 14- Pezzoli/Al-Delaimy/Zaslavsky (RTC & CEC)
- DEC 12- Schroeder (Project 7)

Participation in Outreach

Community engagement/research translation opportunities that our trainees participate in:

- 1. Environmental public health assessment and soil testing of toxic hot spots in Tijuana (with the potential to build on this work and do environmental epidemiology along the U.S.-Mexico border--leveraging Dr. Wael Al-Delaimy efforts as Chief of Global Health. (Dr. Al-Delaimy is a co-leader on both our Community Engagement Core and Research Translation Core).

- 2. Phytoremediation of Brownfields (contaminated sites in San Diego). Tim Jobe in Julian Schroeder's lab is currently training a student to help us test plant tissue.

- 3. Data ethics/ integration, visualization and mapping We are working with the San Diego Supercomputer Center on a web-based "Dashboard" interface for sharing the data we collect relevant to our Community Engagement and Research Translation efforts (e.g., information about vacant lots, potentially contaminated, that community groups want to use as community gardens; soil testing data). Dr. Al-Delaimy is seeking funds for a data ethics conference, he could potentially develop this into an opportunity for trainees. Ilya Zaslavsky (on our SRC team) runs the pertinent lab at the Supercomputer Center building the Dashboard.

All three of these opportunities have strong "out-in-the-real-world" components that are tying in with all the major agencies, local, state and federal.

Camille with Dr. Tukey

Graduate Student: Camille Konopnicki
Lab: Dr. Robert Tukey

2006-2012, Chemistry and Biochemistry Graduate Program
Dissertation: "The Intricacies of UGT Regulation: Protein-Protein Interactions and Environmental Arsenic Exposure"

Current: Postdoctoral Fellow at UCSD

Areas of Interest:

- Investigating how environmental toxicant exposure affects important biological processes, such as drug metabolism.
- Understanding the factors that lead to observed differences in drug metabolism between individuals.

Publications:

Konopnicki C.M., Dickmann L., Tracy J., Tukey R.H., Wienkers L.C., and Foti R.S. "Evaluation of UGT Protein Interactions in Human Hepatocytes: Effect of siRNA Down Regulation of UGT1A9 and UGT2B7 on Propofol Glucuronidation in Human Hepatocytes". *Archives of Biochemistry and Biophysics* (2013).

Konopnicki C.M., Fujiwara R., and Tukey R.H. "The Regulatory Role of Oral Arsenic in Humanized *UGT1* Mice". *In preparation.*

Graduate Student Emily Witham
Pamela Mellon's Laboratory

2008-2012, Biomedical Sciences Program
Dissertation: "Androgen Receptor and Kisspeptin Receptor: Roles in Reproduction"

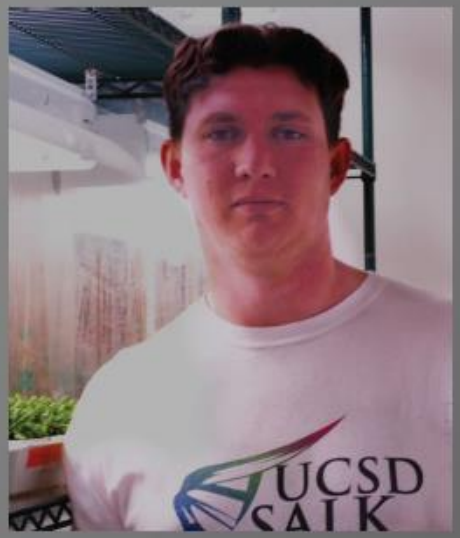
Currently,
Postdoctoral Fellow,
The Scripps Research Institute, La Jolla

Areas of Interest:
Prenatal Exposure
Affects of Endocrine Disruptors

Publications:

1. **Witham, E. A.**, Meadows*, J. D., Shojaei*, S., Kauffman, A. S., and Mellon, P. L. (2012). Prenatal Exposure to Low Levels of Androgen Accelerates Female Puberty Onset and Reproductive Senescence in Mice. *Endocrinology* 153: 4522-4532. *equivalent contributions. PMID 22778229, PMC3423623
2. Xie, H., Cherrington, B. D, Meadows, J. D., **Witham, E. A.**, and Mellon, P. L. (2013). The Homeodomain Protein, Msx1, Represses the αGSU and GnRH Receptor Genes During Gonadotrope Development. *Molecular Endocrinology* 12, 422-436. PMID 23371388, PMC3589667
3. **Witham, E. A.**, Meadows, J. D., Hoffmann, H. M., Shojaei, S., Coss, D., Kauffman, A. S., and Mellon, P. L. Kisspeptin Regulates Gonadotropin Genes Via Immediate Early Gene Induction in Pituitary Gonadotropes. Submitted.
4. Brayman, M. J., Meadows, J. D., **Witham, E. A.**, Hashimoto Partyka, M., Iruela Arispe, M. L., and Mellon, P. L. Decreased Fertility in Female Mice Lacking Neuronal Progesterone Receptor. Submitted.
5. Witham*, E. A., Shojaei*, S., Meadows, J.D., and Mellon, P. L. Androgen Receptor (AR)-mediated regulation of Gonadotropin-Releasing Hormone (GnRH) Receptor. In preparation.

Graduate Student Tim Jobe, Julian Schroeder's Laboratory



Areas of Interest:

- Identification and characterization of toxic heavy metal and arsenic transporters
- Identification and characterization of toxic heavy metal sensing mechanisms
- Genome-wide screens for novel genes involved in toxic metal tolerance
- Systems biology approaches to understand toxic heavy metal regulated gene networks

Publications:

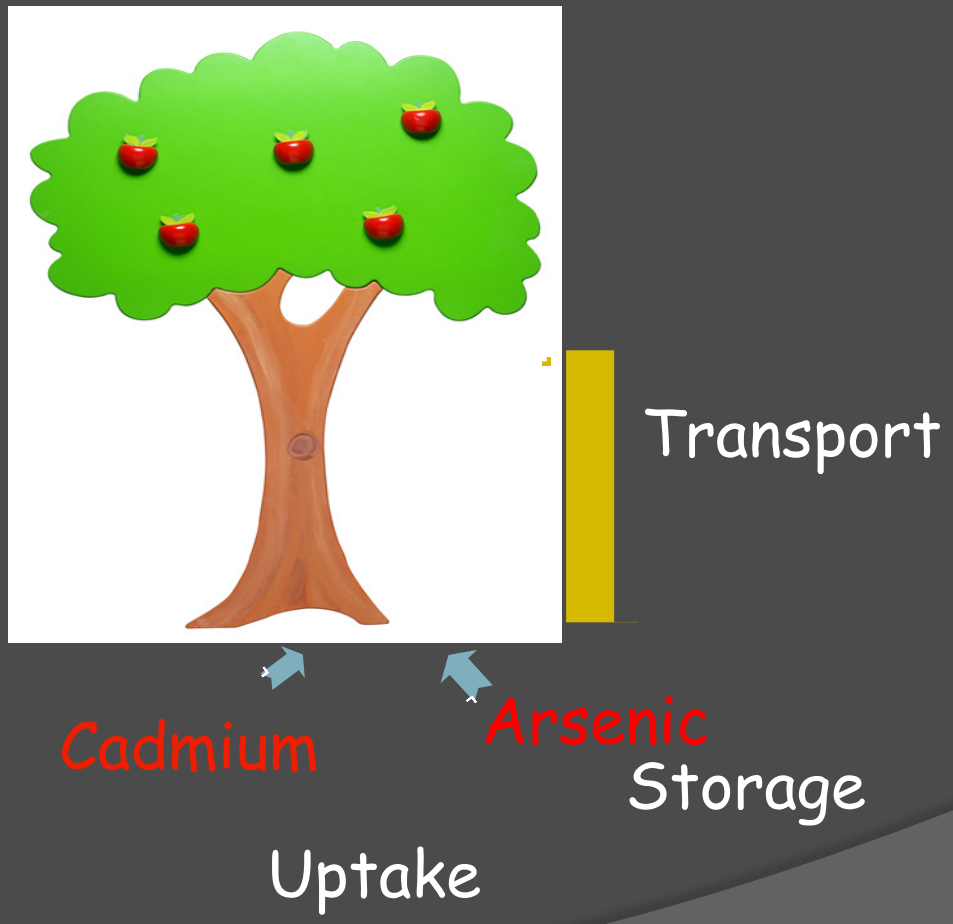
Jobe, T. O., Sung, D.-Y., Akmakjian, G., Pham, A., Komives, E. A., Mendoza-Cózatl, D. G. and Schroeder, J. I. (2012), Feedback inhibition by thiols outranks glutathione depletion: a luciferase-based screen reveals glutathione-deficient γ-ECS and glutathione synthetase mutants impaired in cadmium-induced sulfate assimilation. *The Plant Journal, 70, 783-795.*

Mendoza-Cózatl, D.G., **Jobe, T.O.**, Hauser, F. and Schroeder, J.I. (2011) Long-distance transport, vacuolar sequestration, tolerance, and transcriptional responses induced by cadmium and arsenic. *Current Opinion in Plant Biology, 14, 554-562.*

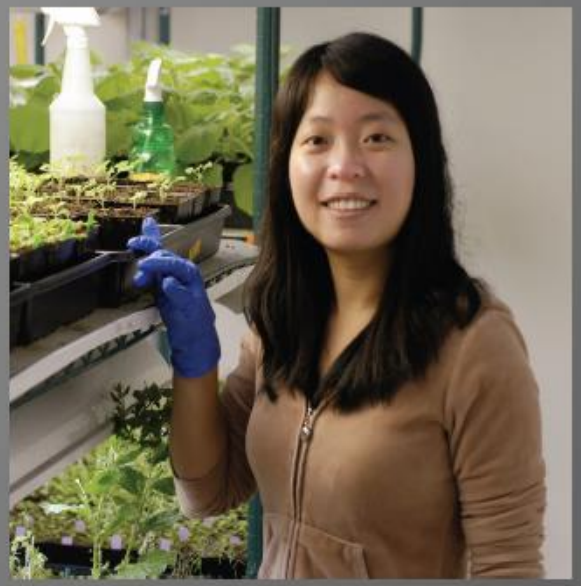
Mendoza-Cozatl, D. G., Zhai, Z., **Jobe, T. O.**, Akmakjian, G. Z., Song, W. Y., Limbo, O., Russell, M. R., Kozlovskyy, V. I., Martinoia, E., Vatamaniuk, O. K., Russell, P. & Schroeder, J. I. Tonoplast-localized Abc2 transporter mediates phytochelatin accumulation in vacuoles and confers cadmium tolerance. *J Biol Chem 285, 40416-26 (2010).PMC30003340*

Mendoza-Cozatl, D. G., Akmakjian, G., **Jobe, T.O.**, Xie, Q. Q., Komives, E., Stacey, G., Stacey, M. & Schroeder, J. I. Impaired cadmium, glutathione and phytochelatin partitioning between shoots and roots in *opt3-2 mutant (revisions requested).*

Prevent toxic heavy metals and arsenic from contaminating food



Graduate Student Xie, Julian Schroeder's Laboratory



Areas of Interest:

1. Engineering plants to enhance plant phytoremediation of arsenic and cadmium

2. Discovery and characterization of genes encoding transporters that affect cadmium accumulation in plants

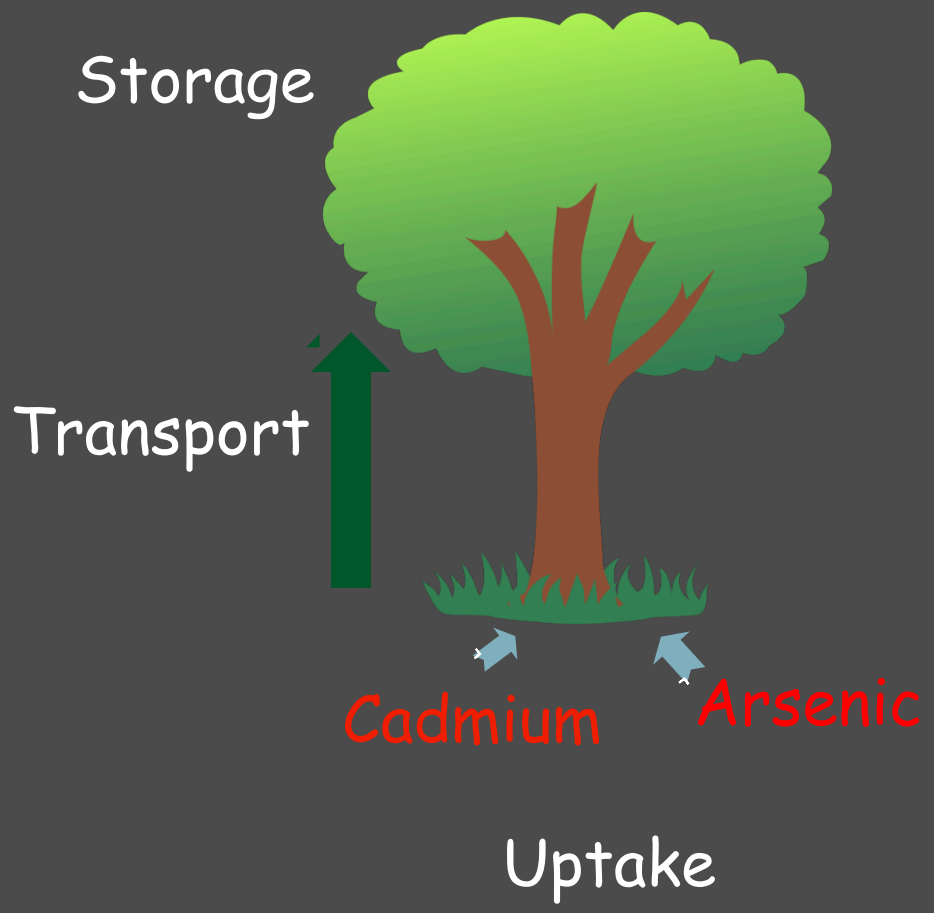
3. Developing new strategies to reduce toxic arsenic and cadmium accumulation in edible plant tissues.

Publications:

Mendoza-Cozatl, D. G., Akmakjian, G., Jobe, T.O., **Xie Q. Q.,** Komives, E., Stacey, G., Stacey, M. & Schroeder, J. I. Impaired cadmium, glutathione and phytochelatin partitioning between shoots and roots in *opt3-2 mutant (revisions requested).*

Phytoremediation

Plants remediate toxic heavy metals and arsenic



Superfund Research Program at Boston University

OVERVIEW OF TRAINING CORE

APRIL 25, 2013

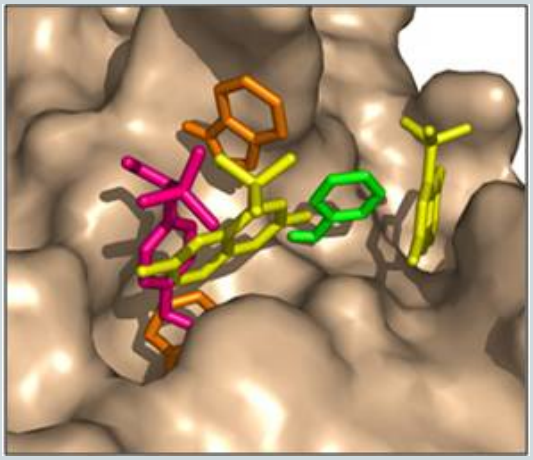
Superfund Research Program

SRP Program at Boston University

- Established in 1995
- Five research projects:
  - Project 1: Prenatal Exposure to Tetrachloroethylene-Contaminated Drinking Water and the Risk of Birth Defects
  - Project 2: Analyzing Patterns in Epidemiologic and Toxicologic Data
  - Project 3: Environmental PPARγ Agonists: Dual B Lymphocyte and Bone Marrow Stromal Cell Toxicants
  - Project 4: Mechanisms and Impacts of Dioxin Resistance in Fish
  - Project 5: Developmental Toxicity of non-Dioxin-like PCBs and Chemical Mixtures
- Five core facilities:
  - Administrative, Research Translation, Community Engagement, Training
  - Research Support Core (Bioinformatics and Molecular Modeling)

Research Support Core: Bioinformatics & Molecular Modeling

(Co-PIs: Stefano Monti & Sandor Vajda)



Develop computational tools and provide expertise in two areas:

- Modeling the interactions between xenobiotics and protein receptors using methods of structural bioinformatics and computational biology

- Statistical analysis of dense datasets and the reconstruction of regulatory pathways

Training Core
(PI: Michael McClean)

- Provide coordinated training in computational, biological and environmental sciences related to research in the BU SRP
- Emphasize skills needed to communicate clearly with others within the scientific community and disseminate scientific knowledge to a broader audience, including both government agencies and members of the lay public
- Orient trainees to the mission, activities and needs of the NIEHS SRP, EPA and state environmental and health agencies and thereby develop a sense of shared mission and peer network

Degree Programs

- Department-specific programs at BUSPH:
  - Department of Environmental Health
  - Department of Epidemiology
  - Department of Biostatistics
- Department-specific programs at BUSM:
  - Department of Microbiology
  - Department of Pathology
- Intercollegiate Program in Bioinformatics (BU Medical Campus, College of Arts & Sciences, College of Engineering)
- Department of Biology at Woods Hole Oceanographic Institute (joint program affiliated with MIT)

Core Curriculum

- EH 765 Survey of Environmental Health (Scammell*, Heiger-Bernays*, Webster*)
- EH 768 Introduction to Toxicology (Schlezinger*, Heiger-Bernays*)
- EP 759 Reproductive Epidemiology (Aschengrau*)
- BF 527 Bioinformatic Applications (Franzosa)
- BI 642 Physiology & Biochemistry of Reproduction (Callard)

* Members of BU SRP

Coordinated with 4 Training Programs

- Integrative Graduate Education and Research Traineeship Program in Bioinformatics (NSF, Co-Director: Waxman)
- Training Program in Reproductive, Perinatal and Pediatric Epidemiology (NICHD, Co-Director: Aschengrau*)
- Training Program in Environmental Epidemiology in Community Settings (NIEHS, Director: McClean*)
- Immunology Training Program (NIAID, Director: Sherr*)

* Members of BU SRP

Program Activities

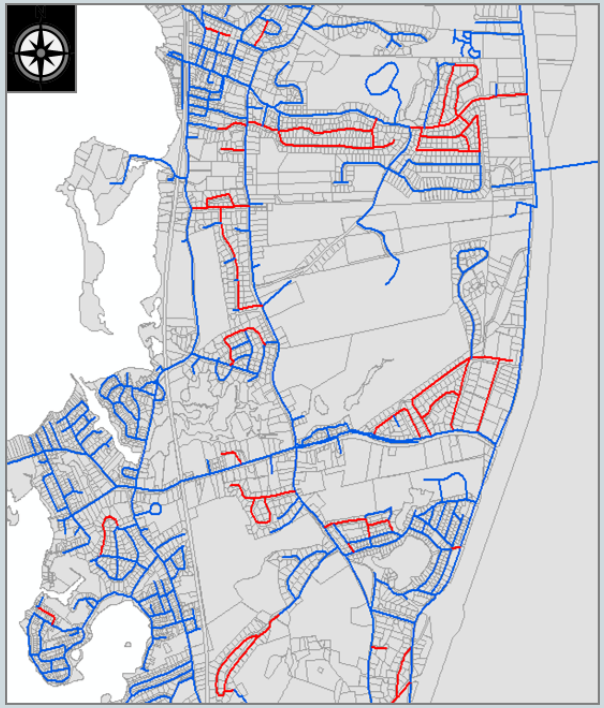
- Weekly seminar series:
  - Medical Campus: *Environmental Health Doctoral Seminar*
  - WHOI Campus: *Department of Biology Seminar*
- Biweekly Proseminar:
  - Topic sessions (e.g. grant writing, data management, data visualization, preparing a CV, etc)
  - Lunch with guest speakers
- Annual Events:
  - 2-Day BU SRP Research & Training Retreat
  - 1-Day BU SRP Trainee Meeting

Research and Training Retreat

- 2-day offsite retreat includes oral and poster presentations
- Attended by:
  - All PIs and trainees affiliated with the BU SRP
  - Community partners (CEC)
  - Representatives of state and federal agencies (RTC)
  - Graduate students and post-doctoral fellows from the other New England SRPs
- The primary goals of the research retreat are to:
  - share ideas and develop new collaborative research opportunities
  - provide trainees with an additional opportunity to present their research
  - orient trainees to the mission, activities and needs of the NIEHS SRP, EPA and state environmental and health agencies
  - encourage new professional connections and networks and promote a sense of community with a shared mission
- Agency representatives invited to participate in a concluding panel session to discuss the ways in which BU SRP research can be translated for government agencies and policymakers

Project 1
(PI: Ann Aschengrau)

Studying risk of birth defects in a population exposed to PCE in drinking water



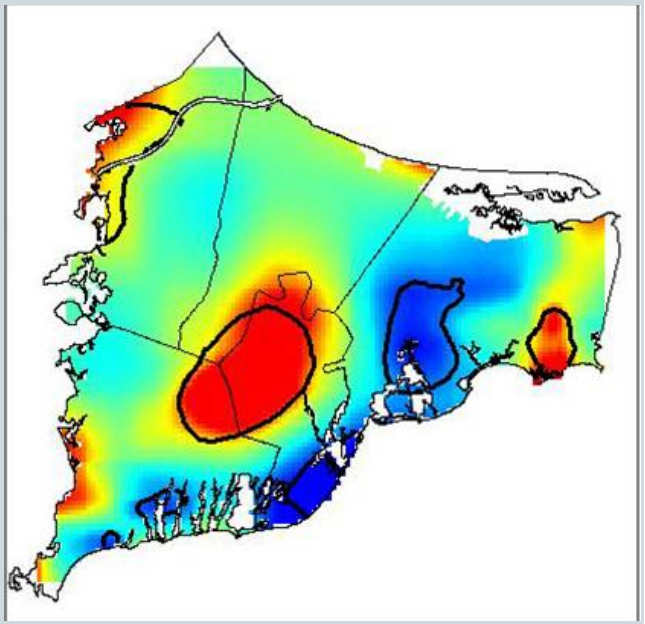
Lisa Gallagher, DSc - Use of a water distribution model to assess exposure to tetrachloroethylene-contaminated drinking water

Patricia Janulewicz, DSc - Behavioral neurotoxicity: Tools of the trade and their application to child and adult research

Kelly Getz, PhD Candidate - Prenatal risk factors for autism addressing the maternal cytokine storm hypothesis

Project 2
(PI: Veronica Vieira)

Improving methods for mapping/modeling epidemiologic and chemical mixture data to investigate reproductive and developmental outcomes



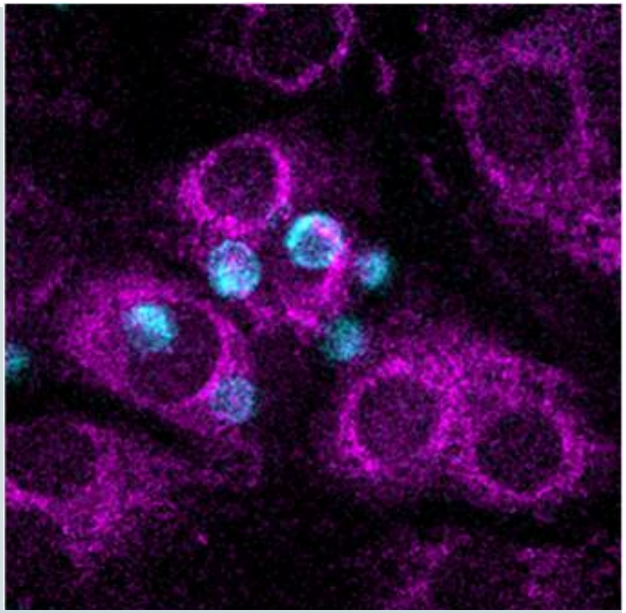
Kate Hoffman, DSc - Learning and developmental disabilities and polyfluoroalkyl chemicals

Jessica Nelson, DSc - Biomonitoring surveillance: Application and implications

Robin Bliss (Young), PhD - Properties of hypothesis tests using generalized additive models with smoothers of geographic location and spatial statistics

Project 3
(PI: Jennifer Schlezinger)

Determining the molecular mechanism by which individual and complex mixtures of environmental chemicals impair the development of the mammalian immune system and accelerate bone aging



Greg Howard, DSc - Synergism in toxicology and epidemiology

Amelia Haas, MD/PhD - Environmental PPAR agonists accelerate aging of bone and impair lymphopoiesis

James Watt, PhD Candidate - Exploring the role of environmental obesogens on bone loss

Project 4
(PI: Mark Hahn)

Understanding mechanisms underlying differential sensitivity to the developmental toxicity of PCBs that act through the AhR receptor

Goran Bozinovic, PhD - Physiology, morphology, and gene expression of sensitive and resistant *Fundulus heteroclitus*

Supraja Narasimhan, PhD - The role of the constitutively active aryl hydrocarbon receptor in mammary tumor progression

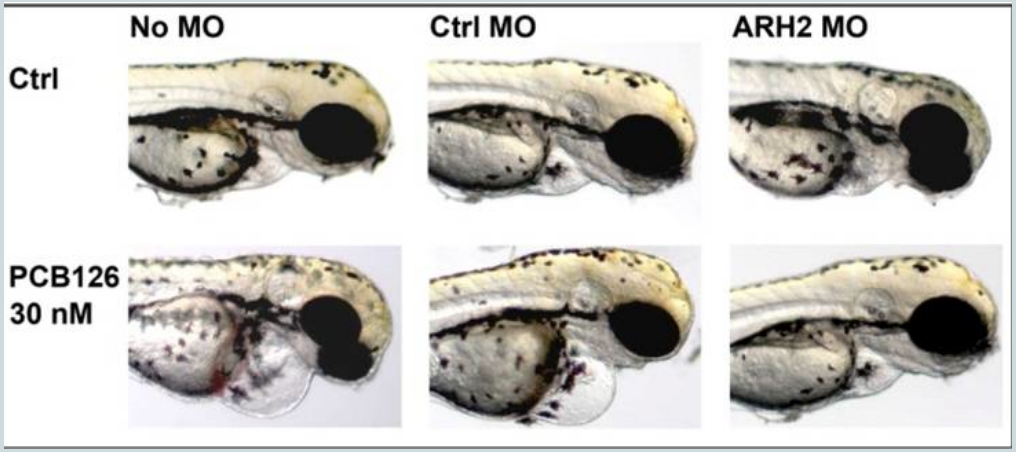
Olga Novikov, MD/PhD Candidate – The effects of environmental and endogenous AhR ligands on AhR-mediated regulation of triple negative breast cancer invasion and metastasis

Project 5
(PI: John Stegeman)

A comprehensive study of ortho-PCB effects on development, and possible mechanisms using fish models

Thiago Parente, PhD - CYP1A evolution in Loricariidae fish

Juliano Zanette, PhD - Identification and characterization of molecular markers to study ecotoxicology in bivalves and fish



Upcoming - 25 Years of the Superfund Research Program: Highlights and Hopes

- Call on May 23, 2013 - Sponsored by The Collaborative on Health and the Environment (CHE)
- Featured speakers include:
  - Dr. Bill Suk, Director of SRP
  - Dr. Joseph Graziano, Director of Columbia SRP

Dr. Dave Ozonoff
Director of BU SRP

Dr. Jennifer Schlezinger
Former trainee and current PI of Project 3