STEEP AIMS:
Renewed Commitment for the Public Good

Fall 2020 Progress

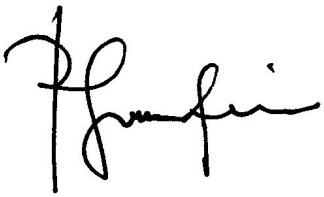
STEEP
Sources, Transport, Exposure & Effects of PFASs
UNIVERSITY OF RHODE ISLAND SUPERFUND RESEARCH PROGRAM

University of Rhode Island

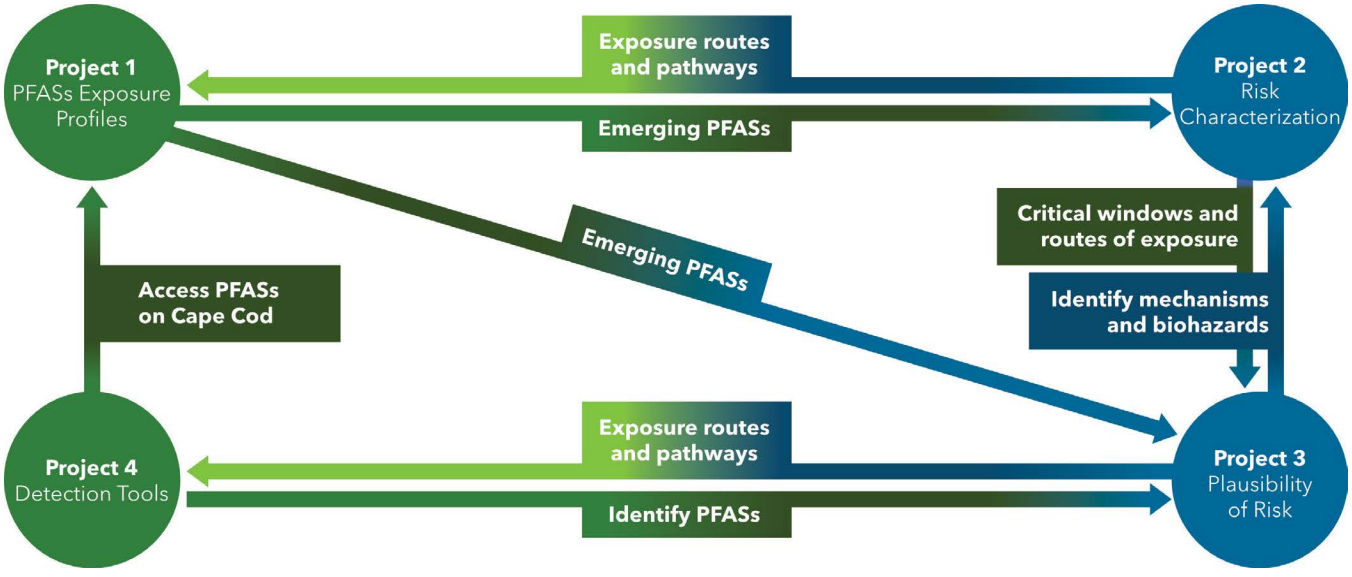
I have been working for nearly 20 years in the field of emerging contaminants with particular focus on the coastal marine environment. From dioxins to PCBs, I have seen the damage that human-produced chemicals have wrought on human and environmental health; however, PFAS present a whole new level of challenges as they are extremely persistent and ubiquitous in the environment. STEEP will continue to work with its stakeholders to ensure that the best available science is used to protect people from undue PFAS exposure, though COVID-19 made progress more difficult. Stay safe!

For over 30 years, I have dedicated my medical research to environmental epidemiology. My main emphasis is on the adverse health effects of environmental chemicals—in particular the long-term implications of early-life exposures. PFAS can negatively affect the maturation of important organ functions, and a major concern is the insidious threat of PFAS exposure to the immune system. In a time with widespread COVID-19 infections, a fully functional immune system is crucial. Through the support of NIEHS, STEEP supports our highest aspirations in addressing and preventing adverse health impacts from the PFAS.

Lead **Rainer Lohmann, PhD**
Graduate School of Oceanography
University of Rhode Island



Co-lead **Philippe Grandjean, MD DMSc**
Harvard T.H. Chan School of Public Health,
Department of Environmental Health



Director Lohmann and co-Director Grandjean combine complementary expertise in environmental and epidemiological science. They brought together a team of individuals that function as an effective and integrated interdisciplinary team. This includes researchers from the University of Rhode Island Graduate School of Oceanography, the Coastal Institute, and Colleges of Pharmacy, Engineering, and the Environment and Life Sciences; Harvard T.H. Chan School of Public Health, Department of Environmental Health; and the Silent Spring Institute.

STEEP Overview

Per- and polyfluorinated alkyl substances (PFAS) are extremely resistant to environmental degradation and are found in humans and the environment around the world.

The most notable PFAS include perfluorooctanoic acid (PFOA) and perfluorooctanoic sulfonate (PFOS). In the U.S., there are industrial PFAS production and manufacturing sites, and over 600 fire/crash training sites nationwide where PFAS-containing aqueous film-forming foams have most likely contaminated groundwater and sediments. Additional human exposure results from widespread use of PFAS in consumer products, e.g., stain-resistant furnishings and carpets, grease-proof food packaging and wrappers. Production and use of PFOS and PFOA have declined in the U.S. since the early 2000s following a voluntary phase-out by 3M, and subsequent stewardship plans by U.S. EPA and international agreements. Industrial production in the U.S. shifted away from PFOA and PFOS as the public was provided evidence of their adverse human health impacts. As production decreased in the U.S., new fluorinated compounds have been and continue to be developed to meet society's demand. As a result, environmental contamination and human exposure continues.

Despite widespread PFAS use since the 1950s, there are still knowledge deficits about their environmental and public health impacts, thus this contaminant is considered emerging. STEEP is committed to researching compelling environmental and human health concerns to inform development of appropriate benchmark dose levels for PFAS. Moreover, STEEP will disseminate these research results to a variety of stakeholders as well as train the next generation of scientists essential to the management of these highly stable and ubiquitous compounds. In the past year, there has been a burgeoning awareness of the ubiquity of PFAS and its transport through consumer goods into the food web. From Vermont dairy farms to global applications of some 4,700 permutations of PFAS, presence of these "forever chemicals" in humans and ecosystems is of growing concern and in urgent need of widespread attention.

RESEARCH PROJECTS OVERVIEW: STEEP Research Projects aim to better understand the pathways of PFAS contamination from entry into the environment through groundwater contamination, dispersal through the food web, and distribution to vulnerable human populations during early development, in part through breast milk. In addition, STEEP supports the development and deployment of in situ passive sampling techniques for PFAS and their precursors in water. STEEP is thereby addressing limitations in the current understanding of human exposure to PFAS by combining targeted human exposure assessment with chemometric approaches to characterize existing PFAS sources.

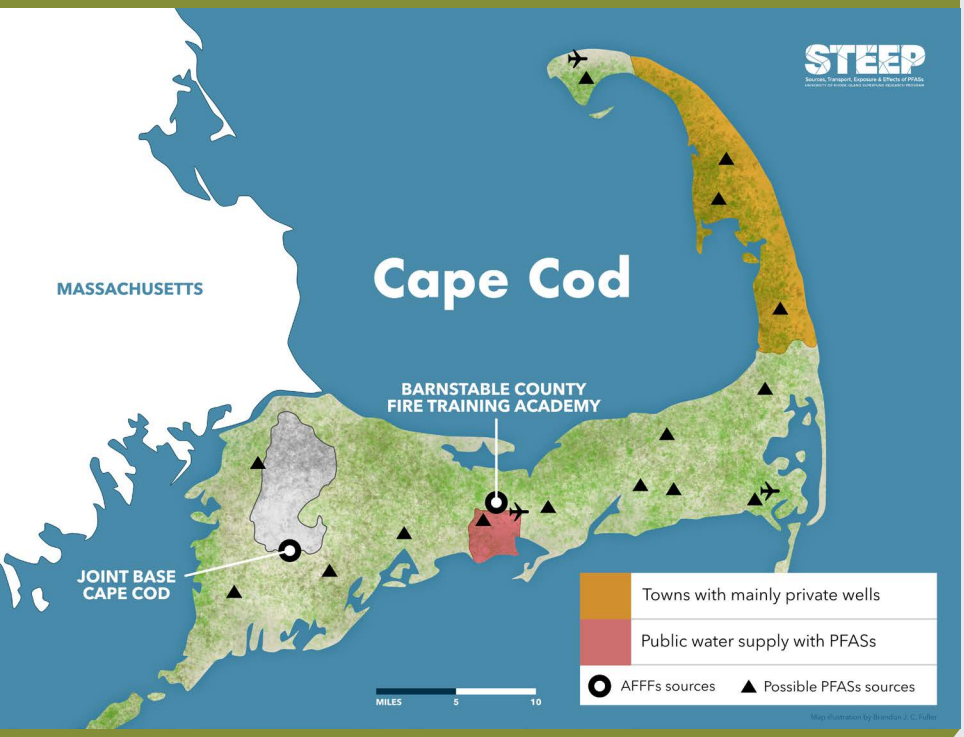
CORE OBJECTIVES OVERVIEW: To ensure a legacy of scientific awareness, dissemination of broadly accessible research findings, and practical application by affected communities, STEEP Cores serve to prepare the next generation of interdisciplinary emerging contaminant researchers, translate scientific findings generated by STEEP projects for internal and external stakeholders, and engage Cape Cod communities on the front lines of PFAS exposure through contaminated drinking water.

Communities

STEEP is focused on two study sites, one on Cape Cod and the other in the Faroe Islands. Barnstable County, MA, is STEEP's primary site for community engagement activities. STEEP partner Silent Spring Institute has conducted community-engaged research and activities focused on water quality and public heath on Cape Cod for more than 20 years.

The Faroe Islands are STEEP's epidemiological research site, where for decades co-director Grandjean, in partnership with Pál Weihe, MD (Adjunct Professor, University of the Faroe Islands; Head, Department of Occupational Medicine and Public Health), has studied the impact of persistent chemicals on pre-natal and post-natal health which enriches STEEP's understanding of the adverse health impacts of PFAS.

The vast majority of people worldwide are exposed to some level of PFAS due to its presence in a wide range of manufactured products and consumer goods; however, some communities akin to STEEP study sites experience increased exposure from secondary sources. In Cape Cod, the additional exposure to PFAS is linked to contaminated groundwater that finds its way to residents' tap water. The Faroe Islands fishing community experiences additional PFAS exposure linked to marine food intake and a cultural tradition of consuming pilot whale meat.



Barnstable County, MA, is a Cape Cod area beloved for its sweeping coastline, quaint villages, and welcoming community ambiance. Groundwater on Cape Cod has been contaminated by PFAS from multiple sources. To date, these sources have been identified as fire training areas, airports, military bases, landfills, municipal wastewater, and septic systems. The spread of PFAS is exacerbated by Barnstable's location in an outwash plain with permeable soil. The result is that groundwater aquifers are highly susceptible to movement of contaminants from the surface of the ground—the place where surface water both contributes to aquifers and enters the food web. Once PFAS get into groundwater, they move with the groundwater and eventually can contaminate both public and private drinking water sources. Given these multiple inputs of PFAS and the unique geology of the area, there is an ongoing threat to Cape Cod's sole source aquifer that provides drinking water for 200,000 year-round and 500,000 summer residents.

The Faroe Islands consist of 18 inhabited volcanic islands, which are connected by a network of roads, ferries, subsea tunnels, and bridges. Located in the Atlantic Ocean between Norway and Iceland, these islands are a self-governing archipelago of the Kingdom of Denmark. With a population of slightly more than 50,000, this fishing community is situated in the heart of the Gulf Stream in the North Atlantic. In a generation, with the help of the fishing trade that accounts for approximately 20 percent of GDP, Faroese affluence has grown in the widespread use of technology and well-established infrastructure. Beginning in 1985, study cohorts of ~2,300 Faroese children have been repeatedly re-examined to ascertain effects of mercury in their diet and later expanded to include PFAS. Consequently, the overall health threats from toxic chemicals to the current and future generations of Faroese are compelling and timely as reflections of widely occurring health risks.

Project 1: Environmental Fate & Transport

Environmental Engineering: Exposure assessment and chemometrics of PFAS

CENTRAL HYPOTHESIS:

Some geochemical and hydrological conditions facilitate PFAS transport and precursor transformation near contaminated sites, increasing their propensity to enter drinking water and fish.

Lead: **Elsie Sunderland**
Harvard T.H. Chan School of Public Health, Department of Environmental Health (HSPH)
Harvard John A. Paulson School of Engineering and Applied Sciences (SEAS)

Key Personnel: **Alan Vajda**
University of Colorado-Denver (UCD)

Overview

More than 600 sites across the U.S. are contaminated by poly- and perfluoroalkyl substances (PFAS) but the extent of transport away from these sites and entry into human exposure pathways (drinking water and fish) is virtually unknown. This information is critical for assessing human health risks associated with exposures to PFAS from contaminated sites.

This project is investigating the diverse potential exposure pathways for PFAS. This work includes new measurements of PFAS present in water (surface waters, private wells, estuaries, tap water) and seafood in the Cape Cod/New England region and the Faroe Islands. The Joint Base Cape Cod (JBCC) is a contaminated Superfund site located on Cape Cod. As part of project 1,

STEEP researchers are investigating the fate of the aqueous film forming foam (AFFF) contaminated plume as it mixes with other PFAS sources and enters surface waters, downstream rivers and ultimately the marine environment. In collaboration with Project 4, researchers at UC Denver are investigating the uptake and bioconcentration of PFAS in laboratory fish. Further, Project 1 is investigating uptake and trophic magnification of PFAS in fish downstream of AFFF impacted locations.

Aims of this project include:

- The development of novel statistical methods to fingerprint profiles of PFAS measured in fish and drinking water to better understand contamination sources. As part of STEEP research, this technique was applied to better understand sources of human exposure to different demographic groups in the Faroe Islands and North America (Hu et al., 2018). In addition, this technique was used to understand how PFAS exposure sources for children in the Faroe Islands have changed over time (Dassuncao et al., 2018). Project 1 has further applied this technique to differentiate contamination in the environment from AFFF and other PFAS sources in surface waters on Cape Cod, MA (Ruyle et al., in review). We have further developed a statistical technique for reconstructing major precursors in contemporary AFFF using information on the known transformations of PFAS precursors into terminal perfluroalkyl acids (PFAA) and measured yields of precursors using the TOP assay (Ruyle et al., in institutional review).
- Better understanding of how environmental factors influence the transport and transformations of PFAS away from contaminated sites and into surface waters and the marine environment. In collaboration with the U.S. Geological Survey (USGS), Project 1 research has studied the dilution and transformations of PFAS and precursor chemicals as contaminated groundwater plumes from AFFF use enter surface waters and rivers on Cape Cod. This research is providing new insights into the lifetime of transport potential for PFAS precursors, measurements of PFAS accumulation at the air-water interface, and new insights into sorption mechanisms that retard PFAS transport (Tokranov et al., in review).
- Improved understanding of the propensity of different PFAS in the contaminated groundwater environment to enter fish and the accumulation in different tissues. The University of Colorado Denver and USGS have developed a mobile laboratory/water-quality characterization approach to assess PFAS bioconcentration. Researchers are investigating associations between PFAS accumulation in laboratory fish and endocrine disruption, metabolic effects and immune responses.

One of the major expected outcomes of this work is a better understanding of the spatial extent of elevated PFAS concentrations in fish and drinking water from contaminated sites, which will also improve our understanding of the vulnerability of exposed communities to PFAS contamination.

Progress to date

New method for measuring organofluorine accumulation at the surface of consumer products

It is well-established that targeted mass-spectrometry is only able to capture a small fraction of the PFAS present in environmental samples, which may result in underestimates of the magnitude of contamination present in the environment and human exposure. In this work, STEEP researchers used an instrument readily available at most major research centers (x-ray photoelectron spectroscopy: XPS) to measure the total organofluorine present at the surface of common consumer products. The new method development allows for a true surface measurement that can identify surface coatings (much shallower depth than the method developed using particle-induced gamma ray emission: PIGE) and also depth profiles for PFAS present at the surface of products. This allows investigators to determine the homogeneity in PFAS application to the product. Results based on XPS measurements agree well with other studies that have shown consumer products contain many PFAS that are not detected using targeted measurement techniques.

Understanding the relative importance of diverse human exposure pathways for PFAS

Project 1 researchers published a number of products this year aimed at better identifying the relative importance of drinking water, seafood and consumer products as exposure sources (reviewed in Sunderland et al., 2019). PFAS concentrations were measured in archived drinking water samples from 1989/1990 at locations across the United States. This work revealed significant associations between PFAS concentrations in drinking water and serum PFAS concentrations in the background US population (away from contaminated sites), indicating the ubiquity of drinking water exposures to PFAS for many US individuals (Hu et al., 2019). Work conducted in

collaboration with Project 2 in the Faroe Islands revealed that even in a remote Faroese fishing community, a large fraction of exposure originates from use of diverse consumer products containing PFAS and non-seafood sources (Dassuncao et al., 2018, Hu et al. 2018). Researchers showed that concentrations of legacy PFAS in the serum of children declined rapidly following the phase-out in PFOS production between 2000-2002, likely reflecting the elimination of PFOS and its precursors from consumer sources. These "steep" declines indicate the potential benefits from coordinated global action controlling production sources.

Bioaccumulation of PFAS in the marine food web

Research conducted collaboratively between Project 1 and Project 4 is providing new insights on accumulation of PFAS in seawater and uptake of PFAS in marine food webs (Zhang et al., 2019). This work suggests that contaminated submarine groundwater discharge may be a concern for some Northeast estuaries and delay recovery of PFAS contaminated sites when sources have been eliminated. It also suggests that short-chain PFAS precursors are contributing to higher than expected concentrations measured in marine plankton from the Northeastern Atlantic Ocean shelf and slope, which is likely to influence their accumulation in higher trophic level organisms consumed by humans and wildlife. Ongoing work is investigating how wastewater and groundwater inputs to Waquoit Bay, MA are affecting marine food web exposures to PFAS.

Tissue distribution of PFAS in marine mammals

Project 1 research, in collaboration with Project 3, has also been studying the toxicokinetics of PFAS distribution among the tissues of marine mammals and the controlling role of phospholipids for tissue distribution (Dassuncao et al., 2019). This research focused on pilot whales, which are an important exposure pathway for individuals in the Faroe Islands — the focus of Project 2 research. Results have shown preferential accumulation of long-chain PFAS in the brain of pilot whales, likely indicating facilitated transport mechanisms for some PFAS. In addition, high concentration of the C-6 carboxylate were found in the liver, which is consistent with the role of specific binding proteins such as liver fatty acid binding proteins (FABP) affecting accumulation in different target sites. These hypotheses are being further evaluated by work associated with Project 3. Overall, this research has shown that a revised toxicokinetic model based on the phospholipid content of different organisms would improve the ability to represent tissue accumulation and bioaccumulation of PFAS.

Research highlight: Uptake and effects of PFAS in fish exposed to AFFF-contaminated groundwater

Project 1 experiments with CU Denver, USGS, and Project 4 on-site at an AFFF-contaminated groundwater

plume have investigated multi-media uptake and effects of PFAS exposure. These experiments demonstrate distinct uptake profiles of PFAS mixtures in fish, mussels, and passive samplers. Specific PFAS compounds were detectable only in fish tissue, and not in water samples or by passive samplers. These findings have implications for environmental monitoring of PFAS concentrations. In collaboration with Project 3, evaluation of biomarkers in fish experimentally exposed to this AFFF-contaminated groundwater plume showed impaired sperm, elevated testicular histopathology, and disrupted liver lipids, paralleling observations in PFAS-exposed humans. Ongoing transcriptomic analysis of liver and testis mRNA aims to characterize the molecular regulatory networks mediating these reproductive and metabolic responses to environmental PFAS mixtures and their relationship to PFAS body-burden. Fish microbiome responses to PFAS have been amplified for 16S and metagenomic sequencing to provide a further linkage between PFAS aqueous concentrations and PFAS body burden. The relationship between molecular uptake mechanisms and tissue-specific PFAS concentrations is under investigation in collaboration with Project 3 and Project 4.

Plans for upcoming year

- Complete first iteration of a mechanistic model for PFAS bioaccumulation in aquatic food webs (Jennifer Sun).
- Evaluate linkages between water sample, individual PFAS body-burden, within-fish multi-omic (liver, testis, microbiome) and organismal biomarkers (reproductive and metabolic) in fish from an FTA dose-response experiment.
- Implement a new method for modeling vulnerability of private wells for high PFAS concentrations using machine learning approaches and monitoring data from the state of New Hampshire (Xindi Hu).
- Measure total organoflurine in Faroese serum, and fish from Waquoit Bay (Heidi Pickard).
- Develop a new atmospheric simulation for PFAS deposition in the Northeastern US using the GEOS-Chem model (Lara Schultes).
- Participate in STEEP renewal development and submission.

SELECTED ACCOMPLISHMENTS

H. Joerss, Z. Xie, **C.C. Wagner**, W-J von Appen, **E.M. Sunderland**, R. Ebinghaus. 2020. Transport of legacy perfluoroalkyl substances and the replacement compound HFPO-DA through the Atlantic gateway to the Arctic Ocean – Is the Arctic a sink or a source? *Environmental Science & Technology*. http://dx.doi.org/10.1021/acs.est.0c00228

Carol F. Kwiatkowski, David Q. Andrews, Linda S. Birnbaum, Thomas A. Bruton, Jamie C. DeWitt, Detlef R. U. Knappe, Maricel V. Maffini, Mark F. Miller, Katherine E. Pelch, Anna Reade, Anna Soehl, Xenia Trier, Marta Venier, **Charlotte C. Wagner**, Zhanyun Wang, and Arlene Blum. Scientific Basis for Managing PFAS as a Chemical Class. *Environmental Science & Technology Letters* 2020 7 (8), 532-543. DOI: 10.1021/acs.estlett.0c00255

B.J. Ruyle, C.P. Thackray, J.P. McCord, M.J. Strynar, K.A. Mauge-Lewis, S.E. Fenton, E.M. Sunderland. 2020. Reconstructing the composition of poly- and perfluroalkyl substances (PFAS) in contemporary aqueous film forming foams. To be submitted to *Environmental Science & Technology Letters*, In Institutional review at EPA and NIH.

B.J. Ruyle, H.M. Pickard, D.R. LeBlanc, **A.K. Tokranov**, C.P. Thackray, **X.C. Hu**, C.D. Vecitis, E.M. Sunderland. 2020. PFAS Precursor Transformations and Unexplained Organofluorine in AFFF-Impacted Coastal Watersheds. *Environmental Science and Technology*. In revision.

A.K. Tokranov, D.R. LeBlanc, **H.M. Pickard**, L.B. Barber, **B.J. Ruyle**, R.B. Hull, E.M. Sunderland, C.D. Vecitis. 2020. PFAS Interfacial Sorption and Precursor Persistence during Transport across Surface Water/Groundwater Boundaries. *Environmental Science and Technology*. In revision.

A.O. De Silva, J.M. Armitage, T.A. Bruton, **C. Dassuncao**, W. Heiger-Bernays, **X.C. Hu**, A. Karrman, C. Ng, **A. Robuck**, M. Sun, T.F. Webster, E.M. Sunderland. 2020. PFAS Exposure Pathways for Humans and Wildlife: A Synthesis of Current Knowledge and Key Gaps in Understanding. *Environmental Toxicology and Chemistry*. In review.

PROJECT 1 TRAINEES

Heidi Pickard, PhD Candidate, Harvard SEAS
Bridger Ruyle, PhD Candidate, Harvard SEAS
Charlotte Wagner, PhD Candidate, Harvard SEAS
Jennifer Sun, PhD Candidate, Harvard SEAS
Lara Schultes, Postdoctoral Fellow, Harvard SEAS

PROJECT 1 GRADUATES

Andrea Tokranov, PhD (June 2019), Harvard SEAS
Clifton Dassuncao, PhD (May 2018), HSPH
Xindi (Cindy) Hu, PhD (May 2018), HSPH

Project 2: Childhood Risk

Epidemiological Study: Inflammation and metabolic changes in children developmentally exposed to PFAS

CENTRAL HYPOTHESIS:

Dietary exposure to PFAS during fetal development and childhood can interfere with immune system development and metabolism and thereby pave the way for later disease development.

Lead: **Philippe Grandjean**, Harvard T.H. Chan School of Public Health, Department of Environmental Health (HSPH)

Clinical Lead: **Pál Weihe, MD**, Adjunct Professor at The University of the Faroe Islands and Head of the Department of Occupational Medicine and Public Health

Key Personnel: **Carmen Messerlian**, Harvard T.H. Chan School of Public Health, Department of Environmental Health and Department of Epidemiology (HSPH)

Overview

Poly- and perfluoroalkyl substances (PFAS) are widely used industrial chemicals, but the extent of human PFAS exposures from contaminated sites and bioaccumulation in food-chains were discovered less than 20 years ago, and the full range of adverse health effects is not completely known. Recent evidence suggests that current PFAS exposures may cause adverse effects on the immune system and other sensitive tissues and organs, even at exposures far below provisional exposure limits. Early-life exposure to PFAS may contribute to the development of metabolic diseases, including obesity and type 2 diabetes. PFAS can also decrease antibody response to certain childhood vaccinations, and most PFAS are transferred through breast milk.

Relying on an already established birth cohort in the Faroe Islands that has been supported by NIEHS, this project is utilizing exposure and outcome data covering

a 9-year span to determine possible links between PFAS exposure profiles, immune dysfunction, and metabolic abnormalities. Due to the homogeneity of the Faroese population, the wide range of exposures, and the high participation rate in the clinical follow-up, this epidemiological setting represents advantages that would be nearly impossible to match anywhere else.

The data analysis takes into account additional factors, including exposures to other environmental chemicals, sex of the child, and diet. Overall, this will allow us to contribute important documentation for possible use in risk characterization in U.S. populations exposed to PFAS.

Progress to date

Through interdisciplinary collaboration and a shared commitment to bettering the health of communities impacted by environmental PFAS contamination, the STEEP Center team has made steady and promising progress in upholding the commitment to the Cape Cod and Faroe Island communities while advancing the science on PFAS exposure.

This project is an epidemiological study which takes advantage of a prospective birth cohort (N = 490) established in the Faroe Islands, a North Atlantic fishing community where early-life exposures to persistent environmental pollutants, such as PFAS, have been linked to immunotoxicity, obesity and related metabolic conditions in previous epidemiological studies. The cohort was generated from consecutive births between 2007 and 2009 and is the largest and most thoroughly examined group of PFAS-exposed children followed since birth. Progress to date includes:

- Completion of all clinical exams and blood work of the cohort members (8-9 years) who accepted the invitation to participate and re-consented (N = 407, 210 boys and 197 girls; 83% participation). Also, 385 DEXA scans have been completed to assess body fat distribution. Clinical data have been entered into the database. Routine blood tests have been completed, and more advanced analyses of vaccine antibodies and metabolic biomarkers have been done.
- At current PFAS exposure levels, vaccine antibody levels appear not as strongly affected by PFAS as in previous studies. However, detailed assessment of lipid metabolism, including serum-cholesterol, shows PFAS-associated increases.
- Serum-PFAS analytical methods have been upgraded and optimized on a new and more sensitive UPLC-MS/MS system comprising a Thermo Scientific EQuan MAX module for online solid-phase extraction and a TSQ Quantiva triple quadropole mass spectrometer. All exposure biomarker analyses have been completed at a high quality level.

Plans for upcoming year

- Carry out further analysis of clinical data, including DEXA scans, in regard to PFAS exposure biomarkers and serum biomarkers.
- Commence advanced statistical data analyses, including calculation of derived parameters and structural equation models, in collaboration with subcontractors. These analyses will also include estimated PFAS exposures during infancy.
- Participate in STEEP renewal development and submission.

PROJECT 2 TRAINEES

The previous trainee for Project 2, Damaskini Valvi, recently accepted a position at the Mount Sinai School of Medicine as an Assistant Professor in Environmental Medicine & Public Health (https://www.mountsinai.org/profiles/valvi-damaskini). Two new postdocs have recently been recruited for trainee roles.

Annelise Blomberg, postdoctoral research fellow, Harvard T.H. Chan School of Public Health.

Yu-Hsuan Aria Shih, postdoctoral research fellow, Harvard T.H. Chan School of Public Health.

SELECTED ACCOMPLISHMENTS

Publications

Ammitzbøll C, Börnsen L, Petersen ER, Oturai AB, Søndergaard HB, **Grandjean P**, **Sellebjerg** F. Perfluorinated substances, risk factors for multiple sclerosis and cellular immune activation. *J Neuroimmunol* 2019; 330: 90-5. PMCID: PMC6461219

Barouki R, Melén E, Herceg Z, Beckers J, Chen J, Karagas M, Puga A, Xia Y, Chadwick L, Yan W, Audouze K, Slama R, Heindel J, **Grandjean P**, Kawamoto T, Nohara K. Epigenetics as a mechanism linking developmental exposures to long-term toxicity. *Environ Int* 2018; 114: 77-86. PMCID: PMC5899930

Budtz-Jørgensen E, **Grandjean P**. Application of benchmark analysis for mixed contaminant exposures: Mutual adjustment of perfluoroalkylate substances associated with immunotoxicity. *PloS One* 2018; 13(10): e0205388. PMCID: PMC6195268

Eryasa B, **Grandjean P**, Nielsen F, **Valvi D**, Zmirou-Navier D, **Sunderland E**, **Weihe P**, Oulhote Y. Physico-chemical properties and gestational diabetes predict transplacental transfer and partitioning of perfluoroalkyl substances. *Environ Int* 2019; 130: 104874. PMID: 31200157

Grandjean P, Abdennebi-Najar L, Barouki R, Cranor CF, Etzel RA, Gee D, Heindel JJ, Hougaard KS, Hunt P, Nawrot TS, Prins GS. Time scales of developmental toxicity impacting on research and needs for intervention. *Basic Clin Pharmacol Toxicol* 2019; 125(3): 70-80. PMCID: PMC6497561

Grandjean P, Prins GS, **Weihe P**. Development Priority. *Basic Clin Pharmacol Toxicol* 2019; 125(3): 3-4. PMCID: PMC6713582

Hu XC, **Tokranov AK**, Liddie J, Zhang X, **Grandjean P**, Hart JE, Laden F, Sun Q, Yeung LW, **Sunderland EM**. Tap Water Contributions to Plasma Concentrations of Poly-and Perfluoroalkyl Substances (PFAS) in a Nationwide Prospective Cohort of US Women. *Environ Health Perspect* 2019; 127(6): 067006. PMID: 31170009

Shelly CE, **Grandjean P**, Oulhote Y, Plomgaard P, Frikke-Schmidt R, Nielsen F, Zmirou-Navier D, **Weihe P**, **Valvi D**. Serum-Adipokine Hormones from Birth to Puberty in Children Exposed to Perfluoroalkyl Substances. *J Clin Endocrinol Metab* 2019; 104: 5338-5348. PMID: 31216000

Presentations

Grandjean P. *New insights into risks to human health*. 2019 Per- and Polyfluoroalkyl Substances: Second National Conference: Northeastern University, Boston, MA. June 12, 2019.

Grandjean P. *New insights into risks to human health: The immune system.* New England PFAS Workshop hosted by the American Groundwater Trust: Westford, MA. September 16, 2019.

Project 3: Metabolic Effects

PFAS compound effects on metabolic abnormalities in rodents

CENTRAL HYPOTHESIS:

PFAS exposure leads to metabolic abnormalities in rodents and can be linked back to preferential sorption of PFAS to biomolecules.

Co-lead: **Angela Slitt**, URI College of Pharmacy (Pharm)

Co-lead: **Geoffrey Bothun**, URI College of Engineering (COE)

Overview

Human exposure to poly- and perfluoroalkyl substances (PFAS) has been linked to immunotoxicity and cancer as well as metabolic disorders and cholesterol levels. Specific to metabolic disorders, PFAS are known to concentrate in the liver and links have been established between PFAS serum levels, specifically perfluorooctanoic acid (PFOA) and perfluorosulfonic acid (PFOS), and liver injury. While these findings are insightful, these two common PFAS chemicals represent only a fraction of PFAS that exist within the contaminated sites. Mechanisms driving biological response to PFAS compounds are still being investigated.

This project will:

- Address whether environmental exposure to PFAS contributes an additional increase risk for obesity-induced fatty liver disease and metabolic disorders.
- Identify the physicochemical and partitioning behavior of PFAS that contribute to bioaccumulation.
- Test the hypotheses that (1) PFAS exposure increases diet-induced fatty liver disease and inflammation, and (2) that the biological changes in the liver can be correlated with the body's response to PFAS.

These project results will inform how PFAS exposure impacts risk factors common in the U.S. population (e.g., diet and obesity).

Progress to date

Slitt Lab

- Completed Aim 1, with additional studies to include proteomics analysis to reveal how 12 PFAS impact the process of adipogenesis. Currently, a manuscript is being developed on the adipogenesis results. A manuscript on the hepatocytes results has been tentatively accepted to *ES&T* (IF=7.1), and a second manuscript is being prepared for publication.
- Completed Aim 2 experiments and currently preparing manuscripts related to Aim 2 progress and results.
- Submitted, and have had accepted, multiple manuscripts related to the work for Aims 1 and 2.
- Continue experiments to complete analysis of livers and brains related to developmental PFAS exposure, and also to identify key uptake mechanisms for PFAS absorption by liver, intestine, and excretion to breast milk.
- Developed collaborations and implemented MTAs for Slitt to receive FABP1, BCRP, and CD36 knockout mice for breast milk disposition (pilot data).

Bothun Lab

- Completed studies that determined serum protein binding (association) constants for perfluorocarboxylic acids (PFOA, PFNA, PFDA, GenX) and perfluorosulfonic acids (PFBS, PFHxS, PFOS). Based on fluorine NMR work, entropy is a dominant factor governing PFAS binding. A manuscript on this novel discovery has been submitted to *Chemosphere* (led by trainee M. Fedorenko). Complementary fluorescence and dialysis-based studies further show that perfluorocarboxylic acids out-compete their hydrocarbon analogs for protein binding. A manuscript on this is under preparation (led by trainee J. Alesio).
- Conducting a comprehensive study comparing analytical techniques for PFAS binding to human serum albumin in collaboration with Dr. Bongsup Cho and trainee A. Crisalli. The goal is to determine molecular mechanisms of PFAS binding to better understand bioaccumulation and biodistribution.
- Prepared a joint manuscript with the Bothun (trainee J. Alesio) and Slitt (trainee E. Marques) groups showing correlations between BSA binding constants and proteomics data associated with lipid metabolism, transport, and synthesis, as well as with drug metabolism, cholesterol, and redox potential. The correlations suggest that PFAS with lower protein affinity lead to greater lipid metabolism and synthesis.
- Ongoing studies to determine PFAS binding to lactalbumin protein — an abundant protein found in breastmilk (trainee J. Alesio, undergraduate S. Hedrick). Binding constants to this protein have not been reported and are important to understanding how PFAS transport during breastfeeding.
- Examined PFAS partitioning using model cell membranes with lipids relevant to eukaryote and bacteria cells. Monolayer studies have shown a previously unreported repulsive interaction between the fluorinated PFAS tails and the hydrogenated lipid tails. This was further observed for membrane extracts of the bacterium *Alcanivorax borkumensis*, where lipid-PFAS repulsion roughly scaled with the hydrophobicity (LogP) of the PFAS. A manuscript is under preparation (led by trainee A. Naumann).

Plans for upcoming year

- Publish adipogenesis manuscripts (Aims 1) and resubmit manuscript to *ES&T* that includes a QSAR analysis. Write and submit another resulting manuscript from Aim 1 work that demonstrates effects of PFAS at 70 ppt on gene expression.
- Publish the resulting studies for Aim 2. These are written and close to submission and have endpoints related to Project 2.
- Complete remaining analysis of key tissues of interest (i.e. liver, brain) related to Alzheimer's Disease Supplement with Nasser Zawia, Dean of URI's Graduate School and Professor of Pharmacy; expect two to three manuscripts to result from this collaboration.
- Continue to publish remaining three to four manuscripts related to Bothun Lab research.
- Complete lactalbumin binding studies and identify correlations with PFAS blood serum concentrations.
- Determine PFAS partitioning into mammalian cell membranes (e.g. hepatocytes) and membrane extracts, and identify PFAS-lipid interactions.
- Participate in STEEP renewal development and submission.

PROJECT 3 TRAINEES

Current Trainees

Jessica Alesio (formerly Orr), PhD Student, URI Engineering
Juliana Agudelo, PhD Student, URI Pharmacy
Emily Kaye, MS Student, URI Pharmacy
Sadegh Modaresi, URI Pharmacy

Graduates

Michael Fedorenko, MS, URI Engineering
Emily Marques (formerly Martell), URI Pharmacy (Postdoctoral Fellow at UMass Amherst with Dr. Alicia Timme-Laragy
Aleksandra Naumann, MS, URI Engineering
Marisa Pfohl, PhD, URI Pharmacy (Postdoctoral Fellow at EPA)

Trainee Awards and Recognition

Juliana Agudelo, recipient of KC Donnelly Award "Develop novel and new analytical methods to understand the possible linkage between PFAS exposure and non-alcoholic fatty liver disease (NAFLD) in humans." Agudelo will travel to the EPA to learn untargeted Mass Spectrometry with Dr. Mark Strynar.

Emily Marques, 2019/2020 Graduate Student Representative of the Mechanisms Specialty Section of the Society of Toxicology.

Naomi Parijillo, Recipient of URI Undergraduate Research Grant, $1000 for "Evaluating gene expression and OATP-mediated mechanisms of Per- and polyfluoroalkyl substances (PFAS) across ethnicities in human hepatocytes".

Lucie Ford, Recipient of Society of Toxicology Pfizer Undergraduate Research Award 2020.

SELECTED ACCOMPLISHMENTS

Poster Presentations

Kaye E, Agudelo J, **Pfohl M, Marques E, Slitt A**. (2020) Developmental PFOS exposure causes changes in liver transcriptome. Late-Breaking 9: Air Pollution; PFAS; Respiratory. Society of Toxicology Annual Meeting, Anaheim, CA, March 19, 2020.

Alesio J, Fedorenko M, Burke D, White A, **Bothun G**. (2019). PFAS Protein Binding by Fluorescence Spectroscopy: A Critical Analysis. Session 3: Susceptibility and Risk Factors: Methods to assess the risks to human health presented by hazardous substances. Superfund Research Program Annual Meeting, Seattle, WA, November 19, 2019.

Marques E, Pfohl M, Wei W, Tarantola G, Ford L, Amaeze O, and **Slitt A**. (2020) Replacement Per- and Polyfluoroalkyl Substances (PFAS) Are Potent Modulators of Lipogenic and Drug Metabolizing Gene Expression Signatures in Primary Human Hepatocytes. *The Toxicologist*, 2435, Society of Toxicology Annual Meeting, March 2020.

Ford L, **Marques E**, Wei W, **Pfohl M**, Agudelo J, and **Slitt A**. (2020) Time to Treatment after Plating Impacts PFAS Induction of Gene Expression in Cryopreserved Human Hepatocytes. *The Toxicologist*, 1974, Society of Toxicology Annual Meeting, March 2020.

Hamilton MC, **Pfohl M, Marques E**, Ford L, **Slitt A**, and Baldwin WS. Increased Toxicity and Retention of Perflourooctane Sulfonate (PFOS) in hCYP2B6-Tg Mice Compared to Cyp2b-Null Mice Is Relieved by a High-Fat Diet. *The Toxicologist*, 2433, Society of Toxicology Annual Meeting, March 2020.

Marques E, Pfohl M, Wei W, Amaeze O, and **Slitt A**. (2019) Gene expression and lipid accumulation profiles for perfluoroalkyl acid (PFAA) and PFAA mixtures in human hepatocytes. Gordon Conference and Seminar: Cellular & Molecular Mechanism of Toxicity, August, 2019.

Manuscripts

Pfohl M, Ingram L, **Marques ES**, Auclair A, Barlock BJ, Jamwal R, Anderson D, Cummings B, and **Slitt AL**. Perfluorooctanesulfonic acid (PFOS) and perfluorohexanesulfonic acid (PFHxS) alter the blood lipidome and the hepatic proteome in a murine model of diet-induced obesity. *Toxicological Sciences*. Accepted for publication.

Marques ES, **Pfohl M**, Wei W, Tarantola G, Ford L, Amaeze O, **Bothun G**, and **Slitt AL**. Replacement per- and polyfluoroalkyl substances (PFAS) are potent modulators of lipogenic and drug metabolizing gene expression signatures in primary human hepatocytes. *Environmental Science and Technology*. Revisions requested.

Marques ES, Pfohl M, Auclair A, Jamwal R, Barlock BJ, Sammoura FM, Goedken M, Akhlaghi F, and **Slitt AL**. PFOS administration shifts the hepatic proteome and augments dietary outcomes related to hepatic steatosis in mice. *Toxicology and Applied Pharmacology*. Revisions requested.

Pfohl M, Marques ES, Auclair A, Jamwal R, Barlock BJ, Goedken M, and **Slitt A**. An 'omics approach to unraveling the paradoxical effect of diet on perfluorooctanesulfonic acid (PFOS) and perfluorononanoic acid (PFNA)-induced hepatic steatosis. Under review.

Amaeze O, Wei W, **Marques ES**, Ma H, Lazzaro S, Johnson N, and **Slitt A**. Inhibitory and inductive effects of Nigerian medicinal plants extracts on human P-glycoprotein and Cytochrome P450 enzymes – implications for herb-drug interaction. *Drug Metabolism and Pharmacokinetics*. In review.

Alesio J, Slitt A, Bothun G. Connecting Physicochemical Properties of Perfluoroalkyl Substances (PFAS) and Fatty Acid Analogs to Bovine Serum Albumin Binding. *Journal of Agricultural and Food Sciences.* In preparation.

Fedorenko M, Alesio J, Fedorenko A, **Slitt A, Bothun G**. Dominant Entropic Binding of Perfluoroalkyl Substances (PFAS) to Albumin Protein Revealed by 19F NMR. *Chemosphere*. Accepted pending revisions.

Crisalli A, Alesio J, Bothun G, Cho B. New mechanistic insight into albumin binding of PFAS and PFAS replacements. In preparation, journal TBD.

Alesio J, Bothun G. Perfluoroalkyl carboxylates and sulfonates lead to membrane ordering in the hydrocarbonoclastic bacteria *Alcanovorax Borkumensis* without impacting growth. *Environmental Science and Technology*. In preparation.

Naumann A, Alesio J, Bothun G. PFAS accumulation in bacterial membrane monolayers: Role of electrostatic and hydrophobic interactions. *Langmuir*. In preparation.

Invited Presentations

Angela Slitt, July 2020, Federal Information Exchange, invited speaker "Evaluating emerging and legacy PFAS as inducers of hepatic steatosis."

Angela Slitt, July 2020, Cleanwater Action, DARK WATERS Expert Panel Discussion.

Other activities

- Slitt served on PFAS Drinking Water Technical Advisory Group formed by the Rhode Island Department of Health.
- Slitt provided written and expert testimony related to RI Bill S-2235 (PFAS in drinking water, groundwater, and surface waters) and S-2068 (PFAS in food packaging), February 2020.
- Slitt represented STEEP SRP to answer questions at a screening of Dark Waters organized by Clean Water Action, February 2020.

COVID-19 Adaptations

Methodologies developed in the Slitt Lab with STEEP support were applied to the COVID-19 pandemic and are represented in the following pending grant submissions:

- Slitt and Messelarian (Project 2), "Leveraging the URI Mobile Health Unit to Understand whether PFAS exposure increases COVID Risk in a RI Vulnerable Population," Time Sensitive R21 submitted to NIEHS for September 2020.
- Slitt, RADX-Tech submission, July 2020 "QuantiCOVID Assay to Detect SARS-CoV-2 mRNA."
- Slitt, RADX-Tech re-submission, August 2020 "QuantiCOVID Assay to Detect SARS-CoV-2 mRNA."
- Slitt, Countermeasures.gov, MCM2020-03098, "Quanti-COVID Assay to Detect SARS-CoV-2 mRNA." August 2020.
- Slitt, Army Advance Laboratory, AAL-7083258, "Quanti-Covid-19 Test to detect Sars-CoV-2 mRNA from nasal swabs and saliva," August 2020.
- Slitt, Army Advance Laboratory, AAL-7083258, "Test to detect Sars-CoV-2 mRNA from nasal swabs and saliva." April 2020.

Project 4: Detection Tools

Environmental Engineering: Develop passive samplers for the detection and bioaccumulation of PFAS in water and porewater

CENTRAL HYPOTHESIS:

Passive sampling can be used to detect PFAS and their precursors in air, water, and porewater.

Lead: **Rainer Lohmann**, Graduate School of Oceanography, University of Rhode Island (GSO)

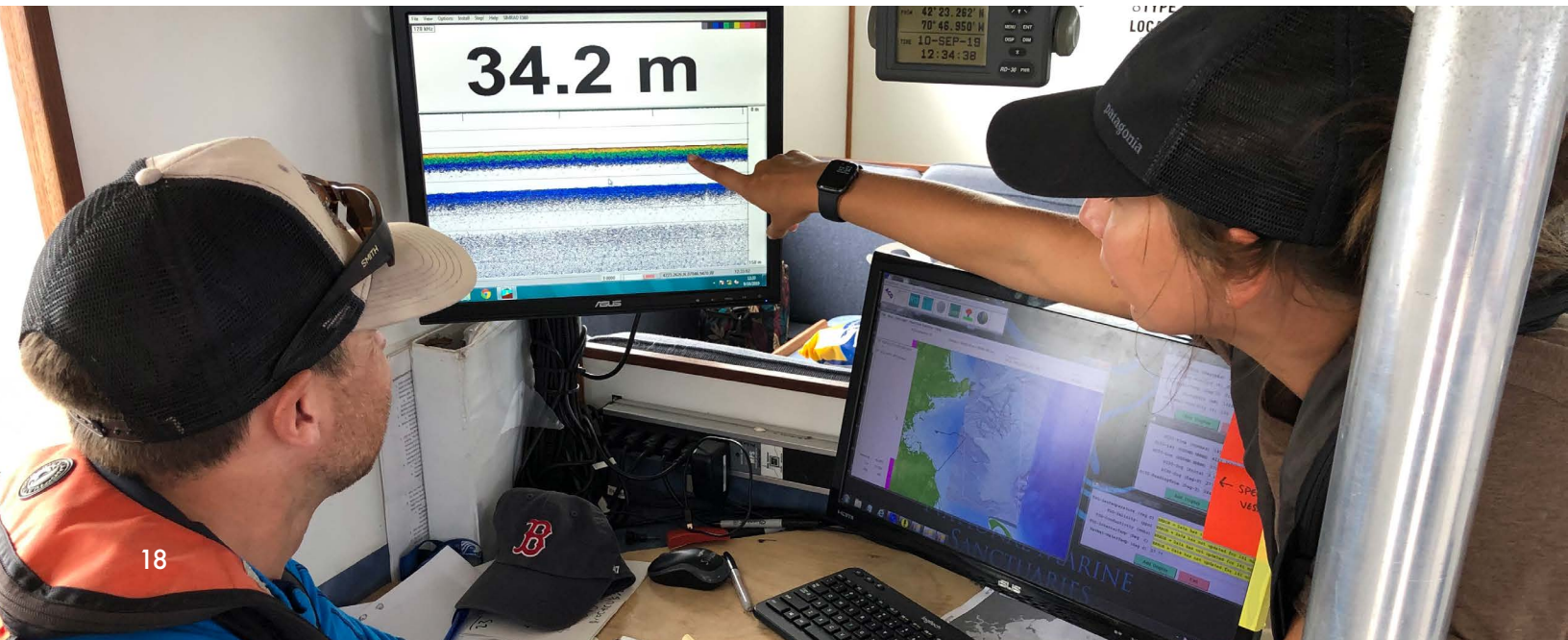
Key Personnel: **Laurel Schaider**, Silent Spring Institute (SSI)

Overview

This project is developing, validating, and deploying novel passive samplers for the detection of poly- and perfluoroalkyl substances (PFAS) in air, water, and porewater (water in the sediment) and as a potential screening tool for bioaccumulation. At contaminated sites, as the extent of a PFAS plume is investigated, the benefits of field-validated passive sampling approaches include ease of handling, shipping, and analysis; reduced potential for contamination; and lower detection limits that will be needed as regulatory agencies adjust their references doses.

This project is:

- Developing a porewater fiber for measuring PFAS concentrations.
- Collaborating with U.S. Environmental Protection Agency (EPA) to determine PFAS accumulation in bivalves (e.g., mussels and oysters), and comparing these results to the novel passive samplers.
- Validating PFAS passive sampling tools.



Sites for field validation and application are located on Cape Cod, MA, including in ponds near Joint Base Cape Cod, where groundwater is contaminated by aqueous film forming foams (AFFF). Researchers are engaging residents and stakeholders to address concerns about long-range PFAS transport and characterizing the extent of impacted ponds, creeks, and estuaries.

Progress to date

- Assessed the distribution of legacy and emerging PFAS in different bird tissues from coastal and offshore seabirds from the US East Coast in collaboration with U.S. EPA (Anna Robuck, trainee).
- Collaborated with Brown University (Dr. Hurt) on testing and modifying nanographites as potential sampling tools for PFAS (Jitka Becanova, trainee).
- Validated polyethylene sheets to detect precursor PFAS indoors (Maya Morales McDevitt, trainee).
- Performed the first laboratory experiments on how to sample PFAS with thin fibers, and first tests linked to measuring the bioavailability of PFAS in controlled lab experiments (Jitka Becanova, trainee).
- Used passive sampling tubes to derive transport and fate of PFAS in Narragansett Bay and two local wastewater treatment plants to derive sampling rates (Christine Gardiner, trainee alumnus).

Plans for upcoming year

- Field-test passive samplers for PFAS in a stream on Cape Cod next to a USGS gauge to evaluate their performance under a range of field conditions (Matt Dunn, trainee).
- Collect shellfish and water samples from additional ponds and estuaries throughout Cape Cod to identify future sampling sites.
- Continue field-testing passive samplers on Guam to identify PFAS sources to groundwater. (Jitka Becanova, trainee)
- Assess transport and fate of PFAS in Narragansett Bay from an AFFF application in collaboration with EPA. (Christine Gardiner, former trainee)
- Derive bioaccumulation of PFAS in mobile lab experiments relative to passive samplers. (Alan Vajda, Project 1)
- Validate PE sheets as outdoor air passive samplers in a waste water treatment plant in collaboration with the Narragansett Bay Commission. (Maya Morales-McDevitt, trainee)
- Test PE-tubes as total PFAS samplers in indoor air. (Melissa Woodward, trainee)
- Derive temporal trends of PFAS in seabirds 2007-2019. (Anna Robuck, trainee)
- Assess novel PFAS in the Delaware River combining fish, water and passive samplers. (Anna Robuck, trainee)
- Participate in STEEP renewal development and submission.

PROJECT 4 TRAINEES

Jitka Becanova, Postdoctoral Researcher, GSO URI
Matt Dunn, PhD Student, GSO URI
Izak Hill, MS student, GSO URI
Maya Morales-McDevitt, MS Student, GSO URI
Anna Robuck, PhD Student, GSO URI
Melissa Woodward, PhD Student, GSO URI
Tatyana Yanishevsky, MS Student, GSO URI

PROJECT 4 GRADUATES

Christine Gardiner, GSO URI
Erik Dixon-Anderson, GSO URI

SELECTED ACCOMPLISHMENTS

Ian T. Cousins, Gretta Goldenman, Dorte Herzke, Andrew B. Lindstrom, **Rainer Lohmann**, Mark Miller, Carla A. Ng, Sharyle Patton, Martin Scheringer, Xenia Trier, Lena Vierke, Zhanyun Wang, Jamie C. DeWitt. The concept of essential use for determining when uses of PFAS can be phased out. *Environ Sci: Processes & Impact* 2019, 21(11):1803-1815. doi: 10.1039/c9em00163h
Selected as one of the Best Papers of 2019

Cordner, Alissa, Vanessa Y. De La Rosa, **Laurel A. Schaider**, Ruthann A. Rudel, Lauren Richter, Phil Brown. Guideline levels for PFOA and PFOS in drinking water: the role of scientific uncertainty, risk assessment decisions, and social factors. *J Exp Sci Environ Epidemiol* 2019, 29,157-171. doi: 10.1038/s41370-018-0099-9
2020 ISES Award for Best JESEE Paper

Ian T. Cousins, Juliane Glüge, Gretta Goldenman, Dorte Herzke, **Rainer Lohmann**, Mark Miller, Carla A. Ng, Sharyle Patton, Martin Scheringer, Xenia Trier, Lena Vierke, Zhanyun Wang, Jamie C. DeWitt: Strategies for grouping per- and polyfluoroalkyl substances (PFAS) to protect human and environmental health. *Environ Sci: Processes & Impact* 2020, 22 (7): 1444-1460.

Anna R. Robuck, Mark G. Cantwell, James McCord, Lindsay Addison, **Marisa Pfohl**, Mark J. Strynar, Richard McKinney, David R. Katz, David N. Wiley and **Rainer Lohmann**. Per- and Polyfluoroalkyl Substances (PFAS) in Juvenile Seabirds from the US Atlantic Coast. *Environ Sci Technol* 2020, June – revised.

Rainer Lohmann, Ian T. Cousins, Jamie C. DeWitt, Juliane Glüge, Gretta Goldenman, Dorte Herzke, Andrew B. Lindstrom, Mark Miller, Carla A. Ng, Sharyle Patton, Martin Scheringer, Xenia Trier, Lena Vierke, Zhanyun Wang. Are fluoropolymers really polymers of low concern and separate from other PFAS? *Environ Sci Technol* 2020 submitted.

Rainer Lohmann: Passive Samplers for PFAS in Surface Water and Air; Presentation at 2-day webinar on PFAS Sampling for Environmental Professionals by Environmental Professionals Organization of Connecticut, webinar June 2020.

Rainer Lohmann, "Passive sampling of PFAS in air and water," US EPA Superfund Contaminated Sediment Forum, webinar March 2020.

Jamie DeWitt and **Rainer Lohmann**, "The Concept of Essential uses of PFAS," Science Response Network webinar. September 2019.

Susmann, Herbert P., **Schaider Laurel A.**, Rodgers Kathryn M., Rudel, Ruthann A. Dietary Habits Related to Food Packaging and Population Exposure to PFAS. *Environ Health Perspect* 2019, in press. doi: 10.1289/EHP 4092. Featured in *EHP* Science Selection "PFAS in Food Packaging: A Hot, Greasy Exposure," 5/28/20. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7255411/

Laurel Schaider. PFAS and other contaminants of emerging concern in the waters of Cape Cod: Understanding exposures and addressing community concerns. Dartmouth College/ Hitchcock Medical, Department of Epidemiology, invited seminar. September 2019.

Laurel Schaider and Phil Brown. Working with communities to understand and address PFAS exposures. NIEHS Partnerships for Environmental Public Health. March 2020. https://www.niehs.nih.gov/research/supported/translational/peph/webinars/pfas/index.cfm

Rainer Lohmann appointed to RI Dept of Health's PFAS Drinking Water Technical Advisory Group.

Administrative Core

Director: **Rainer Lohmann**, Graduate School of Oceanography, University of Rhode Island (GSO)

Co-director: **Philippe Grandjean**, Harvard T.H. Chan School of Public Health, Department of Environmental Health (HSPH)

Project Coordinator: **Wendy Lucht**, Graduate School of Oceanography, University of Rhode Island (GSO)

Overview

The Administrative Core (AC) is the central hub of STEEP, responsible for oversight and management of the Superfund Research Program (SRP). Its main role is to ensure the efficacy of STEEP's activities, which include producing integrated research, communicating findings to multiple audiences, engaging multiple researchers and communities, and training next generation scientists. The AC provides fiscal oversight and is integrated with the rest of the SRP through the Director's and Co-Director's leadership as well as their roles in active STEEP project research, communication, and outreach. The AC, supported by the coordinator, works closely with the STEEP Internal Advisory Committee (IAC), and the External Advisory Committee (EAC).

STEEP plans to engage Harrison Dekker (URI Library) to enhance data sharing within the SRP and promote data integration among projects and cores. With support from a graduate research assistant, Dekker will manage and curate data and move it towards the Open Science Platform. Dekker will assist the STEEP team in adopting fundamental FAIR data practices: data management, code management, project organization and communication. Data sharing will support public-domain release of STEEP chemical and biological data and integrated analysis with nationally available chemical and biological databases.

This core:

- Ensures successful integration of research projects and cores through regular meetings and evaluations from internal and external advisory committees.
- Provides relevant operational insights and tools for stakeholders and communities.
- Coordinates the SRP's timely response to opportunities, challenges, and evaluations.

Completed and ongoing activities

- Administer the grant and subcontracts serving as the liaison between the University of Rhode Island, Harvard T.H. Chan School of Public Health, Silent Spring Institute, and the National Institute of Environmental Health Sciences (NIEHS).
- Provide financial oversight and support to each project and core.
- Manage reporting to NIEHS: Research Performance Progress Report (RPPR), Annual Update, fiscal reporting, and SRP Data Collection Tool.
- Manage the STEEP team calendar.
- Coordinate STEEP-wide interaction with federal and state agencies and stakeholders; support AC leads in maintaining comprehensive interactions with national and international leaders in the field.

HIGHLIGHTS FROM STEEP LEADERSHIP

- Rainer Lohmann appointed to U.S. EPA's Board of Scientific Counselors.
- Conference calls with stakeholders and state agencies on current and future PFAS needs (RIDEM, RIDOH, MassDEP, NHDES, VT DEC, Toxics Action Network; New England Biosolids and Residuals Association).
- Lohmann, Angela Slitt, and Alyson McCann appointed to the RI taskforce on setting MCLs for PFAS
- Submission of STEEP written comments and oral testimony in MA, NH in support of establishing science-based MCLs for PFAS in drinking water.
- Representing STEEP at Senator Sheldon Whitehouse's (RI, D) Annual Energy and Environment Leaders Day.
- Submission and administration of supplemental SRP grants linked to Data Science, Alzheimer's research, trainee externships and new instrumentation.
- Preparation in progress for PFAS in Our World (virtual trainee symposium), October 2020 and FLUOROS 2021 symposium in Providence, RI.
- Participate in STEEP renewal development and submission.

CONTRIBUTIONS TO PEER SRPS

Co-organized 2nd National PFAS conference, Northeastern University, May 2019; co-organizer of 3rd National PFAS conference in NC, 2021.

Planned administrators' session at National SRP meeting, Seattle, WA, November, 2019.

Corresponds with RI Congressional Delegation regarding NIEHS budget and PFAS-related language under consideration in federal legislation.

National and International Collaborations

SRP lead Lohmann and co-lead Grandjean continue to engage in high-level meetings at both the national and international level as well as meeting with Congressional staff. This provides STEEP with an important voice in the international emerging contaminants community, most specifically with regard to PFAS and next generation chemicals. Their work also ensures that STEEP is on the cutting edge of discovery and subsequent regulatory action.

- Grandjean continues to advise on water pollution problems in New Hampshire, Vermont, Alabama, and Michigan.
- Lohmann, as a member of the Global PFAS Science Panel, co-authored "The concept of essential use for determining when uses of PFAS can be phased out" (Cousins et al., 2019) and "Strategies for grouping per- and polyfluoroalkyl substances (PFAS) to protect human and environmental health" (Cousins et al., 2020). These papers have been broadly disseminated and inform policy on PFAS, particularly in the EU.
- Grandjean served as ad hoc expert on the risks to human health from PFAS-contaminated food to the European Food Safety Authority.
- Lohmann provided expert testimony at RI House Environment and Natural Resources Committee on PFAS in drinking and surface waters.

Internal Advisory Committee

Rainer Lohmann, PhD, SRP Director, University of Rhode Island (ex officio)

- **Philippe Grandjean**, MD, DMSc, SRP Co-Director, Harvard University
- **Judith Swift**, MA, Research Translation Core, University of Rhode Island
- **Peter Snyder**, PhD, Vice-President for Research, University of Rhode Island (ex officio)
- **Art Gold**, PhD, Natural Resource Sciences, University of Rhode Island
- **Bongsup Cho**, PhD, Pharmacy, University of Rhode Island
- **Wendy Lucht**, GSO, University of Rhode Island (ex officio)

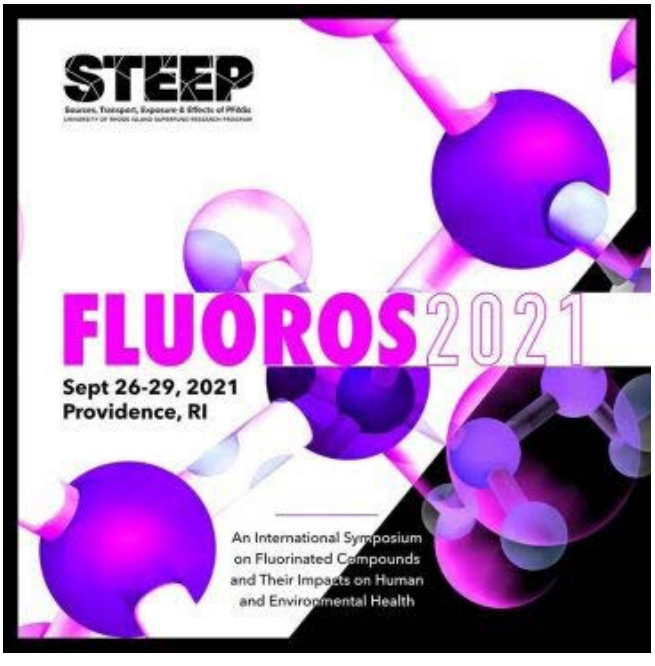
The STEEP SRP reports to Vice President Snyder, and fosters the interaction of STEEP with new colleagues within URI, including the URI Health Collaborative, the URI College of Business Textiles, Fashion, and Design Department, URI Harrington School of Communication and Media, URI Business Engagement Center, and Library Services.

External Advisory Committee

David Sherr, PhD, Professor Environmental Health, Boston University (chair)

- **Linda Abriola**, PhD, Professor, Civil and Environmental Engineering, Tufts University
- **Jane Crowley**, RS, MS, Eastham Health Agent, Director of Health and Environment
- **Gary Ginsberg**, PhD, New York State Department of Health, Director, Center for Environmental Health
- **Marc A. Mills**, PhD, United States Environmental Protection Agency, Office of Research and Development

The primary goals of the EAC are to provide guidance, feedback, and resources to STEEP with a focus on the scientific merit of the research; the relevance and importance of the individual components to the goals of the SRP; the integration of research across disciplines; the effectiveness of research translation activities in linking projects and stakeholders; and the appropriateness of community engagement and training activities. STEEP year 3 evaluation will take place at the EAC meeting in September 2020.



Research Translation Core

Core Lead: **Judith Swift**,
Coastal Institute at URI

Co-lead: **Nathan Vinhateiro**,
Coastal Institute at URI

Co-lead: **Amber Neville**,
Coastal Institute at URI

Overview

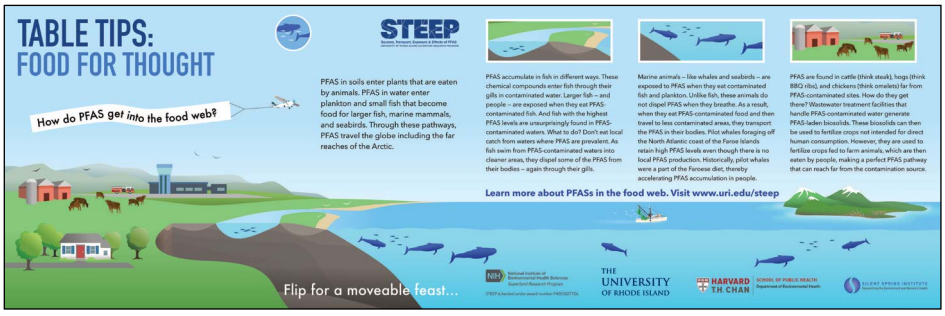
The Research Translation Core (RTC) continues to make STEEP's research results and the implications of these findings readily accessible to stakeholders to assist them in understanding the effects and characterizing the risk of PFAS exposure. As part of this iterative communication strategy, RTC embeds opportunities for stakeholders to provide feedback to SRP researchers at regular intervals, complemented by a clear timeline for researchers to provide updates in response to community concerns.

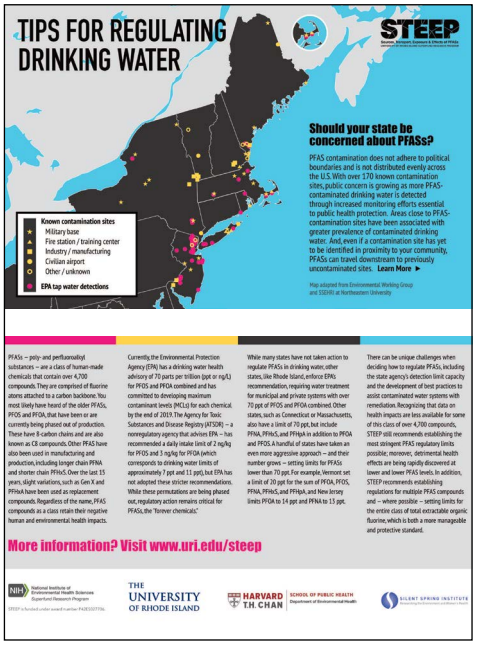
As this process continues, stakeholders and researchers continue to narrow in on scientific questions and research strategies that are essential to management and regulatory applications as well as supporting an informed community.

To accomplish overarching bidirectional communication, RTC develops targeted messages for: 1) researchers within STEEP and the broader SRP network; 2) state and federal agencies including the NIEHS, U.S. EPA, Agency for Toxic Substances and Disease Registry (ATSDR), and Tribal Councils; 3) other end-users with a focus on communities on Cape Cod, MA, and the Faroe Islands; and 4) additional groups as identified or, in turn, reach out to STEEP.

This core:

- Ensures STEEP's results are widely disseminated guided by principles of the Transtheoretical Model of behavior change (TTM).
- Provides information to state and federal regulators as well as industry leaders to influence the mitigation of PFAS use to protect human and environmental health.
- Facilitates technology transfer where appropriate.





PFAS: What are they? Where do they come from? How do they impact your health? What can you do to reduce exposure to them?

Get practical answers to tough questions about "forever chemicals" via the new STEEP Superfund research program's short video series featuring key project researchers.

PFAS: What Are They? with Rainer Lohmann
PFAS: Where Do They Come From? with Rainer Lohmann
PFAS: Where are They in the Environment? with Anna Robuck
PFAS: How Do They Travel in the Environment? with Rainer Lohmann
PFAS: How Do They Impact Ecosystems? with Anna Robuck
PFAS: How Exposed Am I? with Anna Robuck
PFAS: How Might Exposure Impact My Health? with Angela Slitt
PFAS: What Can I Do? with Anna Robuck

- Synergizes relationship with Community Engagement Core (CEC) to ensure wide dissemination of information to affected communities, and improve communication techniques of STEEP trainees, scientists, and researchers.
- Coordinates broad-spectrum outreach and communication efforts in partnership with CEC and Training Core (TC).

RTC is adapting the message complexity to suit individual target audiences without jeopardizing the scientific rigor demanded by the investigation of emerging contaminants

Progress to date

- Developed and launched two conference websites and related promotional graphics for "PFAS in Our World," to be held virtually in October, 2020, and "FLUOROS 2020." (COVID-19 interrupted – postponed to 2021) *CI—2021
- Continued to consistently update website—www.uri.edu/steep—including conceptual design of infographics, illustrations, and mixed-use communication tools to stimulate intellectual and emotional response to engage affected communities. Continue to use social media as a means to drive Gen Zs and millennials to the website.
- Produced, launched, and promoted 8 short videos (3-7 mins), each featuring a STEEP researcher and exploring topics ranging from what PFAS are to their impact on human and environmental health to what can be done to reduce PFAS exposure and use.
- Developed outreach events to complement CEC study site community engagement, focusing on a range of audiences including other SRPs, government agencies, university communities, and environmental groups.
- Continued to enhance STEEP branding and promote PFAS science education through social media.
- Presented on RTC/CEC monthly webinar hosted by NIEHS SRP.
- Published tri-annual STEEP newsletter: https://web.uri.edu/steep/news-events/newsletter/
- Developed library of outreach resource material: https://web.uri.edu/steep/resources/
- Taught two sessions as part of trainee colloquium focused on communication skills, social media implementation, and career development.
- Developed and planned workshops for trainees to develop protocol for colloquia; assisted with development of new trainee orientation packet and

offered face-to-face coaching (hosting speakers, promoting events, engaging with the public, utilizing social media, informing elected officials, applying for awards, fellowships, etc.).

- Planned improvisational workshop for trainees to hone flexible and interpersonal skills for public information sessions. *CI—2021
- Shared STEEP materials at Land & Water Conservation Summit March 2020.
- Attended three *The Virus of Racism* workshops and a 2-day conference on diversity, equity, and inclusion (DEI) with Mi'kmaq Tribe in Nova Scotia, Canada to heighten diversity awareness for presentations and publications, and reviewing materials through DEI lens.

Plans for upcoming year

- Develop tip cards on continued use versus disposal of PFAS-laden products, medical monitoring, and adverse health effects of PFAS exposure. *CI—2021
- Create one-pager for healthcare providers and tip cards for medical waiting rooms focused on ubiquitous and toxic nature of PFAS and potential for long-term—but slow developing—adverse health impacts. *CI—2021
- Full revision of current website to capture accomplishments and additional goals. New features (pop-up videos and podcasts) to assist the public in navigating the complexity of information. Evolving values will reflect DEI. *CI—2021
- Develop additional videos, promote through social media, and make viewable on both the STEEP website and YouTube.
- Develop six 10-minute PFAS-focused podcasts, e.g., history, health risks, regulation and remediation, consumer products, and disposal/phaseout strategies. *CI—2021
- Continue work with CEC to promote current efforts and, as possible, RTC will develop additional programming to reach target groups with specific interests and concerns.
- Develop template for CEC on town-specific testing results.
- Partner with North Carolina State University SRP on community engagement products.
- Seek funding to support translation of tip cards and information sheets to Spanish, et al.
- Promote FLUOROS 2021 via social media using DEI materials to diversify attendees.
- Develop informational 2-pager on COVID-19 and PFAS and their link due to chemicals' immune system adverse health impacts.
- Participate in STEEP renewal development and submission.

SELECTED ACCOMPLISHMENTS

STEEP 8 Short Video Series SILENT CHEMICALS, LOUD SCIENCE, Part 1: PFAS: What Are They? https://web.uri.edu/steep/part-1-pfas-what-are-they/

Amber Neville, Laurel Schaider, **Judith Swift**, Alyson McCann, **Nathan Vinhateiro**, Amanda Hernandez. Communicating private well water testing results and the human health implications of PFAS contamination through targeted messaging and tailored media. NIEHS Superfund Research Program Annual Meeting, Seattle, WA, November 18-20, 2019. https://web.uri.edu/steep/files/SRP-Poster-2019-lowres.pdf

Outreach resources: https://web.uri.edu/steep/resources/outreach/

Promotional social media placards: https://web.uri.edu/steep/science-day/

Social media outreach

Twitter Stats:
7.7K impressions in last quarter

Public health experts, including STEEP co-lead and Harvard Professor Dr. Philippe Grandjean, begin research on the relationship between PFAS exposure and COVID-19:
1424 impressions, 55 engagements

Registration open for the "PFAS In Our World" Virtual Conference, held October 13-14, 2020:
653 impressions, 50 engagements

STEEP director Lohmann and coauthors advise on best scientific and regulatory grouping strategies for PFAS to protect human and environmental health:
1025 impressions, 72 engagements

Community Engagement Core

Co-lead: **Alyson McCann**, College of the Environment and Life Sciences, University of Rhode Island (CELS)

Co-lead: **Laurel Schaider**, Silent Spring Institute (SSI)

Overview

Community Engagement Core (CEC) activities are centered on Cape Cod, MA, a region where groundwater and drinking water have been impacted by per- and polyfluoroalkyl substances (PFAS). The CEC is engaging with residents, local officials, non-profit organizations, and regulators to protect human health and support local water quality protection.

This core is:

- Implementing a PFAS testing and report-back program for private well owners on Cape Cod.
- Hosting an annual STEEP Science Day on Cape Cod for researchers and trainees to share research findings and for stakeholders and community members to ask questions and inform research and engagement activities.
- Participating in community events and responding to the community's needs by providing scientific expertise in response to local questions and concerns.
- Promoting and implementing prevention and intervention strategies to reduce exposures to PFAS.

The CEC is collaborating with its core community partners, the Massachusetts Breast Cancer Coalition (MBCC) and the Sierra Club Cape Cod Group, to expand community outreach by engaging a broader base of each community partners' constituents. The CEC's activities on Cape Cod are connected to STEEP research projects. Private well testing results will inform chemical "fingerprinting" as part of the Environmental Fate & Transport research, and input from Cape residents and stakeholders will inform site selection as part of the Detection Tools research.

Progress to date

PRIVATE WELL STUDY AND INTERVIEWS WITH PARTICIPANTS

As part of its October 2019 Science Day, the CEC shared an overview of the preliminary findings from its Cape Cod private wells study. These findings were based on the first 101 wells from 12 towns that were sampled and summarized in a fact sheet developed in collaboration with RTC. Each participant received a customized report with the results for their own well that was developed using SSI's Digital Exposure Report-Back Interface (DERBI).

While plans to collect the next round of water samples have been on hold due to COVID-19, CEC is moving forward with a series of 20-minute phone interviews with participating private well owners on Cape Cod to capture their perspective on information they received as a participant in the study, particularly their interpretation of the information in their individual well report. Participants were randomly selected from three subgroups: half were participants with any detectable PFAS chemical, one third were participants with no detectable PFAS, and the rest were participants who have not opened their report. Thus far, 19 of 30 planned participants have been interviewed.

Preliminary survey responses indicate that there is a spectrum of awareness on the Cape regarding water issues, ranging from a general awareness of water concerns to specific knowledge of PFAS chemicals. All interviewees expressed appreciation for the information, and particularly preferred viewing the printed report to see how their home compared to others in the study and the ability to share the information with others.

FOCUS GROUPS OF PRIVATE WELL OWNERS

CEC will hold focus group(s) with private well water study volunteers to learn about motivations and barriers to testing private drinking water wells. The resulting information will help CEC to understand what motivates private well owners to test—or not—their drinking water. Due to COVID-19, focus groups scheduled for March 16, 2020, were cancelled, and the revised URI Institutional Review Board Protocol was approved to allow CEC to move forward with remote focus groups beginning in September 2020.

PLANNING FOR SCIENCE DAY SERIES

In response to COVID-19 social distancing requirements, the 2020 annual Science Day event will be a series of online public presentations featuring STEEP researchers and trainees. In collaboration with RTC, CEC is planning a series of four events throughout the fall of 2020. Each presentation will consist of a pre-recorded presentation followed by live Q&A with STEEP team members. The Town of Barnstable has offered to host these presentations via Zoom, and they will be streamed live online and on the local access cable channel.

ENGAGING WITH HIGH SCHOOL STUDENTS ON CAPE COD

2019 Science Day included 80 students from five Cape Cod high schools. Building on this foundation, CEC is collaborating with the head of the Sierra Club Cape Cod Group, who is also a high school teacher, to contact teachers in biology, chemistry, and environmental science.

ENGAGING WITH MASHPEE WAMPANOAG TRIBE

The CEC is developing a partnership with the Mashpee Wampanoag Tribe on Cape Cod to discuss potential collaborations, including measuring PFAS in drinking

water and fish and shellfish, evaluating whether members of the Tribe face uniquely elevated exposures due to their reliance on local resources, and developing strategies for communicating information about risks with Tribe members. Emily Diamond, who holds a joint appointment as professor of Communication Studies and Marine Affairs at URI, is seeking external funding to support these efforts.

CONTRIBUTING TO STATE-LEVEL DECISION-MAKING

CEC PIs have contributed to state-level decision-making processes regarding PFAS in MA and RI. McCann—along with STEEP researchers Rainer Lohmann and Angela Slitt—is a member of the RI Department of Health's PFAS Drinking Water Technical Advisory Committee and is actively providing input on development of PFAS drinking water standards. Schaider, along with other STEEP researchers, submitted written comments to the MA Department of Environmental Protection (MassDEP) in February 2020 on proposed state drinking water standards (MCLs). Schaider and MBCC's executive director Cheryl Osimo also provided oral testimony at a public hearing about the proposed MCLs in January 2020.

COLLABORATION WITH COMMUNITY GROUPS AND ATTENDANCE AT COMMUNITY EVENTS

STEEP trainees, CEC, and RTC met with residents and distributed informational materials at community events, including:

- Cape Cod Moms Parent Resource Fair, Barnstable, MA, Jan. 25, 2020
- Local Environmental Action Conference, Boston, MA, March 7, 2020
- Rhode Island Land and Water Conservation Summit, Kingston, RI, March 7, 2020
- Outreach activities have been curtailed due to COVID-19.
- Barnstable County's Virtual Water Fair (moved to online), starting May 30, 2020

Schaider provided an update of STEEP's private well water testing program at SSI's December 2019 Cape Cod research update, attended by over 60 participants and covered by local media.

Schaider presented at a community event on November 13, 2019, hosted by the Unitarian Universalist Fellowship of Falmouth and co-hosted by the Sierra Club Cape Cod Group and MBCC.

Osimo of MBCC provided PFAS updates to the Barnstable Town Council, the Hyannis Water Board, and Greater Hyannis Civic Association. STEEP materials have been shared at community events on Cape Cod and throughout MA at tables organized by MBCC.

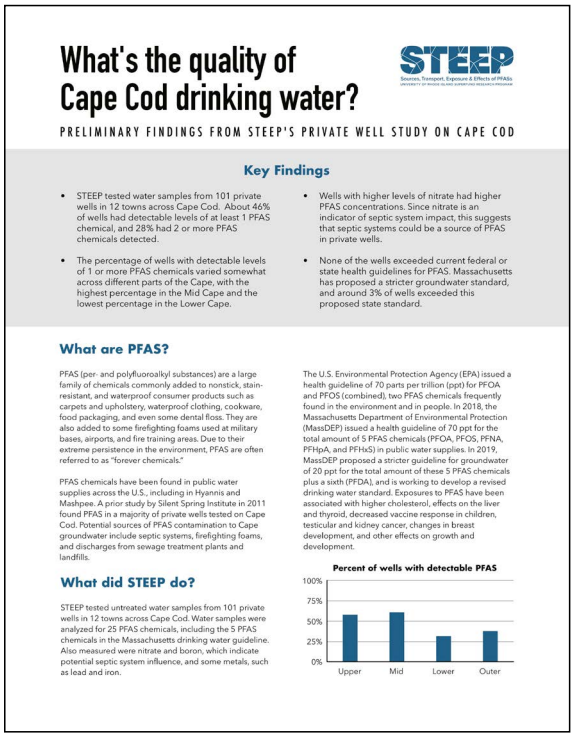
At the request of one of the West Barnstable Water Commissioners, Schaider provided an information session and accompanying one page overview summarizing CEC's private wells study at commissioners' meeting in February 2020.

Plans for upcoming year

- *Follow-up round of private well testing and report-back*. In collaboration with Project 1, CEC aims to collect water samples from another 150 private wells on Cape Cod once COVID-19 restrictions allow. Members of the Mashpee Wampanoag Tribe will be especially welcomed to participate.
- *Interviews with private well study participants*. CEC will complete interviews with study participants and synthesize findings for publication in a peer-reviewed journal article.
- *Focus groups with private well owners*. In August/September 2020, CEC will conduct two Zoom focus groups with Cape Cod private well owners to identify barriers to private well water testing and treatment.
- *Virtual Science Day Series*. In Fall 2020, CEC, with the support of the Town of Barnstable, will host four virtual presentations to update Cape Cod residents about STEEP research and the evolving local and national regulatory and policy landscape. These virtual presentations will be rebroadcast on local access TV and available on the STEEP website.
- *High school engagement*. CEC will organize lessons with high school students on Cape Cod in Fall 2020. Working with a STEEP trainee action team that is developing lessons for high school students, CEC will organize real-time student-to-trainee discussions. CEC foresees a fall 2021 event that would bring together high school students from across the Cape to discuss water quality and emerging contaminants.
- *Mashpee Wampanoag Tribe engagement*. CEC will coordinate collection and testing of additional

samples from tribal lands, work with RTC to translate findings into tribal-specific materials, and develop a series of engagement activities to inform tribal members about PFAS risks.

- *State-level policymaking*. McCann will continue to work on the RI Department of Health's PFAS Technical Advisory Committee and serve as a resource to this committee. Schaider will continue to provide input to MassDEP and will attend its new Stakeholder Process for PFAS & Residuals beginning in Fall 2020.
- *Meetings with Cape Cod Community Advisory Committee and other stakeholders*. CEC will continue to meet with the Cape Cod advisory committee and other stakeholders on the Cape to help identify additional community engagement opportunities and to garner suggestions for the STEEP renewal.
- Participate in STEEP renewal development and submission.



What's the quality of Cape Cod drinking water?

STEEP

PRELIMINARY FINDINGS FROM STEEP'S PRIVATE WELL STUDY ON CAPE COD

Key Findings

- STEEP tested water samples from 101 private wells in 12 towns across Cape Cod. About 46% of wells had detectable levels of at least 1 PFAS chemical, and 28% had 2 or more PFAS chemicals detected.
- The percentage of wells with detectable levels of 1 or more PFAS chemicals varied somewhat across different parts of the Cape, with the highest percentage in the Mid Cape and the lowest percentage in the Lower Cape.
- Wells with higher levels of nitrate had higher PFAS concentrations. Since nitrate is an indicator of septic system impact, this suggests that septic systems could be a source of PFAS in private wells.
- None of the wells exceeded current federal or state health guidelines for PFAS. Massachusetts has proposed a stricter groundwater standard, and around 3% of wells exceeded this proposed state standard.

What are PFAS?

PFAS (per- and polyfluoroalkyl substances) are a large family of chemicals commonly added to nonstick, stain-resistant, and waterproof consumer products such as carpets and upholstery, waterproof clothing, cookware, food packaging, and even some dental floss. They are also added to some firefighting foams used at military bases, airports, and fire training areas. Due to their extreme persistence in the environment, PFAS are often referred to as "forever chemicals."

PFAS chemicals have been found in public water supplies across the U.S., including in Hyannis and Mashpee. A prior study by Silent Spring Institute in 2011 found PFAS in a majority of private wells tested on Cape Cod. Potential sources of PFAS contamination to Cape groundwater include septic systems, firefighting foams, and discharges from sewage treatment plants and landfills.

What did STEEP do?

STEEP tested untreated water samples from 101 private wells in 12 towns across Cape Cod. Water samples were analyzed for 25 PFAS chemicals, including the 5 PFAS chemicals in the Massachusetts drinking water guideline. Also measured were nitrate and boron, which indicate potential septic system influence, and some metals, such as lead and iron.

The U.S. Environmental Protection Agency (EPA) issued a health guideline of 70 parts per trillion (ppt) for PFOA and PFOS (combined), two PFAS chemicals frequently found in the environment and in people. In 2018, the Massachusetts Department of Environmental Protection (MassDEP) issued a health guideline of 70 ppt for the total amount of 5 PFAS chemicals (PFOA, PFOS, PFNA, PFHpA, and PFHxS) in public water supplies. In 2019, MassDEP proposed a stricter guideline for groundwater of 20 ppt for the total amount of these 5 PFAS chemicals plus a sixth (PFDA), and is working to develop a revised drinking water standard. Exposures to PFAS have been associated with higher cholesterol, effects on the liver and thyroid, decreased vaccine response in children, testicular and kidney cancer, changes in breast development, and other effects on growth and development.

Percent of wells with detectable PFAS

SELECTED ACCOMPLISHMENTS

Presentations

Schaider L, McCann A, Hernandez A, Pickard H, Balcom P, Sunderland E. Legacy and alternative PFAS compounds in private wells on Cape Cod, Massachusetts, USA. Oral presentation. Society of Environmental Toxicology and Chemistry North America 40th Annual Meeting, Toronto, 2019.

Schaider L, McCann A, Hernandez A, Pickard H, Balcom P, Sunderland E. Legacy and Alternative PFAS Compounds in Private Wells on Cape Cod, Massachusetts, USA. Poster presentation. NIEHS Superfund Research Program Annual Meeting, Seattle, 2019.

Webinars

"PFAS in Massachusetts Drinking Water: An Update on Research and Regulations." Laurel Schaider. Hosted by Massachusetts Breast Cancer Coalition. October 30, 2019. http://mbcc.org/breast-cancer-prevention/pfas-in-ma-drinking-water-october-webinar-recording/

Local media coverage and editorials

Cape Cod Times, 12/11/19 (Editorial)
Written by Laurel Schaider and Cheryl Osimo. "PFAS: A local and global challenge." https://www.capecodtimes.com/opinion/20191211/pfas-local-and-global-challenge

Cape Cod Times, 12/11/19.
"Researchers: Hyannis PFAS studies will move ahead." https://www.capecodtimes.com/news/20191211/researchers-hyannis-pfas-studies-will-move-ahead

Barnstable Patriot, 12/12/19
"Silent Spring shares latest research on PFAS exposure."
https://www.barnstablepatriot.com/news/20191212/silent-spring-shares-latest-research-on-pfas-exposure

CapeCod.com, 12/12/19
"Silent Spring Institute Provides Updates on PFAS Studies."
https://www.capecod.com/newscenter/silent-spring-institute-provides-updates-on-pfas-studies/

Cape Cod Times, 7/12/20
"Carcinogenic chemicals found in Nantucket well water." https://www.capecodtimes.com/news/20200712/carcinogenic-chemicals-found-in-nantucket-well-water

Other media coverage and editorials

WBUR Boston, 11/8/19
"What Are PFAS Chemicals, And Should I Be Freaking Out About Them?"
https://www.wbur.org/earthwhile/2019/11/08/what-are-pfas-chemicals-and-should-i-be-freaking-out-about-them

National Geographic, 1/24/20
"Toxic 'forever chemicals' more common in tap water than thought, report says."
https://www.nationalgeographic.com/science/2020/01/pfas-contamination-safe-drinking-water-study/

Inverse, 3/2/20
"PFAS: Your home is full of potentially harmful "forever chemicals" – here's what you need to know."
https://www.inverse.com/mind-body/pfas-explained-your-home-is-full-potentially-harmful-forever-chemicals

Environmental Health News, 7/6/20
"Op-ed: PFAS chemicals—the other immune system threat."
https://www.ehn.org/pfas-and-immune-system-2646344962.html

Wired, 8/7/20
"The End Is Nearer for 'Forever Chemicals' in Food Wrappers."
https://www.wired.com/story/the-end-is-nearer-for-forever-chemicals-in-food-wrappers/

Training Core: Next Generation

Co-lead: **Angela Slitt**, URI College of Pharmacy (Pharm)

Assessment Coordinator: **John Stevenson**, Professor Emeritus of Psychology, University of Rhode Island (PSY)

Co-lead: **Elsie Sunderland**
Harvard T.H. Chan School of Public Health, Department of Environmental Health (HSPH)
Harvard John A. Paulson School of Engineering and Applied Sciences (SEAS)

TC Coordinator: **Alicia Crisalli**, PhD Student, Pharm URI, TC Trainee

Overview

The STEEP Training Core (TC) is responsible for shaping the next generation of environmental health scientists into well-rounded researchers with an interdisciplinary approach and the professional skills necessary to succeed after graduate school. The TC will provide pre- and post-doctoral level STEEP trainees with additional resources and opportunities to become skilled scientists and engineers. They will be able to address various aspects of emerging contaminants, specifically empirical research, practical remediation, community engagement, and research translation facets of PFAS.

The primary goals of the Training Core are to:

- Promote and coordinate inter- and intra-institutional as well as interdisciplinary cross-training experiences.
- Provide professional development opportunities to enhance leadership, peer-to-peer mentoring, outreach, and communication skills.
- Collaborate with Research Translation and Community Engagement Cores to provide skills often not addressed in traditional PhD programs.
- Connect trainees through social media to create a cohesive and integrated team.
- Support intra-STEEP lab exchanges and participation in professional conferences.

The TC is capitalizing on STEEP's multi-institutional strength by focusing on innovative and interdisciplinary training activities. The TC supports three distinct groups of research trainees over the entire five-year grant cycle: fully supported pre-doctoral trainees, fully supported post-doctoral trainees, and partially STEEP-funded graduate students and post-doctoral fellows. In addition, two STEEP fellowships for students from underrepresented minority groups are being supported through the URI Graduate School Diversity Program. All graduate trainees will be fully immersed in their rigorous interdisciplinary training activities.

Progress to date

- Organized and completed another iteration of the Colloquium on PFAS I. Due to COVID-19, the colloquium was moved to a conference call format in March 2020.
- Coordinated the virtual colloquium visit by Dr. Carla Ng of the University of Pittsburgh, and Dr. Ng will visit the URI as soon as it is safe to do so.
- Planning for Dr. Mark Strynar of the US EPA to visit URI when it is safe to do so.
- Coordinate and hold a two-day Zoom conference on October 13-14, 2020, entitled "PFAS in Our World." Alicia Crisalli (URI Pharm) and Heidi Pickard (Harbard) are conference co-chairs, and Slitt Lab trainees will chair the associated poster sessions. Full trainee involvement will be solicited for additional conference details.

Plans for upcoming year

- Form and support Trainee Action Teams to provide trainees with active engagement with PFAS science and community policy. Trainees will conduct interdisciplinary projects that have on-the-ground applications.

  — Team 1: Development of pedagogy for high school students (interface with CEC)

  — Team 2: Direct engagement with community stakeholder, including underrepresented groups and ethnic minorities (led by CEC)

  —Team 3: Science translation for a variety of interest groups (led by RTC)

  — Team 4: Policy response and support action team to support local, state and Federal regulatory activities (interface with STEEP Science PIs)
- Encourage small expertise group meetings among STEEP trainees and regular joint group meetings.
- Support and encourage trainee engagement in the STEEP Lab Rotation program.
- Focus on diversity and inclusion/social and environmental justice issues.

SELECTED ACCOMPLISHMENTS

Juliana Agudelo

–Recipient of the URI Graduate School Dean's Diversity Fellowship
–Recipient of the Perry J. Gehring Diversity Student Travel Award for the Society of Toxicology Annual Meeting in Anaheim, CA in March 2020. Invited to be the society's special guest at the Undergraduate Diversity Program dinner.
–Recipient of the 2020 KC Donnelly Externship Award to support an externship at the EPA where she will be quantifying total PFAS body burden in human livers.

Anna Robuck

–Recipient of the Robert and Patricia Switzer Foundation Award in recognition of her current leadership role as well as future leadership potential surrounding PFAS issues. This competitive award includes a monetary research award and leadership development over the course of the fellowship year.
–Recipient of an ORISE EPA Fellowship to commence after the successful completion of her PhD dissertation.

Heidi Pickard

–Represented STEEP trainees at the Environmental Action Conference at Northeastern University.
–Received significant press coverage (35 news stories from 25 outlets) for her paper on the atmospheric transport of PFAS (http://dx.doi.org/10.1029/2020gl087535)

TRAINEE GRADUATES

Michael Fedorenko, MS, URI Engineering
Christine Gardiner, MS, URI GSO
Emily Marques (formerly **Martell**), URI Pharmacy (Postdoctoral Fellow at UMass Amherst with Dr. Alicia Timme-Laragy)
Aleksandra Naumann, MS, URI Engineering
Marisa Pfohl, PhD, URI Pharmacy (Postdoctoral Fellow at EPA)
Andrea Tokranov, PhD, Harvard (Scientist at USGS)
Clifton Dassuncao, PhD, Harvard SEAS (Scientist at Eastern Research Group)
Xindi (Cindy) Hu, PhD, Harvard SEAS (Scientist at Mathematica Policy Research, Inc.)
Damaskini Valvi, Postdoctoral Researcher, Harvard (Assistant Professor at Mount Sinai)

TRAINEE PUBLICATIONS

B.J. Ruyle, C.P. Thackray, J.P. McCord, M.J. Strynar, K.A. Mauge-Lewis, S.E. Fenton, E.M. Sunderland. 2020. Reconstructing the composition of poly- and perfluroalkyl substances (PFAS) in contemporary aqueous film forming foams. *Environmental Science & Technology Letters*, In Institutional review at EPA and NIH.

B.J. Ruyle, H.M. Pickard, D.R. LeBlanc, **A.K. Tokranov**, C.P. Thackray, **X.C. Hu**, C.D. Vecitis, E.M. Sunderland. 2020. PFAS Precursor Transformations and Unexplained Organofluorine in AFFF-Impacted Coastal Watersheds. *Environmental Science and Technology*. In revision.

A.K. Tokranov, D.R. LeBlanc, **H.M. Pickard**, L.B. Barber, **B.J. Ruyle**, R.B. Hull, E.M. Sunderland, C.D. Vecitis. 2020. PFAS Interfacial Sorption and Precursor Persistence during Transport across Surface Water/Groundwater Boundaries. *Environmental Science and Technology*. In revision.

A.O. De Silva, J.M. Armitage, T.A. Bruton, **C. Dassuncao**, W. Heiger-Bernays, **X.C. Hu**, A. Karrman, C. Ng, **A. Robuck**, M. Sun, T.F. Webster, E.M. Sunderland. 2020. PFAS Exposure Pathways for Humans and Wildlife: A Synthesis of Current Knowledge and Key Gaps in Understanding. *Environmental Toxicology and Chemistry*. In review.

Hanna Joerss, Zhiyong Xie, **Charlotte C. Wagner**, Wilken-Jon von Appen, Elsie M. Sunderland, and Ralf Ebinghaus. Transport of Legacy Perfluoroalkyl Substances and the Replacement Compound HFPO-DA through the Atlantic Gateway to the Arctic Ocean–Is the Arctic a Sink or a Source? *Environmental Science & Technology* 2020 54 (16), 9958-9967. DOI: 10.1021/acs.est.0c00228

Carol F. Kwiatkowski, David Q. Andrews, Linda S. Birnbaum, Thomas A. Bruton, Jamie C. DeWitt, Detlef R. U. Knappe, Maricel V. Maffini, Mark F. Miller, Katherine E. Pelch, Anna Reade, Anna Soehl, Xenia Trier, Marta Venier, **Charlotte C. Wagner**, Zhanyun Wang, and Arlene Blum. Scientific Basis for Managing PFAS as a Chemical Class. *Environmental Science & Technology Letters* 2020 7 (8), 532-543 DOI: 10.1021/acs.estlett.0c00255

Pfohl M, Ingram L, **Marques ES**, Auclair A, Barlock BJ, Jamwal R, Anderson D, Cummings B, and **Slitt AL**. Perfluorooctanesulfonic acid (PFOS) and perfluorohexanesulfonic acid (PFHxS) alter the blood lipidome and the hepatic proteome in a murine model of diet-induced obesity. *Toxicological Sciences*. Accepted.

Marques ES, Pfohl M, Wei W, Tarantola G, Ford L, Amaeze O, **Bothun G**, and **Slitt AL**. Replacement per- and polyfluoroalkyl substances (PFAS) are potent modulators of lipogenic and drug metabolizing gene expression signatures in primary human hepatocytes. *Environmental Science and Technology*. Revisions requested.

Marques ES, Pfohl M, Auclair A, Jamwal R, Barlock BJ, Sammoura FM, Goedken M, Akhlaghi F, and **Slitt AL**. PFOS administration shifts the hepatic proteome and augments dietary outcomes related to hepatic steatosis in mice. *Toxicology and Applied Pharmacology*. Revisions requested.

Pfohl M, Marques, ES, Auclair A, Jamwal R, Barlock BJ, Goedken M, and **Slitt A**. An 'omics approach to unraveling the paradoxical effect of diet on perfluorooctanesulfonic acid (PFOS) and perfluorononanoic acid (PFNA)-induced hepatic steatosis. *Toxicological Sciences*. In review.

Amaeze O, Wei W, **Marques ES**, Ma H, Lazzaro S, Johnson N, and **Slitt A**. Inhibitory and inductive effects of Nigerian medicinal plants extracts on human P-glycoprotein and Cytochrome P450 enzymes – implications for herb-drug interaction. *Drug Metabolism and Pharmacokinetics*. In review.

Alesio J., Slitt A., Bothun G. Connecting Physicochemical Properties of Perfluoroalkyl Substances (PFASs) and Fatty Acid Analogs to Bovine Serum Albumin Binding. *Journal of Agricultural and Food Sciences*. In preparation.

Fedorenko M, Alesio J, Fedorenko A., **Slitt A., Bothun G**. Dominant Entropic Binding of Perfluoroalkyl Substances (PFASs) to Albumin Protein Revealed by 19F NMR. *Chemosphere*. Pending revisions.

Crisalli A, Alesio J, Bothun G, Cho B. New mechanistic insight into albumin binding of PFASs and PFAS replacements. In preparation, journal TBD.

Alesio J, Bothun G. Perfluoroalkyl carboxylates and sulfonates lead to membrane ordering in the hydrocarbonoclastic bacteria *Alcanovorax Borkumensis* without impacting growth. *Environmental Science and Technology*. In preparation.

Naumann A, Alesio J, Bothun G. PFAS accumulation in bacterial membrane monolayers: Role of electrostatic and hydrophobic interactions. *Langmuir*. In preparation.

Anna R. Robuck, Mark G. Cantwell, James McCord, Lindsay Addison, **Marisa Pfohl**, Mark J. Strynar, Richard McKinney, David R. Katz, David N. Wiley and **Rainer Lohmann**. Per- and Polyfluoroalkyl Substances (PFAS) in Juvenile Seabirds from the US Atlantic Coast. *Environ Sci Technol* 2020, June –revised.

TRAINEE PRESENTATIONS

Ruyle BJ and Sunderland EM. Reconstructing proprietary PFAS compositions in AFFF. Accepted oral presentation at upcoming SETAC North America 41st Annual Conference, Fort Worth (virtual), November 2020.

Ruyle BJ, Pickard HM, Tokranov AK, LeBlanc DR, Sunderland EM. Detection and transformations of poly- and perfluoroalkyl acids downstream from fire training areas in groundwater-fed coastal watersheds. Oral Presentation at SETAC North America 40th Annual Meeting, Toronto, November 2019.

J. Sun, M. McDougall, C. Dassuncao, F.A.P.C. Gobas, B.C. Kelly, E.M. Sunderland. Development of a food web bioaccumulation model for poly- and perfluoroalkyl substances (PFAS). Poster presentation at the Society for Environmental Toxicology and Chemistry (SETAC) 40th Annual Meeting in North America, Toronto, Canada, November 3-7, 2019.

H.M. Pickard, A. Chovancova, **C. Dassuncao, A.K. Tokranov**, E.M. Sunderland. The legacy of long-chained PFAS in seafood: Implications for risk-based guidance in New Hampshire. Poster presentation at the Society for Environmental Toxicology and Chemistry (SETAC) 40th Annual Meeting in North America, Toronto, Canada, November 3-7, 2019.

Alicia Crisalli. Investigation of Protein-PFAS Interactions and the Potential Interference of PFAS in Protein-DNA Interactions. NIEHS Superfund Research Program Annual Meeting, Seattle, WA, November 18-20, 2019.

Kaye E, Agudelo J, **Pfohl M, Marques E, Slitt A**. (2020) Developmental PFOS exposure causes changes in liver transcriptome. Late-Breaking 9: Air Pollution; PFAS; Respiratory. Society of Toxicology Annual Meeting, Anaheim, CA, March 19, 2020

Alesio J, Fedorenko M, Burke D, White A, **Bothun G**. (2019). PFAS Protein Binding by Fluorescence Spectroscopy: A Critical Analysis. Session 3: Susceptibility and Risk Factors: Methods to assess the risks to human health presented by hazardous substances. Superfund Research Program Annual Meeting, Seattle, WA, November 19, 2019.

Marques E, Pfohl M, Wei W, Tarantola G, Ford L, Amaeze O, and **Slitt A**. (2020) Replacement Per- and Polyfluoroalkyl Substances (PFASs) Are Potent Modulators of Lipogenic and Drug Metabolizing Gene Expression Signatures in Primary Human Hepatocytes. *The Toxicologist*, 2435, Society of Toxicology Annual Meeting, March 2020

Ford L, **Marques E**, Wei W, **Pfohl M**, Agudelo J, and **Slitt A**. (2020) Time to Treatment after Plating Impacts PFAS Induction of Gene Expression in Cryopreserved Human Hepatocytes. *The Toxicologist*, 1974, Society of Toxicology Annual Meeting, March 2020

Hamilton MC, **Pfohl M, Marques E**, Ford L, **Slitt A**, and Baldwin WS. Increased Toxicity and Retention of Perflourooctane Sulfonate (PFOS) in hCYP2B6-Tg Mice Compared to Cyp2b-Null Mice Is Relieved by a High-Fat Diet. The Toxicologist, 2433, Society of Toxicology Annual Meeting, March 2020

Marques E, Pfohl M, Wei W, Amaeze O, and **Slitt A**. (2019) Gene expression and lipid accumulation profiles for perfluoroalkyl acid (PFAA) and PFAA mixtures in human hepatocytes. Gordon Conference and Seminar: Cellular & Molecular Mechanism of Toxicity, August, 2019

Trainees

Juliana Agudelo
PhD Student
College of Pharmacy, URI
Slitt Lab

Jessica Alesio
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College of Engineering, URI
Bothun Lab

Jitka Becanova
Postdoctoral Researcher
Graduate School of Oceanography, URI
Lohmann Lab

Annelise Blomberg
Postdoctoral Researcher
School of Public Health, Harvard
Grandjean Lab

Alicia Crisalli
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College of Pharmacy, URI
Cho Lab/TC Grad Assistant

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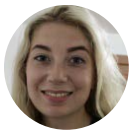

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THE UNIVERSITY OF RHODE ISLAND

HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH
Department of Environmental Health

SILENT SPRING INSTITUTE
Researching the Environment and Women's Health

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