Laue Department of Epidemiology Travel Award Budget Justification

Total Amount Requested: $3,513
Destination: Athens, Greece
Purpose of Travel: Annual Conference of the International Society for Environmental Epidemiology (ISEE)
Dates of Trip: September 16, 2022* – September 23, 2022

I am committed to environmental epidemiology and plan to remain an academic researcher in the field. I would like to attend the annual meeting of ISEE because the opportunity to network in person is unparalleled. As a junior researcher, building my scientific network is especially important to me. I plan to be on the job market soon, and it is crucial that I showcase my research and commitment to the field to potential employers. Attending in person this year would be especially beneficial given that ISEE has been remote for the past two years. In addition to the invaluable networking opportunities, feedback on my presentations at past ISEE conferences has been essential to advancing my research and scientific thinking.

I have regularly attended ISEE annual conferences since 2016 and presented abstracts annually since 2017. This year I have submitted two abstracts, which I will present if accepted. One, titled "Contribution of gut bacteria to arsenic metabolism in the first year of life in a prospective birth cohort," elucidates the bidirectionality of associations between arsenic exposure and features of the gut microbiome in the New Hampshire Birth Cohort Study (NHBCS). This work is conducted with my primary mentors, Drs. Margaret Karagas and Juliette Madan, who both hold appointments in the Department of Epidemiology. The second abstract, titled "Early-life exposure to per- and polyfluoroalkyl substances and gut microbial composition," explores the associations between human milk concentrations of per- and polyfluoroalkyl substances (PFAS), which are of great concern in New Hampshire, and the developing gut microbiome. This work is the result of a collaboration with other members of the Department in addition to Drs. Karagas and Madan, most notably Dr. Megan Romano, who spearheads PFAS work within NHBCS.

Item	Amount
Bus to/from Logan	$62
Airfare: Roundtrip from Boston to Athens on U.S. airline + checked bag	$1300
Hotel: Average nightly cost of conference-recommended hotels: $200 x 6 nights	$1200
Meals: $50 x 7 days	$350
Conference Registration: ISEE Member Subsidized/Early-Career Fee, Early Bird Registration: 550 €	$601

*arrival in Athens on September 17

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MEDICINE

Megan E. Romano, MPH, PhD
ASSOCIATE PROFESSOR,
DEPARTMENT OF EPIDEMIOLOGY

31 March 2022

Dear Dr. Karagas:

I am writing to nominate Hannah Laue for the Department of Epidemiology Trainee Travel Award to support her attendance at the International Society for Environmental Epidemiology (ISEE) Annual Meeting in Athens, Greece (September 18-21, 2022).

As you know, Dr. Laue is a postdoctoral research associate in the Department of Epidemiology, and we are currently collaborating on a project to examine the influence of per- and polyfluoroalkyl substances (PFAS) on the infant gut microbiome in the New Hampshire Birth Cohort Study (NHBCS). Dr. Laue has extensive knowledge of environmental epidemiology and the infant microbiome, and it has been a pleasure to work with her while she begins her first forays into PFAS research. While working with her, I have been impressed with her commitment to the research, her thorough attention to epidemiologic theory, and passion for conducting impactful science. She is submitting an abstract of this work to ISEE for consideration and will present the work at the conference if accepted.

Human milk is an under-appreciated source of toxic exposures for infants. This includes PFAS, which have documented associations with immune-related outcomes. One potential mechanism by which PFAS may affect the immune system is through the gut microbiome. Dr. Laue's work leverages rich data from the NHBCS, including concentrations of PFAS in human milk and shotgun metagenomic sequencing reads of the infant gut microbiome. These data allowed Dr. Laue to investigate changes in bacterial diversity, species relative abundance, and the relative abundance of genes that may impart immunological effects. This research is critical to our understanding of the broad health effects of PFAS.

Attendance at the ISEE Annual Meeting will give Dr. Laue a timely opportunity to engage with her peers and to network with colleagues as she approaches independence. The ISEE Annual Meeting is an unparalleled opportunity for Dr. Laue to disseminate her work to a global audience and to engage with both peers and senior researchers within the field of environmental epidemiology. Particularly given the recent lack of networking opportunities due to the COVID-19 pandemic, the opportunity to attend in person is especially critical for Dr. Laue given her current career stage. I strongly endorse Dr. Laue's application for these travel funds, and I know that she will make the most of the opportunity to attend this epidemiological conference.

Sincerely,

Megan E. Romano, MPH, PhD

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Early-life exposure to per- and polyfluoroalkyl substances and gut microbial composition

Hannah E. Laue[1], Yuka Moroishi[1], Thomas J. Palys[1], Brock C. Christensen[1], Rachel Criswell[2], Emily R. Baker[3], Margaret R. Karagas[1], Juliette C. Madan[1,4], Megan E. Romano[1]

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Background and Aim: Human milk is an under-appreciated source of toxic exposures, including immunomodulatory per- and polyfluoroalkyl substances (PFAS), for infants fed human milk. The immune-related effects of PFAS may, in part, be due to alterations of the microbiome. We aimed to identify changes in the infant gut microbiome related to milk PFAS exposure.

Methods: In the New Hampshire Birth Cohort Study, PFAS were quantified in human milk samples from ~six weeks postpartum using solid-phase extraction coupled to high-performance liquid chromatography-isotope dilution tandem mass spectrometry. A molar sum (ΣPFAS) was calculated. Caregivers collected infant stool samples at six weeks (n=116) and/or one year postpartum (n=119). Stool DNA was extracted and underwent metagenomic sequencing. We profiled bacterial species and KEGG Orthologies (KOs) using BioBakery pipelines. Diversity was quantified with the Shannon Index. We estimated the association of PFAS with alpha diversity and relative abundances of species and KOs with linear regression. Single- and multi-pollutant models adjusted for confounders and predictors of the microbiome, with missing covariate data imputed. Each outcome timepoint was considered separately and analyses at six weeks were restricted to infants who were exclusively fed human milk (n=90).

Results: Perfluorooctanesulfonic acid (PFOS) and perfluorooctanoic acid (PFOA) were detected in 94% and 83% of milk samples, respectively. PFOS was associated with increased Shannon Index at six weeks [β=0.24 per PFOS doubling, (95%CI: 0.03, 0.45), p=0.03]. Estimates were stronger in multi-pollutant than single-pollutant models, and among complete cases. ΣPFAS was associated with one-year-old *Bacteroides vulgatus* relative abundance [(β=-2.48 % per doubling (-3.77, -1.18), FDR q=0.05]. No other associations were observed.

Conclusions: PFAS may increase diversity of the infant gut microbiome and alter the relative abundance of cardiometabolically-active bacteria. Additional analyses may highlight susceptible populations and identify related health outcomes.

Keywords: per- and polyfluoroalkyl substances, microbiome, human milk

Contribution of gut bacteria to arsenic metabolism in the first year of life in a prospective birth cohort

Hannah E. Laue[1], Yuka Moroishi[1], Juliette C. Madan[1,2], Margaret R. Karagas[1]

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[2] Departments of Pediatrics and Psychiatry, Children's Hospital at Dartmouth, Lebanon, NH

Background and Aim: Gut bacteria are at the interface of environmental exposures and human systems, and may aid host metabolism and excretion of toxic chemicals. We investigated whether arsenic metabolism by gut bacteria is related to arsenic exposure and metabolism.

Methods: In the New Hampshire Birth Cohort Study, urine and stool samples were obtained at six weeks (n=186) and one year (n=190) of age. Inorganic arsenic (iAs), monomethylarsonic acid (MMA), dimethylarsinic acid (DMA), and arsenobetaine (AsB) were quantified in infant urine samples using high-performance liquid chromatography with inductively coupled plasma mass spectrometry. Total arsenic exposure (tAs) was summarized as Σ(iAs, MMA, DMA) and $\log_{10}$-transformed. Fecal DNA underwent metagenomic sequencing and the relative abundance of bacterial gene pathways were grouped as KEGG Orthologies (KOs) using BioBakery algorithms. In the first set of models, arsenic-related KOs with >80% detection were $\log_{10}$-transformed and modeled continuously using linear regression, those with <10% were not evaluated and those with 10-80% detection were analyzed dichotomously (detect/non-detect) using logistic regression. Models adjusted for age at sample collection and child's sex. Effect modification by delivery mode was assessed in stratified models. In the second set of models, the association between the relative abundance/detection of the KOs and arsenic speciation (%iAs, %MMA, %DMA) was assessed with linear regression.

Results: tAs was associated with the increased relative abundance/detection odds of several arsenic-related KOs, including K16509, an arsenate reductase transcriptional regulator, with stronger associations among six-week-olds than one-year-olds. K16509 was also associated with increased %MMA and %DMA at six weeks and one year, suggesting it contributes to host metabolism. Notably, many associations were stronger among Caesarean-delivered than vaginally-delivered infants, suggesting vertical transfer of arsenic-related genes.

Conclusions: Our findings suggest that the infant gut microbiome may be responsive to arsenic exposure and may aid host metabolism and excretion.

Keywords: arsenic, microbiome