Undergraduate Education Program
Sunday, March 15, 2020
# Undergraduate Education Program

March 15, 2020

The materials listed below are resources for participants in the Undergraduate Education Program, in order of use during the program. Many of the items are in this booklet. Those with page numbers preceded by “W” are found at www.toxicology.org/diversityprogram.

To access: Username: Diversity2020 and Password: UEP15Sun!

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| W Becoming a Toxicologist—SOT Career Guide |
| W Academic Program Directors and Internship Sponsors List |
| W SOT Annual Meeting Session Types |
| W Toxicology Specialty Areas |

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Acknowledgments

The 2020 Undergraduate Education Program has received support from:

Society of Toxicology

Daniel and Patricia Acosta Diversity Student Fund

Perry J. Gehring Diversity Student Travel Fund

National Institute of Environmental Health Sciences of the National Institutes of Health under Award Number 5R13ES029028

Pfizer, Inc.

Eastman Charitable Foundation

NSF International

SRC, Inc.

We also recognize the outstanding efforts of the members of the SOT Committee on Diversity Initiatives. Their dedication and year-round inspiration and work undergird the Undergraduate Diversity Program. Thanks as well to the speakers, mentors, and the many other volunteers who make this program possible.
Schedule
## Undergraduate Diversity Program Schedule

### Sunday, March 15 | Anaheim Marriott

<table>
<thead>
<tr>
<th>TIME</th>
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<th>PRESENTER(S)</th>
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<tbody>
<tr>
<td>7:45 AM</td>
<td>Undergraduate Education Program registration</td>
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<tr>
<td><strong>8:00 AM–12:05 PM</strong></td>
<td><strong>Toxicology Presentations</strong></td>
<td><strong>Chairs: James P. Luyendyk, PhD, Michigan State University; and Frederic J. Moulin, DVM, PhD, US FDA</strong></td>
<td></td>
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<tr>
<td>8:00 AM–8:10 AM</td>
<td>Welcome</td>
<td>James P. Luyendyk, PhD, Michigan State University, East Lansing, MI; and Ronald N. Hines, PhD, ATS, SOT President</td>
<td></td>
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<tr>
<td>8:10 AM–9:00 AM</td>
<td>To Vape or Not to Vape: Is That the Question?</td>
<td>Judith T. Zelikoff, PhD, New York University School of Medicine, New York, NY</td>
<td></td>
</tr>
<tr>
<td>9:00 AM–9:50 AM</td>
<td>Drug Discovery Toxicology: From Target Assessment to Translational Biomarkers</td>
<td>J. Eric McDuffie, PhD, MBA, Janssen Pharmaceutical Companies of Johnson &amp; Johnson, San Diego, CA</td>
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<tr>
<td>9:50 AM–10:05 AM</td>
<td>Break</td>
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<tr>
<td>10:05 AM–11:15 AM</td>
<td>Case Study: Metal Levels in Whales from the Gulf of Maine: A One Environmental Health Approach</td>
<td>Mindy F. Reynolds, PhD, Washington College, Chestertown, MD; John P. Wise Sr., PhD, University of Louisville, Louisville, KY; and Bryanna Rupprecht, Washington College Class of 2020, Chestertown, MD</td>
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</tr>
<tr>
<td>11:15 AM–12:05 PM</td>
<td>Characterization of Chemistry and Toxicity of Ambient Particulate Matter Air Pollution Near Uranium Mine Sites on Tribal Lands of the Southwest</td>
<td>Matthew J. Campen, PhD, MSPH, University of New Mexico, Albuquerque, NM</td>
<td></td>
</tr>
<tr>
<td>12:05 PM–1:00 PM</td>
<td>Lunch and Networking</td>
<td>James P. Luyendyk, PhD, Michigan State University, East Lansing, MI</td>
<td></td>
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**Preview of Afternoon**

**Chairs: James P. Luyendyk, PhD, Michigan State University; and Frederic J. Moulin, DVM, PhD, US FDA**
### Sunday, March 15 (Continued)

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<td>1:00 PM–2:00 PM</td>
<td>Breakout Sessions for Students</td>
<td><strong>Graduate School: How to Get In and What to Expect: Graduate Student and Academic Advisor Perspectives</strong>&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;<strong>Chairs:</strong> Hong Wang, PhD, DABT, Genentech Inc, South San Francisco, CA; and Enrique Fuentes-Mattei, PhD, University of Texas MD Anderson Cancer Center, Houston, TX&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;<strong>Academic Advisor Facilitator:</strong>&lt;br&gt;Lauren Aleksunes, PhD, Rutgers University, Piscataway, NJ  &lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;<strong>Graduate Student Facilitator:</strong>&lt;br&gt;Catheryne L. Chiang, PhD, US EPA, Troutman, NC</td>
<td>Grand Ballroom</td>
</tr>
<tr>
<td>Breakout 1</td>
<td>Breakout 2</td>
<td><strong>Academic Advisor Facilitator:</strong>&lt;br&gt;Craig Marcus, PhD, Oregon State University, Corvallis, OR  &lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;<strong>Graduate Student Facilitator:</strong>&lt;br&gt;Courtney McClure, BS, University of California Los Angeles, Los Angeles, CA</td>
<td>Grand Ballroom B</td>
</tr>
<tr>
<td>Breakout 2</td>
<td>Breakout 3</td>
<td><strong>Academic Advisor Facilitator:</strong>&lt;br&gt;Judith T. Zelikoff, PhD, New York University School of Medicine, Tuxedo Park, NY  &lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;<strong>Graduate Student Facilitator:</strong>&lt;br&gt;Monika A. Roy, MSPH, University of Massachusetts Amherst, Amherst, MA</td>
<td>Grand Ballroom D</td>
</tr>
<tr>
<td>Breakout 3</td>
<td>Breakout 4</td>
<td><strong>Academic Advisor Facilitator:</strong>&lt;br&gt;Courtney E. W. Sulentic, PhD, Wright State University, Dayton, OH  &lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;<strong>Graduate Student Facilitator:</strong>&lt;br&gt;Olushola M. Awoyemi, MSc, PhD, Texas Tech University, Lubbock, TX</td>
<td>Grand Ballroom G</td>
</tr>
<tr>
<td>Breakout 4</td>
<td>Breakout 5</td>
<td><strong>Academic Advisor Facilitator:</strong>&lt;br&gt;Angela Slitt, PhD, University of Rhode Island, Kingston, RI  &lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;<strong>Graduate Student Facilitator:</strong>&lt;br&gt;Giovanna Pozuelos, MS, University of California Riverside, Riverside, CA</td>
<td>Grand Ballroom H</td>
</tr>
<tr>
<td>Breakout 5</td>
<td>Breakout Session for Advisors</td>
<td><strong>Facilitator:</strong>&lt;br&gt;José E. Manautou, PhD, ATS, University of Connecticut School of Pharmacy, Storrs, CT  &lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;&lt;br&gt;<strong>Facilitator:</strong>&lt;br&gt;Conference Planning Committee, SOT</td>
<td>Grand Ballroom J</td>
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<tr>
<td>2:00 PM–2:10 PM</td>
<td>Break</td>
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| 2:10 PM–3:10 PM  | **Career Roundtables: Opportunities in Toxicology**       | **Academia:** Antonio T. Baines, PhD, North Carolina Central University, Durham, NC  
**Government:** Ofelia A. Olivero, PhD, ATS, NIH, Rockville, MD  
**Industry:** Robert P. Casillas, PhD, ATS, Latham Biopharm Group, Cambridge, MA | Grand Ballroom B |
|                  | **Breakout 1**                                            | *Academia:* Alexandra Noël, PhD, Louisiana State University, Baton Rouge, LA  
*Government:* Shaun D. McCullough, MS, PhD, US EPA, Chapel Hill, NC  
*Industry:* Kristini Miles, PhD, DABT, Venture Chemical Consulting LLC, Atlanta, GA | Grand Ballroom C |
|                  | **Breakout 2**                                            | *Academia:* Larissa Williams, PhD, Bates College, Lewiston, Maine  
*Government:* Pedro Del Valle, PhD, ATS, US FDA, Division of Hematology Oncology Toxicology, Silver Spring, MD  
*Industry:* Jacqueline Kinyamu-Akunda, DVM, PhD, Novartis Institutes for BioMedical Research Inc, Spring House, PA | Grand Ballroom D |
|                  | **Breakout 3**                                            | *Academia:* Darryl B. Hood, PhD, Ohio State University, Columbus, OH  
*Government:* Xinrong Chen, PhD, DABT, US Consumer Product Safety Commission, Rockville, MD  
*Industry:* Colleen E. McLoughlin, PhD, DABT, ERT, Scivera LLC, Charlottesville, VA | Grand Ballroom G |
|                  | **Breakout 4**                                            | *Academia:* Barbara L.F. Kaplan, PhD, Mississippi State University, Mississippi State, MS  
*Government:* Aimen Farraj, PhD, DABT, US EPA, Research Triangle Park, NC  
*Industry:* Joe (Junguo) Zhou, PhD, DABT, Johnson & Johnson, Raritan, NJ | Grand Ballroom H |
| 3:15 PM–5:00 PM  | **Open Time with Academic Toxicology Program Directors and Internship Sponsors** | Chair: Kymberly M. Gowdy, PhD, East Carolina University | Marquis South |
| 5:15 PM–6:30 PM  | **Awards Ceremony**                                       |                                                                                                                                  | Convention Center (CC) Ballroom A |
| 6:30 PM–7:30 PM  | **Welcome Reception**                                     |                                                                                                                                  | CC Grand Plaza |
| 7:30 PM–9:00 PM  | **Student/Postdoctoral Scholar Mixer**                    |                                                                                                                                  | Anaheim Marriott Marquis Center |
Program Participants
Artwork Credits (Top to Bottom): "Students" and "Engineer" by Wilson Joseph, "Peer to Peer" by Sharon Showalter, "Conversation" by Gregor Črešnar, and "Community" by Bruno Castro; all from the Noun Project. These images are used on pages 15, 16, 18, 19, 20, and 23.
Participant Roles
Who are the participants and what are their roles?

Undergraduate Students
All undergraduate students who register for the Annual Meeting also can register for the Sunday Undergraduate Education Program. Some students, selected by the Committee on Diversity Initiatives (CDI) based on a nationwide competitive application, receive travel support to attend the meeting and have special activities on Saturday and Monday.

The students’ role is to interact with toxicologists, learn more about toxicology, discover strategies for success in applying to and completing graduate school, and consider careers in the biomedical scientists.

Undergraduate Faculty Advisors
These are faculty members who are not SOT members and who have been involved with supporting the career development of undergraduate students, especially those from groups that are underrepresented in the sciences. CDI also selects these participants by competitive application from a national pool. Faculty advisors can communicate readily with the students, peer mentors, and toxicologists. They play an important role in helping everyone benefit from the unique experience of the Undergraduate Program. At their home institution, they assist with the graduate school application process as well as recruiting future program participants.

Peer Mentors
Typically toxicology graduate students, but sometimes undergraduate students or postdoctoral scholars, these participants contribute to the cohesiveness of the mentor groups. Some peer mentors participated in the SOT Undergraduate Program when they were baccalaureate students. Peer mentors are excellent resources for questions about what graduate school is really like and for good reasons to consider a career in toxicology.

Host Mentors
Host mentors are toxicologists who are established in a toxicology career. These participants have a broad perspective on the benefits of a graduate research degree, employment opportunities in the biomedical sciences, and what life is like as a toxicologist. Group participants can network, network, network, during the program and in the future.

Committee on Diversity Initiatives
The members of this SOT Committee have planned the Undergraduate Program, selected all the participants and speakers, and thought about all the details that make this program a well-rounded introduction to toxicology and graduate school. They want to meet the participants during the program, may be contacted in the future, and will follow up to see what career paths the student participants select.
2020 Peer Mentors

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## 2020 Host Mentors

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
<th>Contact Information</th>
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<tbody>
<tr>
<td><strong>Marie M. Bourgeois, PhD, MPH</strong></td>
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### Committee on Diversity Initiatives 2019–2020

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<th>Institution</th>
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<td>Office of Science Education and Diversity</td>
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<td><a href="mailto:krychli1@jhmi.edu">krychli1@jhmi.edu</a></td>
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<tr>
<td>Catherine Lyn (Katie) Chiang, BS</td>
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<td>University of Illinois at Urbana-Champaign</td>
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Dr. Zelikoff, a tenured Full Professor in the NYU Department of Environmental Medicine at the New York University School of Medicine, has over 25 years of extensive experience in environmental health and toxicology, focusing on laboratory models to assess the toxicology of inhaled single contaminants and complex mixtures, including metals, nanoparticles, gaseous and particulate (PM) air pollutants, smokeless and combustible products from tobacco cigarettes, biomass burning, and diesel exhaust. Over the last decade, studies in her laboratory have focused on the effects of early-life exposure (prenatal, neonatal, and adolescent exposures) to environmental toxicants, including electronic cigarettes (e-cigs) and ambient particulate matter (PM) on neurodevelopment, fetal cardiovascular structure and function, obstetric consequences, and later-life disorders (obesity, heart disease, immune dysfunction, cognitive behavior, and reproductive success in male and female offspring). Her studies with e-cig aerosols demonstrate that maternal exposure during pregnancy and early life alters neurodevelopment and produces hyperactivity- and anxiety-like behavior in adult offspring in a sex-dependent manner, obesity in adult female offspring, and increases in brain biological mediators correlated with memory performance. Furthermore, these studies also demonstrate that early-life exposure to e-cig aerosols with nicotine and flavorings alter bone marrow immune cell development. Altogether, these studies have shown the lack of safety associated with prenatal and early-life exposure to e-cig aerosols for the developing fetus and offspring.

As the Community Engagement Core (CEC) Director for the NYU NIEHS Core Center, Dr. Zelikoff has worked with several environmentally impacted minority and underserved communities and community-based organizations throughout the New York and New Jersey metropolitan areas. In cooperation with Massachusetts Institute of Technology, University of New Mexico, and the New York University Center CEC, Dr. Zelikoff also has partnered with student and staff nurses who work closely with Native American tribes and with members of the Ramapough Lunaape Tribal Nation to increase environmental health literacy. In addition to having served as a member of numerous Federal Advisory Committees, including the Institute of Medicine and National Research Council, National Toxicology Program Board of Scientific Advisors, and US Environmental Protection Agency and having chaired a NASA Panel to determine potential health effects of moon dust exposure, Dr. Zelikoff is a current ad hoc member on other study panels.
Dr. McDuffie is the Scientific Director of the Predictive & Investigative Toxicology group at Janssen Pharmaceutical Research & Development LLC, in San Diego, California. Dr. McDuffie’s career began at Pfizer Inc.’s Ann Arbor, Michigan (2000–2007), and Plymouth, Michigan (2006–2007), sites. At Pfizer, he was responsible for providing investigative pathology support for multiple therapeutic area projects. As a member of a global group of collaborative preclinical safety assessment scientists, Dr. McDuffie supports early discovery and/or late development projects at Janssen. Dr. McDuffie has more than 19 years of experience in preclinical toxicology, including applications of in vivo and in vitro models and related biomarkers to support early target liability assessment as well as investigate mechanisms of potentially translatable inducible organ-specific liabilities for late-stage drug candidates.

He earned a BS in biology from Benedict College in Columbia, South Carolina (1994); a PhD in pharmacology from Meharry Medical College in Nashville, Tennessee (1998); postdoctoral research training from the University of Michigan Medical School in Ann Arbor, Michigan (1998–2000); and an MBA from the University of Phoenix in San Diego, California (2009). He has presented at various national and international conferences and co-authored over 30 peer-reviewed manuscripts and book chapters. Dr. McDuffie also co-edited the benchmark book Drug Discovery Toxicology: From Target Assessment to Translational Biomarkers (2016).
Dr. Reynolds graduated from Brown University, where she studied the effect of repair and vitamin C in hexavalent chromium–induced toxicity. She then completed a postdoctoral appointment at Brown, where, in addition to continuing her research, she was an Adjunct Professor at Salve Regina University in the Department of Biology and taught a course in the Brown Pre-college Summer Program. In 2008, she joined the faculty of Washington College, where is now an Associate Professor and Chair of Biology, as well as Chair of the Natural Science Division. Dr. Reynolds teaches courses in general biology, biochemistry, cell biology, and toxicology. Over the course of her teaching career, Dr. Reynolds has transformed her teaching pedagogy to almost exclusively rely on active learning and inquiry-based design. All her courses employ principles of toxicology, allowing students to be introduced to the subject early in their undergraduate careers.

Dr. Reynolds’ commitment to undergraduate education extends beyond the classroom. She has chaired the SOT Undergraduate Education Subcommittee and the SOT Education Committee. She is currently Co-Chair of the SOT Faculty United for Toxicology Undergraduate Recruitment and Education Committee and has served as a mentor and speaker for the CDI Undergraduate Diversity Program. SOT awarded Dr. Reynolds the Undergraduate Educator Award in 2015. Within her community, Dr. Reynolds collaborates with public school teachers and offers STEM events for middle school and high school students, and she is particularly interested in introducing young women and students of color to the STEM fields. Dr. Reynolds has an active research lab examining the molecular mechanisms of cytotoxicity and genotoxicity following co-exposure to cobalt, cadmium, and nickel. She has published several research and review articles on this subject with undergraduates as co-authors. Many of her students, including several SOT award recipients, have presented their research at the Society’s Annual Meeting. Washington College has recognized Dr. Reynolds for her contribution to undergraduate education and service by awarding her the Gold Pentagon Leadership Award and inducting her into Omicron Delta Kappa, a national leadership honor society.
Dr. Wise is head of the Wise Laboratory of Environmental and Genetic Toxicology, Professor of Pharmacology and Toxicology, and University Scholar and Chair of the Center for Environmental and Occupational Health in the School of Medicine at the University of Louisville. Dr. Wise’s formal education includes a bachelor’s degree in biology with high distinction and recognition from George Mason University and a PhD in pharmacology from the George Washington University. His postdoctoral training focused on molecular epidemiology followed by training in occupational health and risk assessment.

Dr. Wise leads a team of faculty, staff, and students who conduct state-of-the-art research aimed at understanding how chemicals in the environment affect health from a One Environmental Health perspective. His work includes experimental approaches involving cell biology, molecular biology, toxicology, molecular epidemiology, and genomics to study the health impacts of environmental chemicals at the molecular, cellular, tissue, individual, community, and population levels in humans and wildlife.

He has earned the SOT Education Award, the SOT Career Achievement Award from the Metals Specialty Section, and the Environmental Mutagenesis and Genomics Society’s Education Award. Dr. Wise has mentored and trained over 200 faculty; postdoctoral fellows; and graduate, undergraduate, and high school students in biomedical and environmental health research. His students have won numerous local, national, and international awards and grants and have gone on to successful careers in academia, government, industry, and nongovernmental organizations. His undergraduate students have flown in zero gravity with NASA, biopsied whales at sea, caught and sampled live alligators at Kennedy Space Center, and studied sea turtles on the beaches of Puerto Rico. His work has been featured in numerous articles in local, national, and international press and social media sites, including short documentaries with Alexandra Cousteau and Miles O’Brien.
Dr. Campen is a Regents’ Professor of Pharmaceutical Sciences at the University of New Mexico College of Pharmacy and an expert in the cardiopulmonary health effects of air pollution. He also is broadly interested in the cross talk of the cardiovascular and respiratory system in health and disease, conducting basic and clinical research into the nature of comorbidities that promote cardiovascular illness. His primary research focus involves the impact of inhaled toxicants, especially common air pollutants, on vascular function and injury. After graduating from the University of North Carolina School of Public Health, Dr. Campen trained in a pulmonary medicine postdoctoral fellowship at the Johns Hopkins University School of Medicine. Before his current appointment, he worked as an independent scientist at the Lovelace Respiratory Research Institute in Albuquerque, New Mexico, conducting both grant- and contract-funded research. Dr. Campen has published over 90 peer-reviewed articles and recently authored the “Toxic Responses of the Heart and Vascular System” chapter in the ninth edition of Casarett and Doull’s Toxicology: The Basic Science of Poisons. Dr. Campen currently serves as an Associate Editor for Toxicological Sciences, and in 2013, he shared the Toxicological Sciences Editor-in-Chief position with John Lipscomb. Dr. Campen also was awarded the 2014 SOT Achievement Award. He has been a regular contributor and advisor to the US Environmental Protection Agency Clean Air Scientific Advisory Committee.
Breakout Session Facilitators
Graduate School: How to Get In and What to Expect?
Graduate Student and Academic Advisor Perspectives

Breakout 1

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Exploring Careers in Toxicology Roundtables

This is your opportunity to talk informally with SOT members who are employed in different areas of toxicology, learn what their career paths were like, and explore how these toxicologists manage work-life balance. Your group will meet with three toxicologists—one from academia, one from government, and one from industry.

These toxicologists will tell you what working in their employment sector is like from their perspective. You can discuss the advantages and differences for employees in this area versus other areas. Please ask any questions you might have about what life is like in their positions. You will gain insights into where you might find your best balance and use your interests and aptitudes pursuing a career in toxicology.

What would you like to know about life as a toxicologist?
Be sure to ask your questions.

Toxicologists Meeting with Your Group

Breakout 1

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Toxicology Presentations
To Vape or Not to Vape: Is That the Question?

Judith T. Zelikoff, PhD
Professor
Department of Environmental Medicine
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Electronic cigarette
An electronic cigarette, developed by a Chinese company, gives the user nicotine but no fire, no tar, no carbon monoxide, no ash and no stub.

- Light Simulates cigarette glow, indicates when device is ready for use and works as battery indicator
- Electronic components Such as control circuits, pneumatic airflow sensor
- Vaporizer Atomizes the nicotine smoking liquid in the liquid container
- Nicotine liquid container

Battery

Electronic cigarette
Comparison
Regular cigarette

One e-cigarette
100
6-24 mg.

6-7 cigarettes
15
0.6-2.4 mg.

Nicotine per puff
E-cigarette with 24 mg of nicotine: 0.16 mg/puff
Cigarette with 1.8 mg of nicotine: 0.16 mg/puff

Source: E-Cig
Graphics: Eski Poli, Elizabeth Nielsen
© 2018 NCT
Evolution of E-cigarette Devices: How Many Do You Know?

One vapor unit, 59 mg nicotine/pod = >one pack of cigarettes

The smoke generated by iQOS contains substances from pyrolysis and thermogenic degradation that are identical to the constituents found in traditional tobacco cigarette smoke.

How about These?

E-cigarettes: Thumbs Up or Down . . .

- No cancer-causing chemicals
- Healthy alternative to the real thing
- Smoke in smoke-free areas
- Cheaper alternative
- No cancer-causing tobacco
- No fire; therefore, not a fire risk
- No passive smoke to those around us
- No bitter aftertaste

E-cigs Can Help You Quit Smoking

- Cessation rates were 28% lower in those who used e-cigarettes compared with those who did not use e-cigarettes
- As currently being used, e-cigarettes are associated with significantly less quitting among smokers

Kalkhoran and Glantz, 2016.
E-cigarettes: Thumbs Up or Down . . .

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- Healthy alternative to the real thing
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- Cheaper alternative
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- No bitter aftertaste

E-cigs Can Help You Quit Smoking

- Cessation rates were **28% lower** in those who used e-cigarettes compared with those who did not use e-cigarettes
- As currently being used, e-cigarettes are associated with significantly **less quitting** among smokers

Kalkhoran and Glantz, 2016.
### Table 1

Sample Characteristics and E-cigarette use by Sub-Groups, CHIS 2014 (N=1,052)

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<td>68</td>
<td>8.26%</td>
</tr>
<tr>
<td>Language Spoken at Home</td>
<td>Not English Only</td>
<td>501</td>
<td>50.3%</td>
</tr>
<tr>
<td></td>
<td>English Only</td>
<td>551</td>
<td>49.7%</td>
</tr>
<tr>
<td>Secondary Education</td>
<td>High School</td>
<td>591</td>
<td>51.09%</td>
</tr>
<tr>
<td></td>
<td>Not Attending School</td>
<td>460</td>
<td>44.01%</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>113</td>
<td>10.30%</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>558</td>
<td>51.11%</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>494</td>
<td>48.89%</td>
</tr>
<tr>
<td>Age</td>
<td>1,052</td>
<td>14.5 15.13</td>
<td>**</td>
</tr>
<tr>
<td>Poverty Level</td>
<td>≤ 200% FPL</td>
<td>591</td>
<td>51.09%</td>
</tr>
<tr>
<td></td>
<td>&gt; 200% FPL</td>
<td>461</td>
<td>44.01%</td>
</tr>
</tbody>
</table>

1 Percentages and means represent the percent of each sub-population that has ever used e-cigarettes and mean values among e-cigarette ever users.

N represents unweighted sample size

FPL = Federal Poverty Level

* ≤ .05  
** ≤ .01  
*** ≤ .001

---

**Statistics: Youth and Adolescents**

- Misconception among youth that e-cigs are harmless and pose no long-term risks
- 36% of young adults (18–24) report ever using an e-cigarette; 14% report current use
- Adolescent years are important for brain development that continues to age 25
- Adolescents can get more easily addicted than adults because of increased synapese activity
  - Studies are surfacing that identify the health risks posed to young people who vape:
    - delayed brain development
    - respiratory health
    - poor impulse control, and
    - mood disorders
- Long-term health consequences of adolescent use is unknown
- Risks of second-/thirdhand exposure is still in question as well
Patterns of E-cig Use Vary by Age, Gender, Race, and Ethnicity

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Level</th>
<th>Sample Characteristics</th>
<th>E-cigarette Use</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ever-Use</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Overall</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td>90%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Yes</td>
<td>10%</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>395</td>
<td>32.79%</td>
<td>15.53%</td>
<td></td>
</tr>
<tr>
<td>Latino</td>
<td>451</td>
<td>47.00%</td>
<td>8.61%</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>101</td>
<td>10.59%</td>
<td>5.79%</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>105</td>
<td>9.61%</td>
<td>5.74%</td>
<td></td>
</tr>
<tr>
<td>Citizenship Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>US Citizen</td>
<td>916</td>
<td>86.43%</td>
<td>11.44%</td>
<td>**</td>
</tr>
<tr>
<td>Naturalized Citizen</td>
<td>68</td>
<td>5.32%</td>
<td>5.68%</td>
<td></td>
</tr>
<tr>
<td>Non-Citizen</td>
<td>68</td>
<td>8.26%</td>
<td>1.46%</td>
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<tr>
<td>Language Spoken at Home</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not English Only</td>
<td>501</td>
<td>50.3%</td>
<td>6.76%</td>
<td>*</td>
</tr>
<tr>
<td>English Only</td>
<td>551</td>
<td>49.7%</td>
<td>13.89%</td>
<td></td>
</tr>
<tr>
<td>Secondary Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High School</td>
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<td>12.42%</td>
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<tr>
<td>Middle School or Lower</td>
<td>339</td>
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<tr>
<td>Not Attending School/Other</td>
<td>113</td>
<td>7.09%</td>
<td>6.01%</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
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<td></td>
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<td>8.21%</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td>15.13%</td>
</tr>
<tr>
<td>Poverty Level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 200% Federal Poverty Line</td>
<td>591</td>
<td>51.09%</td>
<td>13.69%</td>
<td>*</td>
</tr>
</tbody>
</table>

Percentages and means represent the percent of each sub-population that has ever used e-cigarettes and mean values among e-cigarette ever users. N represents unweighted sample size. FPL = Federal Poverty Level.

* \( \leq 0.05 \)
** \( \leq 0.01 \)
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• Respiratory health
• Poor impulse control
• Mood disorders

Long-term health consequences of adolescent use is unknown

Risks of second-/thirdhand exposure is still in question as well

State-Specific Prevalence of Current E-cigarette Use

Nicotine and Tobacco Control, 2018.

What Is in E-cigarettes?

E-cigarette aerosol contains at least 10 chemicals on California’s Prop 65 list of chemicals known to cause cancer, birth defects or other reproductive harm.

TobaccoFreeCA

IT’S NOT JUST "HARMLESS WATER VAPOR"

Acetaldehyde
Benzene
Cadmium
Formaldehyde
Isoprene
Lead
Nickel
Nicotine
N-Nitrosornicotine

Cigarettes, aerosol, and smokeless tobacco products contain over 700 chemicals, many of which are known to cause cancer and other harmful effects.

Los Angeles County Department of Public Health

Judith T. Zelikoff
7,000 Different Vape Flavors

What about Secondhand Vape?

• A main selling point of e-cigs is that they can be used anywhere because they don't produce toxic “smoke” that puts others at risk

• Experts say e-cig secondhand smoke contains a similar amount of tiny particles of heavy metals and other substances that can damage the lungs
Are E-cigarettes Less Harmful Than Regular Cigarettes?

Yes, but that doesn’t mean e-cigarettes are safe!

E-cigs: Toxicology

- E-cig studies *in vivo* and *in vitro* report inflammation
  - Mitogen-activated protein kinase
  - Janus tyrosine kinase/signal transducer and activator of transcription
  - Nuclear factor-κB signaling

- Immune-compromised state and increased susceptibility to microbial infections *in vivo*

- Prolonged exposure to some constituents of e-cig aerosols results in inflammation, asthma, and/or COPD
**E-cig “Smoke” Is Carcinogenic**

1. Induction of DNA Damage
2. Inhibition of DNA Repair
3. Increase of Cell Mutation and Tumorigenic Transformation Susceptibility

Tang et al., 2018. *PNAS*.

---

**Individual Responses Can Be Different . . .**

- The variety of responses among organisms that get the same dose of chemical is due to individual susceptibility

- Dose and individual susceptibility play roles in all situations involving chemicals, including medicines, tobacco, and caffeine
Lack of Toxicological Studies on Susceptible Populations

- There is a known risk for e-cigarettes, as nicotine crosses the placenta and is a known developmental neurotoxicant

- About 6% of pregnant women use e-cigs alone; 8.5% are dual users of tobacco cigarettes and e-cigarettes

- Although uncertain about health effects, pregnant smokers are attracted to e-cigarettes as a harm-reduction strategy

- At present, the risk-benefit ratio of e-cigarette use during pregnancy is unknown

Opposing Governmental Viewpoints on E-cigarette Use during Pregnancy

"The evidence is already sufficient to provide appropriately cautious messages to pregnant women and women of reproductive age, as well as adolescents about the use of nicotine-containing products such as smokeless tobacco and e-cigarettes, and newer forms of nicotine-containing tobacco products, as alternatives to smoking."

-2014 Report of the Surgeon General
Does Early-Life Exposure to E-cigarettes, with or without Nicotine, Alter Neurodevelopment, Produce Neuroinflammation, and/or Change Adult Offspring Behavior?

- Maternal exposure to FA, e-cig, or e-cig+nic
- Day 1: e-cig exposure started directly after mating
- Day 18–21: Dams give birth
- Lactational period exposure
- Offspring mature
- One-month sacrifice
- Four-month sacrifice
- Transcriptome
- Neuroinflammation-markers/peripheral inflammation
- Persistence of genomic changes
- Behavioral testing

Generation system developed by Gordon and Corbett, NYU.

Neuro-Related Outcomes Associated with Conventional Cigarette Smoke Exposure Early in Life

- Fetal, childhood, and adolescent exposure to cigarette smoke is associated with adverse neurocognitive outcomes, including:
  - Decreases in general intellectual ability
  - Decreases in auditory and visual learning
  - Development of conduct disorders
  - Increased hyperactivity-impulsivity behaviors
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Pre- and Postnatal Exposure to E-cig Aerosols Alters Frontal Cortex Gene Expression in a Sex-Dependent Manner and in the Absence of Nicotine

Total Significant Gene Changes per Treatment Group and Sex
- Female offspring without nicotine: 2,630
- Male offspring without nicotine: 2,615
- Female offspring with nicotine: 1,393
- Male offspring with nicotine: 152

IPA-Predicted Disease and Biological Functions in Common with Conventional Cigarette Smoke

Figure 1. Treatment and sex groups have both overlapping and unique genes that were significantly changed (p<0.01)
Aerosols without Nicotine Enhanced Hippocampus Iba-1 Expression in Adult Offspring

IBA-1 & GFAP Expression in CA1

Mean Intensity

[Graph showing mean intensity of Iba-1 and GFAP expression in Control, +Nic, and -Nic groups]

For each sample 3-6 slide replicates measured.

*Significantly different than control p ≤ 0.01

Representative Images of the CA1 Region

FA, Iba-1 (red), GFAP (green) and DAPI (blue)

Testing Behavior Associated with Early-Life E-cigarette Exposure

<table>
<thead>
<tr>
<th>Behavior</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperactive Behavior, Exploratory Behavior, Activity Levels</td>
<td>Locomotor Testing</td>
</tr>
<tr>
<td>Short-Term Memory</td>
<td>Repeated Acquisition and Performance Chamber (RAPC) Testing</td>
</tr>
<tr>
<td>Long-Term Memory and Learning</td>
<td>Operant Conditioning Chamber Testing</td>
</tr>
</tbody>
</table>

In collaboration with Dr. Cory-Slechta, U of Rochester. Lautenbain et al., 2016.
Pre- and Postnatal Exposure to E-cig Aerosols with and without Nicotine

*Increased Activity in Adult (4-mo-old) Male and Female Offspring Measured as Jump Time*

- Female Jump Time
  - Significantly different (p<0.01)

- Male Jump Time
  - Significantly different when compared to control (p<0.01)

n=10 mice/treatment group

Pre- and Postnatal Exposure of Mice to E-cig Aerosols with and without Nicotine

*Increased Adult (4-mo-old) Male and Female Speed of Movement (Average Velocity Time)*

- Female Average Velocity
  - Significantly different (p<0.01)

- Male Average Velocity
  - Significantly different (p<0.01)

n=10 mice/treatment group
Study 2: E-cig Prenatal Exposure

<table>
<thead>
<tr>
<th>Behavioral Task</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FA</td>
<td>PGVG</td>
</tr>
<tr>
<td>Locomotor Activity</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Anxiety and Arousal</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Behavioral Despair</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>(depression)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Repetitive Digging</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Learning and Memory</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

J. Schwitzer et al., In revision, EHP 2019.

Translational Take-Home Messages

- Consideration of offspring sex is an important factor for evaluating health outcomes

- The fetus and offspring from a pregnant woman using e-cigs without nicotine are as vulnerable to “vape” effects on neurodevelopment as those exposed to nicotine-based e-cigs

- Predicted adverse health outcomes (memory, learning, activity) of early-life exposure to e-cigs appear similar to those seen in offspring prenatally exposed to cigarette smoke

- Behavioral phenotypes in adult offspring are consistent with attention deficit hyperactivity disorder and anxiety disorder

- While health impacts of second-/thirdhand e-cig aerosol exposures are not clear, caution is recommended for pregnant smokers and babies living with “vapers”
Study 2: E-cig Prenatal Exposure

J. Schwartzer et al., In revision, EHP 2019.

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---

Vaping: Constrictive Bronchiolitis (Popcorn Lung)

E-cig or Vaping-Associated Lung Injury (EVALI)

• Patients have reported symptoms such as:
  - cough, shortness of breath, or chest pain
  - nausea, vomiting, abdominal pain, or diarrhea
  - fever, chills, or weight loss

• Some patients reported symptoms over a few days; others reported symptoms developed over several weeks

• A lung infection does not appear to be causing the symptoms
Pulmonary Toxicity: Vaping

"Vaping-Associated Lung Injury"

- NEJM Correspondence 10/2/2019
- Histopathology
  - New evidence to add to clinical and imaging data
  - New diagnostic clues
- Exogenous lipoid pneumonia?
  - Does the histology/imaging data thus far support this hypothesis?
- Exposure versus toxicity

CDC (2019): Most People Who Died from Vaping-Linked Disease Used Products Containing THC

Potential Culprits in Mystery Lung illnesses: Black-Market Vaping Products

Some of the THC vaping cartridges seized by Minnesota law enforcement officials in a record drug arrest in Anoka County in September (AP)

Advertising logos for cannabis brands are displayed on the side of a vape shop in downtown Los Angeles. (Richard Vogel/AP; Washington Post, 2019)
EVALI: The Search Continues

- A substance that has turned up in many THC samples is vitamin E oil
- Experts in the legal marijuana industry say it is added to THC oil to fill vape cartridges
- Legally sold vitamin E acetate is commonly used as a nutritional supplement and in skin-care products
- Health officials warn it could be hazardous when inhaled, potentially causing the sorts of symptoms many patients have reported: cough, shortness of breath, and chest pain

Toxicology: Food for Thought

- What e-cig design features alter the production of and user exposure to different toxicants, and are we using the correct parameters for our studies?
- What about the health effects of dual e-cig and tobacco users? Does e-cig use lead to nicotine addiction and the dual use of tobacco cigarettes?
- What exposure biomarkers should be used to determine e-cig toxicant exposure, disease risk, morbidity, and mortality?
- On which short- and long-term health endpoints should toxicology research focus?
- How well do toxicology studies reflect effects on vulnerable populations?
- Can toxicology studies help us move the e-cigarette health and science field forward, or can we solely rely on human studies?
Acknowledgement and Thanks

**NYU Researcher**
Jason Blum

**Collaborators**
C. Klein (NYU School of Med)
D. Cory-Slechta (U. of Rochester)
M. Aschner (Albert Einstein)
J. Schwartzer (Mt. Holyoke)

**Funding Support**
NYU NIEHS Center Pilot Grant
NYU NIEHS Molecular, Biostatistics and Bioinformatics Cores
Drug Discovery Toxicology:  
*From Target Assessment to Translational Biomarkers*

J. Eric McDuffie, PhD, MBA  
Scientific Director  
Predictive & Investigative Toxicology  
Nonclinical Safety

What Do You Think It Takes to  
Make a Prescription Drug?
Presentation Overview

• Candidate drug discovery, target engagement, and preclinical efficacy
• Drug target validation and lead generation
• Preclinical testing and Investigational New Drug (IND) application filing
• Clinical trials (Phases 1, 2, and 3)
• New Drug Application (NDA) filing
• NDA review/decision on approval
• Phase 4 clinical studies


On Average, How Many Years Does It Take to Generate Sufficient Research Data to Support Approval of a Prescription Drug?
The Importance of Preclinical Safety Testing

- The estimated cost for developing a new drug is ~$2.6 billion
- Preclinical safety studies constitute ~15% of total drug development costs
- Clinical trials constitute ~30% of total drug development costs
- Approximately 70% of all discovery compounds do not become drugs due an early identification of preclinical safety findings
- The approval rate for candidate drugs entering clinical development is <12%
- The importance of preclinical safety testing is to decrease discovery research efforts for toxic compounds that are unlikely to become drugs

https://www.policymed.com/2014/12/a-tough-road-cost-to-develop-one-new-drug-is-26-billion-approval-rate-for-drugs-entering-clinical-de.html
During the Initial Discovery Phase, How Many Steps Do Chemists Often Perform in Efforts to Discover a Candidate Prescription Drug?

Drug Discovery, Target Engagement, and Preclinical Efficacy

The drug discovery and target validation processes are intended to demonstrate potential correlations between preclinical and clinical readouts:

- Demonstrating drug-like properties (Target Engagement)
- Preclinical data (e.g., efficacy biomarker profiles) should inform backup compound selections

What Emerging Technology Do You Believe May Be Used to Help Validate a Candidate Prescription Drug?

Drug Target Validation

Lead Candidate Drug Generation

The identification of a “lead compound” to progress towards preclinical safety testing includes:

- In vitro assays and in vivo studies aid the prioritization of compounds to identify a “lead compound” to progress towards preclinical safety testing
- Predict compound-induced toxicologic risks to humans using in vitro, in vivo and/or in silico models


Case Example – In Vitro Assay: Receptor Selectivity for Ibrutinib

Ibrutinib

- Bruton’s Tyrosine Kinase (BTK) inhibitor
- Used to treat B-cell malignancies
- Hits several other kinases at clinically and toxicologically relevant levels

<table>
<thead>
<tr>
<th>Kinase</th>
<th>IC50 (nM)</th>
<th>Median Cmax (unbound)/IC50 Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Btk</td>
<td>0.53</td>
<td>12.27</td>
</tr>
<tr>
<td>Blk</td>
<td>0.94</td>
<td>6.92</td>
</tr>
<tr>
<td>BmxEtk</td>
<td>1.1</td>
<td>5.91</td>
</tr>
<tr>
<td>ErbB4/Her4</td>
<td>1.23</td>
<td>5.29</td>
</tr>
<tr>
<td>Tnk</td>
<td>2.87</td>
<td>2.27</td>
</tr>
<tr>
<td>Tec</td>
<td>5.49</td>
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<tr>
<td>Itk</td>
<td>11.7</td>
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</tr>
<tr>
<td>EGFR</td>
<td>11.86</td>
<td>0.55</td>
</tr>
<tr>
<td>ErbB2/Her2</td>
<td>21.57</td>
<td>0.30</td>
</tr>
<tr>
<td>Jak3</td>
<td>51.9</td>
<td>0.30</td>
</tr>
</tbody>
</table>

Image adapted from: Honigberg et al PNAS v107;29:13075-13080. 2010
What Do You Think It Takes to Ensure a Candidate Drug Is Safe for Humans?

Preclinical Safety Testing

Preclinical Safety Testing

Preclinical Safety Study Design Considerations

- **Species selection:**
  - Typically default to rat and dog
- **Dosing formulation testing**
- **Dose level testing:**
  - At high enough exposure in good laboratory practice (GLP) studies to support Phase 1 clinical trial
- **Study duration:**
  - 5–14 days
- **Clinical endpoints:**
  - Clinical observations, body weights, and food consumption
- **Pathology endpoints:**
  - Clinical, routine, and molecular pathology


Some images have been removed from this slide.

What Is Your Perceived Definition of a Translatable Safety Biomarker?
Translatable Safety Biomarkers

Investigational New Drug (IND) Application Filing

- **US FDA/CDER has 30 days to assess safety per the IND application**
  - No comments or minor → proceed with Phase I trial
  - Phone call or letter → clinical hold

  - **Why?**
    - Duration of toxicology studies (in two species) insufficient to support proposed clinical duration
    - Doses/exposures not high sufficient enough in toxicology studies
    - NOAEL not established in toxicology studies
List a Toxicity That Would Cause Regulatory Authorities to Enforce a “Clinical Hold” (aka Delay or Suspend Ongoing Research) for a Candidate Drug Trial in Humans.
Clinical Trial Holds: Partial or Complete

A Few Key Example Reasons for a Clinical Trial Hold

The reason for a clinical hold is concern for the safety of clinical trial participants.

- **Partial Clinical Hold**
  - *Drug Delivery Device–Related Issues*
    - When a gene therapy (e.g., brain) delivery device poses risk to humans

- **Complete Clinical Hold**
  - *Developmental or Reproductive Toxicology*
    - When a candidate drug is intended to treat a life-threatening disease or condition affecting both genders
Case Example: Candidate Drug-Induced Testicular Toxicity

- Candidate drug-induced testicular toxicity can lead to a clinical hold or very restrictive clinical enrollment and/or robust monitoring

In this session, using actual data from a research study, students will review the level of metals from whale biopsies to analyze trends and make inferences about ecosystem health in the Gulf of Maine.

The Gulf of Maine serves as an important aquatic ecosystem for many marine organisms. Whales are one of the most important species in the ocean that migrate there each year; however, scientists have begun to see a drop in whales’ overall fitness. These whales—such as humpback, fin, and minke—play a key role in supporting the phytoplankton population by fertilizing the water. These plankton absorb copious amounts of carbon dioxide from the atmosphere, which in turn creates a healthier environment. Scientists have put whale health on high priority given whales’ prolonged stretch on the endangered species list. To research whale fitness and health in relation to their connections to their environment’s health, the One Environmental Health approach has emerged.

One Environmental Health recognizes relationships between human health, organism health, and ecosystem health. Scientists are working together with the goal to understand the relationship between the health of an organism and the health of the environment.

*The One Environmental Health approach in the Gulf of Maine.*
Characterization of Chemistry and Toxicity of Ambient Particulate Matter Air Pollution Near Uranium Mine Sites on Tribal Lands of the Southwest

Matthew J. Campen, PhD
University of New Mexico
Native Environmental Health Equity: Addressing the Impacts of Abandoned Mines on Native Communities

- >1/2 of Native population of US lives in 13 western US states, where 161,000 abandoned hard rock mines also located
- >600,000 Native Americans live within 10 km of abandoned mines
- Greater reliance on local resources creates increased concern over potentially greater exposure and resultant impacts


Hot Spots in the Four-Corners Region for Environmental Lung Disease: Silicosis and Interstitial Lung Disease/Sarcoidosis

Community-Based Concerns Drive Our Research

Demographics and Cardiometabolic Disease Prevalence in a Navajo Nation Cohort: The Diné-Navajo Environmental Health Study

<table>
<thead>
<tr>
<th>Variable</th>
<th>DiNEH Subset (n = 252)</th>
<th>Original DiNEH (n = 1304)</th>
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</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>55.3 (± 14.3)</td>
<td>51.5 (± 17.4)</td>
</tr>
<tr>
<td>Female, %</td>
<td>57.5</td>
<td>56.4</td>
</tr>
<tr>
<td><strong>Self-reported health conditions:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 2 Diabetes, %</td>
<td>26.2</td>
<td>25.1</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>38.1</td>
<td>35.9</td>
</tr>
<tr>
<td>Heart Disease, %</td>
<td>6</td>
<td>5.4</td>
</tr>
<tr>
<td>Myocardial Infarction, %</td>
<td>4.4</td>
<td>3.1</td>
</tr>
<tr>
<td>Stroke, %</td>
<td>5.2</td>
<td>3.5</td>
</tr>
<tr>
<td>Body mass index (BMI), kg/m²</td>
<td>29.7 (26.8-33.6)</td>
<td>28.3 (25.1-32.6)*</td>
</tr>
<tr>
<td>Obesity (BMI ≥ 30), %</td>
<td>47.6</td>
<td>41.2</td>
</tr>
</tbody>
</table>

High prevalence of diabetes, hypertension, and obesity

Harmon et al., PLoS ONE, 2016

* self-report
Multivariate Regression Modeling

### Covariates

**Exposure metrics:**
- Water intake of metals
- AUM proximity

**Age, gender, BMI, HbA1c**

### Response variables

mRNA endothelial cell responses to serum
- VCAM-1
- ICAM-1
- CCL2

*Reduced models derived by model selection using AIC*

---

Uranium Mine Proximity (NOT Oral Intake of Arsenic or Uranium) Correlates with Inflammatory Markers in Navajo Participants

CCL2 (Inflammatory Marker)

Proximity to Uranium Mine Sites (Weighted by Surface Area of Sites)

Harmon et al., JESEE, 2017
Community Research Interim Results

Closer proximity to abandoned uranium mines predicted increased serum inflammatory potential

\[ \text{Broader effect of overall burden of mining waste exposure} \]

- Other pathways → windblown?
- Other mining metals/mixtures

Could windblown contaminated dusts negatively impact public health in affected communities?

Steps in Risk Assessment:

- Hazard Identification
- Exposure Assessment
- Dose-Response Assessment
- Risk Characterization
Particulates

• “Dust” ranges in size greatly; respirable particles are generally <10 microns
• Size of particle determines how they deposit in the lungs
• Mass mean aerodynamic diameter (“MMAD”) is used to describe the size of particles
  – BASED on empirically determined particle buoyancy rather than physical shape
• PM toxicity is a function of:
  o Aerodynamic diameter
    • Deposition and retention
  o Chemical composition

PM Characteristics:
- PM10: 10 microns
- PM2.5: 2.5 microns
- <2.5: Inhalable
- >2.5: Respirable

Location of Claim 28 Mine Site in the Blue Gap Tachee (BGT) Chapter of the Navajo Nation

- > 500 abandoned mines
- 4 mill sites
- 1,100 exposure features
- 100s of contaminated wells (Arsenic, Uranium)

DiNEH Study Area
- Monument Valley Area
- Cove/Mesa Area
- Blue Gap Tachee
- Chinle
- Gallup
- Navajo Nation
- New Mexico
- Arizona
- Utah
- Colorado

EPA and HIS, 2010

Matthew J. Campen | 63 |
Metal Contaminants in Surface Soils

- Sediments from Claim 28 mine site contains respirable metallic mineral grains
- XANES analysis suggests many of these metallic grains are likely carnotite, a mineral composed of uranium and vanadium

Metal Contaminants in Resuspended Sediments

- Soils were resuspended in air and captured in a Next Generation Impactor to characterize respirable fractions
- Sub-micron (respirable) PM contained significant amounts of carnotite
Carnotite Particulates Exhibit Nano-agglomerated Ultrastructure

Zychowski et al., *Toxicol Sci*, 2018

---

**Initial Toxicity Assessments**: Comparing Cardiopulmonary Toxicity of Contaminated “Claim 28” PM vs Background PM

- **Dose groups** (C57BL/6, male):
  - Vehicle control aspiration
  - 100µg Claim 28 PM<sub>10</sub>
  - 100µg Background PM<sub>10</sub>
- **Euthanized 24h post aspiration**
- **Pulmonary inflammation**
  - Lavage Cellularity, Cytokines
- **Aortic vasomotor dysfunction**
- **Cytotoxicity assay** (*in vitro*)

---

[Diagram showing pulmonay and vascular endpoints]
**Lung Outcomes:** Lavage Inflammatory Cells and Cytokines

*Following particulate exposure in mice*

*P<0.05; **P<0.001 by one-way ANOVA with Dunnett’s Post-Hoc test*

---

**Relative Cytotoxicity Assessment**

- Treated THP-1 cells with increasing concentrations of Claim 28 and Background PM$_{10}$
- Dihydroethidium and caspase-1 levels were both elevated in THP-1 cells treated with Claim 28 PM$_{10}$

Zychowski et al., *Toxicol Sci*, 2018
Conclusions

• Proximity to mine sites may be linked to circulating inflammatory potential
• Mine site soils contain mixed metal contaminants
  – Many in respirable grains
  – Mine site–derived PM clearly more toxic to the pulmonary tract than background soil PM samples
• Both vanadium and uranium, key components of the ore carnotite, have independent and complementary pulmonary toxicity
• But how realistic are these exposures . . . ?

Where Are We in Understanding the Range of Inhaled Uranium Ore Health Impacts?

<table>
<thead>
<tr>
<th>Duration</th>
<th>Pathology</th>
<th>Exposure</th>
<th>Risk Assessment</th>
<th>Uranium Mine Site Ores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>Pulmonary T1,1/2/17</td>
<td>Aspiration</td>
<td>Hazard ID</td>
<td>Carnotite/Tyayuminite (Vanadium)</td>
</tr>
<tr>
<td>Subacute, single dose</td>
<td>Chronic Vascular Remodeling (Athero, HTN)</td>
<td>Dose-Response</td>
<td></td>
<td>Uraninite</td>
</tr>
<tr>
<td>Subacute/repeated</td>
<td>Neuropathy—AD, neuroinflammation</td>
<td>Exposure Assessment</td>
<td></td>
<td>Thucholite (pyrobitumen)</td>
</tr>
<tr>
<td>Chronic/repeated</td>
<td>Fetal exposure/birth outcomes</td>
<td>Inhalation</td>
<td>Risk Management</td>
<td>Coffinite (Uranium Silicates)</td>
</tr>
</tbody>
</table>
Steps in Risk Assessment:

- Hazard Identification
- Exposure Assessment
- Dose-Response Assessment
- Risk Characterization

Study Limitations, Next Steps

**Limitations:**

- Fate and transport
  - How much contaminated dust is the community actually exposed to?
  - Doses of mine dust administered to the mice are much larger than anyone living near the mine would receive.
  - Navajo residents have lived most of their lives near the site, receiving low but chronic doses over time.
  - The duration and extent of dust exposures are not well understood. On-site monitoring in 2017 will address these limitations.

**Proposed next step: Mobile Laboratory**
The Long Drive . . .

Arrival at UNM

Traffic in Blue Gap Tachee, AZ
Lung Inflammation: Pilot Study

- Exposures to concentrated PM from the Blue Gap Tachee, AZ, region caused increased levels of inflammatory cells in the lung
- We will need to compare with PM$_{2.5}$ from other regions
Overall Metals in PM from Completed Exposures, Spring 2018
(Compared with Published PM Levels from Other Regions of the Planet)

Next Steps

- Move trailer to Laguna Pueblo
  - Jackpile mine is much larger and different ore type (uranium silicates) for spring 2019
  - A “neutral” or unaffected site (TBD)
  - Other??
- Assay tissues
- Complete wind dispersion modeling for SE Navajo region
The Long Drive . . .

Leaving BGT, AZ

Setting Up in Paguate, NM

Current Location in Paguate, NM

St. Anthony’s mine

Jackpile mine
Interim Conclusions

• Dusts arising from uranium mine sites are more toxic than background dusts
  – Toxicity is either due to metal contaminants or morphology of PM
• However, even at close ranges, metal-contaminated dusts do not seem to make up a substantial portion of the PM$_{2.5}$ that communities experience
• Metals data from Paguate, NM, will be very informative to finalizing these conclusions

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- May 15, 2020: Scientific Session/CE Course Proposal Submission Deadline
- October 9, 2020: SOT Awards Nomination and Application Deadline
- October 16, 2020: 2021 Abstract Submission Deadline
- October 16, 2020: Undergraduate Diversity Awards, Perry J. Gehring Diversity Student Travel Award, and Other SOT Undergraduate Awards Deadline

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