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Welcome!

Major Felipe and I would like to extend our gratitude to you for participating in the inaugural Total Exposure Health Conference. We are particularly excited that this is the first conference to focus on opportunities that are emerging at the interface of exposure science and precision medicine. We wouldn’t be here today if it weren’t for the historic contributions of programs and activities such as the Air Force’s Total Exposure Health Program, NIH’s All-of-Us Program, and National Academy of Sciences Reports, to name a few.

We are happy to share that the conference advisory board succeeded in bringing together an exceptional slate of speakers reflecting military, academic, industry, and national laboratory leaders across multiple disciplines including bioethics, industrial hygiene, toxicology, exposure science, precision medicine, and more.

Over the next two days, we’re looking forward to a rich exchange of ideas and solutions that could improve the future of human health. Our key note speakers will set the stage by laying out the major scientific goals and obstacles that must be addressed in order to leverage 21st century genetics to deliver individualized protection to the public and improve operational readiness of our military and first responders. We think you’ll agree that now is the ideal time for these exchanges of expertise given the transformation we’re seeing in the fields of exposure science, toxicology and genetics.

Our thanks to all of you who are attending, and especially to our sponsors: Battelle, DailyBreath, HESI, MyExposome, and Soylent.

Sincerely,

Justin G. Teeguarden, Ph.D., DABT
Conference Co-Chair
Total Exposure Health Conference
Chief Scientist, Exposure Science
Pacific Northwest National Laboratory
Department of Environmental and Molecular Toxicology, Oregon State University

Major Alfred J. Felipe, USAF BSC
Conference Co-Chair
Total Exposure Health Conference
KEYNOTE AND PLENARY SPEAKERS

Major General Robert Miller
U.S. Air Force Office of the Surgeon General
Making a Difference Together

Dr. J. Michael Gaziano
Harvard Medical School and Million Veteran Program
The Million Veteran Program: A Modern Mega-Cohort Within a Large Healthcare System – Progress, Challenges and Future Directions

Colonel Philip Goff
Air Force Medical Support Agency
Optimizing Human Performance through Precision Health

Colonel (ret.) Kirk A. Phillips
Battelle
Conference Reflections and the Future of Total Exposure Health
## AGENDA

### WEDNESDAY, SEPTEMBER 5

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<th>TIME</th>
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<tbody>
<tr>
<td>5:00 – 7:00 pm</td>
<td>Early Registration</td>
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### THURSDAY, SEPTEMBER 6

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<th>TIME</th>
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<tbody>
<tr>
<td>7:00 – 8:00 am</td>
<td>Registration</td>
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| 8:00 – 8:15 am  | Conference Welcome & Overview  
*Dr. Justin Teeguarden, Pacific Northwest National Laboratory*  
*Major Alfred Felipe, Air Force Medical Support Agency*  

### THURSDAY, SEPTEMBER 6

<table>
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<th>TIME</th>
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| 8:15 – 8:45 am  | Opening Plenary: Making a Difference Together  
*Major General Robert Miller, U.S. Air Force Office of the Surgeon General*  

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<th>TIME</th>
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| 8:45 – 9:15 am  | Optimizing Human Performance through Precision Health  
*Colonel Philip Goff, Air Force Medical Support Agency*  

### THURSDAY, SEPTEMBER 6

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<th>TIME</th>
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| 9:15 – 9:45 am  | The Engines and Outcomes of Growth In the Field of Exposure Science  
*Dr. Justin Teeguarden, Pacific Northwest National Laboratory, Oregon State University*  

### THURSDAY, SEPTEMBER 6

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<th>TIME</th>
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| 9:45 – 10:15 am | The Million Veteran Program: A Modern Mega-Cohort Within a Large Healthcare System – Progress, Challenges and Future Directions  
*Dr. J. Michael Gaziano, Harvard Medical School & Million Veteran Program*  

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<tbody>
<tr>
<td>10:15 – 10:30 am</td>
<td>Break</td>
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### THURSDAY, SEPTEMBER 6

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<th>TIME</th>
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| 10:30 – 12:00 pm| Session 1: Stakeholder Challenges in Precision Medicine & Environmental Health  
*Chair: Dr. Steven Lacey, Indiana University Fairbanks School of Public Health*  

### THURSDAY, SEPTEMBER 6

<table>
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<th>TIME</th>
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| 10:30 – 10:35 am| Introduction  
*Dr. Steven Lacey, Indiana University Fairbanks School of Public Health*  

### THURSDAY, SEPTEMBER 6

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<th>TIME</th>
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| 10:35 – 11:05 am| Geisinger’s Genomics & Precision Health Initiative  
*Dr. David Ledbetter, Geisinger*  

### THURSDAY, SEPTEMBER 6

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<tr>
<th>TIME</th>
<th>TOPIC</th>
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| 11:05 – 11:35 am| Key Occupational and Environmental Exposure Challenges in the Department of Defense  
*Mr. Steven Jones, DoD Health Affairs*  

### THURSDAY, SEPTEMBER 6

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<tr>
<th>TIME</th>
<th>TOPIC</th>
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</table>
| 11:35 – 12:00 pm| Precision Health Protection: Barriers and Opportunities for Industry  
*Dr. Steven Lacey, Indiana University Fairbanks School of Public Health*  

### THURSDAY, SEPTEMBER 6

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<th>TIME</th>
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</table>
| 12:00 – 1:30 pm | Break for Lunch (on your own)  
Exhibitors will be available at this time  

### Thursday, September 6 (continued)

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<thead>
<tr>
<th>TIME</th>
<th>TOPIC</th>
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<tbody>
<tr>
<td>1:30 – 2:30 pm</td>
<td><strong>Session 2: Bioethics in Precision Medicine</strong></td>
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<td><em>Chair:</em> Dr. Lesa Aylward, Summit Toxicology, LLP</td>
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<tr>
<td>1:30 – 1:35 pm</td>
<td>Introduction</td>
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<tr>
<td></td>
<td>Dr. Lesa Aylward, Summit Toxicology, LLP</td>
</tr>
<tr>
<td>1:35 – 2:00 pm</td>
<td>Bioethics and Precision Medicine: From Little Genes to Big Data</td>
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<td>Dr. Kenneth Goodman, University of Miami</td>
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<tr>
<td>2:00 – 2:25 pm</td>
<td>The Ethics of Incidental Findings and Genomic Sequencing Research</td>
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<td>Dr. Benjamin Berkman, National Institutes of Health</td>
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<tr>
<td>2:25 – 2:35 pm</td>
<td>Break</td>
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<tr>
<td>2:35 – 5:00 pm</td>
<td><strong>Session 3: Advances in Toxicology</strong></td>
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<tr>
<td></td>
<td><em>Chair:</em> Dr. Lesa Aylward, Summit Toxicology, LLP</td>
</tr>
<tr>
<td>2:35 – 2:40 pm</td>
<td>Introduction</td>
</tr>
<tr>
<td></td>
<td>Dr. Lesa Aylward, Summit Toxicology, LLP</td>
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<tr>
<td>2:40 – 3:10 pm</td>
<td>Translating Innovations in Toxicology into Chemical Safety Decision Making</td>
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<td></td>
<td>Dr. Russell Thomas, U.S. Environmental Protection Agency</td>
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<tr>
<td>3:10 – 3:35 pm</td>
<td>A Predictive Toxicology Approach for Acute Toxicity of Chemical Warfare Agents</td>
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<td></td>
<td>Dr. Morgan Minyard, U.S. Department of Defense</td>
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<tr>
<td>3:35 – 4:00 pm</td>
<td>Using Population-Based Mouse Models for Environmental Exposures, Toxicity, &amp; Disease</td>
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<td>Dr. Danila Cuomo, Texas A&amp;M University</td>
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<tr>
<td>4:00 – 4:30 pm</td>
<td>Employing a Systems Biology Approach to Total Exposure Health</td>
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<td>Dr. Heather Pangburn, U.S. Air Force School of Aerospace Medicine</td>
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<tr>
<td>4:30 – 5:00 pm</td>
<td>Design, Implementation, and Strategies for Toxicity Assessment and Force Health Protection in the U.S. Army Public Health Center and Beyond</td>
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<td>Dr. Emily Reinke, U.S. Army Public Health Center</td>
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<tr>
<td>5:00 – 7:00 pm</td>
<td><strong>Expo &amp; Poster Session</strong></td>
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<td></td>
<td><em>Light hors d’oeuvres and refreshments will be served</em></td>
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<tr>
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<td><em>Poster presentations will be given at this time</em></td>
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<td><em>(Details will be sent via email or provided at the registration desk)</em></td>
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**FRIDAY, SEPTEMBER 7**

<table>
<thead>
<tr>
<th>TIME</th>
<th>TOPIC</th>
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<tbody>
<tr>
<td>8:00 – 8:05 am</td>
<td><strong>Day 2 – Welcome and Announcements</strong>&lt;br&gt;Dr. Justin Teeguarden, Pacific Northwest National Laboratory</td>
</tr>
<tr>
<td>8:05 – 10:50 am</td>
<td><strong>Session 4: Advances in Precision Medicine</strong>&lt;br&gt;<em>Chair:</em> Dr. J. Michael Gaziano, Harvard Medical School</td>
</tr>
<tr>
<td>8:05 – 8:10 am</td>
<td><strong>Introduction</strong>&lt;br&gt;Dr. J. Michael Gaziano, Harvard Medical School</td>
</tr>
<tr>
<td>8:10 – 8:40 am</td>
<td><strong>Covering All the Bases: A Primer on Today’s Sequencing Technologies and Their Applications in Precision Medicine Research</strong>&lt;br&gt;Dr. Dana Crawford, Case Western Reserve University</td>
</tr>
<tr>
<td>8:40 – 9:00 am</td>
<td><strong>Exposome Scale Metabolomics and Precision Medicine</strong>&lt;br&gt;Dr. Gary Miller, Emory University</td>
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<tr>
<td>9:00 – 9:20 am</td>
<td><strong>Gene-Environment Interaction = the Missing Piece of Precision Medicine?</strong>&lt;br&gt;Dr. Marylyn Ritchie, University of Pennsylvania</td>
</tr>
<tr>
<td>9:20 – 9:40 am</td>
<td><strong>New Technologies for High Throughput Multi-Omics Measurements</strong>&lt;br&gt;Dr. Richard Smith, Pacific Northwest National Laboratory</td>
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<tr>
<td>9:40 – 9:50 am</td>
<td>Break</td>
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<tr>
<td>9:50 – 10:10 am</td>
<td><strong>Population Genomics in Military Cohorts for Detection of Rare Variation Associated with Mental Health Issues</strong>&lt;br&gt;Dr. Clifton Dalgard, Uniformed Services University of the Health Sciences</td>
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<tr>
<td>10:10 – 10:30 am</td>
<td><strong>Personalizing Environmental Health in the Military</strong>&lt;br&gt;Dr. Christopher Bradburne, Johns Hopkins University</td>
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<tr>
<td>10:30 – 10:50 am</td>
<td><strong>Organs-on-Chips: A Platform for Drug Development, Disease Modeling and Precision Medicine</strong>&lt;br&gt;Daniel Levner, Emulate</td>
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<tr>
<td>10:50 – 12:00 pm</td>
<td>Break for Lunch (on your own)  &lt;br&gt;Exhibitors will be available at this time</td>
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<tr>
<td>12:00 – 3:00 pm</td>
<td><strong>Session 5: Advances in Exposure Science</strong>&lt;br&gt;<em>Chair:</em> Dr. Justin Teeguarden, Pacific Northwest National Laboratory, Oregon State University</td>
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<tr>
<td>12:00 – 12:05 pm</td>
<td><strong>Introduction</strong>&lt;br&gt;Dr. Justin Teeguarden, Pacific Northwest National Laboratory</td>
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### FRIDAY, SEPTEMBER 7 (continued)

<table>
<thead>
<tr>
<th>TIME</th>
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<tr>
<td>12:05 – 12:25 pm</td>
<td>Biomonitoring for Assessing Exposure to Environmental Chemicals</td>
<td>Dr. Antonia Calafat, Centers for Disease Control and Prevention</td>
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<tr>
<td>12:25 – 12:45 pm</td>
<td>Non-Invasive Personal Wristband Sampler to Assess Chemical Exposures</td>
<td>Dr. Kim Anderson, Oregon State University</td>
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<tr>
<td>12:45 – 1:05 pm</td>
<td>Emerging Approaches and Opportunities to Inform In Vitro-In Vivo Extrapolation and Exposure Reconstruction</td>
<td>Dr. Barbara Wetmore, U.S. Environmental Protection Agency</td>
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<tr>
<td>1:05 – 1:25 pm</td>
<td>High Throughput Exposure Science for Chemical Decision Making</td>
<td>Dr. John Wambaugh, U.S. Environmental Protection Agency</td>
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<td>1:25 – 1:40 pm</td>
<td>Break</td>
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<tr>
<td>1:40 – 2:00 pm</td>
<td>Air Force Noise Exposure Demonstration Project</td>
<td>Dr. Dirk Yamamoto, U.S. Air Force School of Aerospace Medicine</td>
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<td>2:00 – 2:20 pm</td>
<td>Gut Microbiome and Host Interactions in Military Environments</td>
<td>Dr. J. Philip Karl, U.S. Army Research Institute of Environmental Medicine</td>
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<tr>
<td>2:50 – 3:00 pm</td>
<td>Closing &amp; Remarks</td>
<td>Dr. Justin Teeguarden, Pacific Northwest National Laboratory</td>
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<td>Major Alfred Felipe, Air Force Medical Support Agency</td>
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<tr>
<td>3:00 pm</td>
<td>Conference Adjourned</td>
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KEYNOTE AND PLENARY SPEAKERS’ ABSTRACTS

Opening Plenary: Making a Difference Together


Rapid advancements and investments in research, technology, partnerships as well as a smaller and more connected world have offered bold and innovative solutions to address healthcare’s most pressing challenges. Virtual health, Telegenetics, Analytics, Blockchain, and Artificial Intelligence are only a few of a growing number of disruptors and multipliers that are shifting the paradigm in healthcare and leading to an increased focus on value-based care, patient experience, virtual health, personalized health, and marketplace collaborations.

While transformation is occurring broadly across healthcare, Military Health System-specific drivers have also charged the Military Health System with building a more lethal force, innovating and taking risks, collaborating with industry, and bringing business reform to the Department of Defense. Regardless of the sector, striving towards optimal human performance and worker health challenges are of utmost importance to the Department of Defense as well as interagency government agencies, industry, non-profit and academia.

Total Exposure Health (TEH) aims to capture workplace, environment, and lifestyle exposures to the individual (i.e., N=1, genome) using advances in science, technology, and informatics to deliver preventive, proactive, and precise healthcare solutions. TEH provides a new tool in the toolbox that is aiming to develop an individual’s comprehensive profile by combining their genetics, personal exposure, analytics, and ultimately integrating the data into the Electronic Health Record. TEH offers an avenue to answer long-standing cross-sector questions and challenges that would not only impact the Department of Defense, but also industry to ultimately enhance human performance and worker health, increase lethality and productivity, and reduce healthcare costs.

A bold, innovative, and cross-sector approach such as TEH has many unanswered questions and opportunities ahead, but they can’t all be solved alone. With questions and challenges applicable to interagency government, industry, non-profit and academia sectors, we all have an opportunity to learn and leverage knowledge and resources from one another. This first ever Total Exposure Health Conference itself is an example of the basic concept of what TEH is – bringing the pieces together to make a whole. Through this conference we hope all attendees will have an opportunity to exchange ideas and build relationships across sectors, gain an understanding of the current state of science and technology, and ultimately – Make a Difference Together!

Optimizing Human Performance through Precision Health

Colonel Phillip Goff, Air Force Medical Support Agency

When we work, our employer is required to assess our exposures to determine if there is a health threat from the noise, chemicals, ergonomic stressors or anything else that might be harmful and mitigate those risks. The Environmental Protection Agency assesses some environmental toxics in water, air and soil that could pose health or environmental risks. However, what about the combination of workplace, environmental stressors, and lifestyle choices; are there additive or synergistic effects to those exposures? Likewise, does an individual’s unique genetic and microbiomic makeup play a part? Do genes make individuals more susceptible or more resistant to disease or illness?

Total Exposure Health (TEH) aims to answer all these questions by capturing an individual’s exposures through their work, hobbies and lifestyles, food choices, medications, and comparing them with their unique genetic and microbiomic predispositions to more fully understand, communicate and protect our military members and their beneficiaries.

Bringing together the plethora of work from various disciplines such as genetic testing, informatics, exposure science, and information technology under one portfolio is no easy task, and therefore partnerships and collaborations are needed to leverage resources and data to collectively improve the health and welfare of all people.
A demonstration project to prove the concept of Total Exposure Health will be also discussed. The Noise Exposure Demonstration Project (NEDP) was conducted at an active Air Force Base to determine participant’s 24/7 total-noise exposure while wearing personal noise dosimeters around-the-clock. The NEDP took into account key study confounders, such as: occupation, noise duration, and location as well as confounder, as well as genetic proclivities, lifestyle.

Ultimately, by leveraging the resources and concepts of TEH, health care can be enhanced through proactive, precise, and preventive actions to care for our most important weapon system, the human weapon system.

The Engines and Outcomes of Growth In the Field of Exposure Science
Dr. Justin Teeguarden, Pacific Northwest National Laboratory

The influence of “environment” on human’s disease is widely understood to equal that of the genome. Yet equality of exposure data and genome data is not a condition of the field of environmental health. Acquisition of DNA sequence data has been on a long trajectory of increasing speed, accuracy, and completeness with parallel declines in cost. Only more recently has the field of exposure science begun to undergo a similar transformation toward more rapid, cost effective and comprehensive collection of information related to environmental exposures. The engines of this transformation are not just the widening understanding of the importance of exposures on human health. Seminal reports from the National Academy of Sciences and major strategic investments in new measurement technologies and integrated research by the National Institutes of Health, among other institutions, collectively provide the vision and fuel for growth and transformation in exposure sciences. This talk will introduce a selection of National Academy of Science reports that helped catalyze the recent growth and evolution in the field of exposure science and the NIH programs that support that growth. Examples of how changes in the field position the field of exposure science to support precision medicine and the goals of the Total Exposure Health Program will be described.

The Million Veteran Program: A Modern Mega-Cohort Within a Large Healthcare System – Progress, Challenges and Future Directions
Dr. Michael Gaziano, Harvard Medical School

The revolutions in various scientific fields are making it possible to rethink our approach to how we conduct large-scale trials and observational studies. These include exponential growth in computing power, the widespread availability of electronic health record (EHR) data and low cost genetic and other omic testing. We can now use larger amounts of and more complex data to answer questions in population science. The Million Veteran Program (MVP) and our pragmatic trial program are examples of how this is being executed within the VA Healthcare System.

With a current enrollment of more than 650,000 participants, MVP is the largest cohort within a healthcare system with rich data of health, lifestyle, military exposure and genetic information in the United States, and is expected to enroll one million veterans. This longitudinal cohort serves as a resource for cutting-edge precision medicine research, such as understanding the genetic risk for diseases and genetic basis for differential response to treatment (pharmacogenomics), and identification of molecular targets for new treatments. Participants provide a blood sample for genomic and other omic analysis, complete health, lifestyle and military exposure surveys, grant access to their electronic medical records and agree to be contacted for potential participation in future research. MVP enrollment is conducted at approximately 60 sites. Three coordinating centers and a toll-free information (call) center support site recruitment. Enrollment is monitored by Genomic Information System for Integrated Science (GenISIS), a secure IT/Informatics infrastructure, which also serves as the data warehouse, and provides a secure scientific computational environment where researchers conduct their analyses. Concurrently, the Veterans Informatics and Computing Infrastructure (VINCI) assists in access to VA electronic medical record data that spans 20 years.
We are collaborating with the Department of Energy (DOE) to jointly leverage the VA's vast array of clinical and genomic data with DOE's computer science and exa-scale computing expertise and infrastructure. A collaboration with the Department of Defense (DOD) will allow us to enroll recently separated veterans and active duty military personnel in MVP, starting with the Millennium Cohort Study enrollees beginning in 2017.

Approximately 25 teams are conducting projects using MVP genotype and clinical data in schizophrenia, bipolar disorder, Gulf War Illness, PTSD, multi-substance abuse, cardiovascular disease, metabolic disease, chronic kidney disease, cancer, suicide, and age-related macular degeneration and other health conditions. I will present some lessons learned in curation of our extensive data and early GWAS results.

Our pragmatic trial program uses the EHR data to support many trials and has also launched a trial comparing two antihypertensive medications without recruitment sites. Participants are identified using EHR data and contacted by phone. If they are willing to participate, they are enrolled by phone. Progress of the study is followed by EHR.

These are two of several examples of how big health data are used to conduct large-scale modern epidemiology within a large healthcare system. In collaboration with many partners we will be pursuing innovations in big data analytics, statistics and mathematics, computational biology and computer science to support this endeavor. This will involve interaction with other global leaders working in this new field of big data population science and groups with similar data assets such as the UKBiobank.

**Closing Plenary: Conference Reflections and the Future of Total Exposure Health**

Colonel (ret.) Kirk A Phillips, Battelle

Wrapping up the first ever conference on Total Exposure Health, Kirk will cover the origins of Total Exposure Health and provide a vector for developing objective methods and groundbreaking tools to measure, assess and provide exposure information to individuals and their healthcare providers in a way that returns the provider-patient relationship to a conversation and achieves behavioral change in everyday life decisions. To do this we need to better understand the impact of ALL exposures (workplace, lifestyle and environment). The information needs to be personal and not just population based to affect change and while individual exposures achieve some goals matching those exposures to individual genetic proclivity is essential to achieve true behavioral change. Understanding these genetic proclivities and the molecular biology driving disease from those changes opens whole new areas of research to develop protective and clinical interventions.

The attendees and presenters at the TEH 2018 represent the scientific and medical professions, researchers and leaders in precision health. Never before has such a group come together to align themselves to deliver Total Exposure Health. Battelle’s research under TEH will be described as an example of a gateway to the next generation of innovation and development in health. Breaking the “stove pipes” of our professions will allow us collectively together be “exposure scientists.”
INVITED SPEAKERS’ ABSTRACTS

Non-Invasive Personal Wristband Sampler to Assess Chemical Exposures
Dr. Kim Anderson, Oregon State University

Background: We have pioneered the development of silicone wristbands as a passive sampling tool for assessing personal exposure monitors. The nature of the silicone wristband passive sampler will be explored. Aims: Describe the development and demonstrate that the application of the wristband sampler, assess the recovery of 150 organic chemicals in transport and storage stability studies, compare the wristband with other technologies and approaches and demonstrate the application of wristband in diverse real-world settings. Methods: Wristband were tested with over 150 organic chemicals in a series of transport and storage conditions, up to 22 months at -20, 4, and +30C. The chemicals tested include organic phosphates, PBDE and OP flame retardants, polycyclic aromatic hydrocarbons, oxygenated polycyclic aromatic hydrocarbons, volatile aromatic compounds, volatile alkanes, polychlorinated biphenyls, fragrance and other consumer products, fungicides, herbicides, insecticides, pesticide bi-products and precursors, and phthalates. Two studies measured chemicals in the wristband and correlated with the measured metabolites in urine and traditional exposure measures. Results: Over 1,500 chemicals were analyzed in single method screen. All volatile and semi-volatile chemicals tested were found to be within 30% of the true value throughout the storage and transport stability studies. All semi-volatile chemicals tested were stabile during transport at all temperatures including +30C, volatile chemicals were stable up to 28 days transport at 4C (and -20C). More PAH urine metabolites correlated with the wristbands then active samplers, and more urine flame retardant metabolites correlated with the wristband than hand-wipes. Wristbands used in several cohorts in Peru, Africa, and North America were in compliance with the wristband protocols >95%. The 1,500 chemicals screened generated geographic differences of exposures to chemical mixtures. Gender and occupational differences were observed. Conclusions: The wristband is easy to use by study participants. The wristband may be used for many chemicals. Comparisons with other technology/approaches, such as active samplers and biological samples like urine suggests the wristband is as good indicator of chemical exposures. Limitations of the technology will be discussed.

The Ethics of Incidental Findings and Genomic Sequencing Research
Dr. Benjamin Berkman, National Institutes of Health

Since the advent of next-generation sequencing a decade ago, the research community has been struggling with the ethical issues raised by incidental findings in genetic research. This talk will explore some of the ethical controversies and questions that remain unresolved and that must be addressed by any investigators employing large scale sequencing in their research. Topics will include: 1) When is reconsent required to conduct genomic sequencing on legacy samples? 2) Do researchers have a duty to look for incidental findings? 2) When is it appropriate to disclose genetic information to relatives of the proband? 4) Should subjects have a robust right not to know medically important genetic information about themselves?

Personalizing Environmental Health in the Military
Dr. Chris Bradburne, Johns Hopkins University

Recent efforts in genomic and precision medicine present unique opportunities for military environmental and occupational health. The US Military represents a relatively well-monitored population, with service-wide databases to monitor exposures and one of the world's largest biobanks of serum samples available for health surveillance. Current gaps in military environmental health science and practice could be better addressed by ‘exposome’ research and application initiatives that align these monitoring capabilities with national efforts in both precision medicine and the microbiome. Risk assessments can be refined with individualized risk factors, genetic susceptibilities, and exposure records, while biomarkers of exposure and biomarkers of affect could be elucidated. This talk focuses on current research and application in which combined efforts in these fields could provide better quantitative and mechanistic understanding of chronic and acute exposure risks, leading to actionable information for military environmental health stakeholders.
Biomonitoring for Assessing Exposure to Environmental Chemicals

Dr. Antonia Calafat, Centers for Disease Control and Prevention

The health significance of human exposure to many current-use chemicals is limited and often contradictory. Investigating the prevalence of such exposures is of public health importance because of the potential harmful health effects of some of these chemicals. Biomonitoring (i.e., trace level measurement of environmental chemicals or their metabolites in biospecimens) provides a quantitative measure of the amount of a given chemical present in the human body after integrating all sources and routes of exposure. Analytical methods for biomonitoring must be highly sensitive, selective, and specific, and follow rigorous quality control and quality assurance programs to ensure reliable measures of target chemicals. Even when such analytical methods exist, establishing whether such measures truly reflect the exposure of interest requires additional information. For example, biomonitoring requires toxicokinetic information to properly select the biospecimen and identify the specificity of target biomarkers. Furthermore, collection and sample processing procedures can impact integrity and usefulness of biospecimens. We will discuss the relevance of the above factors to ensure that biomonitoring measurements adequately reflect the intended exposures.

Covering all the Bases: A Primer on Today’s Sequencing Technologies and Their Applications in Precision Medicine Research

Dr. Dana Crawford, Case Western Reserve University

Recent advances in efficient and cost-effective sequencing and array-based genotyping technologies have made this era of bench to bedside research possible. This primer will briefly overview the latest in sequencing, including the strengths and remaining challenges of its more popular laboratory techniques. We will also briefly discuss applications of this technology with an emphasis on precision medicine research and clinical applications.

Using Population-based Mouse Models for Environmental Exposures, Toxicity, and Disease

Dr. Danila Cuomo, Texas A&M University

Most human diseases result from a complex interplay of genetic, epigenetic and environmental factors, and current scientific approaches do not adequately capture these complex interactions. Intrinsic variability across the human population is associated with variable responses to environmental exposures, which can contribute to whether an individual is susceptible or resistant to a particular adverse outcome. Understanding such gene-environment interactions will enable a more accurate toxicant risk assessment and public health protection. Traditional epidemiological approaches are limited in exploring factors contributing to differential susceptibility and in determining mechanisms underlying differential responses. To overcome this limitation, new genetically-diverse mouse resources such as the Collaborative Cross and Diversity Outcross have been developed to better model the genetic diversity found in human populations. These population-based mouse models allow controlled exposures in a population setting to identify genetic polymorphisms that drive either susceptibility or resistance to toxicity and to elucidate the underlying mechanisms. Integrating genetic and mechanistic toxicity data could lead to the identification of sensitive biomarkers of exposure associated with toxicity that can be translated to human exposure settings. Mouse population models offer substantial advances to classical toxicity testing paradigms by including genetically diverse individuals that may inform toxicity risks for sensitive subpopulations.

Population Genomics in Military Cohorts for Detection of Rare Variation Associated with Mental Health Issues

Dr. Clifton Dalgard, Uniformed Services University of the Health Sciences
Bioethics and Precision Medicine: From Little Genes to Big Data

Dr. Kenneth Goodman, University of Miami

The intersection of science and values has long been shaped by new technologies. Precision Medicine is one of those new technologies. It presents novel and important challenges, not least in shaping the frontier between genomics and the use of machine learning on large data sets: If it is so good, will we ensure fair access to all? Will the research programs to develop and improve it be guided by sound data policies and employ appropriate software? How should we decide if the costs of Precision Medicine are worth the benefits, and will those costs undermine more basic public health needs? Will we ensure the beneficiaries include military personnel and veterans? The tools of bioethics are essential to answering these questions – essential to getting this right.

Key Occupational and Environmental Exposure Challenges in the Department of Defense

Mr. Steven Jones, DoD Health Affairs

The Department of Defense requires a medically ready force to sustain readiness and accomplish all missions across the full spectrum of military operations conducted in a myriad of complex environments. Force health protection efforts from prevention to care to recovery are key to sustaining a medically ready and fighting force.

The myriad of operational environments across the globe create an expansive array of occupational and environmental health exposure challenges with potential acute and chronic detriments to the health of the force. These exposure challenges necessitate implementation of policy and robust tactics, techniques, and procedures to continuously monitor, assess, mitigate, and where possible, eliminate, health threats from exposures. The difficulty of this challenge and task, as well as knowledge that the best of efforts will not eliminate all exposure risks, further necessitate the need to routinely monitor the health of individuals and units, with a particular focus on quantifying exposures and assessing the impact of these exposures on health. Quantifying exposures—whether past, current or predicted future exposures—to individuals and populations informs prevention, diagnosis, treatment, and many other aspects of providing care for those we entrust to our nation’s defense. Application of exposure science principles as seen in Total Exposure Health (TEH) is a promising approach to the challenge of better understanding and mitigating exposures and potential health effects, which in turn enables a medically ready force and mission success.

Gut Microbiome and Host Interactions in Military Environments

Dr. Philip Karl, U.S. Army Research Institute of Environmental Medicine

The human gastrointestinal tract is home to trillions of microorganisms collectively known as the gut microbiome. The gut microbiome and its human host coexist in a dynamic, bidirectional relationship that is largely mutually beneficial, but can be perturbed by exposures that directly impact the host, the microbiome or both. As such, the gut microbiome is increasingly recognized as a modulator of host responses to environmental, physical, and psychological stress exposure. There is growing recognition that supporting a healthy and resilient gut microbiome may contribute to health and performance optimization of Warfighters. However, the extent to which military-relevant stressors modulate the Warfighter gut microbiome, and the implications for Warfighter health and performance are just now beginning to be explored. This talk will consider the potential role of the gut microbiome in Warfighter health and performance, and discuss findings of recently completed studies conducted within the U.S. Army Research Institute of Environmental Medicine (USARIEM) examining relationships between dietary and environmental exposures, the gut microbiome, and host responses during military relevant stress.

Disclaimer: The views expressed in this abstract are those of the authors and do not reflect the official policy of the Department of Army, Department of Defense, or the U.S. Government.
**Precision Health Protection: Barriers and Opportunities for Industry**  
**Dr. Steven E Lacey, Indiana University Fairbanks School of Public Health**

There is a laundry list of financial, ethical, and technical obstacles in creating the future of occupational health protection. These obstacles are apparent across all stakeholders, including workers, management, healthcare providers, and occupational hygienists. Nevertheless, none of the issues identified to date are insurmountable, and the return on addressing these challenges is clear: more effective health protection for more people.

**Geisinger’s Genomics & Precision Health Initiative**  
**Dr. David Ledbetter, Geisinger**

Despite decades of hopeful discussions about its potential value and impact, the pace of incorporating genetic and genomic information into the actual practice of clinical medicine has lagged, delayed by concerns about potential risk of harm, costs, and an inadequate evidence base. Calls for ever more research have pushed back adoption of clinical genomic sequencing to a long-promised ‘someday’. Such delays fuel what is ultimately a false dichotomy between the need for ongoing research to deepen understanding and knowledge and the imperative to responsibly and thoughtfully, but urgently, transition the early lessons from genomic testing and screening into clinical care for our patients and communities. This presentation will focus on lessons learned at Geisinger over the past decade as we expanded a research-based biobank to include a genome screening and counseling program that reports confirmed clinically actionable findings and now to launch clinical exome sequencing, offering population health screening as part of routine clinical care to all of our patients.

**Organs-on-Chips: A Platform for Drug Development, Disease Modeling and Precision Medicine**  
**Dr. Danny Levner, Emulate, Inc.**

Organ-Chips—such as the Lung-, Liver-, Brain- and Intestine-Chips—are micro-engineered systems that display physiological functions consistent with human *in vivo*. Each Organ-Chip is composed of a clear flexible polymer about the size of a AA battery that contains hollow channels lined by living human cells; these cells are cultured under continuous flow and mechanical forces, which recreate key aspects of the *in vivo* cellular microenvironment. We have found that cells cultured within the engineered 3D microenvironments of Organ-Chips go beyond conventional *in vitro* models, making Organ-Chips more predictive of *in vivo* physiology. Accordingly, Organ-Chips enable the study of normal physiology, pathophysiology, and mechanisms of action or toxicity in an organ-specific context. In this presentation, we will highlight studies from collaborative efforts across our Human Emulation System with various academic and industry partners to demonstrate the utility of the system as a more predictive human-relevant platform for efficacy, safety and mechanistic studies, and precision medicine.

**Exposome Scale Metabolomics and Precision Medicine**  
**Dr. Gary Miller, Emory University**

Derived from the term exposure, the exposome is an omic-scale characterization of the nongenetic drivers of health and disease. With the genome, it defines the phenotype of an individual. The measurement of complex environmental factors that exert pressure on our health has not kept pace with genomics and historically has not provided a similar level of resolution. Recently, high-resolution mass spectrometry (HRMS) has provided a means of precise detection of over 20,000 signals, revolutionizing the ability to measure biologic responses (metabolomics) to cumulative exposures such as environmental chemicals, diet and drug metabolites (exposomics). Such approaches make it possible to obtain detailed information on drugs, toxicants, pollutants, nutrients, and physical and psychological stressors on an -omic scale. Examples of the use of the exposome approach in clinical populations will be presented along with strategies to harmonize analyses among laboratories. The exposome model can provide data on exposures at the individual level for precision medicine as well as the group level for clinical trials and population health.
A Predictive Toxicology Approach for Acute Toxicity of Chemical Warfare Agents

Dr. Morgan Minyard, U.S. Department of Defense

The Defense Threat Reduction Agency (DTRA) is focused on providing acute human toxicity estimates of chemical warfare agents to the warfighter at the speed of relevancy. Traditional in vivo methods are time consuming and require large numbers of animals. In order to provide a quicker response to the warfighter, newer in silico and in vitro tools should be incorporated into current toxicology capabilities in order to provide the faster turnaround time on relevant agents of interest. A proof of concept approach was tried with one of the opioids, providing evidence that a systematic in silico, in vitro and select in vivo approach to provide acute human toxicity estimates is possible and needed for the DoD mission.

Employing a Systems Biology Approach to Total Exposure Health

Dr. Heather Pangburn, U.S. Air Force School of Aerospace Medicine

Healthcare in the 21st century has been transformed with the availability of a reference human genome sequence accompanied by intensive efforts to understand the genetic basis of disease and treatment on an individualized level as exemplified by the President Obama’s Precision Medicine Initiative. A strategic vision of the Air Force Medical Service is to craft the healthiest and highest performing segment of the U.S. by 2025. In a step towards realizing this strategic vision, the Air Force Surgeon General launched the Total Exposure Health (TEH) initiative. TEH envisions transforming healthcare from a reactive stance to a proactive stance by harnessing informatics to integrate all available data (genomic, lifestyle, occupational, environmental exposures etc.) to inform the warfighter and commanders of their health risks, fostering health engendering behaviors and actions. This presentation will address how the Air Force is employing a systems biology approach, combining computational modeling with cell biology, proteomics, genomics, metabolomics, epigenetics, and bioinformatics to address TEH requirements in hopes of elucidating underlying mechanisms of effects based on given sets of exposures from a molecular to human level perspective and from an omics perspective. Application of modern omics technologies will be highlighted as employed in assessing the expected impact of genetic variation in metabolic and transporter processes related to chemicals commonly encountered in the U.S. Air Force environment. Using a Systems Biology approach to address TEH requirements has great potential to determine/deliver personalized safe exposure levels and knowledge supporting the development of individualized treatment and mitigation strategies.

Design, Implementation, and Strategies for Toxicity Assessment and Force Health Protection in the U.S. Army Public Health Center and Beyond

Dr. Emily Reinke, U.S. Army Public Health Center

The assessment of toxicity for new compounds and rapid assessment for emerging contaminants are critical for protection of the Force and surrounding communities. Within the U.S. Army, a set of Army regulations, policies, and guidances provide the groundwork for assessing the toxicity of new chemicals alongside of performance prior to being fielded. Development of toxicology data throughout all phases of research, development, testing, and evaluation allows for mission sustainment, life cycle cost reduction, and reductions in human health and environmental impacts. To meet the need for rapid emergency response capabilities, increased prediction of toxicity from exposure and decreased reliance on traditional animal assessment strategies, the implementation of new approach methods is critical to providing accurate and comprehensive toxicity data to accurately predict consequences from manufacturing and use. With these drivers in mind, DoD works closely with the Interagency Coordinating Committee for the Validation of Alternative Methods (ICCVAM), which consists of 16 Federal Agencies that collect or rely on toxicity data. In
January 2018, ICCVAM published a strategic roadmap for the design, validation, and implementation of new approaches to toxicity testing that highlights the relationship between assay developers, users, and regulators. It suggests a new paradigm for validation that will accelerate the process while maintaining confidence in these methods as they emerge and encourages regulatory use. A recent workshop hosted by ICCVAM/NICEATM was dedicated entirely to the development of acute toxicity prediction through the use of computational modeling. The results showed great success in prediction of a wide-range of chemicals and will result in the development of a consensus model from the most successful submitted models. As a limited number of DoD-relevant compounds were included in the training and test sets, the full predictability for DoD relevant compounds (e.g. high nitrogen energetics) has not been determined. On-going efforts to include these compounds in further testing of the consensus model will help to refine the model. In the future it is critical that these types of compounds are included in the training and testing of the models, or that supporting models specifically designed to handle them are included. The most recent efforts by both ICCVAM and the U.S. Army Public Health Center to meet testing needs while decreasing animal use will be highlighted in this talk.

**Gene-Environment Interaction = The Missing Piece of Precision Medicine?**

**Dr. Marylyn D. Ritchie, University of Pennsylvania**

Advances in genome technology have brought us into the current era of precision medicine. The idea that we can use information about our genetic make-up to inform disease risk, prevention, and treatment is becoming a reality. In genomic medicine and pharmacogenomics, we now have a growing list of genes that are strongly associated with Mendelian (rare) disease and/or drug response phenotypes; however, in complex disease, there are a limited number of genes where we have been able to translate the genome-wide association study (GWAS) finding and clinical care. Most of these GWAS findings have small effect sizes, which means that individually, they explain a small proportion of the heritability of the complex trait of interest. It is possible that the role of the environment is more significant than previously appreciated and when including gene-environment interactions, our ability to explain a higher proportion of the heritability improves. In this presentation, we will discuss why gene-environment interactions are important to consider; review some of the state-of-the-art examples; and discuss the challenges with integrating the environment with precision medicine.

**New Technologies for High Throughput Multi-omics Measurements**

**Dr. Richard D. Smith, Pacific Northwest National Laboratory**

The ability to broadly, quantitatively and quickly access an individual’s exposures as well as their responses to such exposures is a common need for both advances in exposure science and precision medicine. Key to this are multi-omics measurements that include the proteome, metabolome, lipidome, glycome, and other components of an individual’s ‘exposome’. Such measurement capabilities are rapidly maturing in research settings and are increasingly based upon the use of separations combined with mass spectrometry (e.g., GC-MS LC-MS). However, all present platforms fall far short of what is desired for exposome measurements, being challenged by the need for greater speed (i.e. throughput), lower cost, higher sensitivity and the ability to much more broadly detect and effectively identify the diverse components of potential interest. This presentation will briefly summarize the current state-of-the-art and present challenges, and then describe how the use of ion mobility separations combined with mass spectrometry (i.e. IM-MS) can help address the challenges, as well as the limitations of current IM-MS measurement platforms. The presentation will then describe major advances based upon new approaches for IM-MS developed at PNNL utilizing Structures for Lossless Ion Manipulations (SLIM), including the capabilities for broad measurements, facilitating compound identification, resolving previously problematic isomers, and providing sensitive high throughput measurements.
Translating Innovations in Toxicology into Chemical Safety Decision Making

Dr. Russell Thomas, U.S. Environmental Protection Agency

The field of toxicology has struggled with rapidly and efficiently integrating technological and computational advances into decision making due to the potential public health and regulatory implications of the underlying science. Over the past ten years, these technologies and approaches include high-throughput and high-content in vitro screening, complex tissue culture models, and computational modeling. The endpoints and uncertainties associated with these new technologies are qualitatively and quantitatively different than the traditional toxicological responses. To bridge this gap and more effectively translate advances to regulatory decisions, a multi-pronged effort is underway to systematically address limitations in in vitro test systems, characterize the uncertainty and variability associated with the new approaches as well as the existing in vivo models, and use computational modeling to integrate data at different levels of biological complexity. The application of the data and models to different decision context are occurring in partnership with regulatory scientists through the development of decision support tools and focused case studies. The talk will provide an update on the current state of the technologies and approaches as well as the effort to enable translation of the advances to chemical safety decisions. This abstract does not necessarily reflect U.S. EPA policy.

High Throughput Exposure Science for Chemical Decision Making

Dr. John Wambaugh, U.S. Environmental Protection Agency

In 2012 the National Research Council (NRC) report Exposure Science in the 21st Century identified significant data needs for the estimation of chemical risk. Estimating chemical risks is a consideration of both hazard and exposure—if the exposure level is low relative to hazardous doses, then there is minimal risk potential. Efforts to make accelerated chemical safety decisions using high throughput in vitro screening data have historically been limited because there are few exposure estimates for many chemical classes. The EPA’s Exposure Forecasting (ExpoCast) project was initiated to provide exposure context for 21st Century toxicity testing. Through a combination of statistical analysis, model development, and new experimentation—particularly the advent of new, non-targeted screening mode high resolution mass spectrometry (e.g., metabolomics and exposomics)—ExpoCast has begun to implement the NRC’s vision. The views expressed in this abstract are those of the authors and do not necessarily reflect the views or policies of the U.S. EPA.
Emerging Approaches and Opportunities to Inform In Vitro-In Vivo Extrapolation and Exposure Reconstruction

Dr. Barbara Wetmore, U.S. Environmental Protection Agency

Recent advances in vitro assays, in silico tools, and systems pharmacology approaches provide opportunities to capture the exposure continuum from the external exposure space to anticipated systemic and target tissue concentrations. With the U.S. commercial and industrial chemical landscape encompassing tens of thousands of chemicals with limited safety data, efficient characterization of this continuum and its use to link internal exposures to the potential for subsequent human health effects using high-throughput toxicity data is a high priority. Ongoing efforts at the US Environmental Protection Agency (EPA) have advanced the science underlying quantitative in vitro-in vivo extrapolation (QIVIVE), a methodology that facilitates the quantitative application of in vitro experimental data and in silico modeling to predict in vivo system behaviors (e.g., toxicokinetics, toxicodynamics and population variability). To date, in vitro toxicokinetic data generated on over 500 chemicals have been employed to develop and validate IVIVE models of varying levels of complexity and have been used to predict dose and exposure metrics along this continuum. Assessments of predictivity, uncertainty and variability of these IVIVE approaches have critically evaluated the predictions to identify the appropriate use and application of these datasets across the broad chemical space requiring data. Leveraging the in vitro datasets, in silico tools predicting hepatic clearance and plasma protein binding have also been developed for broad application across the untested space. Efforts to quantitate anticipated ranges of population variability have involved incorporating physiologic and metabolic profile information with chemical toxicokinetic data, allowing assessments across the US population and different life stages. These data and models reside in the EPA’s open source CompTox Dashboard and the R-based HTTK (High-Throughput ToxicoKinetics) platform. The positioning of IVIVE at the crossroads of new approach methodology (NAM)-based risk assessments underscores the importance of continued advances in this space. Multi-disciplinary collaboration, data and model transparency and education will be key to facilitate the application of these alternative methodologies in chemical safety assessments. This abstract does not necessarily reflect U.S. EPA policy.

Air Force Noise Exposure Demonstration Project

Dr. Dirk Yamamoto, U.S. Air Force School of Aerospace Medicine

This presentation summarizes research conducted by the US Air Force School of Aerospace Medicine, Force Health Protection Branch (USAFSAM/FHOF), in support of the Air Force Medical Service Total Exposure Health (TEH) program. Intended to be an initial demonstration of Total Exposure Health, the primary objective of this study was to develop low-cost sensor technology, in order to capture noise exposure data on a 24-hour basis for study participants. Here, the final product was a Bluetooth Low Energy noise microphone/sensor, connected to a special “app” developed for Apple iOS/Android devices and designed to extend battery life.

A total of 19 study participants (12 male, 7 female; 17 enlisted, 2 officer) were enrolled and consented at Moody AFB, GA. Field data collection over a 7-10 day period yielded 10,607 noise events, defined as being ≥70 dB. The majority (77%) were categorized as low noise events (≥70 dB, but < 95 dB). Questionnaire data indicated that noise exposures are due to various occupational, environmental, and lifestyle activities. Results of this study include demonstrating the ability to incorporate low-cost technology to capture data around-the-clock to provide insight into the types and extent of noise exposures experienced by military members. Further, this TEH approach to characterizing 24-hour noise exposures helps identify potential interventions (“personalized care”) to reduce the risk of hearing loss. Such interventions might include increased training, audiograms, and medical monitoring. Data on preferred types of hearing protection devices, e.g., foam plugs, ear muffs, custom-fitted plugs, were gathered, also.
POSTER ABSTRACTS

1) Evaluating Children’s Exposures to Semi-Volatile Organic Compounds Using Silicone Wristbands
Stephanie C. Hammel, Duke University; Allison L. Phillips, Kate Hoffman, Amelia M. Lorenzo, Albert Chen, and Heather M. Stapleton, Duke University; Thomas F. Webster, Boston University

Silicone wristbands have been used as passive sampling tools to evaluate personal exposures to a variety of semi-volatile organic compounds (SVOCs). Because SVOCs are applied as flame retardants, plasticizers, and stain repellants in common household products, human exposure to these compounds is common. Early-life exposure is of particular concern for children, who often experience greater exposure than adults and could be especially vulnerable to long-term adverse health effects. In this study, we evaluated the ability of wristbands to measure children’s exposure to organophosphate esters (OPEs), phthalates, brominated flame retardants (BFRs) and per- and polyfluoroalkyl substance (PFAS) precursors. In 2014–2016, children (ages 3–6) and their families were recruited to participate in a study examining children’s SVOC exposures in the home environment. Paired samples of house dust, hand wipes, pooled urine (3 samples collected over 48 hrs), and serum were collected during home visits, and children wore pre-cleaned silicone wristbands (n=74) for 7 days. The wristbands were analyzed for a suite of SVOCs using gas chromatography/mass spectrometry (GC/MS), and statistical analyses were performed to evaluate relationships between levels on the wristbands and other paired samples, as well as with biomarkers in urine and serum. All measured OPEs were frequently detected on >85% of the wristbands. Geometric means ranged from 6.1 to 614.8 ng/g band, with triphenyl phosphate (TPHP) having the highest concentration overall. OPEs on the wristbands were positively associated with metabolites from pooled urine samples. In particular, tris(1,3-dichloroisopropyl)phosphate (TDCIPP) on the wristbands was significantly correlated with its corresponding urinary metabolite, bis(1,3-dichloroisopropyl)phosphate (r=0.51, p<0.01). Isopropylated triaryl-phosphate esters (ITPs) were also significantly correlated with their metabolite, isopropylphenyl phenyl phosphate (ip-PPP; r=0.24–0.38; p<0.05). Average outdoor temperature was positively and significantly associated with TDCIPP on the wristbands (i.e., a 5% increase in TDCIPP concentration per 1°C increase in outdoor temperature), which reflects a similar trend observed for its urinary metabolite; however, this association was not observed for hand wipes. The magnitude of correlation between OPEs in exposure matrices and paired urinary metabolites for wristbands was roughly equivalent to hand wipes and was consistently greater than house dust. PFAS precursors were also commonly detected on children's wristbands, with geometric means ranging from 1.0 to 136.7 ng/g band. Further analyses will be performed to quantify phthalates and BFRs on the wristbands and to evaluate associations with house dust, hand wipes, and corresponding biomarkers.

2) The Utah PRISMS Informatics Ecosystem: An Infrastructure for Generating and Utilizing Exposomes for Translational Research
Ram Gouripeddi, University of Utah; Scott Collingwood, Bob Wong, Mollie Cummins, Julio Facelli, and Katherine Sward, University of Utah

Quantifying effects of the modern environment on health requires taking into account data from all contributing environmental exposures (exposome) which can span endogenous processes within the body, biological responses of adaptation to environment, and socio-behavioral factors. Exposomic research is translational in nature as the exposome includes direct biological pathway alterations as well as mutagenic and epigenetic mechanisms of environmental influences on the phenome. Generating exposomes requires integration of data from wearable and stationary sensors, environmental monitors, physiology, medication use and other clinical data, genomic and other biospecimen-derived, person-reported and computational models. This aggregation and integration requires to support variable spatio-temporal resolutions due to differences in study, experimental and analytical designs. Gaps in measured data may need to be filled with modeled data along with characterization of uncertainties.

We are developing a scalable computation infrastructure, the Utah PRISMS (Pediatric Research Using Integrated Sensor Monitoring Systems) Informatics Ecosystem (UPIE) to address these needs. UPIE is a comprehensive, standards-based, open-source informatics platform that provides semantically consistent, metadata-driven, event-based management of exposomic data. Using an event-driven architecture always the modeling and storage of all activities related to the study itself and its operations in their
primitive form on a timeline as events that can be transformed to higher/analytical models based on use-cases. It is aligned with the goals of modern environmental health research supporting meaningful integration of sensor and biomedical data. It consists of the following components:

1. Data acquisition pipeline: Hardware and software tools, wireless networking, and protocols to support easy system deployment, robust sensor data collection, and feedback to study participants.
2. Participant facing tools: Collect and annotate various patient reported and activity data, as well as inform participants on their current clinical and environmental status.
3. Computational modeling: Generate comprehensive spatio-temporal data in the absence of measurements and for recognition of activity signatures from sensor measurements.
4. Central big data federation/integration platform: Standards-based, open-access infrastructure that integrates measured and computationally modeled data with biomedical information along with characterizing uncertainties associated with using these data.
5. Researcher facing platforms: Tools and processes for researchers undertaking exposomic studies for a variety of experimental designs and for clinical care.

In this presentation, we discuss the architecture of UPIE, and the generalizability of this multi-scale and multi-omics platform for providing robust pipelines for reproducible exposomic research using results from pilot projects using real-time, low-cost air quality sensors to provide spatio-temporal records of particulate matter exposures. These pediatric studies are aligned with the National Institutes of Health (NIH) ECHO program and NIH PRISMS program and evaluated participant acceptance of personal and home-based Internet-of-Things sensor monitoring; demonstrated the feasibility of gathering environmental exposure data from low-cost sensors at a very fine level of resolution; demonstrated the efficacy in integrating heterogeneous data for building and analyzing exposure profiles.

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3) Silicone Dog Tags Examine Occupational Firefighter Chemical Exposures

Carolyn Poutasse, Oregon State University; Lane G. Tidwell, Peter Hoffman, and Kim A. Anderson, Oregon State University; Carlos Poston, Sara Jahnke, and Christopher Haddock, National Development and Research Institutes, Inc.

Firefighters are charged with protecting the citizens and property in the communities they serve, but occupational hazards specific to the fire service are hypothesized to play a role in the increased risk of cancers. These hazards include exposures to recognized or probable carcinogens, such as benzene, polycyclic aromatic hydrocarbons, diesel fumes, polychlorinated biphenyls, and asbestos. However, exposure classification for fire service studies is often rudimentary and based solely on job title or other inexact surrogates (e.g. department fire call volume), resulting in tremendous variability between and within departments with respect to exposures to environmental carcinogens. Silicone wristbands have recently been used to provide personal exposure assessments, and are often partnered with demographic data assessed by questionnaires to infer lifestyle and behaviors that are associated with chemical concentrations. This study presents the dog tag as a new necklace configuration of the silicone passive sampling device. Firefighters (on-shift vs. off-shift) recruited from two different stations (high volume vs. low volume) will wear the dog tag for 24 hours to capture accurate measurements of bioavailable occupational chemical exposures. This research will provide the first comprehensive characterization of chemical exposures to firefighters with the analysis of over 1500 analytes using gas chromatography mass spectrometry.
4) Hearing Health Education Delivery Using a Precision Preventative Medicine Approach

Dr. Tanisha Hammill, M.P.H., DoD Hearing Center of Excellence; Natasha Gorrell, MSPH, and Julieta Scalo, PhD, PharmD, DoD Hearing Center of Excellence, zCore Business Solutions

Background: The Department of Defense (DoD) Hearing Center of Excellence (HCE) developed the Comprehensive Hearing Health Program (CHHP) to prevent one of the most pervasive service-related injuries: noise-induced hearing loss (NIHL). Developed in 2013, the CHHP delivers wide-ranging hearing-health support for Service members (SMs) and hearing professionals; this includes a variety of military-focused educational materials and messaging for delivery by audiology providers, and is currently being piloted with a study assessing its impact on SM’s knowledge, attitudes, beliefs, and behaviors (KABB). The study also evaluates environmental noise exposures and genetic risk factors for NIHL. Although genetic susceptibility and noise exposure are established in the literature as risk factors, no literature has been found incorporating these into a precision-medicine approach to NIHL risk-profiling. This effort is the first to bring together KABB, environmental exposure, and genetic susceptibility to identify individualized hearing-injury risk-profiles.

Objective: To inform development of next-generation educational strategies that are customizable to individual SM’s needs, this study will characterize three precision preventative-medicine elements: KABB, noise exposures, and genetic susceptibility. Specific Aims: 1) Evaluate short- and long-term impacts of CHHP education on SM’s hearing-health KABB; 2) Identify genetic factors underlying NIHL susceptibility; 3) Use personal noise-exposure dosimetry and diaries to estimate the relationship between noise exposure and NIHL; 4) Create a hearing-loss risk-profile matrix to inform development of tailored educational messaging.

Study Design: This non-randomized, quasi-experimental study takes place at four participating military installations (one per Service). SMs stationed at either a Hearing Conservation or an Audiology Clinic/Center of Audiology are provided with CHHP educational materials. Surveys measuring KABB are administered immediately before and after the educational intervention and at 3-month follow-up visits. Non-intervention control groups recruited from each participating base complete baseline and 3-month follow-up surveys. All participants provide saliva samples for genetic analysis. To quantify noise-exposure, a convenience-sampled sub-cohort (n = 100 to 260) will wear personal noise-dosimeters and keep noise-exposure diaries for 7 days. Finally, DoD databases will provide relevant demographic, medical, employment, and deployment histories. Planned analyses will evaluate: 1) effects of CHHP education on KABB (mixed effects modeling); 2) relationships between genetic markers and NIHL (logistic regression); and 3) relationships between noise exposures and NIHL (generalized linear modeling). Findings will be synthesized into a hearing-injury risk-profile matrix for identifying individual prevention needs.

Results: Data collection is ongoing and anticipated to conclude September 2018. Preliminary data will be presented on sample characteristics, self-reported tinnitus and hearing loss, and unadjusted KABB question scores. Initial review of trends in pre-post KABB changes will be discussed, along with overviews of planned analytic models.

Relevance: To facilitate creation of novel strategies for personalized education and prevention, this study will characterize individual NIHL risk factors in three domains: environmental exposure, genetics, and personal hearing-health KABB. Findings will be relevant to the Military Operational Medicine Military Health System (MHS) Priority Area, in both Injury Prevention and Reduction and Environmental Health and Protection, as well as the Clinical and Rehabilitative Medicine MHS Priority Area as a hearing loss/dysfunction-related initiative.
5) Application of Total Exposure Health Practices to Solve Difficult Environmental Regulatory Problems: A Study of Low-Level Occupational Exposures to Trichloroethylene (TCE) in Air

Mr. John Lowe, CIH, Jacobs; David Patterson, Project Manager, Jacobs; Tim Smith, CPHIMS, KBRwyle

Total Exposure Health (TEH) combines exposure science, bioinformatics and information technology to prevent disease, preserve health and deliver precision medicine solutions. In the Air Force Medical Service’s (AFMS) TEH Strategic Plan FY19-23, two research goals are to: synthesize, identify and understand current and emerging trends through studies and analysis to advance prevention strategies, and ensure compliance with regulatory standards. Low-level inhalation exposure to the chlorinated volatile organic compound (VOC) trichloroethylene (TCE) from legacy soil and groundwater contamination provides an interesting case study of the challenges involved with translating TEH principles into practice. An example of a research need is for methods which more fully characterize the TCE exposome, such as real-time air monitoring based on wearable VOC sensors supplemented by exhaled breath sampling and monitoring for biomarkers of exposure. “Omic” studies of TCE have begun to identify genomic and metabolomic profiles associated with human toxicity, forming the basis for relating biological effects on a molecular level with low-level inhalation exposures. Expanding beyond the occupational health and medical fields, challenges exist in applying TEH solutions to exposures managed by environmental agencies such as the U.S. Environmental Protection Agency (EPA). With TCE, current EPA practices in regulatory toxicology include animal models of toxicity combined with limited air sampling for assessing exposures; the large margins of uncertainty associated with these practices result in overly conservative (and not always optimal) risk management outcomes. Though research is ongoing under EPA’s Computational Toxicology Program, environmental agencies currently do not embrace the principles embodied in TEH for site cleanup (CERCLA), waste management (RCRA) or toxic substances (TSCA) regulation. Using the example of TCE, this poster examines these potential regulatory barriers to the TEH vision of assessing work, environment and lifestyle exposures, and discusses potential solutions and associated research needs.

6) Comparing Chemical Exposures Across Diverse Communities Using Silicone Wristbands

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Assessing personal chemical exposure is critical to linking environmental contaminants with adverse health effects. Yet, for most environmental chemicals, there is little information about the frequency of chemical mixtures encountered by human populations. In this study, silicone wristbands were used to capture chemical detection frequencies in six distinct populations from Africa, South America, and North America. Wristbands were worn by residents in Senegal (n=25), the Alto Mayo region of Peru (n=69), Eugene, Oregon (n=25), Ohio (n=24), near the East Coast of the U.S. (n=24), and Corvallis and Bend, Oregon (n=21). Gender and age were also recorded. All 188 wristband extracts were analyzed for the presence/absence of >1,400 chemicals. Combining all locations, the average number chemical detections per individual was not significantly different for participants of ages 11-20, 21-40, 41-60, and >61 (Tukey-Kramer HSD, p<0.05). However, the children in Oregon, making up the <10 age bracket, had a significantly higher average number of chemical detections than all five other populations investigated (p<0.05), largely due to flame retardant and plasticizer chemicals. Examining location further, Senegal participants had a significantly lower average number of chemical detections per individual than all five other populations (p<0.05). In the U.S., Oregon adults had significantly higher average number of chemical detections than both Ohio and East Coast residents (p<0.001). There were no significant differences in the number of chemical detections for males compared to females even when stratified by continent or age (p>0.05). These wristband results help unlock the complexities that age, built environment, consumer products, and geographic location have on chemical exposures.
7) Unbiased High-Content Phenotyping for Personalized Chemical Exposure Risk Assessment


**Background:** Humans experience varying biological responses to chemical/environmental stimuli. Predicting differential responses involves understanding how an individual’s genetic profile can influence diverse responses to exposure/treatment. Understanding how genetics influences response to chemical exposure at the cellular level is critical for advancing personalized medicine initiatives and next generation prognosis and/or treatment methods. This unmet need is critical in the unique environment of the warfighter, as improved predictive measures could significantly reduce the risk of chemical exposure or better inform response measures.

**Methods:** Genetically characterized human B-lymphoblast cell lines (LCLs) were treated for 48 hours with a panel of nine compounds representing diverse mechanisms of action over a concentration range (based upon the average LCL response). Every plate contained vehicle (0.1% DMSO) and positive controls (10% DMSO) for cell death using both Jurkat control cells and the LCL of interest. The LCLs (and Jurkat controls) were stained with viability dyes and imaged. To analyze the images and extract phenotypic information, we developed an automated high content analysis pipeline (Clarity Bioanalytics) to measure 11,000+ morphological cell features. Redundant features (i.e. those features that were similar between positive and negative controls) were eliminated, and the remaining informative features were scored, ranked, and analyzed. Clarity Bioanalytics was used to manage, analyze, and score the high content analysis data. Novel algorithms and statistical tests were used to define the phenotypic signature for each chemical toxicant and identify outlier wells (i.e. hits). Single nucleotide polymorphism (SNP) data for each LCL were downloaded from the dbSNP repository and processed for genome-wide association. Pharmacologic quantitative trait loci were mapped based on the genetic profiles of LCLs displaying “non-normal” (i.e., outliers) phenotypic signatures. The statistical relevance of various SNPs were organized by chromosome using Manhattan plots.

**Results:** Preliminary results from the feature evaluation and selection phase of the project indicate we can identify unbiased (sets of) features that are specific for one or more of the individual compounds. We have screened nearly 300 LCLs with the compound panel, identified phenotypic signatures that signify exposure to a specific compound, and correlated differential phenotypic responses to particular genetic polymorphisms (i.e., SNPs) using Genome Wide Association Screening (GWAS). Interrogation of SNPs with publicly available databases allowed us to identify genes/genetic elements and signaling pathways that may be involved in differential cellular response to toxicant exposure.

**Conclusions:** The results of our proof-of-concept experiments demonstrate that we can use unbiased phenotyping to identify and characterize the cellular response to chemical exposure and, using our novel analysis pipeline, correlate phenotypic changes to with genetic information. The identification of genetic correlations to differential response patterns is an important step toward personalized assessment of biological effects of chemical exposure, which will allow predictive assessment of exposure risk on the basis of genetic information.
8) Health Surveillance Program Helps Define the Exposome of Former Workers

Dr. Ashley Golden, ORAU; Wendy Benade, Bill Stange, John McInerney, Donna Cragle, Zachariah Hubbell, Jeffrey Miller, and Barbara Neill, ORAU; Lee Newman, University of Colorado Denver

The National Supplemental Screening Program (NSSP), a Department of Energy (DOE) Former Worker Medical Screening Program, provides exposure-based medical examinations to identify health conditions that are occupational or non-occupational in origin. This approach extends disease surveillance and health promotion into the post-employment years of the participants and provides valuable data that are useful for understanding the occupational exposure profile of individuals and how it relates to adverse outcomes. The organizational framework of the NSSP ensures performance standards of the highest quality on a nationwide scale through the implementation of a single, web-based relational data management health records system to collect and process all demographic, occupational exposure, clinical, and health outcome data, resulting in over 1000 pieces of data for each participant for a single exam.

This poster describes the design of a former worker integrated health screening and health promotion program and the outcomes for DOE former workers, within which 17,227 participants completed an initial NSSP medical screening exam and 3,411 had also completed at least one follow-up exam prior to December 31, 2017. We discuss the DOE former worker NSSP participant population, the exposure-based and non-occupational medical screening tests used, as well as information that indicates the value of a program to inform former workers of addressable health conditions in an integrated manner. The NSSP comprehensive medical screening examinations are performed through a network of clinics such that participants are provided access within 75 miles of their residence. The medical protocol is tailored to each participant based on medical and occupational exposure history. Occupational hazards considered in the evaluation include, but are not limited to: radiation, beryllium, asbestos, silica, diesel exhaust, heavy metals, solvents, other chemicals, noise, and laser energy.

Occupationally-related health conditions are commonly identified in NSSP participants in all exam phases (initial and follow-up), as expected for a former worker group of this kind. Notably, however, we have observed steadily higher proportions of non-occupational health findings (many previously undiagnosed) than conditions associated strictly with occupational exposures, demonstrating the utility of this program model for more comprehensive worker health surveillance. Common non-occupational findings include diabetes, hypertension, colon cancer, cardiovascular disease, and renal disease. Asbestos, mesothelioma, and beryllium sensitization/chronic beryllium disease are prevalent occupational conditions identified in the NSSP population. Indeterminate health conditions, those that are not explicitly occupational or non-occupational, typically include obstructive and restrictive lung disease, lung cancer, and skin cancer.
9) Integrated Proteomic and Metabolomic Network Analysis of Reveals Circadian Misalignment Patterns

Jason McDermott, Pacific Northwest National Laboratory; Jason Wendler, Jon Jacobs, Hans Van Dongen

People with schedules misaligned to their circadian pacemaker such as shift workers and military personnel involved in short notice transmeridian deployment can experience a host of adverse health effects from short term deficits in mental acuity to long term metabolic disorders. In a controlled cohort study of patients performing a constant routine after adaptation to either day or night schedules, we previously showed that metabolites stratified into three distinct clusters 1) those that showed 24 h rhythmicity under constant routine following both the day and night shift schedules, but reversed their rhythms following the night shift schedule; 2) those that showed significant 24h rhythmicity under constant routine only after the day shift schedule; and 3) those that did not show significant 24-h rhythmicity under constant routine after the day shift schedule, but were rhythmic after the night shift acclimation. To further assess the mechanisms associated with circadian- and behavior- driven metabolite rhythms, we performed proteomic assay on four timepoints from the same cohort, and integrated these results with the metabolomic data. We used Linear Mixed Models with random effects to account for within-subject variation to contrast the day and night cohorts at each timepoint. We then calculated pathway enrichment statistics for the significant proteins at each timepoint. Consistent with metabolomic signatures of acute phase response, one of the top proteins that differentiates Alpha-1-acid glycoprotein 1 is a protein that in humans is encoded by the ORM1 gene. Pathways associated with glucose and glycolysis, and mitochondria dominated differences at early timepoints. Pathways that differentiated the day and night cohorts at all timepoints include oxidative stress, humoral immunity, and the melanosome. To place these in context with each other we inferred an integrated association network using a machine learning approach. We identified modules composed of sets of proteins and metabolites with similar dynamic profiles, and then mapped the functional pathways to this network model. This analysis allows an improved representation of the complex relationships and patterns inherent in the data.

10) Susceptibility to Severe Disease and Death in Patients with Ebola Virus Disease (EVD) is Associated with Host Genetics and Multi-Omic Expression Quantitative Trait Loci (eQTL)

Jason P. Wendler, Pacific Northwest National Laboratory; Joe Brown, and Katrina M. Waters, Pacific Northwest National Laboratory; Amie J. Eisfeld, Peter J. Halfmann, and Yoshihiro Kawaoka, University of Wisconsin-Madison

A paradox in most infectious diseases is that some individuals develop serious, life-threatening illness, while others present mild symptoms or none at all. Disparate disease outcomes are mediated by differential host responses to infection, and those that influence survival or fitness face a variety of evolutionary selective pressures. In heterogeneous populations, these selective forces lead to characteristic genomic signatures that are detectable by GWAS and other population-genomic analyses. The power to detect selective signatures associated with infectious diseases will be dampened if penetrance and exposure are low, however this could be offset if different microorganisms select for common host factors. Our pan-viral, multi-omic analyses indicate that a finite number of host responses are associated with virulence, most of which are common to more than one virus. We have performed genome-wide scans for loci associated with survival using peripheral blood mononuclear cells from patients infected with Zaire Ebola virus (EBOV) during the 2015 outbreak in Sierra Leone. Genotypes were ascertained using RNA-seq reads, which also enabled us to investigate allele-specific expression patterns (ASE) that are associated with disease outcome. ASE and GWAS are distinct approaches that test for associations with different types of factors. We also expanded transcriptomic eQTL scans to include expression of proteins, metabolites, and lipids. Genotype resolution was enhanced by imputation to 1000-genomes reference populations. We used SNPTEST to scan for association with outcome using additive, dominant, recessive, and heterozygous genetic models. Cis-eQTL and ASE of immune response genes are associated with survival. Polymorphisms near genes related to T-cell homeostasis and oxidative stress response are also associated with disease outcome.
Currently, genome sequence analysis cannot independently and completely characterize the threat of exposure to a natural, engineered, or synthetic biological agent. The pathogenic potential of a microbe is often determined by subtleties of strain variations that become apparent only after post-transcriptional or post-translational events that target host cells. Pathogenesis is also dependent on the host defenses to the invading organism, where either a weak or overly strong response can ultimately result in disease. Thus, interrogating the unique repertoire and magnitude of molecular responses from host cells is an alternative solution for evaluating potentially dangerous biological exposures. This approach is especially attractive because it does not require exhaustive cataloging and is agnostic to synthetically altered or generated agents. We applied a Support Vector Machine (SVM) learning approach with bootstrapping to transcriptomic data from in vitro infections of human cells infected with either H1N1 influenza (low virulence) or H5N1 influenza (high virulence). In this preliminary analysis, we were able to maximize the area under the ROC curve (AUC) to 0.83 with a signature of 110 out of 1,352 differentially expressed genes, demonstrating the feasibility of this method to distinguish between viral strains based on pathogenic potential. Analysis of key predictive features of the model revealed genes involved in cell signaling and inflammation. These genes are consistent with known host modulators during viral infection and increase our confidence that the model can accurately assess data that may cross-validate with cell response data from other infections. Future analysis of new datasets will be used to further refine and validate this method for biological threat characterization and can also be evaluated for potential therapeutic targets.
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