AGILENT EMERGING OMICS RESEARCH TOUR

Environmental Exposure Science Symposium

The Measure of Confidence

TUESDAY, SEPTEMBER 30, 2014 | **The Hamner Institutes for Health Sciences**

Agenda	
8:00 am – 8:45 am	Registration and continental breakfast
8:50 am – 9:00 am	*Welcome and Introductions* **Anthony Macherone**
9:00 am – 9:25 am	*The exposome and analytical strategies to measure it* **Anthony Macherone, PhD – Agilent Technologies & Visiting Scientist, Johns Hopkins School of Medicine**
9:25 am – 9:50 am	*Challenges & Opportunities in Implementing the Exposome* **David Balshaw, PhD – NIEHS**
9:50 am – 10:15 am	*Use of 'Omics' to Charcterise Human Exposure* **Martyn Smith, PhD – UC Berkeley**
10:15 am – 10:30 am	Break
10:30 am – 10:55 am	*The Endogenous Exposome* **James Swenberg, PhD – UNC School of Medicine**
10:55 am – 11:20 am	*Future platforms for in vitro-based toxicity testing* **Mary McBride, PhD – Agilent Technologies**
11:20 am – 11:45 am	*A Pathway-centric Approach to Multiomics Research Powered by GeneSpring Analytics* **Nigel Skinner, PhD – Agilent Technologies**
11:45 am – 12:00 pm	*Closing remarks* **Anthony Macherone, David Balshaw**
12:00 pm – 1:00 pm	Lunch

Environmental exposure science is moving away from a single point bottom-up strategy of measuring one exposure and one effect to a top-down discovery approach. The exposome paradigm incorporates these non-targeted techniques to identify relevant biomarkers followed by a targeted approach to differentiate biomarkers of exposure and disease.

This event will define the exposome, current trends and analytical strategies to measure the exposome and toxicity pathways in real case studies. It will further illustrate how the exposome paradigm can be applied to elucidate exposure-response relationships, sources of exposure and mechanisms of action in chronic human health.

Date: September 30, 2014

Location: The Hamner Institutes for Health Sciences
Main Conference Room 521
6 Davis Drive
Research Triangle Park, NC 27709-3547

Time: 8:00 am – 1:00 pm
Register Today!

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Abstracts & Bios:

The exposome and analytical strategies to measure it.

Anthony Macherone

The growing realization that 70% to 90% of chronic human disease risks result from exposures to nongenetic factors is influencing a new paradigm that considers gene × environment matrix and how these interactions affect human health. This new paradigm of the exposome is defined as the sum of all exposures over a complete lifetime. At its essence the exposome is represented by the thousands of chemicals circulating in human blood that are outside of genetic control. Exposomics is the measurement of the exposome using "omics" tools. The instrumentation includes LC/MS, GC/MS, ICP-MS, NMR and personal sensors and sensor arrays. In a comparative model similar to genome-wide associated studies (GWAS), exposome-wide associated studies (EWAS) will interrogate exposomes in a discovery-based metabolomics mode followed by multi-technique, targeted analyses to differentiate biomarkers of exposure (causal pathways) and biomarkers of disease (reactive pathways). This two-step model will elucidate exposureresponse relationships, sources of exposure and human kinetics and mechanisms of action.

Anthony Macherone is a Senior Applications Chemist with Agilent Technologies and worked for the past two decades in a number of disciplines ranging from forensics, biotech and drug discovery. His main focus over these years has been the development of core laboratories for the identification and quantification of known and unknown substances in biological and non-biological matrices. To this end, Anthony has developed expertise in liquid and gas phase chromatography technologies including but not limited to single and tandem quadrupole, time-of-flight and quadrupole time-of flight mass spectrometry and nuclear magnetic resonance spectroscopy. The accumulation of these cross disciplinary skills has afforded him a unique insight into laboratory design and method development for the identification of biomarkers using "omics" technologies. Anthony holds a visiting scientist appointment at the Johns Hopkins University School of Medicine and is a member of the American Chemical Society, the American Association for the Advancement of Science and the American Society of Mass Spectrometry.

Challenges & Opportunities in Implementing the Exposome

David Balshaw

Dr Balshaw is a program director in the Center for Risk and Integrated Sciences at the National Institute of Environmental Health Sciences. Dr Balshaw is responsible for planning and administration of NIEHSfunded research programs in bioengineering, integrated systems, and computational methods to understand complex systems; development of sensor technologies for environmental exposure assessment; discovery and validation of emerging biomarkers; and application of innovative "omics" research for reducing the risk of exposure and disease including development of databases. He is the primary NIEHS scientist overseeing the development of emerging technologies with particular emphasis on enabling innovative approaches to improving exposure and risk assessment. To this end, Dr Balshaw has been a leading figure in the development of the Exposure Biology Program to develop a new generation of tools to characterize the personal environment integrating direct, personal assessment of multiple chemical factors, dietary intake, physical activity and psychosocial stress as well as assessment of the biological response to these factors on major biological pathways. Dr Balshaw received training in pharmacology and biophysics from the University of Cincinnati and University of North Carolina at Chapel Hill. His interdisciplinary training has enabled him to effectively bridge between disparate communities including engineering, mechanistic toxicology, and both clinical and public health application. These successes have led to recognition of his leadership as an expert translational scientist at the NIH and leadership roles in the NIH Common Fund, the NIEHS DISCOVER Program, and the NIH Genes, Environment, and Health Initiative Exposure Biology Program.

Use of 'Omics' to Charcterise Human Exposure

Martyn Smith

Dr. Smith has expertise and a broad background in molecular epidemiology, toxicology and genomics, aimed at finding the causes of chronic disease including lymphoma and leukemia. His interest in the subject of benzene toxicity began in the mid-1980's and he has published extensively on this topic, most recently as a review for the 2010 Annual Reviews of Public Health. Dr. Smith has led the Superfund Research Program at Berkeley since its inception in 1987. This program has been peer reviewed and renewed 5 times. The overall goal of the Program is to improve understanding of the relationship between exposure and disease; provide better human health risk assessments; and, develop a range of prevention and remediation strategies to improve and protect public health and the environment. In addition, he is a collaborator on numerous other projects examining emerging technologies to develop biomarkers for human studies, improve chemical detection, and facilitate waste remediation. Dr Smith received his BSc and PhD from the University of London (UK), and conducted Post-doctoral training at the Karolinska Institute in Sweden.

Future platforms for in vitro-based toxicity testing

Mary McBride

Toxicology is moving from traditional high dose testing in animals to an in vitro approach based on a deep mechanistic understanding of key toxicity pathways. Major components of this new approach include the use of human cell-based assays combined with high-content multi-omics measurements, computational systems biology models and pharmacokinetic tools to evaluate perturbations in key cell-signaling pathways. By integrating all of these tools —termed "integrated systems toxicology" — it may be possible to map and annotate toxicity pathways, conduct systems analysis of pathway function, and link pathway perturbations to cell and tissue responses thereby enabling both dose-response modeling and in vitro to in vivo extrapolation. Using a case study approach focused on a few key prototype nuclear receptor and stress-response pathways, we can now identify specific technologies and experiments that will accelerate completion of the first-phase of pathway mapping and modeling. Here, we describe the suite of technology platforms used in these studies and show how these tools have been applied in our studies. We also discuss how these integrated data packages are shaping, informing and modifying our conventional views of toxicity pathways.

Mary McBride is the Director of Government Relations for Life Sciences and Chemical Analysis at Agilent Technologies. She works to identify and develop strategic business opportunities, working with government agencies, academic and industrial partners and non-for profit organizations. She recently established a private sector partnership designed to demonstrate the feasibility, potential benefits and risks of using toxicity pathway-based approaches to toxicity testing that inform human health risk assessments. Prior to joining Agilent in 2007, Dr. McBride was an Associate Division Leader within the Chemical and Biological National Security Program at Lawrence Livermore National Laboratory. There, she directed and managed the research and development activities of a large team working to develop and deploy technologies to prepare for, detect and respond to biological terrorism. These technologies have transitioned from proof of concept projects to operational systems with successful commercialization of multiple diagnostic and detection products. Dr. McBride earned a B.S in Biochemistry and a Ph.D. in Analytical Chemistry, both from the University of California, Davis. She has published more than 40 peerreviewed papers and holds 5 patents related to biodetection instrumentation and assays.

A Pathway-centric Approach to Multiomics Research Powered by GeneSpring Analytics

Nigel Skinner

The talk will discuss the advantages of analyzing multiple omics data sets, enabling such data to be visualized in a biological context through the use of bioinformatics. Several examples will be provided that illustrate the acceleration of biomarker discovery & drug safety research. One example will show how the integration of transcriptomic and metabolomics data enables improved experimental design of proteomics workflows, and accelerated identification of druggable targets forming the basis for subsequent structural studies and characterization.

Dr Nigel Skinner is Global Market Segment Manager for Life Science Research Disease Research & Toxicology Solutions in Agilent Technologies Life Sciences Group. Dr Skinner has worked in Marketing and Business Development at Agilent since 2007, prior to which he has held various marketing and business development positions at GE Healthcare, Life Technologies and Affymetrix, working in the U.S., U.K. and Switzerland. Dr Skinner holds a PhD from Cambridge University (UK), together with an MBA, MEng and BSc. He has published more than 30 peer-reviewed publications and holds 6 patents.