TRANSFORMING TOXICOLOGY

WITH INTEGRATED
MULTI-OMIC SOLUTIONS

The Measure of Confidence

Agilent Technologies

SYSTEMS TOXICOLOGY SOLUTIONS

With leading analytical products across the four major omics—genomics, transcriptomics, proteomics, and metabolomics—Agilent empowers research toxicologists who are moving from traditional high-dose testing in animals to integrated systems toxicology approaches that enable deeper understanding of biological processes.

Researchers are applying this new approach to toxicity testing using Agilent systems toxicology solutions to link exposures to outcome-specific patterns obtained from omics profiles. By integrating multi-omic data sets, they are better able to identify toxicity pathways, modes of action, mechanisms of disease, and biomarkers of toxicity.
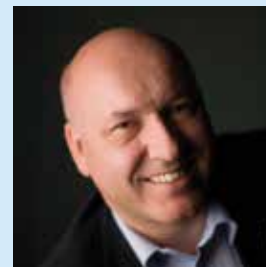
As a trusted partner, we provide comprehensive tools for leading researchers like the ones featured here. Our systems and software help them stay on the forefront of toxicology research—and they can do the same for you.

CHEMICAL SAFETY USING SYSTEMS TOXICOLOGY

At Johns Hopkins University, **Dr. Thomas Hartung** directs the Center for Alternatives to Animal Testing, where he is a tireless champion for systems toxicology. He sees the future of toxicity testing as increasingly based on omics technologies.
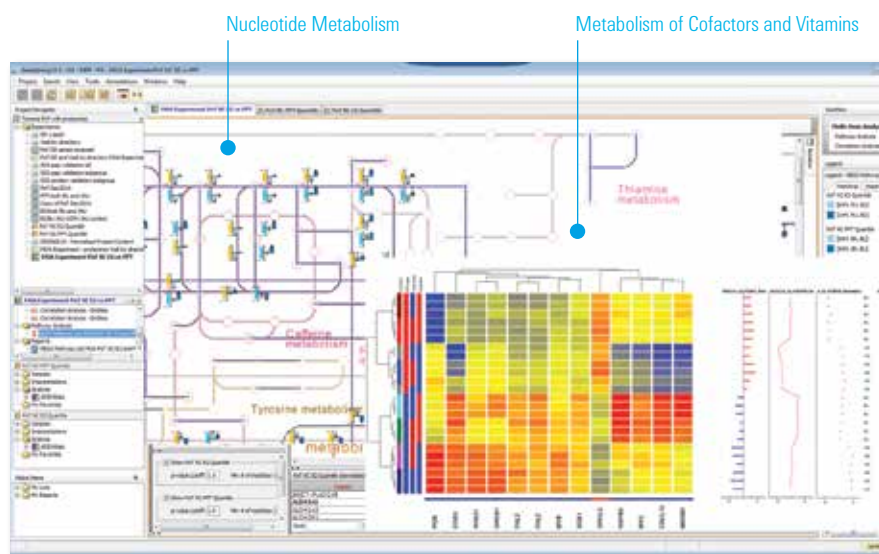
In an NIH-funded project, Dr. Hartung and his team are mapping pathways of **endocrine disruption**, a first step toward mapping all cell-signaling pathways. Using Agilent gene expression microarrays, liquid chromatography coupled with mass spectrometry, and the GeneSpring software suite—the team is integrating transcriptomic, metabolomic, and proteomic data to understand mechanisms of toxicity.

Nucleotide Metabolism   Metabolism of Cofactors and Vitamins

The Agilent GeneSpring software suite enables you to integrate and analyze multi-omics data. Providing powerful statistics and rich visualization, it gives biological context to your data.

> *"Our work with Agilent's GeneSpring bioinformatics platform has really demonstrated the power of integrated omics. Multi-omics data, considered collectively, reveals critical biological connections that were not considered significant in the individual omics analysis."*

DR. THOMAS HARTUNG,
JOHNS HOPKINS UNIVERSITY

> *"We are using an Agilent 6550 Q-TOF LC/MS to perform exposome-wide association studies to discover causal exposures."*

DR. STEPHEN RAPPAPORT,
UNIVERSITY OF CALIFORNIA AT BERKELEY

Dr. Stephen Rappaport, director of the Berkeley Center for Exposure Biology at the University of California at Berkeley, is applying a multi-omics approach in his work to identify the causal linkages between environmental exposures and disease. His research is substantially advancing the emerging field of **exposure biology**, and he was one of the first to define and promote the concept of the "exposome" as the totality of lifetime exposures that might contribute to disease.

PHARMACEUTICAL SAFETY USING SYSTEMS TOXICOLOGY

"We hope to better anticipate and prevent possible adverse reactions to medications. With Agilent we have been using their SurePrint G3 Microarrays and metabolomics workflow to identify genetic risk factors that are common among hepatotoxic drugs".

DR. PAUL WATKINS, HAMNER INSTITUTES

Roughly 30 percent of drugs tested in clinical trials fail due to unanticipated and unacceptable toxicology profiles. That's one reason Agilent is working with **Dr. Paul B. Watkins**, who directs the Institute for Drug Safety Sciences at the Hamner Institutes. Dr. Watkins has been doing extensive research on **drug-induced liver injury**, or DILI, a form of hepatotoxicity, which often terminates the development of promising new drug candidates. Dr. Watkins and his team of researchers are developing integrative methods to predict DILI.

"We are performing pathway-guided global metabolomics using Agilent's 6550 Q-TOF LC/MS, followed by targeted metabolomics with the 6460 Triple Quadrupole LC/MS. We use kidney-toxic drugs as molecular probes to investigate renal mechanisms of toxicity and enable identification of pharmaco-metabolomic biomarker profiles."

DR. LAWRENCE LESKO, UNIVERSITY OF FLORIDA

Kidney toxicity is a leading cause of compound attrition and of formerly approved drugs being withdrawn from the market. Although a few clinical biomarkers of kidney injury are available, they lack adequate sensitivity and/or specificity. **Dr. Lawrence Lesko**, who directs the Center for Pharmacometrics and Systems Pharmacology at the University of Florida, leads a team of researchers working to identify novel biomarkers for early detection of drug-induced nephrotoxicity.

The Agilent 6550 Q-TOF (left), combined with the 1260 HPLC system (center) is the perfect choice for discovery metabolomics, biomarker discovery, and clinical research. The Agilent 6460 Triple Quadrupole mass spectrometer (right) provides ultra-sensitive detection, ideal for quantitation and targeted analysis.

"In collaboration with Agilent Technologies, we have developed methods based on Agilent's ChIP-on-chip microarray platform to measure both the distribution of DNA damage throughout the genome and the rates of repair. Methods to predict response to drug treatments will enable improved selection."

PROFESSOR SIMON REED, CARDIFF UNIVERSITY

At the Institute of Cancer and Genetics at Cardiff University, Professor Simon Reed is working to unravel the mechanisms of DNA damage and repair. This understanding is critical for clinical research. Drugs like cisplatin—used to treat cancer—may cause kidney damage as a result of damage to DNA. Using technology from Agilent, Professor Reed has developed a microarray-based method—3D-DIP-chip— for measuring cisplatin-induced DNA damage in blood.

Agilent's microarrays provide superior sensitivity and maximum design flexibility with either defined or completely customizable content.

DETECTING EMERGING CONTAMINANTS

"The combination of Agilent GC/MS, LC/MS, and ICP-MS offers tremendous advantages for analysis, enabling us to comprehensively evaluate environmental exposures. Using Mass Profiler Professional, we are able detect otherwise subtle trends in occurrence and to discover new substances within highly complex environmental mixtures."

DR. SHANE SNYDER, UNIVERSITY OF ARIZONA

An internationally recognized authority on water contamination, Dr. Shane Snyder is a professor of chemical and environmental engineering at the University of Arizona. His research is focused on the identification, fate, and health relevance of emerging water pollutants, such as pharmaceuticals and personal care products. He applies Agilent's broad analytical product portfolio and bioinformatics tools in his work to comprehensively identify emerging water contaminants.

The Agilent 7200 Q-TOF GC/MS system (left) combines unmatched separation power with advanced high-performance accurate mass analysis. It enables you to screen your samples for virtually unlimited numbers of known analytes, or analyze for unknown or emerging contaminants. The Agilent 8800 Triple Quadrupole ICP-MS (right), combined with our 1200 Infinity Series LC (center), delivers accurate and sensitive mass detection. It is especially well-suited for trace level analysis from complex sample matrices.

"China faces many pressing environmental issues, and a systems toxicology approach offers a way to link environmental factors to health consequences. Toxicology will play a more and more important role in Chinese scientific research, government decision making, and other industries going forward."

DR. GUIBIN JIANG, CHINESE ACADEMY OF SCIENCES

As director of the Chinese Academy of Sciences' Research Center for Eco-Environmental Sciences, Dr. Guibin Jiang is a world-renowned expert in persistent organic pollutants and the speciation of organometallic compounds. His work has significantly advanced analytical and environmental chemistry and ecotoxicology in China.

Dr. Jiang uses Agilent instruments such as our Q-TOF GC/MS systems for nontargeted screening of organic pollutants in water and soil samples from across China. His laboratory also employs Agilent Q-TOF GC/MS and triple quadrupole ICP-MS systems to follow the transport of nanoparticles in environmental systems and to better identify and quantitate heavy metals and metalloids in polluted waters.

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