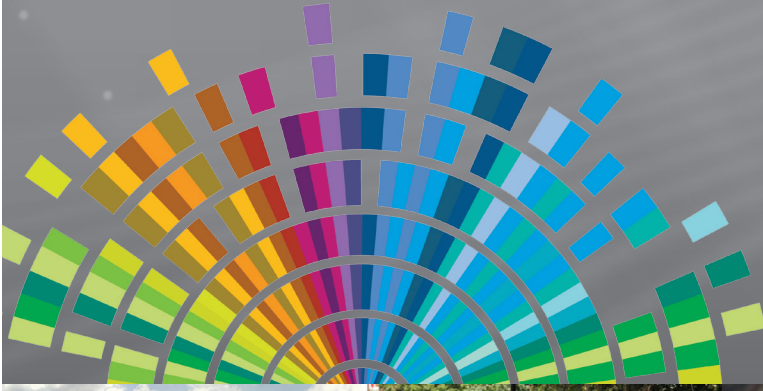




Integrating workflows and Bioinformatics
for Exposome and Environmental Health Research

ADVANCING EXPOSOMICS RESEARCH



EXPOSOMICS AND ENVIRONMENTAL HEALTH RESEARCH

Agilent empowers exposome and environmental health research with leading analytical products and solutions across omics technologies. This enables a deeper understanding of how chemical exposures effect biological processes and disease causality.



The exposome is the cumulative sum of environmental exposure and associated biological responses spanning an individual's lifetime. Exposomics is the application of omics-based technology including mass spectrometry and bioinformatics to characterize and quantify the exposome.

Researchers apply these techniques of systems biology using a multiplatform, multi-omics approach to achieve greater insights into disease pathways.

Differences in exposure profiles can be determined between healthy and diseased populations by using well-designed case-control studies nested from prospective, longitudinal cohorts.

THE EXPOSOME

The term “exposome” was first used by Dr. Christopher Wild, a cancer epidemiologist, in 2005 in the article “Complementing the Genome with an “Exposome”: The Outstanding Challenge of Environmental Exposure Measurement in Molecular Epidemiology”. In this article Dr. Wild discussed the importance and potential impact of environmental exposures on human health. He posited that the best way to characterize these impacts would be to apply tools used in genomics, proteomics and metabolomics.

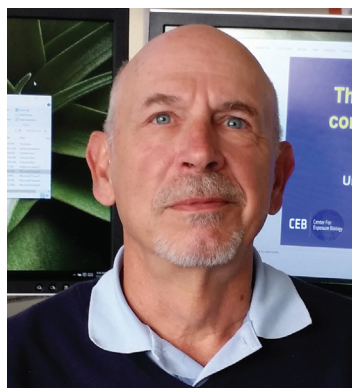


The exposome complements the genome and integrates nongenetic exposures with associated biological response pathways in research of the causative factors of chronic human disease. Within the exposome paradigm, the internal environment is composed of all bio-active chemicals circulating in an organism. Examples include dietary chemicals, drugs, persistent organic pollutants, biotransformation products (metabolites), foreign DNA, reactive electrophiles adducted to serum albumin and molecules from the biochemical response from other sources of exposure (such as noise pollution, place of residence, and lifestyle choices).

The Exposome and Environmental Health Research

An individual's phenotype, their physical and observable characteristics, is a complex combination of genetic expression (the genome), exposures (the exposome), epigenetic modifications, and stochastic events. Genome-wide association studies (GWAS) are applied to elucidate gene expression and protein function and to identify biochemical pathways implicated in chronic diseases. Exposome research elaborates the exposure profiles of all circulating chemicals in a given system using omics technologies to understand its contribution to chronic disease.

Exposome-wide association studies (EWAS) are complementary to GWAS and use similar tools, technologies, and workflows as those used in proteomics, metabolomics, and genomics studies. Metabolomics profiling can be used to track population exposure effects in case control studies.



Stephen M. Rappaport, PhD
University of California at Berkeley

Exposome-Wide Association Studies: Mass Spectrometry

Dr. Rappaport's research is substantially advancing the emerging field of exposure biology. He was one of the first to define and promote the concept of the "exposome" as the totality of lifetime exposures that may contribute to disease.

"The 6550 Q-TOF offers many advantages for our Exposome-Wide Association Studies. The high mass resolution, wide dynamic range and sub-ppm mass accuracy of the 6550 allow us to broadly and accurately elucidate the chemical complexity of human blood samples and annotate molecular identities using high mass accuracy MS/MS.

The Agilent Jet Stream (AJS) and ion-funnel technologies provide the sensitivity necessary to measure low concentrations of many small molecules of interest."

STEPHEN M. RAPPAPORT, PHD, UNIVERSITY OF CALIFORNIA AT BERKELEY



Agilent LC/MS system: 1290 Infinity II HPLC with a 6550 Q-TOF with iFunnel technology for femtogram level sensitivity.

As in all omics-based studies, the analytical challenges in exposure biology and environmental health research are manifold. Common sample types include biopsy samples, cell cultures, urine, blood, serum, or plasma with a broad range of bioactive chemicals. The analyses of these complex samples are performed on multiple mass spectrometers coupled to separation technologies (LC, GC, SFC, CE). Genomics workflows address genotype, epigenomic DNA modifications and gene expression of mRNA and microRNA through microarrays or NGS based assays. Combining the results of different techniques and workflows greatly enhances the ability to identify associations between exposures and disease in environmental health studies.



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The Agilent 6470 Triple Quadrupole LC/MS system with 1290 Infinity II LC System

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Environmental Human Health Measurements: Orchestration of Technologies

Dr. Kingston's research is focused on the establishment of physical test for the definitive environmental quantification of suspected exposures of disease causation such as autism. Inductively coupled plasma mass spectrometry, gas and liquid chromatography tandem mass spectrometry allow his research team to identify and quantify markers of environmental toxin exposure in a targeted approach. By integrating multi-omic data sets, Kingston's lab is better able to identify and differentiate patterns, modes of action and mechanism of disease.

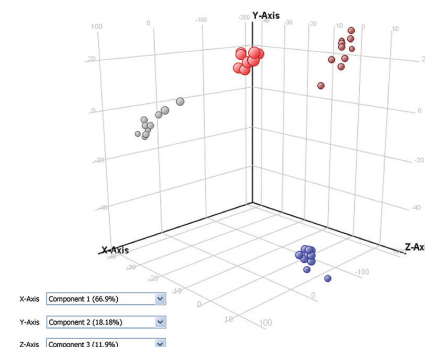


H. M. (Skip) Kingston, PhD
Duquesne University

A Single, Consistent User Experience Across all your Agilent MS Platforms

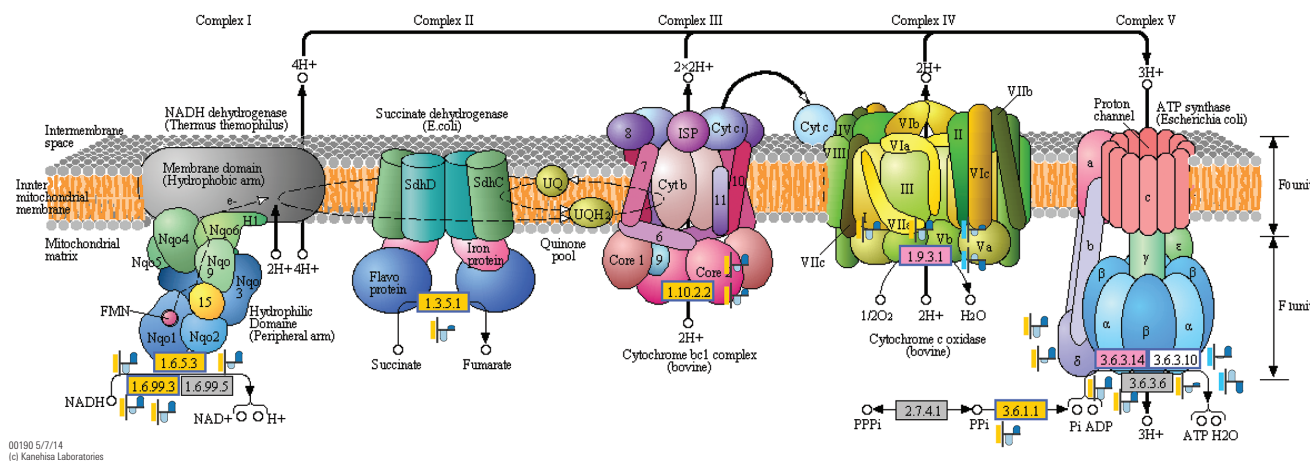
Agilent MassHunter software is designed to make your MS analyses faster, easier, and more productive. In addition to data acquisition and instrument control for your Agilent LC/MS, GC/MS, CE/MS, and ICP-MS, the software incorporates advanced data mining and processing tools. These tools let you rapidly and accurately extract all available information from the analytes in your samples—not just peaks and data points, but answers.

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- **Spectrum Mill** quickly identifies proteins and peptides through fast database searches with automatic or manual match validation and unique algorithms that minimize false positives.
- **Agilent-METLIN Personal Metabolite Database Software** greatly improves metabolite identification by narrowing the list of possible identities.
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- **VistaFlux Software** features integrated programs for creating target lists, extracting batch isotopologues, and visualizing qualitative flux results on pathways.
- **Mass Profiler Professional Software** is a powerful statistical software package designed to exploit the high information content of MS data.
- **GeneSpring GX** offers an interactive environment that promotes investigation and enables understanding of transcriptomics, metabolomics, proteomics and NGS data within a biological context.



Principle Component Analysis (PCA) of metabolites with Mass Profiler Professional Software

OXIDATIVE PHOSPHORYLATION



Multi-omic analysis in Pathway Architect, a module for Mass Profiler Professional and GeneSpring GX

AGILENT TECHNOLOGIES OFFERS SOLUTIONS FOR EXPOSOME AND ENVIRONMENTAL HEALTH RESEARCH

Over the last several decades, significant progress has been made in understanding the genome, the proteome and, the metabolome and their influence on chronic human diseases. However, environmental exposure and its role in disease progression has been largely overlooked. Exposomics has emerged to understand this interplay of environment and biology by applying the sophisticated systems biology tools developed for the measurement of the other “-omics” to characterize and correlate internal and external chemical exposures with disease risk.

Agilent Technologies offers solutions for exposome and environmental health research covering genomics, proteomics, metabolomics, cell metabolism and bioinformatics. These solutions include microarrays and NGS reagents, automated sample preparation, separation systems, mass spectrometry, cell analysis and bioinformatics software.

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