Exposomics: A shift in biomedical research with potential to improve human health

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Recent advances in exposomics offer an exciting opportunity to comprehensively catalog human exposures and link them to biological responses determining health and disease. Pamela J. Lein, Ph.D. from the University of California, tells us more

The sequencing of the human genome was heralded as a major scientific achievement that would revolutionize medicine by identifying genetic causes of disease, which could then be cured using gene therapy. However, while genomic research has identified numerous genetic variants in the human genome that confer risk for disease, it has become increasingly clear that only a small fraction of disease can be attributed solely to genetic causes. Indeed, genetic evidence indicates a critical role for diverse environmental factors in determining an individual's health throughout their life.

These environmental influences include the chemical, physical, and social environments in which people live and the impact of these environments on their opportunities and health behaviors. Put another way, environmental factors that influence human health can be exogenous (e.g., originating from outside the body, such as environmental pollutants, climate, noise, and light), endogenous (e.g., within the body, like the microbiome, metabolism, pre-existing medical conditions) and behavioral (e.g., lifestyle, stress). Tracking the complexity of environmental factors experienced by an individual across their lifetime to identify those that modify health is a significant scientific challenge. However, recent advances in the rapidly evolving field of exposomics offer an exciting opportunity for not only comprehensively cataloging human exposures across the lifespan but also linking them to biological responses that determine health and disease.

In December 2023, investigators representing diverse research fields and expertise convened at the Banbury Center at Cold Spring Harbor Laboratory to develop an updated and unified definition of the exposome. [(1)] The consensus definition reached during this meeting was that the exposome is the integrated compilation of all physical, chemical, biological, and psychosocial influences that impact biology. Exposomics was defined as the field that studies the comprehensive and cumulative effects of the exposome on biological systems by integrating data from a variety of interdisciplinary methodologies and data streams. In contrast to more traditional environmental health or psychosocial research that has largely focused on the effects of a specific environmental factor on a particular outcome at a given point in time, exposomics is explicitly, and, by definition, multifactorial with the goal of enabling discovery-based analysis of environmental influences on health across the lifespan.

Toolbox for Exposomics

While the tools for exposomics are rapidly evolving, many are currently available and 'research-ready.' Examples include high-resolution mass spectrometry for the detection of environmental chemicals and metabolic perturbations, epigenomics to measure environmentally mediated alterations to the genome, and geospatial techniques for mapping the proximity of individuals to exposure sources. Recent studies integrating exposomics with genomics have revealed exciting new discoveries regarding the etiologies of some of the most debilitating human diseases, including cancer, Alzheimer's and Parkinson's diseases, lung disease, and diabetes.

Especially promising is the application of exposomics to understand the root causes of health disparities and adverse health impacts of climate change. Numerous factors are known to contribute to health disparities, including suboptimal nutrition, exposure to chemical pollutants, and psychosocial stress. Climate change also disproportionately impacts disadvantaged communities via extreme heat conditions, vector-borne disease, and insecurity around food and housing. Although some of these environmental influences cannot be quantified using classical biochemical measurements, there are molecular signatures like altered stress pathways and epigenetic modifications that can be readily quantified using currently available exposomic technologies. Thus, exposomics will improve our ability to systematically identify the upstream drivers and molecular transducers of environmental impacts on health to help define strategies for achieving health equity at individual and population levels.

For exposomics to be incorporated into the biomedical enterprise, the field must develop a toolbox that is readily accessible and deployable by those not familiar with the methods. In addition to developing training programs in exposomics, the Banbury Exposomics Consortium outlined five additional focus areas that would propel the field forward: (1) develop advanced biomedical measurement technologies (for blood, tissue, or environmental samples) and strategies for their integration with other omic (e.g., genomics, metabolomics, etc.) technologies and use at the point of care; (2) establish new methods to estimate individual exposures over the life-course that can be applied in research, public health, and clinical applications; (3) create a human exposome reference map enabling analysis at the population scale to support epidemiological research and policy decisions; (4) develop wearable or minimally-invasive tools that measure an individual's exposome and develop strategies for commoditization; and (5) create a framework for the standardization and harmonization of language, protocols, data collection, and data analysis methods, as well as best practices, including quality control and quality assurance, in order to maximize the value of data in a FAIR (findable, accessible, interoperable, and reusable) format.

Ethical, legal, and social aspects (ELSA) of exposomics

It was also recognized by the Banbury Exposomics Consortium that widespread adoption of exposomics requires attention to the ethical, legal, and social aspects (ELSA) of its use, similar to what the field of genomics faced decades ago. There are many questions

that need to be addressed about the value and consequences of exposomics research across many sectors. For example, how does the field preserve privacy while capturing residential, school, and occupational history for geospatial analysis? How do investigators prevent exposome data from being misused? What is the moral imperative if exposomics can unequivocally detect a negative impact related to living in a particular city or part of town? How do we prevent discrimination based on one's exposome profile?

In summary, the Human Genome Project launched in 1990 revolutionized biomedical research, enabling significant conceptual and technical advances in genetics, omics technologies, database infrastructures, etc. Exposomics is poised to build upon the advances made in genomics to provide a more comprehensive understanding of human health and disease. The incentive to invest in exposomics is significant: many of the factors of the exposome, in contrast to the genome, may be modifiable and thus present novel strategies for preventing or curing disease at both the individual and population level.

References

1. "The Banbury Exposomics Consortium. Report from the Integrating Exposomics into the Biomedical Enterprise Banbury Conference," https://www.cshl.edu/banbury/meeting-reports/, 2024.

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