Scientists highlight potential of exposome research

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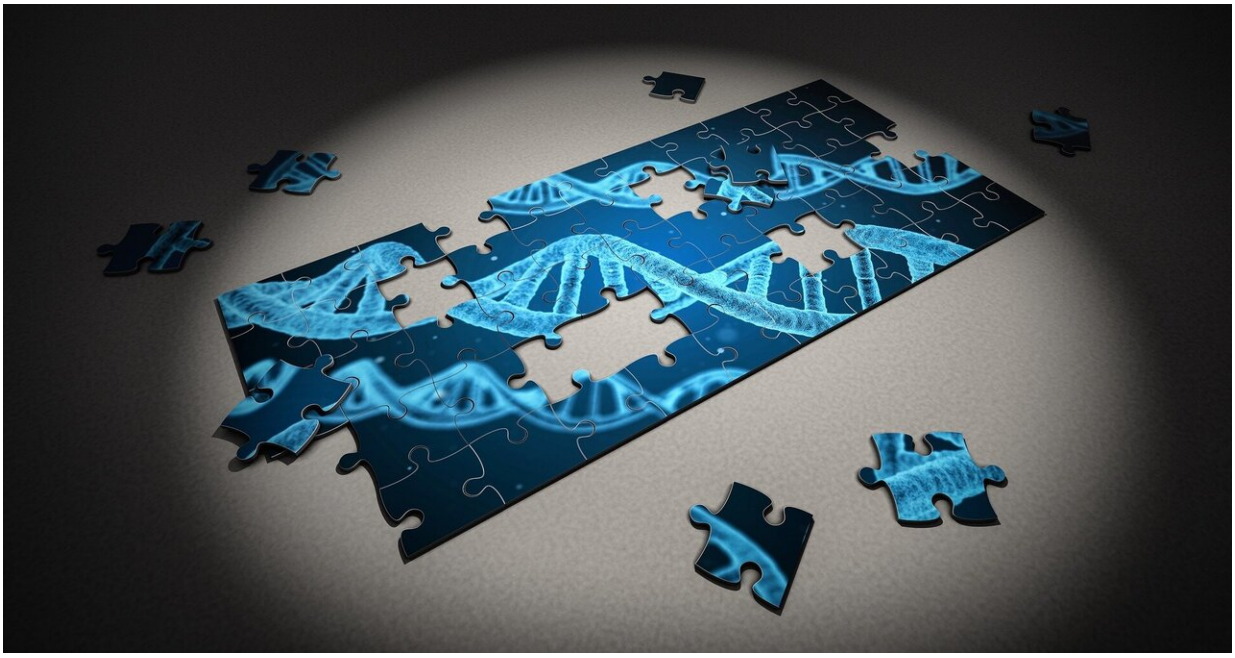

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Over the last two decades, the health sciences have been transformed by genomics, which has provided insights into genetic risk factors for human disease. While powerful, the genomics revolution has also revealed the limits of genetic determinants, which account for only a fraction of total disease risk. A new article in the journal *Science* argues that a similar large-scale effort is needed to ensure a more complete

picture of disease risk by accounting for the exposome, defined as our cumulative exposure to environmental agents such as chemical pollutants.

The article by researchers at Columbia University Mailman School of Public Health; Utrecht University, the Netherlands; University of Luxembourg; and Northeastern University reviews progress in assessing the components of the exposome and its implications on human health.

"Our genes are not our destiny, nor do they provide a complete picture of our risk for disease," says senior author Gary Miller, Ph.D., Vice Dean for Research Strategy and Innovation and professor of environmental health sciences at the Columbia Mailman School. "Our health is also shaped by what we eat and do, our experiences, and where we live and work."

"Less than half of the nongenetic risk burden for disease is accounted for, suggesting the existence of environmental risk factors, exposure to which may largely be preventable," says first author Roel Vermeulen, Professor of Environmental Epidemiology and Exposome Science at Utrecht University. "With growing recognition of the important role nongenetic factors play in disease, we need a coordinated and international effort to characterize the exposome at a scale comparable to that of the human genome."

What Is the Exposome?

The exposome was conceived by the scientist Christopher Wild in 2005 as a way to represent the environmental, nongenetic, drivers of health and disease. These exposures are not restricted to the thousands of chemicals that enter our bodies through the air, water, or food, for example, but also our body's response to our environment, including the built environment and social circumstances, through inflammation,

oxidative stress, infections, and gut flora, for example.

Embracing Complexity

Traditionally, our understanding of the health effects of chemicals has come from epidemiological and toxicological studies that analyze one or a small number of pollutants at a time. "However, our exposures are not a simple sum of a handful of chemicals," the authors write. To capture a fuller picture of environmental exposures, scientists are beginning to employ environment-wide association studies (EWAS), the exposome equivalent of genome-wide association studies (GWAS). Complementing GWAS, EWAS studies take advantage of high-resolution mass spectrometry (HRMS) to measure small molecules originating in the environment, such as air pollution, pesticides, plasticizers, and flame retardants, as well as nutrients and biological metabolites.

"A reductionist approach might isolate the role of a single variable, but it will inadequately capture the complexity of the exposome," the authors write. "The challenge in understanding the role of the exposome on our health lies not only in the large number of chemical exposures in our daily lives, but also in the complex ways that they interact with cells."

Scaling Up

Among the challenges to exposome research are that enrollment in studies of nongenetic environmental exposures remains relatively low. Sample sizes in excess of 100,000 are needed to explain a substantial portion of the genomic heritability of common chronic diseases. The authors posit that similar or even greater sample sizes are required for future environmental studies. A step in that direction, efforts are underway to create a Human Exposome Project representing

environmental and biological exposures for tens of thousands of people, large enough to identify the most prevalent and strongest chemical risk factors, although larger studies are needed to understand the impact of many exposome factors in combination. In addition to sample size, the authors call for improvements in screening technology and data resources to identify associations; network theory to elucidate the constellation of the chemical environment and its biological consequences; and replication in independent studies and the use of methods to establish causation.

Exposome Research for Policy and Personalized Medicine

Large-scale exposome studies will give regulatory bodies new information on those chemicals that have the largest adverse effects on health. "If systematic analysis reveals major adverse effects on human health from exposure to currently approved or potential replacement chemicals, then those compounds should be removed from the marketplace," the authors write. Moreover, data on the effects of classes of chemicals on specific biological pathways known to be perturbed could help in the design of new compounds with minimal impact on human health and the environment. "Current research approaches and regulatory policies fail to address the chemical complexity of our world," the authors write.

In the realm of medicine, more complete information on the impact of nongenetic factors and chemical exposures would also enable the creation of an exposome risk score (ERS) akin to the polygenic risk score (PRS) which could give individuals and their clinicians a better understanding of their likelihood of developing certain diseases.

"Consolidating knowledge garnered from GWAS [genome-wide

association studies] and EWAS [environment-wide association studies]," the authors conclude, "would allow us to map the gene and environment interface, which is where nature meets nurture and chemistry meets biology."

More information: R. Vermeulen at Utrecht University in Utrecht, Netherlands el al., "The exposome and health: Where chemistry meets biology," *Science* (2020). science.sciencemag.org/cgi/doi … 1126/science.aay3164

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