Researchers assert importance of diversity in genomics research

October 10 2019

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Broadening diversity among participants in human genomics research will maximize its potential to discover causes and possible treatments of diseases, requiring thoughtful study design and methodological

considerations, write members of an international genomics consortium in the journal *Cell*.

In the journal's Oct. 10 issue, a working group in the Psychiatric Genomics Consortium examined the scientific and ethical benefits of including underrepresented groups in genomics research and provides guidance on strategy for analyzing such data. The consortium of scientists is dedicated to conducting analyses of genomic-wide genetic data with a focus on psychiatric disorders. "Genome-wide Association Studies in Ancestrally Diverse Populations: Opportunities, Methods, Pitfalls, and Recommendations," whose first author is Virginia Commonwealth University's Roseann Peterson, Ph.D., an assistant professor of psychiatry at the Virginia Institute for Psychiatric and Behavioral Genetics, concludes that despite perceptions that diversity can present challenges when analyzing genetic results, "it is scientifically and ethically imperative, and there is an expanding analytical toolbox to do it well."

Most participants in genome-wide association studies are of European genetic ancestry. That was a practical starting point when the field of genomic research was young, given available data and tools, the authors write, but has given rise to striking disparities in representation.

"We recognize the immense problem of underrepresentation" in human genomic studies, Peterson said of the 31-member author group. "One of the major barriers to conducting cross-ancestry studies is that it appears challenging and few studies have done it. Statistically and methodologically, it requires additional considerations."

The committee reviewed the impact the lack of ancestral diversity can have on genome-wide association studies, which scientists use to search the human genome for common variations that occur more frequently in people with a specific disease than in those without the disease. This

method has been used to identify what are known as genetic polymorphisms, or differences in DNA sequence among individuals, groups or populations, related to psychiatric disorders, diabetes, heart abnormalities and other diseases. Scientists hope to use these association studies to identify risk and protective genetic factors that affect an individual's chance of developing certain diseases and responding to certain medications, and which potentially influence interactions between their inherited genes and the environment.

"Thanks to many collaborative efforts, we have now started to build more diverse genomic resources across the world. However, it is still unclear what is the best analytic strategy when samples of diverse population ancestries are available in a study," said joint senior author Hailiang Huang, Ph.D., of the Stanley Center for Psychiatric Research at Massachusetts Institute of Technology's Broad Institute and Harvard University. "In this paper we outlined key methodological considerations and highlight opportunities, challenges, solutions and areas in need of development, providing a conceptual overview of how to think about and tackle challenging questions in the field."

The authors suggest 11 "best practices" that can help make studying diverse populations more straightforward and accurate. Among the potential issues that can affect the outcome of genomic studies on only or mostly participants of a single ancestry: loss of statistical power that weakens conclusions, gives false positives, or leads to misinterpretation of results.

"Right now, there is a need for guidance about best practices in the analysis of data from global populations, and this primer provides the necessary practical information about how to conduct such analyses," said Laramie E. Duncan, Ph.D., an assistant professor in the Department of Psychiatry and Behavioral Sciences at Stanford University, and joint senior author of the paper.

With genomics moving into health care and genetic testing growing in popularity, individuals who did not descend from European ancestors may receive false positives or ambiguous results. They are also more likely to get false negatives because of the lack of available research data for their genetic background. Genetic risk prediction, according to a previous paper authored by Duncan, is three times more accurate among Americans of European descent than African Americans. This is a direct consequence of the available research data being based largely on European populations.

As clinical researchers develop precision medicine to fight disease, everyone benefits if genetic risk assessments are based on diverse populations, Peterson said. Not doing so could help widen global health disparities.

"If we don't have representation in our genetic studies, we will not be able to identify those that are at risk for these diseases, because we don't have the research data," Peterson said. "If we're only studying Europeans, we're missing out on a lot of genetic diversity which will help us identify causal variants" of diseases and develop medicines to target them.

More information: Peterson et al., Genome-wide Association Studies in Ancestrally Diverse Populations: Opportunities, Methods, Pitfalls, and Recommendations, *Cell* (2019), doi.org/10.1016/j.cell.2019.08.051

Provided by Virginia Commonwealth University