Ethics complicate clinical interpretation and reporting of human genome sequence results

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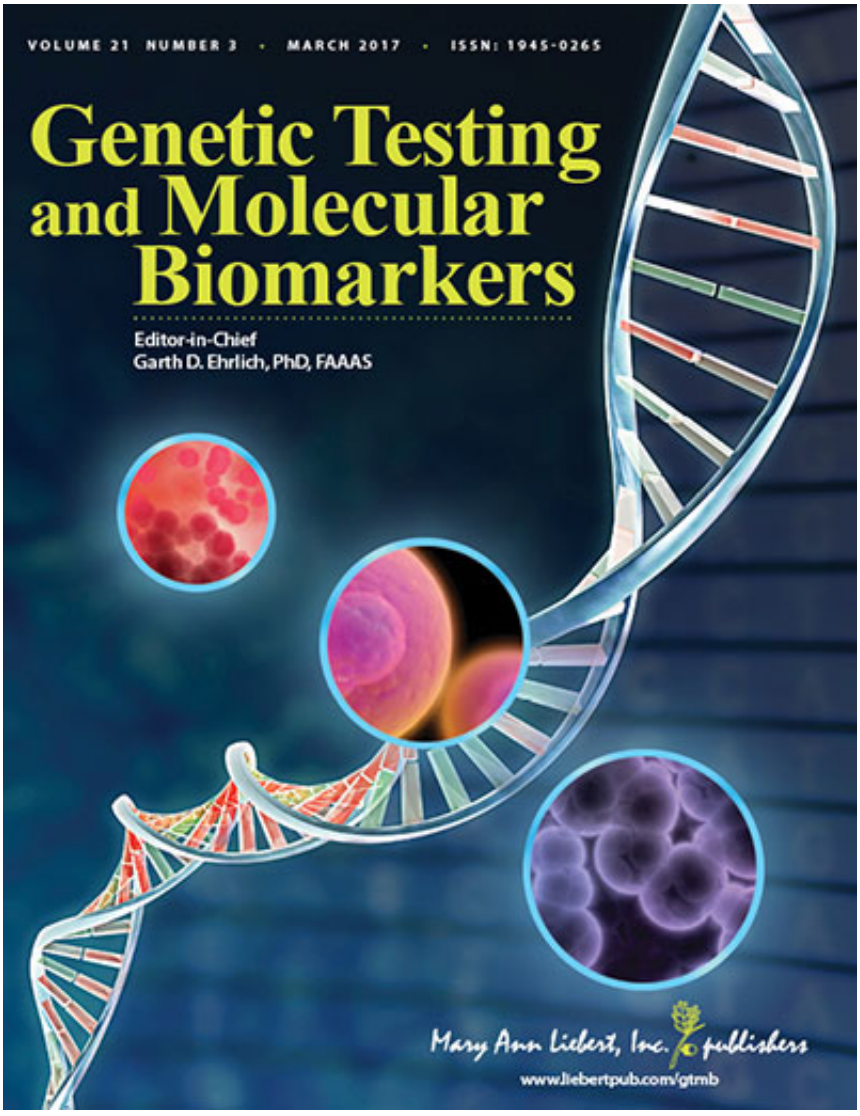

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Medical use of a patient's genomic sequence information can improve diagnostic capabilities and enable personalized therapies, but technical and practical barriers to understanding the clinical implications of sequence data and interpreting them for patients are contributing to ongoing ethical concerns. Current practices in genome sequencing and ethical controversies related to results reporting, including when to inform patients of incidental findings, are discussed in an article published in *Genetic Testing and Molecular Biomarkers*.

Ingrid Holm and Timothy Yu, Boston Children's Hospital, Harvard Medical School, Boston, and Broad Institute of MIT/Harvard, Cambridge, MA, and Steven Joffe, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, describe how human genomic data is collected and interpreted. The researchers provide an insightful perspective on how current scientific and clinical limitations make it difficult even for expert laboratories to determine what is an actual "result" and which results should be reported to patients.

In the article entitled "From Sequence Data to Returnable Results: Ethical Issues in Variant Calling and Interpretation," the authors discuss the potential harm that can be caused by overstating a result or reporting a false-positive finding.

"In the article by Holm and colleagues, the authors address multiple issues that should impact when and if to report incidental findings of potential clinical importance that are uncovered during whole genome sequence (WGS) analyses performed on research study participants," says *Genetic Testing and Molecular Biomarkers* Editor-in-Chief Garth D. Ehrlich, PhD, FAAAS, Center for Genomic Sciences and Center for Advanced Microbial Processing, Institute for Molecular Medicine and Infectious Disease, Drexel College of Medicine (Philadelphia, PA). "The researchers point out that most variants are novel or imperfectly annotated making it difficult for even clinically experienced teams to

determine what results should and should not be returned to the participant. Some of the multiple compounding complexities articulated by the authors that must be considered prior to returning research results to study participants include: the participants indicated preferences; the risk of technical error (false findings); and ascertainment bias of variant risk in predicate studies. They might have also added the lack of knowledge of potential compensating variants elsewhere in the genome."

More information: Ingrid A. Holm et al, From Sequence Data to Returnable Results: Ethical Issues in Variant Calling and Interpretation, *Genetic Testing and Molecular Biomarkers* (2017). DOI: 10.1089/gtmb.2016.0413

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