



GOING PUBLIC WITH PERSONAL GENETICS

BY MARIE BALFOUR

IN THE MODERN DAY, PERSONALIZED GENETIC TESTS ARE INCREASINGLY COMMON.

Imagine walking into your doctor's office and having them pull up your entire biological profile online, tailoring your medical care plan to every molecular piece that makes you unique. This healthcare strategy is the future envisioned by the precision medicine (PM) movement, and it could potentially become the standard for patient care in a few years. As PM becomes more common, it has the ability to dramatically impact the healthcare industry through specialized healthcare solutions molded directly onto a patient's genome. Even though this approach represents the medical technology of the future, efforts should be made to understand and regulate disease dynamics models, adverse effects of testing results, and genetic discrimination that can arise from PM testing.

PM is part of the rise of the "personalized omics" or "multi-omics" movement in which multiple, comprehensive molecular testing mechanisms are used to assess individual profiles of biological molecules

such as RNA, peptides, fatty acids, carbohydrates, and gut microbiota. In 2015, the movement gained momentum through the implementation of the Precision Medicine Initiative by President Obama during his State of the Union address.¹ This approach seeks to integrate multiple lines of molecular data in order to get a wider view of the kinds of interactions which produce and maintain a disease in someone's body.² According to the National Institutes of Health, PM will take into account "individual variability in genes, environment, and lifestyle."³ One sub-section of this movement, genomics, has recently risen to popularity and is often used alone, without a full set of multi-omics data, to detect risk factors for certain diseases. Unfortunately, while genomic tests can help people understand their unique disease risk factors and plan for their future, they also open the door for genetic discrimination, oversimplification of the causes of disease, and unanticipated psychological distress. As this technology

begins to emerge at the forefront of medical advancement, it is important to understand and address the aforementioned challenges in order to properly assimilate precision medicine into modern healthcare.

Personalized genomics tests can help people understand their personal health profile, and this is one of the main reasons why personal genetic tests have been on the rise since their commercial inception in the 1990s and early 2000s through companies such as 23andMe, MyHeritage, and HomeDNA.^{4,5,6} In a recent study, one-third of participants surveyed on their reasons for undergoing genetic testing indicated that they were interested in having their genomes tested because of a known family history of disease. An additional quarter of participants sought to have their genomes tested in order to prepare for their healthcare future, even if they could not treat or prevent their genetic disease.⁷ These results suggest that the personalized genetics movement draws much of

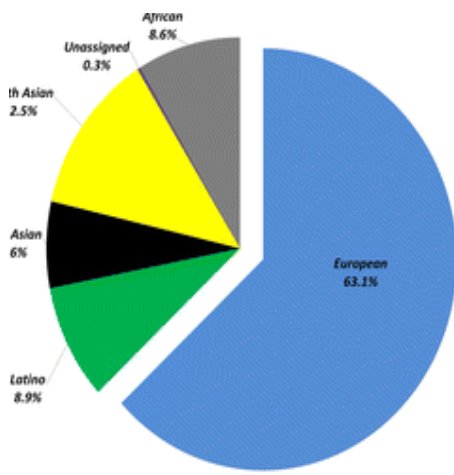


Figure 1. Percentage representation of ancestry/ethnic groups across 66,217 individuals tested by the Institute for Genomic Medicine and the Exome Aggregation Consortium in 2016.¹⁹

“In a recent study, one third of participants surveyed on their reasons for undergoing genetic testing indicated that they were interested in having their genomes tested because of a known family history of disease.”

its support from people who are genuinely curious about how their genetics can influence their lifestyle and healthcare plan.

As genetic testing increases in popularity, there has been a recent global effort to end discrimination based on genetic testing results, but legal action may not catch all of these genome-based injustices. The United Kingdom has already codified protections to prevent insurance premium increases for people who may receive unfavorable genetic testing results, but other countries, such as Canada, have struggled to pass bills that would protect those who participate in personalized molecular tests from discrimination.⁸ In 2009, the United States passed the Genetic Information Nondiscrimination Act (GINA) in order to

ensure legal protection against workplace discrimination based on genetics testing results. However, since GINA’s implementation, at least one study has actually shown an increase in reports of genetic discrimination in the workplace.⁹ Because of this, some researchers argue that the act cannot address newly adopted testing technologies and the U.S. should add additional clauses to prevent further discrimination.¹⁰

Additionally, although personalized genetic tests are becoming increasingly common, the scientific community has not yet established a definitive causal relationship between genetic mutations and disease. Currently, there is not a plausible genetic interaction model for human disease based on personalized data that also

incorporates environmental and social factors such as diet, exercise, and socioeconomic status.¹¹ The multi-omics and PM perspective seeks to improve this outlook by gathering additional molecular data that provides a clearer picture of multiple markers for certain diseases. For example, microbiomics data analyzes human gut microbiomes, which strongly mirror diet patterns, an environmental factor. Results from the Integrated Personal Omics Profiling (iPOP) study, a longitudinal study assessing extensive biochemical profiling data, have suggested links between omics data and disease outcomes. Although iPOP results from microbiome, metabolome, and genome analysis have indicated a possible genetic association with disease indicators such as inflammatory response and mitochondrial dysfunction, more data must be collected in order to confirm these connections and integrate them into a conceivable disease model.^{12,13} Furthermore, there are still limitations to this method because not all environmental and social factors have known molecular markers that can be traced with multi-omics technologies.

Another complication to this testing approach is that the PM movement has the potential to misrepresent certain groups. According to recent analysis, patients of European ancestry are disproportionately represented in genetics testing, which makes it harder for scientists to analyze diseases in other populations.¹⁴ From these results, the precision medicine movement may have a Eurocentric bias that requires more testing from outside populations in order to paint a more accurate picture of many different types of human disease across the globe. Additionally, such mo-



Figure 2. President Barack Obama shakes hands with the Director of the National Institutes of Health, Dr. Francis Collins, after his remarks on the Precision Medicine Initiative on January 30, 2015.²⁰

Table 2 Motivations and concerns: themes emerging from the qualitative interviews

Themes
<i>Motivations</i>
1. To learn personal disease risk or health-related information (30) To avoid or reduce their risk of disease (23) Via lifestyle, diet and/or exercise (10) Via medical intervention (4)
Prepare or plan for the future (9) Emotionally prepare (2) Financially plan (3)
Stored personal information could be of potential value to them in the future (4) For medication prescribing purposes (ie, pharmacogenomics) (3) For diagnostic purposes (1) As the science advances (4)
Because of a known family history of disease (12) Because of a known or suspected personal history of disease (5) Because of a lack of information about family history (3)
2. Curiosity (23) General curiosity (14) Interested in or curious about the science (11) The field of genetics/genomics (8) Science (2) Research (1) Curiosity about their genes (7)
3. To contribute to research (15) Altruistic desire to help others and the field of medicine (3) To contribute to the advancement of science (5)
4. Interested in their ancestry (13)
5. To provide disease risk information for their children and other family members (11) For their existing children (7) For their family members generally (3) For their future potential children and family planning (3)
6. Self-exploration (7)
7. Novel opportunity (3)
8. Useful professionally (1)

Figure 3. Motivations for genetic testing revealed by qualitative interviews from a 2016 study by Sanderson et al.²¹

“The process of acquiring informed consent from patients for these kinds of tests is complicated, because most patients may be truly unaware of what they are consenting to until they receive their results.”



lecular tests will most likely end up categorizing patients into set subgroups that match their molecular profiles instead of developing specific individualized medicines, which could have a stratifying effect on the healthcare industry that focuses more on the differences between genetic groups instead of the similarities that bind everyone together in the medical setting.¹⁵

Because genetic tests are just starting to become more user-friendly and commercially available, the “personalized omics” movement may not currently have the existing infrastructure to educate and support people who receive potentially distressing test results. Currently, personal genetics testing companies have protected themselves from liability for any discrimination or distress their results can cause, even

though reports indicate that many people who receive their testing results experience anxiety and psychological distress. Some researchers have even called for personalized genetics companies to provide genetic counseling services, in addition to their analysis software, to explain testing results to clients.¹⁶ The process of acquiring informed consent from patients for these kinds of tests is complicated, because most patients may be truly unaware of what they are consenting to until they receive their results.¹⁷ Even after patients have received their results, some may not be able to afford the medical therapies available for their personal disease profile.¹⁵ As these tests become increasingly popular and develop a larger pool of client data, there is also a concern for patient privacy. Although molecular testing companies promise total patient privacy and responsible data-sharing practices, unintended security breaches could have lasting consequences.¹⁸

In many ways, the scientific community has missed the opportunity to preemptively regulate the PM movement, and it is quite possible that some or all of its tenets will become commonplace in the next generation. PM technology provides a streamlined way for lots of people to receive their biological information at steadily decreasing costs, making this movement increasingly popular. However, although PM shows great promise, care should be taken to properly address disease dynamics, adverse effects of testing results, and genetic discrimination as the movement progresses.

REFERENCES

1. The Precision Medicine Initiative. Retrieved from <https://obamawhitehouse.archives.gov/node/333101>.
2. Ashley, E. A. (2016). Towards Precision Medicine. *Nature Reviews Genetics*, 17, pp. 507-522.
3. 23andMe. (2018). Retrieved from <https://www.crunchbase.com/organization/23andme#section-overview>.
4. MyHeritage. (2018). Retrieved from <https://www.crunchbase.com/organization/myheritage#section-overview>.
5. About HomeDNA. (2018). Retrieved from <https://homedna.com/about>.
6. What is precision medicine? (2018, April 3). Retrieved from <https://ghr.nlm.nih.gov/primer/precisionmedicine/definition>.
7. Sanderson, S. C., Linderman, M. D., Suckiel, S. A., Diaz, G. A., Zinberg, R. E., Ferryman, K., . . . Schadt, E. E. (2015). Erratum: Motivations,

- concerns and preferences of personal genome sequencing research participants: Baseline findings from the HealthSeq project. *European Journal of Human Genetics*, 24(1), 153-153. doi:10.1038/ejhg.2015.179
8. Nicholls, S. G., & Fafard, P. (2016). Genetic discrimination legislation in Canada: moving from rhetoric to real debate. *Canadian Medical Association Journal*, 188(11), 788-789. doi:10.1503/cmaj.151170
 9. Contreras, J.L. (2016). Genetic Property. *The Georgetown Law Journal*, 105(1).
 10. Ajunwa, I. (2016). Genetic Data and Civil Rights. *SSRN Electronic Journal*, 75-114. doi:10.2139/ssrn.2460897
 11. Moore, J. H., & Williams, S. M. (2009). Epistasis and Its Implications for Personal Genetics. *The American Journal of Human Genetics*, 85(3), 309-320. doi:10.1016/j.ajhg.2009.08.006
 12. Contrepois, K., Coudreau, C., Benayoun, B. A., Schuler, N., Roux, P. F., Bischof, O., ... Mann, C. (2017). Histone variant H2A.J accumulates in senescent cells and promotes inflammatory gene expression. *Nat. Commun*, 8(14995).
 13. Chennamsetty, I., Coronado, M., Contrepois, K., Keller, M. P., Carcamo-Orive, I., Sandin, J., ... Knowles, J. W. (2016). Nat1 Deficiency Is Associated with Mitochondrial Dysfunction and Exercise Intolerance in Mice. *Cell Reports*, 17(4), pp. 527-540.
 14. Petrovski, S., & Goldstein, D. B. (2016). Unequal representation of genetic variation across ancestry groups creates healthcare inequality in the application of precision medicine. *Genome Biology*, 17(1). doi:10.1186/s13059-016-1016-y
 15. Juengst, E., McGowan, M. L., Fishman, J. R., & Settersten, R. A. (2016). From "Personalized" to "Precision" Medicine: The Ethical and Social Implications of Rhetorical Reform in Genomic Medicine. *Hastings Center Report*, 46(5), 21-33. doi:10.1002/hast.614
 16. Middleton, A., Mendes, Á, Benjamin, C. M., & Howard, H. C. (2017). Direct-to-consumer genetic testing: where and how does genetic counseling fit? *Personalized Medicine*, 14(3), 249-257. doi:10.2217/pme-2017-0001
 17. Tomlinson, A. N., MA, LSW, Skinner, D., PhD, Perry, D. L., MS, CGC, Scollon, S. R., MS, CGC, Roche, M. L., MS, CGC, & Bernhardt, B. A., MS, CGC. (2016). "Not tied up neatly with a bow": Professionals' Challenging Cases in Informed Consent for Genomic Sequencing. *Journal of Genetic Counseling*, 21(1), 62-72. doi:10.1007/s10897-015-9842-8
 18. Adams, S. A., & Petersen, C. (2016). Precision medicine: opportunities, possibilities, and challenges for patients and providers. *Journal of the American Medical Informatics Association*, 23(4), 787-790. doi:10.1093/jamia/ocv215.
 19. Petrovski, S., & Goldstein, D. B. (2016). Unequal representation of genetic variation across ancestry groups creates healthcare inequality in the application of precision medicine. *Genome biology*, 17(1), 157.
 20. Souza, P. (2015, October 19). Multimedia: NIH framework points the way forward for building national, large-scale research cohort. Retrieved from <https://www.nih.gov/news-events/multimedia-nih-framework-points-way-forward-building-national-large-scale-research-cohort>.
 21. Sanderson, S. C., Linderman, M. D., Suckiel, S. A., Diaz, G. A., Zinberg, R. E., Ferryman, K., ... & Schadt, E. E. (2016). Motivations, concerns and preferences of personal genome sequencing research participants: baseline findings from the HealthSeq project. *European Journal of Human Genetics*, 24(1), 14.

IMAGE REFERENCES

1. Jarmoluk. (2017, October). [Scientist holding test tubes.]. Retrieved April 8, 2018, from <https://pixabay.com/en/laboratory-analysis-diagnostics-2815631/>
2. Souza, P. (2015, January 30). Precision Medicine Initiative [Digital image]. Retrieved April 17, 2018, from <https://www.nih.gov/news-events/multimedia-nih-framework-points-way-forward-building-national-large-scale-research-cohort>
3. Sanderson, S. C., Linderman, M. D., Suckiel, S. A., Diaz, G. A., Zinberg, R. E., Ferryman, K., ... & Schadt, E. E. (2016). Motivations, concerns and preferences of personal genome sequencing research participants: baseline findings from the HealthSeq project. *European Journal of Human Genetics*, 24(1), 14. Reprinted with permission.
4. Petrovski, S., & Goldstein, D. B. (2016). Unequal representation of genetic variation across ancestry groups creates healthcare inequality in the application of precision medicine. *Genome biology*, 17(1), 157. Reprinted with permission.