Genetics for your whole life

The multiple standardized clinical measurements that make up one's lifetime path through health and disease are essential information for yourself and your healthcare system. Aggregated into a population cohort study across a single-payer network, these data become an extraordinary tool for improving the efficiency of healthcare delivery and new discoveries in genomic medicine.

Elevated blood lipids both cause cardiovascular disease and act as markers warning of its onset via atherosclerosis. A single LDL cholesterol measurement from an annual physical checkup is usually stated relative to the reference threshold, where intervention is justified according to current clinical guidelines. However, this single point in the history of your serum is part of your individual trajectory from health to disease. It is not the point measurement that you need to intercept via diet, exercise or cholesterol-lowering drugs, but the trajectory. Now, for the first time, Thomas Hoffmann and colleagues (https://doi.org/10.1038/s41588-018-0064-5) have been able to predict time to treatment with lipid-lowering statins on the basis of the genetic risk score of the LDL cholesterol measurement alone. The study was possible because of multiple consecutive measurements within the electronic medical records of a longitudinal cohort from a single standardized healthcare system. Encouragingly, 78% of the study's participants consented for their genotype and lipid measurements to be made anonymously available via the database of Genotypes and Phenotypes (dbGaP) repository, and the rest of the study can be accessed by contacting the authors in accordance with their data access statement.

This month's Perspective by Cisca Wijmenga and Alexandra Zhernakova (https://doi.org/10.1038/s41588-018-0066-3) emphasizes the importance—to the evolution of genomics research—of lifetime cohort studies with multiple measurements prior to the onset of disease. The ideal is to have everyone recruited at birth so that all of the effects and environmental interactions of the preexisting genotype can be taken into account. These authors suggest that determining the tissue-specific effects of noncoding genetic variation will require subsets of research participants nested within the larger study to provide cells, microbiota and metabolic measurements not usually obtained in clinical practice. On one hand, most tissues are impossible to biopsy in large numbers of healthy individuals, and it is currently expensive to generate banks of hundreds of cell types from large numbers of individuals. But this vision is not unrealistic in future regenerative medical practice as procedures based on pluripotent stem cells become more commonly used. Even current practice might provide many of the necessary tissues and measurements if research standards were to be properly coordinated across a health network. For example, umbilical cord blood could be sampled in a birth cohort. Adipose tissue and adult stem cells can be retrieved via cosmetic and reconstructive procedures, as can single cells and circulating DNA from donor and patient blood samples.

The Perspective emphasizes the importance of genetic nondiscrimination to the future of cohort research, and we note that this needs to occur systemically via legislation within society as a whole, by the healthcare system and its payers, and within the study. Participants need to control their own information from the outset and to own the study for their own understanding and use, as well as to help shape the objectives of future research with their own choices. We believe that demonstration of the utility of genome variation will be increasingly important as inducement for millions more healthy people to volunteer their medical information in lifetime cohort research. At the population scale required to make new medical discoveries, these studies must be sustained by providing individuals with useful feedback, and they must continually provide information that improves the healthcare system. ❐

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