APPLICATIONS

Personal Genome Analysis

As sequencing costs drop, it has become feasible to analyze large portions of a human genome relatively quickly and comparatively inexpensively. This has most often been performed in either a research setting to better understand the functional impact of genetic variation or in the clinic to identify the molecular cause of a suspected genetic disease. However, there is a growing market for providing genomic information to what are sometimes termed "ostensibly healthy participants" — individuals without visible disease or health complications but who want to know their genomic information and understand how it informs their ancestry, personal traits and potential future risks for developing certain diseases.

An initial step towards personal genome analysis has been direct to consumer genotyping – a targeted analysis of between 500,000 and 1,000,000 variable regions from across the genome. A small but increasing proportion of these variants is connected to ancestry, physical traits or disease risk, although the predictive value of medical decisions of these risks is often unclear. The FDA ordered the health-related versions of these tests halted in 2013, although it has recently allowed a limited number of direct to consumer genetic tests back onto the market. Consumer genotyping is also available for individual genes such as the *ACTN3* genetic variant involved in muscle strength and spring ability. These genetic differences are poor predictors of athletic skill as well as musical or artistic talent and overall intelligence, as most of the genetic and environmental influences on these traits are still unknown.

Today, predispositional (or presymptomatic) genomic screening — PPGS — analyzing the exome or entire genome of an ostensibly healthy individual — is controversial. There is little data about the response of people who have received genomic information about their trait and disease risk factors. At the same time, there is a powerful and growing recognition among personal genomic stakeholders that such information may provide a positive benefit on an individual's life and actions, even if the direct health benefit is uncertain or marginal. A number of research projects have been initiated to inform our understanding of these impacts, collectively involving more than 1,000 individuals. Common motivations for participating in PPGS initiatives include the desire to learn health-related information, a sense of general curiosity about personal genomic information and the desire to contribute to research that may benefit others. In keeping with the early adopter status of these studies, current participants tend to be highly educated, technically savvy and from a high socio-economic status. There have been few published studies of the impact of PPGS on the participants and the short and long-term benefits and concerns are primarily speculative. A long-term analysis of this sort of information is being conducted by the PeopleSeq Consortium, a collaboration between multiple PPGS projects using a common set of questions and techniques.

Personal genome studies offered direct-to-consumer should be a component of students' efforts to obtain, evaluate and communicate information about advancements in genetic technology. This provides fertile ground for a discussion of the implications of genetic information. (Biology COS standard 3) These topics can also be incorporated into an AP Biology course in Big Idea 3: Information. Personal Genome Analysis provides modern content and context for students in Health (COS objective 6) and the Career/Tech course Foundation of Health Sciences (COS objective 10) and Health Informatics (COS objective 5) outlining valid and essential information for the safe use of consumer goods and health products.

Determining the significance of a particular variant identified through genome sequencing is still in its infancy. Classifying a variant as benign or pathogenic requires multiple lines of supporting evidence, curated by a team of researchers and clinicians. For many variants, such supporting evidence either doesn't exist, or is contradictory, resulting in a classification of "variant of uncertain significance (VUS)." Currently in pilot testing, HudsonAlpha has developed a card-based kit that brings the process of variant analysis to high school classrooms. Making Sense of Uncertainty provides opportunities for students to classify variants and argue from evidence to justify their classification. A pilot version of this kit was available to Alabama high school life science educators who attend the two-day GREAT workshops scheduled across the state during the 2016-17 school year.