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If You Don't Know Where You Are Going, You Might Wind Up Someplace Else: Incidental Findings in Recreational Personal Genomics

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Clayton and colleagues (2014) discuss important issues with regard to incidental findings in genomic screens of children. But while the authors seem to limit their analysis to findings that arise as a result of a medically proscribed screen, many children as they grow will likely be exposed to genetic screens outside of a medical establishment and/or the oversight of a physician. For example, as a result of a "recreational," analysis, such as those to discover nonmedical genomic predispositions, promised to consumers by the growing personal genomics industry.

These analyses run the gamut from ancestry to the ability to perceive bitter tastes to earwax type. Thus, in addition to the use of genomics within the predictive, prophylactic, and/or diagnostic contexts, there is a growing group of actionable, albeit arguably nonmedical, uses of genomic data. One such area where there may be significant growing consumer interest is in the area of genetics as it relates to sports and athletics.

There are a number of genes thought to indicate a genetic predisposition to certain athletically desirable skill sets. One of these genes is the ACTN-3 gene, which provides the genetic code for skeletal muscle α-actins that are expressed in fast-twitch muscle fibers. Numerous research studies seem to suggest that certain ACTN-3 alleles (e.g., R577X, which includes a premature stop codon

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polymorphism) influence athletic ability and performance (Yang, Garton, and North 2009).

However, actionable information in the area of athletics is not necessarily associated only with athletic achievement. Perhaps more informative and useful, particularly to aspiring, college-level, and/or professional athletes, are those genetic associations that indicate propensity to injury or those sequences that can provide crucial information regarding the nature of postinjury recovery. These include, for example, genotypes related to bone frailty, likelihood of injuring or tearing ligaments, chances of dying on the field from a sudden cardiac arrest, or the nature of recovery from concussions.

With actionable genomic information, college and professional teams are likely to promote the sequencing of their athletes such that they can design and personalize practice, nutrition, game play, and postinjury recovery to each particular athlete's genetically determinable potential and limitations.

The complicated interplay of genetics that seeds both the homogeneity and heterogeneity of the human race may also result in many of the athletic-related genes having potential medical implications as well. And without anything near a complete picture of what genes may be specifically relevant to athletes, genomic testing companies may include not necessarily athletic-related genetic sequences in their screens. As a result, athletic and other recreational-type sequencing efforts may include genes that have medically important functions and/or numerous potentially heretofore undiscovered medically related functions. And in some instances, teams may use off-the-shelf technology that just also happens to return medically relevant results.

Dealing with these anticipated and unanticipated secondary and incidental findings is nontrivial. And a confluence of events has made the issue of incidental genomic findings a very timely topic, and may also change the way we ought to respond to these issues.

In a letter dated November 22, 2013, the Food and Drug Administration (FDA) sent what seems to be an exasperated warning letter to 23andMe (FDA 2013). The surviving member of the first three big companies to offer direct to the consumer personal genomic analysis (both Navigenics, founded in 2008 and Icelandic deCode Genetics were bought by Life Technologies and Amgen in 2012, respectively), 23andMe, the famously Google-backed personal genomics company, has, by ignoring the FDA on the issues of direct-to-consumer (DTC) genomics, perhaps committed the "single dumbest regulatory strategy" in at least one reporter's extensive experience in the field (Herper 2013).

The FDA, which claims that it hasn't heard anything from 23andMe in months, effectively forced the shutdown of much of its testing services, particularly those aimed at disease-related genes and all the related marketing. 23andMe's national campaign to garner 1 million data subjects seems to now be on hold until the FDA can be satisfied with 23andMe's clinical, research, and business practices.

The FDA views the tests and related technologies run by 23andMe and similar organizations as medical in nature: "within the meaning of section 201(h) of the FD&C Act, 21 U.S.C. 321(h), because it is intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or is intended to affect the structure or function of the body" (FDA 2013).

While the Food and Drug Association may consider recreational personal genomics a misnomer, hundreds of thousands of consumers continue to submit genetic samples for ostensibly nonmedical genomic analysis.

This growing consumer interest in DTC genomics is likely partially responsible for the recent December 12, 2013, report by the Presidential Commission for the Study of Bioethical Issues. The report included the commission's ethical analysis based on standard principles of freedom of information, autonomy, access and fairness, and a set of overarching broad recommendations for clinicians, researchers, and even direct-to-consumer testing companies regarding managing the increasingly common issue of incidental and secondary findings in medical and genomic testing.

Summarizing some of the concerns, the report, which really didn't get down into the particulars of this complicated issue, notes:

> Incidental findings—traditionally defined as results that arise that are outside the original purpose for which the test or procedure was conducted—can create a range of practical, legal, and ethical challenges for recipients and practitioners. Discovering an incidental finding can be lifesaving, but it also can lead to uncertainty and distress without any corresponding improvement in health or wellbeing. For incidental findings of unknown significance, conducting additional follow-up tests or procedures can be risky and costly. Moreover, there is tremendous variation among potential recipients about whether, when, and how they would choose to have incidental findings disclosed. Information that one recipient regards as an unnecessary cause of anxiety could lead another recipient to feel empowered in making health-related decisions. (Presidential Commission 2013, 2)

By categorizing 23andMe's and other DTC types of testing as medical tests within the purview of the FDA, the FDA is effectively creating a more stringent moral duty for DTC genetic testing companies, that is, one arising out of the medical nature of the tests. This duty takes the customer's relationship with the company beyond the corporate and contract worlds and into a potentially more ethically onerous medical context. And the principle of regulatory parsimony that suggests limiting regulatory oversight to only that which is truly necessary to ensure responsible business practices may require more oversight when the business practices are perceived as more medical than recreational.

Moreover, as the cost of sequencing plummets, DTC genomics companies are unlikely to center their business models on the increasing volume of cheap tests, but, like innovative genetic companies before them, they are likely to switch, if they haven't already, to that of a data-heavy information provider and analysis model where the collected

genomes can be mined for increasingly relevant genetic data that can be sold to (hopefully only) the biopharmaceutical sector for drug and diagnostic development.

In this capacity, many DTC genomics companies will likely be tripping over medically actionable genomic information that they are compiling and packaging to sell. However, the level and degree of informed consent suggested by the recent Bioethics Commission report and the legal duties potentially created by the a medical standard of care may serve to inhibit the collection of potentially important genomic data both from the spooked consumer who would be presented with an unexpectedly weighty informed consent process and from the risk-averse corporations who might not be comfortable with an increased level of duty to their customers.

These same DTC genomics companies will be providing information to the aforementioned athletes that will in all likelihood include the aforementioned medically actionable genomic information.

Many of the suggestions that are proposed by the Presidential Commission's report may not be suitable for that particular situation. The level of informed consent outside of the medical context, while possible, does not carry the necessary weight to provide the full meaning to that information, lessening the nature of the consent. In the alternative, the required informed consent may disincentivize participation, which not only hinders the collection of valuable information but could lead to otherwise avoidable harm to the athletes. Further, the multitiered click-wrap-like consent suggested by the report may be as meaningless to the athletes as the similarly phrased licenses and terms of service that they clicked through to update their privacy settings on their favorite social media site.

And, unlike many instances of DTC genomics, the consumers themselves may not be the parties communicating directly with the genomics companies that are trained and prepared to provide incidental findings. Rather, in these instances, the third-party providers of the testing service, such as the coaches or team managers, may be ill prepared to communicate or deal with incidental findings and, unlike medical providers, may not anticipate even the anticipatable and, to many in the medical field, obviously inevitable incidental findings when planning and ordering up the tests for their teams.

Irrespective of the complicated legal tangential issues such as whether or not the FDA has a right to limit access to information provided by DTC genomic companies (*Thompson v. Western States Medical Center* 2002), or whether or not the FDA has the ability to exert control over what people do with medical devices once they enter the marketplace, or whether the growth of smart-phone applications that act as medical devices will change the way the FDA chooses to regulate nonconventional medical devices aimed at the consumer (U.S. Department of Health and Human Services, Food and Drug Administration 2013), there are no easy answers for teams looking to help their athletes train and play better based on their genomics. It is clear, however, that the decision to pursue genetic testing for the team is not one that should be taken lightly and it might need to be done in conjunction with medical specialists, genomic counselors, institutional review boards, and other qualified individuals that may need to present some very heady information to some ill-prepared kids and their families. ■

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