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Direct-to-Consumer Genetic Testing: Failure Is Not an Option

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Abstract

Direct-to-consumer genetic testing is an unavoidable consequence of our ability to cheaply and accurately measure the genome. Some are troubled by the loss of control over how and when this information is disclosed to individuals, but it is difficult to imagine any way to prevent the wide availability of these data. Therefore, the key challenge is to set up social, educational, and technical means to support individuals who have access to their genome.

The progress in genetic sequencing and genotyping technologies in the past two decades has been breathtaking. DNA sequencing in the early 1980s was a cumbersome, low-throughput process requiring considerable skill. The recognition that polymorphisms in DNA lead to differences in how restriction enzymes cut it provided an easy way to genotype a basic set of DNA markers.¹ Current DNA-sequencing machines are producing gigabases of DNA sequence, with one company recently announcing its intention to provide a \$5,000 genome (3 billion bases) within a year.² Genotyping 1 million single-nucleotide polymorphisms now costs a few hundred dollars. The trends are clear: the cost of DNA sequence and genotype data is asymptotically approaching...free.

What are the consequences of this precipitous drop in the cost of containing genetic information? First, in the long run, no company is likely to be able to distinguish itself on the basis of DNA sequencing or genotyping capabilities. There are many competing and effective technologies, and DNA sequencing is rapidly becoming a commodity; many vendors can supply it with relatively indistinguishable quality. One could argue that DNA-sequencing companies have a challenge: what is their business plan once all human genomes have been sequenced? There may not be many repeat customers. Second, given the universal availability of DNA information, the ongoing opportunity will be for interpretation of this information. Our ability to measure DNA has far outpaced our ability to provide rational interpretation, and the next few decades will very likely provide increasing ability to understand these measurements. The business plan for companies that interpret the genome is clear: provide easy access and interpretation of genomic information, in order to help individuals learn about their heritage, traits, and health risks.

What does this have to do with direct-to-consumer (DTC) genetic testing? Such testing has arisen precisely because genotyping is sufficiently inexpensive and straightforward that it is easy for a company to set up shop. The cat is out of the bag: genotyping is already a commodity, and full-genome sequencing is well on the way. The technologies can be acquired for modest capital and can be mastered by technicians with reasonable skill and

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CONFLICT OF INTEREST

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care. Thus, consumers can order information about their DNA directly via the Internet; barring major interventions from the government to restrict commerce in this area, they do not need to gain this information through health care–related gatekeepers.

Why do patients pay for this information? The value of DTC testing is clear: avoidance of involving health-care professionals means that there may be better guarantees of privacy, at least with respect to insurance and employers. The consumer feels more in control of what information is generated and who has it. They can provide DNA samples anonymously in pursuit of information about ancestry, paternity, traits, and disease risk. In addition, the consumer can control what questions are asked; for example, they may want to test genetics for ancestry but have no interest in health risks. With their genome on their personal computer, they can then refer to it whenever they have a genetics-related question.

We can expect attempts by the federal or state governments to control this phenomenon (New York, California, and other states have already made attempts³) as they grapple with the challenges of a changing reality, but the only eventual stable situation is the recognition that any motivated individual will have relatively inexpensive access to their genetic information. The benefits of this reality could be substantial, because genetic information will increasingly provide knowledge about ancestry, physical traits, risk for serious diseases, and likely drug-response phenotypes, among other aspects. Knowledge from genetics may allow individuals to make lifestyle and environmental choices that prolong the quality and length of their lives. Some also believe that genetics will become the basis for emerging social networks (“Hi, we share a similar Y chromosome; maybe we should be friends?”). The risks of this reality could also be substantial: insurance and/or employment discrimination, troubling manipulation of embryos in the quest for the perfect offspring, social marginalization based on genetic traits, dangerously simplified views of genetic determinism, and even panic at discovering complex genetic traits without immediate access to information resources and counselors to help interpret the information. How can we manage these risks and reap the potential rewards? This is not primarily a technical problem but a social one.

It is absolutely critical that we use social mechanisms (such as laws and regulations) to protect individuals from discrimination based on their genetics. The recently passed Genetic Information Nondiscrimination Act (GINA⁴) is an important step in preventing employers and insurance companies from using genetic information unfairly to discriminate against employees and customers. The definition of “unfair” in this context is difficult, because the insurance industry is based on the principle of shared risk and statistical chance. Is it fair to allow a customer who knows he or she has an increased risk for an “expensive” disease to purchase inexpensive insurance, while not allowing the insurance company to know about this risk? Society must make these decisions.

If DNA information becomes ubiquitously available, we must also use social mechanisms to consider how to protect privacy and confidentiality. There have been an increasing number of examples of allegedly “de-identified” data sets being reidentified by combining multiple disparate databases.⁵ If one database has genetic information and disease information, another one allows disease information to be linked to clinic visits, and a third database allows clinic visits to be linked to individual patients, then we have a network of databases that may allow for routine association of individuals to their DNA sequences. Social mechanisms must be put into place that basically say “You are technically able to do this, but you are not allowed to do it; if you do, you will be subjected to significant civil, even criminal, penalties.”

It is important that any business that purports to measure genetics be regulated with respect to the quality of its genotype or sequencing product, and performance metrics should be provided along with regular reports of quality control to regulatory agencies. There has recently been alarm about fraudulent DTC companies that either did not perform any test or did testing of terrible quality. Thousands of biologists worldwide know the principles by which a genotype or sequencing product should be validated both initially and in ongoing tests. The reputation of the entire industry will rely on effective regulation to protect consumers.

We must separate the activities of companies that measure DNA from those that interpret it. Currently, these activities are often bundled together, but they are fundamentally different and should be considered separately. The measurement of DNA is becoming inexpensive and accurate and can be checked for quality control, whereas the task of interpreting DNA measurements is still expensive and difficult. Even though many companies are participating in both activities, we must keep them separate as we think about the proper methods for regulation and oversight.

The task of interpreting DNA measurements will, for the foreseeable future, be imprecise and in large part subjective. The typical uses of DNA measurements are currently for determination of ancestry, fetal gender, paternity and other relatedness measures, medical/health-related risk assessment, and frivolous or vanity genetics (measuring traits that generally have little obvious significance). All these activities can be based on science but still admit of substantial variability in interpretation—particularly to lay audiences who cannot easily understand the technical limitations of most genetic studies. Because the interpretation of DNA measurements is imprecise and difficult, it will be the area in which many DTC companies compete. Some principles of effective competition have begun to emerge. One is focus—some companies have elected to focus on ancestry uses of DNA measurements and have avoided making statements about medical/health risks. This strategy is attractive because ancestry is of great interest but is of lower stakes relative to health, and so these companies can claim focused excellence and avoid operating in dangerous waters. Another strategy is customer support—some companies have created informative websites or “operators are standing by” call centers where customers can learn more about their test results. These are particularly important in cases in which medical information is dispensed, to support customers who may be receiving bad news. A third strategy is social networking—some companies have encouraged their customers to release information to others, in the hopes of defining groups with shared interests/traits—on the model of the remarkably successful social networking sites such as Facebook. Each of these strategies has obvious potential weaknesses, but it is clear that genome interpretation is likely to be very competitive for a while.

A critical consequence of all this information availability is the urgent need to educate the public and health-care workers. The basics of genetic interpretation should be provided to all, probably starting in the health-education units in grade school and high school. There must be education for health-care workers, who will now meet patients with access to their genome on a cell phone or music player. The key message to the public is that most genetics are not deterministic—they simply alter probabilities—and that people can modify genetic health risks through lifestyle interventions. The key message to health-care workers is information about how to follow up on genetic information with appropriate testing (or simple reassurance). In a sense, the DTC companies are competing with the healthcare system in providing genetic “advice” (differences highlighted in Table 1), and we have not worked out methods to hold them accountable for the accuracy and uses of this advice; it may require more than market forces.

Finally, with the rise of DTC genetic testing there will be obvious pressures on health-care practitioners whose workflow must change. Most significantly, clinical geneticists and genetic counselors must rethink how their professions work. No longer will they be the only gatekeepers to genetic information. However, they will continue to be important professional interpreters who are licensed not primarily to measure the DNA but to act on the results with medical interventions, further tests, and patient counseling. Patients may come to them already knowing their genotypes and wondering about their significance. Similarly, primary care physicians will need to learn how to manage patients who come into their offices with 1 million data points, hundreds or thousands of which may have implications for their risk for disease. Finally, clinical pharmacologists will increasingly need to consider drug choice and dose in the context of genetics. In the same way that detection and management of drug interactions fall to the pharmacologist, the detection and management of pharmacogenomic effects may fall to this group as well.

In summary, the universal availability of DNA information to individuals seems unavoidable. Our efforts should be directed not at stopping this deluge of information but instead at creating the scientific, regulatory, and business climate to maximize its benefits and minimize its unfavorable effects.

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Table 1

Key points of comparison for direct-to-consumer testing vs. “traditional” genetic testing

Direct-to-consumer testing^a	Traditional testing
Patient initiates test	Health-care worker initiates test
Companies are currently lightly regulated on privacy issues	Health-care systems are tightly regulated on privacy issues
Patient controls genetic information	Health-care system controls information
Patient chooses interpreter of information	Health-care system interprets information
Test quality is currently unregulated	Careful quality control systems are in place
Interpretation can be for multiple purposes (ancestry, paternity, traits, health)	Interpretation is typically for health issues only
Intense competition drives down prices	Price is tied to health-care payment system
Information may come without support or counseling services	Information is delivered by knowledgeable health-care professionals
Patient has genetic knowledge before others	Health-care system has genetic knowledge before patient
Interpreters typically are not accredited	Interpreters typically are licensed/accredited