The contractual genome: how direct-to-consumer genomic services may help patients take ownership of their DNA

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The sequencing and genotyping of personal genomes by commercial services outside traditional clinical settings may help to shape the expectations of research subjects and patients regarding control of and responsibility for the information contained in their DNA. A greater sense of individual ownership of personal genomic information could replace overly complex and paternalistic institutional proxies for the protection of personal genotype and sequence data, and also could encourage research participants and patients to become better educated regarding genetic contributors to disease.

As financial and technical barriers are reduced along the path to the US\$1000 genome [1,2], personal sequencing will soon be available to anyone with sufficient curiosity and discretionary income. Already, Craig Venter, James Watson and anonymous Chinese and Yoruba donors have had their whole genomes analyzed, with plans for that sequence data to be made available to others via the internet [3]. A US\$10 million dollar incentive, the 'X Prize' in genomic sequencing, will generate more such data by requiring sequencers to analyze the personal genomes of at least 100 individuals in just 10 days [4].

Direct-to-consumer genomics companies are not far behind. An online business, 23andMe, is premised on a business plan for providing personal genotyping information and health-related interpretation of those data outside traditional clinical settings, and DeCODE and Navigenics have also announced similar personal genotyping services [5,6]. A Harvard-based project is actively recruiting altruistic donors to take part in an alternative personal genome research project [7], and Knome, a company based in Cambridge (MA, USA), is recruiting clients interested in knowing their complete personal sequences.

These developments suggest that whole-genome analyses of individuals' DNA sequences may debut not as clinical services validated by extensive trials but as non-medical alternatives to traditional forms of genetic testing, with an initial existence as curiosities available primarily to the wealthy and well-connected scientists. Public reaction to those initial non-medical experiences will play a crucial role in shaping attitudes regarding the value of whole-genome technologies and determining

how downstream whole-genome diagnostic tools are (or are not) adopted as they become more widely available for a broad range of health-related purposes to larger segments of the population.

Is the client always right?

Unlike medical research or clinical data, commercial personal sequencing and genotyping data are presumably the property of the client whose sample is sequenced, to be used as he or she sees fit. While professional ethics and government regulations govern relationships between clinicians and patients, as well as between researchers and subjects, contract law is the dominant framework that governs relationships between genomic vendors and individual clients. Those contractual arrangements for obtaining one's personal sequence may well create a greater expectation of individual ownership and control over sequence and other genetic information in research and clinical contexts.

This means that genetic researchers, most of whom currently do not return individual sequence and genotype information to research subjects (except in cases of genetic variants for which there is clear evidence of significant health effects or for which some clinical intervention is possible), may find that the full return of all personal genomic data becomes the standard. In addition, the creation of a non-medical business for identifying health-related variants (such as 23andMe) may shift some interpretation of genomic information from clinical providers to automated software programs available to the general public, enabling healthcare consumers to examine their own genetic susceptibilities outside the framework of more traditional doctor-patient relationships.

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But will all consumers benefit equally? At least for the present, the new generation of sequencing machines, and the extensive sequence and other whole-genome data that they produce, constitute a scarce resource. As with any emerging technology, the initial benefits of personal sequencing and genotyping will not be distributed equitably across the larger population, and those who have greater financial means will tend to have greater initial access. Does that mean that manufacturers of new genomics technologies, and the organizations and individuals who purchase these technologies, have a social obligation to decline to provide personal genomics services outside traditional clinical and biomedical research contexts, given that those medical contexts are more likely to amplify any early benefits beyond the individuals whose genomes are sequenced?

Perhaps, but inevitably, large-scale personal genotyping and sequencing services will become an increasingly common feature of the consumer-driven health-services' landscape, so staying out of the market does not forestall the consequences for public perception. Generally, unless the consequences of marketing non-invasive health services directly to clients are harmful to identifiable individuals, we do not impose this level of social obligation on for-profit corporations. Moreover, by staying out of the market, ethically informed players would forfeit the opportunity to proactively establish standards for non-medical applications of genomic technologies and to shape the ways in which the media and public come to frame personal genomics, with significant implications for subsequent clinical applications of more affordable versions of that technology. Consequently, engaging with direct-to-consumer genomics companies in developing emerging standards for personal genomic information is not necessarily a bad thing, depending on how non-medical vendors promote their services, protect personal privacy, and provide access and interpretive assistance for economically disadvantaged populations.

Indeed, the growing popularity of direct-to-consumer services may well do more to pave the way to the promised era of personalized medicine than the more usual path of using genetic research studies as precursors for subsequent clinical applications, developing often-complex institutional procedures and protections for using and protecting personal genomic

information [8]. Commercial personal genotyping and sequencing could shift public expectations regarding responsibilities for privacy protections, as well as for initiating and understanding current and future uses of individual genetic information from researchers and physicians to study participants and patients. The challenge of the impending era of the personal genome, then, is not how to make researchers and clinicians better gatekeepers of individual genomic information, but rather how to better educate study subjects and patients as they gain increasing access to the information contained in their DNA, outside the usual research and clinical settings.

Expecting unanticipated findings

Clearly, whether in a clinical, research or commercial setting, anyone agreeing to have his or her genome sequenced or genotyped should do so only after careful consideration of the potential implications, including that not all future consequences can be anticipated at the present time and that many current risk estimates will be of dubious clinical value at best [9]. Where clinically validated genetic tests already exist, medical interpretation of personal sequence data will require additional follow-up to resolve diagnostic ambiguities. For suspected genetic contributors to health and disease for which there are no established diagnostic tests, including recently identified associations between genetic features and particular health conditions that have not yet been sufficiently replicated to serve as the foundation for clinically validated diagnostic tests [10], medical response may be unclear. A large number of those associations also involve gene–gene and gene–environment interactions, which present further empirical and interpretive challenges [11]. As a result, in the foreseeable future, most personal-sequence findings will exist in a medical limbo between 'unknown' and 'verified' significance.

Clients of genomic service providers should be made aware that the only way they can control the current and future implications of those largely ambiguous findings is to carefully limit who has access to their data and for what purposes. Direct-to-consumer genomics providers will have some responsibility for protecting that personal information while it is in their databases – and conspicuous failures to do so will have serious negative implications for their businesses, as well as for subsequent medical applications of whole-genome technologies – but the

signal difference between a direct-to-consumer service and genomic services provided in traditional medical or research settings is that the former places primary responsibility for purposive dissemination of personal genomic data in the hands of the person who is genotyped or sequenced (absent identity theft or intentional violation of individual privacy on the part of the consumer genomics company). That is a revolutionary shift in the locus of control for personal genomic data, one that should motivate many clients to become more involved in the interpretation, management and use of their personal information.

In particular, many clients will be motivated to become better educated regarding the meaning of their genomic information. As cheaper whole-genome analysis becomes available to much larger numbers of people than are currently evaluated clinically for targeted genetic markers, this will require a very different kind of genetic counseling than is currently provided. Commercial services that interact with clients primarily online may develop innovative alternative models for that emerging clinical challenge, although potentially at the expense of the more robust pre- and post-test face-to-face counseling that has been the hallmark of medical genetics to this point. Perhaps inevitably, though, genetic counseling may become more of a process of self education.

Already, many health consumers make use of the internet as a first step in linking self-identified symptoms with possible disorders in trying to understand the diagnoses and advice of healthcare providers. Consumers with direct access to their own genotypes or sequence data will extend that practice to include internet-assisted self interpretation of their genetic risks and susceptibilities for disease. Some direct-to-consumer genomics services provide convenient summary estimates of those risks. A key question going forward will be how useful those risk estimates, and the underlying software programs that calculate them, are in helping individuals manage their health (largely by raising awareness of specific disease risks and susceptibilities). We stress self management and health awareness as criteria for measuring the effectiveness of direct-to-consumer genomics services because those services are not intended as substitutes for medical genetic tests, which are measured in terms of clinical validity and utility. No one will be medically diagnosed by an online genotyping or sequencing service,

but many clients will change their personal health-surveillance practices and health-related behaviors as a result of genomic data generated by these services (including when and how often they consult physicians regarding perceived problems).

In many ways, purchasing one's genotype or sequence is to engage in a process of education. How can that educational process be optimized to have the greatest benefits for one's health? Rather than just giving clients summary estimates of their risks for particular disorders, it may be more effective to involve them more actively in calculating those risks. For example, a software program or internet portal can empower clients to search online public databases for new disease-relevant genetic discoveries, and then to compare those findings with their own genetic information, as well as contributing behaviors, environmental exposures and family histories. In most cases, clients will learn that disease risk prediction depends on multiple variables, some of which are within individual control and others are not, and can, at best, identify a range of possible outcomes. This interactive exercise would also be an opportunity to correct common public misconceptions regarding genetic influences on the development of complex human diseases, such as naively deterministic attitudes regarding behavioral genotypes.

Of course, not all consumer genomics providers will present a nuanced version of genetic contributors to health, disease and behavior. Exaggerated claims regarding the influence of genetic traits or inaccurate estimates of risks conferred by specific genetic variants could significantly discredit not only specific companies providing direct-to-consumer services but also future clinical iterations of personalized medicine. However, those genomics companies that provide more transparent reports in the form of actual genotypic and sequence data along with interpretive annotations will empower consumers to more directly manage and interpret their personal genomic information and thereby engender greater understanding, while those that provide only summary risk estimates will perpetuate a less informed, 'black box' view of genetic information.

Having clients personally engage in exploring the multiple potential meanings of their personal genomic information will increase the educational and health values of consumer genomics services and make it more likely that

direct-to-consumer genomics will be integrated as a front-end, patient-driven, health-surveillance component in a broader spectrum of health services that also includes clinical genetic testing in medical settings. Charging consumers with protecting personal genomic information, making their own decisions regarding its dissemination and learning more about its potential significance could also constitute a superior paradigm to the more paternalistic approach that is currently taken by medical researchers, who, for the most part, tend not to return genomic data to research volunteers, and physicians, who function as gatekeepers in limiting access to clinically validated genetic tests to those with specific indications of a higher risk.

Taking ownership

Would we be better off as research subjects and patients if we were conceptualized as owning our personal sequences by researchers and clinicians? Rather than donating samples for research studies, subjects would loan their personal genomic data (or defined segments of it) for specific limited uses by researchers. Already, some patient advocacy groups are building their own tissue and DNA repositories that maintain control over researcher uses, and individual ownership of personal genomic data is, in some senses, just a step or two further in participant involvement in the research enterprise [12]. Similarly, patients would give clinicians limited permission to examine particular genes or variants when other indications (including, perhaps, online analyses of their complete sequences from non-medical sources) suggest that a genetic component may be relevant to their current or future health status. Taking medical action on the basis of genetic signs of illness would not be that great a departure from the growing numbers of patients today who seek medical care after recognizing what they believe to be signs of illness, according to health-focused websites.

While some patients might be reluctant to grant permission to clinicians to examine their personal sequence data, that reluctance would be of a kind with patients who decline a variety of existing medical tests today. Indeed, clinicians currently ask patients to agree in writing to give them permission to have access to all kinds of personal medical information from cholesterol measures to ECGs to clinically validated genetic tests. Asking patients to provide limited-use access to non-medically generated sequence data would be similar to asking patients for family

health history; both non-medical sequences and family history data can give important extra-medical indications regarding disease risk that must then be confirmed using clinically validated tests and procedures. A patient–physician contractual arrangement may also help to limit the extent to which a patient is obligated to provide health insurers access to genetic test results [13], especially if the patient owns his or her complete non-medical sequence (which would exist outside medical records, access to which is required by most US insurers) prior to a clinical encounter.

In addition, patients might establish other contractual relationships with third-party trusts that hold personal genomic information for ongoing review of new health-related findings as well as for the benefit of biological relatives whose own genomes would be partially reflected in those of their close kin [14]. Such procedures would move us further along the path of greater patient control of access to medical records, a development that could provide added contractual protections for privacy concerns, as well as contribute significantly to patient autonomy. A disadvantage of greater patient control of personal genomic information is that medical researchers and healthcare institutions would lose opportunities to aggregate de-identified individual genomic data in medical databases that could be used for population-level analyses and might result in improvements to the delivery of clinical genetic testing services.

However, on the whole, generating personal genomic information outside of traditional medical settings could be a positive development in better educating the public regarding the limited influence of genetic contributors to health, as well as in demystifying the perceived risks involved in genetics. Encouraging personal initiative in obtaining one's genomic information, vesting individuals with primary responsibility for protecting the privacy of their own information, and offering tools for individuals to explore and gain greater knowledge of the implications that genomic information may have for their present and future health will create a premedical status and utility for personal genomic data that is different from, yet integrated with, its clinical utility.

Up to now, the medicalization of genetic information has had the effect of placing researchers and clinicians between individuals and their personal genomes, as both research subjects and patients have, in effect, surrendered

control over their genomic information to researchers, physicians and the biomedical institutions that they represent (universities and hospitals directly, and insurance companies indirectly). The latter have developed elaborate procedures for determining when research subjects and patients can be told about their own DNA [15,16]. Extra-medical whole-genome analyses have the potential for redefining the roles of those medical gatekeepers and making genetics a more familiar, and thereby less fearful, aspect of our everyday identities. As a result, in addition to individualized treatment, personalized medicine may also come to denote greater individual ownership of personal genomic and other health-related information.

Conclusion

Direct-to-consumer genomic services have the potential for giving research participants and patients a greater sense of ownership of and responsibility for their personal genomic information, including issues of privacy protection, dissemination and interpretation. By engaging direct-to-consumer providers now, physicians, bioethicists and others have the opportunity to integrate non-medical personal genomic analysis into the emerging personalized medicine paradigm as a consumer-driven health-surveillance practice. Rather than attempt to regulate direct-to-consumer genomics services as though they were equivalent to medical genetic tests, we would be better served by treating them as equivalent to

other kinds of extramedical health information that can motivate individuals to make healthy changes in their behavior, to be more aware of health risks and symptoms, and to consult medical providers in a more timely manner. We believe that direct-to-consumer genomic services should be viewed as an opportunity for improving personal health instead of an occasion for concern, caution or over-regulation.

Future perspective

An open question for that future in which inexpensive whole-genome analysis and personalized genomic sequencing are readily available is: to what extent will those personal genomic data be provided to members of the public in medical or non-medical settings? We believe that question will be answered by the success of emerging non-medical consumer genomics companies in providing their initial clients with transparent personal genomic information that:

- Empowers clients to engage in their own personal analyses through a software-assisted portal;
- Gives clients primary responsibility for maintaining the privacy of their own data.

If consumers are directly engaged in interpreting the health significance of their personal genomic information and in protecting the privacy of that information, direct-to-consumer genomics companies can occupy an important long-term role in a health-surveillance continuum

Executive summary

- Large-scale genotyping and personal sequencing are increasingly becoming both more efficient and less expensive.
- Direct-to-consumer genomics companies have begun to offer whole-genome analysis and sequencing services to individual clients.
- Those personal genomics services are offered outside traditional medical settings, and could shape public perceptions of genomic technologies and become models for the delivery of future personalized medical services in clinical settings.
- Direct-to-consumer genomics could shift responsibilities for data privacy from medical providers and healthcare institutions to individual consumers by creating a greater sense of personal ownership of one's DNA.
- Direct-to-consumer genomics could shift at least some of the initiative for understanding one's genomic information and taking appropriate health-related actions based on that understanding from physicians and other health professionals to individuals.
- Direct-to-consumer genomics companies that provide clients with actual genetic information rather than just summary estimates of disease risk are more likely to empower clients and provide information than can be integrated with genetic testing services offered in medical settings.
- Instead of ignoring or aggressively regulating direct-to-consumer genomics companies, we should take this opportunity to work with those companies to develop a more seamless continuum of genomics-based health-surveillance tools that begins with individual self awareness and extends all the way to clinical diagnosis and treatment.

that includes individual self management based on personal genomic data generated in non-medical settings.

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