

# The \$1000 Genome: Ethical and Legal Issues in Whole Genome Sequencing of Individuals

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## Abstract

*Progress in gene sequencing could make rapid whole genome sequencing of individuals affordable to millions of persons and useful for many purposes in a future era of genomic medicine. Using the idea of \$1000 genome as a focus, this article reviews the main technical, ethical, and legal issues that must be resolved to make mass genotyping of individuals cost-effective and ethically acceptable. It presents the case for individual ownership of a person's genome and its information, and shows the implications of that position for rights to informed consent and privacy over sequencing, testing, and disclosing genomic information about identifiable individuals. Legal recognition of a person's right to control his or her genome and the information that it contains is essential for further progress in applying genomic discoveries to human lives.*

## Introduction

The prospect of greatly improved DNA sequencing techniques has led some geneticists to predict that in 10-15 years a person's entire genome could be fully characterized for \$1000 or less (National Institutes of Human Genome Research 2001). Whole individual genotyping is not now practical, but in a future world of genomic medicine it might be an efficient or even essential tool for diagnosis, prevention, and therapy. Once whole genotyping is within easy financial reach, it is likely to be used on a mass or even a population basis for medical and other purposes.<sup>1</sup>

If sequencing whole individual genomes makes good medical sense, it will raise the same ethical, legal, and social issues that now arise with our more fragmentary knowledge of the genome and our more limited genotyping ability. Those issues will assume even greater importance as knowledge of the genome grows and full genotyping of individuals routinely occurs. Looking at those issues in the context of the \$1000 genome will help prepare us for the likely expanded use of genomics in the future and the ethical and policy issues that it will bring.

## The Future of Genomic Medicine

Genomics is likely to play an important role in a future world of health care and medical practice (Collins et al 2003). Its contributions to understanding the pathogenesis of disease and to drug design will be enormous. The ability to predict disease and take preventive action will grow significantly. Molecular staging is becoming an indispensable tool in oncology, and the need for pharmacogenetic

assessments before prescribing drugs is likely to become routine. Within ten years there may also be more effective gene therapies that correct the genomic or molecular basis of existing disease (Guttmacher and Collins 2002).

Many clinical applications of genomics will require that an individual's genome or sections of it be sequenced, so that the presence or absence of disease mutations or other relevant information can be ascertained. In many instances it will be possible to test directly for the segment of DNA under scrutiny. But some relevant testing may require scanning the whole genome for mutations at many different loci at the same time. Also, it may be more efficient to have a person's entire genome sequence *in silico* for later rapid testing as new medical needs arise.

Whether rapid whole genotyping of individuals becomes an established part of health care and medical practice will depend on whether the benefits of whole genotyping outweigh its costs and the threats to privacy of having that information electronically available. One scenario of likely use would be a young adult accepting whole genome sequencing as part of an annual physical exam, with the results stored on a server or a CD-ROM for easy access for later *in silico* testing. Many variations on this scenario could occur as well, including genotyping children at birth or screening fetuses and embryos for reproductive decision-making.

A medical world in which whole individual genotyping is routine will require physicians, nurses, and insurers to be much more knowledgeable about genetics and genomics than they now are (Collins and Guttmacher 2002; Varmus 2002). Consumers and patients will also have to be much better informed and more accepting than they now are about genomics and genetic risk factors in medical care. An increased fund of genetic knowledge on the part of both health care providers and consumers is essential to bring a genomics era in health care into being.

## Technical Issues

The idea of rapid, whole genome sequencing of individuals is now a wild surmise. However, with cheaper and easier sequencing techniques and the growing importance of genomic information in medicine, routine whole genome sequencing might easily occur and be attractive to both patients and physicians. Human genome sequencer Craig Venter has announced that he will embark on this project, and many geneticists expect that it is only a matter of time before rapid whole genome sequencing is feasible (Nature

2002).

Three technical issues and one legal one will determine when, if ever, a \$1000 genome will be cheap, accurate, and useful enough to justify the costs of obtaining it: (1) the cost and ease of sequencing; (2) the development of fine-grained single nucleotide polymorphism and haplotype maps; (3) progress in functional and medical genomics; and (4) the absence of patent barriers.

#### *Reduction in the Cost of Sequencing*

It cost \$3 billion spent over 13 years to sequence the human genome (about \$1 per base pair) (Davies 2001). However, much of that cost was used to perfect the high throughput sequencing techniques that by 2001 enabled the entire human genome to be sequenced in ten months at a cost of \$.05 per base pair. Comparable improvements in efficiency would make it feasible to reduce the price well below \$.01 per base pair in the next 10-15 years (Lander 2002).

The technology that will reduce the cost of sequencing so dramatically is likely to involve cheaper and quicker ways of preparing DNA for reading by automatic sequencers, with fewer passes and assembly issues. Currently DNA is cut at many places, put into bacterial or yeast artificial chromosomes, and then sequenced in pieces, which are then reassembled. The process is complicated by the need to replicate DNA by the polymerase chain reaction, do many sequencing runs, and then determine how the pieces fit together.

Techniques for reading DNA linearly as occurs in DNA replication might provide a cheaper and quicker sequencing strategy. For example, a U.S. patent has been granted on an invention that places DNA on a chip and causes it to straighten out as DNA does naturally when it prepares to copy itself (Riordan 2002). The chip then passes through an optical detector that records the stretched-out DNA as it flies by, working much the same way as an optical sensor in a DVD player does. According to its inventors, this device has the potential to decipher an entire genome in the 30 minutes or so that it takes DNA to replicate itself (Riordan 2002). This approach, however, is still in development, and may not prove to be as effective as claimed. Still, given the enormous technological progress in gene sequencing that occurred over the life of the Human Genome Project, techniques to greatly reduce the cost and speed of sequencing are likely.

#### *Haplotype and SNP Maps*

Another important factor in moving us toward a \$1000 genome is the recognition that full characterization of an individual's genome for most medical purposes may not require sequencing each of the 3 billion base pairs of human DNA. Rather, it will be sufficient to sequence enough of an individual's genome to determine where medical or other relevant departures from a reference sequence for humans are. Developing single nucleotide polymorphism (SNP) and haplotype maps that associate with genes of importance but distinguish among individu-

als could provide whole genome characterization without the need to sequence every base pair. Although still an enormous amount of information, whole genome characterization through SNP and haplotype comparisons using microarrays (which are also expected to drop in cost) would be more easily brought within the \$1000 price constraint.

Progress toward a \$1000 genome may thus be intimately linked to progress in developing fine-grained, accurate SNP and haplotype maps of humans and their correlations with genes, polymorphisms, and mutations of importance. The SNP Consortium and other efforts have produced over 1.5 million SNPs, and the NIH has embarked on a major effort in haplotype mapping (The SNP Consortium 2002; National Institute of Human Genome Research 2002). In the next 10 years these efforts should bear much fruit, with SNP and haplotype maps of humans, including many different ethnic and population groups, likely to be available for finding genes and polymorphisms in the genome.

#### *Functional Genomics*

Having the genomic sequence and SNPs and haplotype maps, however, is not the same as knowing where the genes are and what they do, and thus how they may be used to design drugs and predict, prevent, and treat disease. Unless much more is known about human genes and how they function, having a full human genome sequence would provide limited benefits, and probably not justify the costs of rapid sequencing.

But progress in functional genomics is rapidly occurring, itself fueled by new sequencing and bioinformatic techniques. Comparative genomics has greatly aided the search for human genes by identifying coding sections of DNA that have been conserved for millions of years across many families of organisms. With a draft of the mouse sequence now available and that of the rat and chimpanzee on the horizon, in addition to the sequences of yeast, *c elegans*, *drosophila*, and many microorganisms, the ability to home in on most human genes will be greatly increased (Wade 2002). Several thousand Mendelian disorders have already been identified, as well as polymorphisms that affect metabolism, drug transport, and other issues influencing drug responsiveness (Evans and Johnson 2001). A complete human transcriptome—the part of the genome that is transcribed to RNA prior to translation into proteins—will soon be available (Cyranoski 2002). With microarrays to test the expression of thousands of genes simultaneously, great progress in deciphering the network of genes influencing complex, multifactorial diseases and conditions will also occur.

By the time that sequencing technology is ready for cheap and rapid whole genotyping, geneticists will know a great deal more about what genes do and their connections with both single gene and multifactorial diseases. This knowledge will help to make whole genome sequencing a cost-effective way to obtain global genomic information about a person and to facilitate genetic testing as new med-

ical situations are presented. The most important uses may be susceptibility testing for preventive purposes, genetic testing for diagnosing and staging disease, and pharmacogenetic testing for drug responsiveness. Carrier testing for reproductive purposes will also be sought, and social uses to establish identity or family connection may also occur.

#### *Patent Law Barriers*

Potential barriers to whole genotyping of individuals are patent rights in sections of the human genome. The United States, Europe, and Japan allow the patenting of sequenced molecules of DNA when that sequence is novel, non-obvious, and useful. Many genes or parts of genes have already been patented, and more may be patented in the future. If genome sequences are patented, a sequencer may need a license from the patent holder to sequence that gene in a person, just as they would if they wanted to test for a particular patented gene.<sup>2</sup> Alternatively, if genotyping occurs through comparison with a reference set of SNPs or haplotypes using DNA microarrays, licenses from holders of that information may also be needed.

The need to obtain multiple licenses for whole genome sequencing raises “anticommons” problems of too many rights-holders for efficient licensing to occur (Heller and Eisenberg, 1994). Excessive royalty demands or refusals to license could limit the economic feasibility or completeness of whole genotyping (Merz 2002). If so, it would provide additional evidence for those who argue that patent rights interfere with research and good medical care, and should be limited through mandatory licensure or provisions to protect access to clinical uses of gene patents (Nuffield Council on Bioethics 2002).

#### **Ethical, Legal, and Social Challenges of Whole Genotyping**

Even if rapid whole genotyping is technically and financially feasible, several key ethical, legal, and social issues about control and use of genomic data will have to be resolved before widespread whole sequencing of individual human genomes is adopted. Current genetic testing practices raise most of these issues and the applicable ethical principles have long been known. But many questions about their application remain and protection in many areas is inadequate. Strong protection for the rights of persons who are genotyped will be necessary if health care providers and consumers are to embrace whole genome sequencing or genomic characterization of individuals as an integral part of medicine.

The main ethical, legal, and social issues concern who controls acquisition of a person’s DNA and the information it contains; what uses may be made of that information; and who decides how that information is used. The ethical and legal challenge is to fairly resolve the ownership, consent, and privacy questions so that consumers and the public will have confidence that whole genome sequencing will benefit rather than harm them.

#### *Ownership of the Genome*

A key foundational issue is determining who has disposi-

tional rights over an individual’s genome. In discussing ownership or dispositional control of the genome, we must distinguish between the physical embodiment of the genome in DNA and its informational content. With regard to its informational content, we must also distinguish between information about unique identifiers and medical information. Different rules may apply to each aspect.

Concerning physical embodiment—the tissue sample that contains the DNA or the DNA molecules isolated from it—the question is whether a property or a liability rule should apply. Under a property rule a person would have dispositional rights over or “own” the DNA in their body and continue to do so unless they abandon their DNA or grant control to others. A liability rule, on the other hand, would require that another pay them damages for intruding on their body to get their DNA and then using it without consent. Such a rule would give no rights in DNA that was not taken from their body or in the information that the DNA contains, for example, DNA on postage stamps, envelopes, or cigarette butts.

*Moore v. Regents of the University of California*, the leading case on this topic, adopted a liability rather than property approach to resolve a dispute about commercial exploitation of spleen cells removed during a splenectomy and used in research without the patient’s consent. The case rejected a property right in the tissue itself, but held that the patient had a right to informed consent from his physician about removal and use of those cells (*Moore v. Regents of the University of California* 1990). Informed consent—a type of liability rule—protects an individual’s right to decide whether to provide tissue to a doctor or researcher, including the right not to provide it if it will be sequenced or tested for purposes to which the person objects. But it gives no rights over the genomic information that is derived from that DNA, whether removed with or without his consent or retrieved from objects that a person has touched or discarded.

The prospect of a \$1000 genome is a strong reminder of the need for legal clarification of a person’s control over DNA samples from his body and the information that they contain. Because DNA provides a unique identifier for a person and information about potential diseases and conditions, the information that it contains is too personal and too subject to misuse and misunderstanding to be taken from the body or used to obtain other than identifying information without the person’s consent. Individuals should in general have dispositional control over their DNA and the information it contains until they freely and knowingly waive or transfer those rights to others. Some of that protection already exists, for example, the need under *Moore* to obtain consent before removing DNA from a person. Also, 15-20 states explicitly protect against genetic testing or disclosure without consent (Gostin, Hodge, and Calvo 2001). In most cases, however, new law will be needed to protect the informational content of DNA, including DNA, which is shed or cast off and then tested for medical purposes.<sup>3</sup>

### *Informed Consent to Genotyping*

An important corollary of assigning ownership or dispositional control of identifiable DNA to the person is that only that person can grant to others the right to take or use their DNA or the information that it contains (other than unique identifiers used for valid law enforcement purposes). Public policy, as well as ethical guidelines, should require that no physician, laboratory, or other entity may sequence, store, or test identifiable DNA unless the person tested has given written, informed consent or there has been compliance with conditions for exceptions for persons incompetent to consent. Such a policy will be essential to protect individuals and instill confidence that personal rights in one's own DNA and its information are protected.

Under such a policy an individual's informed consent would be necessary to sequence an identifiable whole genome or any part of it, to access it for later testing, or to disclose the results of any testing that has occurred. The consent requirement should apply to every stage of the sequencing and testing process, including obtaining identifiable DNA, sequencing it, and then testing it for polymorphisms or mutations. The requirement for sequencing and testing should apply even if the DNA has been lawfully obtained for other purposes or recovered from discarded objects or materials. A person's consent should also be required to store his or her identifiable genomic information, to disclose or transfer that information to others, or to use information derived from it for medical or other purposes.

To comply with a legal and ethical policy of informed consent prior to acquiring, sequencing, or testing identifiable DNA and disclosing the results, persons undertaking any of those actions should inform the individual of the relevant risks and benefits of the proposed sequencing and testing, so that he or she can make a free and informed choice. The calculus of benefits and risks will include the tests and medical or other uses of the information which will occur, who will have access to the information, how it will be stored and protected, and what harms could occur from authorized or unauthorized access to that information.

### *Benefits of Genotyping*

An individual should be offered full sequencing of his genome only if there were good reasons to do so. In most cases a request for whole genome sequencing would arise in a medical context as part of a physical exam or some other health-related event. Consider, for example, a hypothetical physical exam of a 25 year-old man fifteen years from now when whole genome sequencing or characterization is available for under \$1000. The physician proposes sequencing the entire genome so that mutations or polymorphisms in thousands of genes can be identified for which the patient could take preventive action. The physician explains that whole genome sequencing will also provide information about pharmacogenetic responsiveness to drugs, and facilitate genetic testing in future medical situ-

ations. Mutations indicating a nontreatable future disease would not be tested, or if tested, would not be disclosed to the patient (Collins 1999).

Because genetic testing of smaller segments of DNA could occur when needed, proponents of whole genome sequencing or characterization of individuals will have to make the case that there are substantial benefits from having a person's whole genome available for current and future testing needs rather than waiting until particular tests are needed. As noted, that case would rest on the greater knowledge that comes from whole genome comparisons, many of which may be necessary to identify genes, polymorphisms, or mutations related to multifactorial conditions, and the convenience of having had one's genome already characterized for later *in silico* testing by computer.

### *Risks of Genotyping*

In addition to explaining benefits, persons offering whole genome sequencing to individuals should also inform them of the potential risks of genotyping and the range of tests that it will make possible. The scope and seriousness of those risks will depend on what information whole genome sequencing of an individual might reveal, what the personal and social significance of that information might be, how the individual's DNA and genotypic information will be stored, what types of misuse could occur, and what penalties and protections exist for use of genomic data without consent.

A major risk of sequencing an individual's whole genome is that much more medical information will be known about him and his family than he might find acceptable. Because a person's genome reveals much of his "future diary" (to use George Annas' evocative term) (Annas 1993), sequencing it makes it much more likely that tests will occur which reveal information that the person would prefer not to know or have known by others. Many persons, for example, may not want to know about late-onset diseases or behavioral tendencies which they could do little to prevent, especially if that information could also lead to stigmatization or discrimination. They may not even want to know about susceptibility conditions for which preventive actions are possible because of their unwillingness to engage in the behavioral or life-style changes that would then be necessary. With identity theft a growing problem, others might object to reducing their "genetic identity" to a computer file that can be stolen and misused (Weiser 2002).

Other persons might be quite interested in having their genome sequenced but fear the risks to privacy that would result from having their entire genome in a computer file or on a CD-ROM where it would be vulnerable to unauthorized testing or disclosures that could lead to stigma and discrimination. Access to unauthorized genomic information could also be used to determine identity or kinship connections, which could prove to be personally embarrassing or legally onerous.<sup>4</sup>

### *Storage Issues*

The extent of many of those risks depends on how DNA and genomic information is gathered, stored, and processed; the security systems that protect it; and the penalties and legal rules that guard against the unauthorized use of genetic data. An important set of protections will depend on how DNA used to obtain a person's whole genome is collected and stored and how access to it and its information is regulated.

Tissue or DNA must be obtained to have genotyping occur, but it may not be necessary to keep tissue or DNA samples once sequencing has occurred. The most secure arrangement would be to destroy the DNA and tissue sample after genotyping, so that only electronic or *in silico* information is then available. If later DNA samples are needed for gene expression studies, DNA could be obtainable from tumors, blood, or other patient tissue. Only if difficulties in obtaining more DNA are likely should a need to store the patient's DNA also exist. In that case the ease of quick clinical testing would have to be weighed against the risks that other persons would obtain unauthorized access to a person's DNA.<sup>5</sup>

A second set of storage issues concerns how the resulting genotypic information about an individual will be maintained and how it may be released. A person's full genotype (or haplotype or SNP map of it) could be stored electronically in a computer or *in silico* on a CD-ROM. The least protective model would keep the entire genotype in a patient's medical records in electronic form, which could then be retrieved as needed for diagnosis, treatment, or other purposes. An intermediate level of protection would have the genotype kept electronically in a place protected by privacy firewalls and other protective mechanisms, but which a physician, with patient consent, could easily access. In the most protective model a trusted third party intermediary would hold genomic data and tissue samples in a secure system (Marshall, 2001). When genotypic information was needed for some medical or other authorized purpose, the patient would instruct the intermediary to provide it to the physician or other user for that purpose. Depending on the use, only part of the genome needed be provided, *e.g.*, the haplotypes or SNPs that relate to pharmacogenetic uses rather than the entire genotype. Determining the best way to protect the security and privacy of genomic information must await future developments in bioinformatics and storage mechanisms.

### *Other Privacy Protections*

In addition to secure storage of genome sequence information and genetic test results, explicit rules for protecting the privacy of genetic information will also be necessary. Because of the personal nature of genotypic information (and hence the tissue or DNA which would yield it), it is important that a person's privacy interest in that information be protected. As the discussion of ownership and consent has shown, the person whose DNA is sequenced should have the right to decide whether and how identifi-

able medical information about him is obtained, used, or disclosed to others. In addition to laws protecting ownership rights over the tissue and DNA molecules it contains, there should also be legal protection against unauthorized use of that material and any genomic information derived from it.

Although tort and property law doctrines will provide some protection, legislative enactments to protect the privacy of DNA and tissue samples will most likely be necessary, with civil and criminal penalties imposed on persons who sequence, use, or transfer identifiable DNA of another without that person's permission. There is no federal constitutional right of informational or disclosure privacy.<sup>6</sup> Even if there were, it would not protect against private intrusions into genetic privacy. Only a small number of states now protect the privacy of a person's identifiable DNA and tests done on it (Gostin, Hodge, and Calvo 2001). Strong state law protection of privacy will be essential for public willingness to accept the increased genetic testing that genomic medicine will require. Those laws should also make it illegal to use wrongfully acquired genetic information in ways adverse to the individual.

In addition to legislation, much protection of the privacy of genetic information will occur through contract. If individuals have dispositional rights over their DNA and its information, they can refuse to provide DNA for sequencing or testing unless the privacy of the results will be protected and disclosures made to others only with the person's express consent. An important set of legal protection for genetic privacy will thus arise from the contractual conditions agreed to in providing DNA for genotyping or testing. Physicians, medical centers, biobanks, or other entities requesting DNA, sequencing, or storing it should agree not to release DNA or genetic information except in accordance with specified procedures for protecting privacy, including written consent for storing, testing, or disclosing identifiable genetic information. Such entities should also make their privacy protection provisions public. Without strong safeguards for privacy, the risk that that contributed material could be used in unauthorized ways could discourage participation.

### *Protecting Against "Unfair" Genetic Discrimination*

There is a strong public sentiment against "genetic discrimination" in health insurance and employment that derives from a pervasive fear that genetic testing could adversely affect a person's access to health care and jobs. To be denied something as important as health insurance or employment because of an inborn factor over which a person has no control seems unfair. But it is recognized that some employment and insurance uses of genetic information might be appropriate (Nowlan 2002). Some genetic factors might so predispose a person to injury in certain industries, *e.g.*, beryllium mining, that testing and excluding them on that basis is justifiable (United States Supreme Court 2002). Access to one's whole genotype could also lead to adverse selection in purchases of life and health insurance, to the detriment of other policyholders.

The “fairness” of genetic distinctions in insurance and jobs depends on the balance among these competing concerns. In the health insurance context, for example, the use of genetic testing to determine access to health insurance would protect policyholders against the higher premiums resulting from adverse selection by those at much higher genetic risk of illness. But it does so at the cost of denying those persons affordable health insurance and discouraging others who might benefit from genetic testing to seek it. Congressional enactment of the Genetic Information Nondiscrimination Act that has passed the United States Senate should instill confidence that whole genotyping for medical purposes will not adversely affect a person’s access to jobs and health insurance (United States Senate 2003).

### **Genotyping Infants, Embryos, and Fetuses**

The discussion has assumed that a competent adult is considering whole genotyping. But situations involving those who are incompetent to consent will also arise, for example, the need to identify the genome of embryos, fetuses, infants, children, and others who lack present competency to consent to medical care. Indeed, some persons have speculated that genotyping will first occur *in utero* or shortly after birth and become part of a person’s medical records throughout their life.

Genotyping and maintenance of genomic data on persons incompetent to consent should not occur unless there is a strong medical justification for doing so. Unless genome-wide comparisons are needed, most gene-related medical needs of persons incapable of consent could be served by more narrow tests or by time-limited storage of the resulting information. Given the potential for misuse, a lack of compelling need to genotype, and the ease with which later genotyping could occur, the need to fully genotype and maintain the results on infants, fetuses, and embryos may be rare.

Conflict between parents interested in whole genome sequencing of their children and the child’s interest in genomic privacy and more limited testing could arise. All states now screen newborns for treatable genetic conditions, such as phenylketonuria. In some states parents have lobbied vigorously for expanded screening, including for some conditions that are not treatable (Goldberg 2000). However, requests for whole genome sequencing of infants or children should respect the privacy of the child and not occur except when directly necessary for present health needs of the child. Unless a clear medical, behavioral, or learning benefit to the child can be shown, no sequencing or genetic testing of children should occur (American Society of Human Genetics 1995). If whole genome sequencing to identify preventable diseases or SNPs or haplotypes associated with drug responsiveness does occur, the child’s DNA should be discarded afterwards and genomic information erased or stringently protected. If protective measures are not feasible, a decision will have to be made whether to genotype them at all

Requests for genotyping fetuses and embryos may also

arise, with DNA obtained through amniocentesis, fetal cell sorting, or blastomere biopsy of embryos. Although most women are not likely to terminate a pregnancy unless a fetus has a severe genetic disease, many more persons might be willing to undergo *in vitro fertilization* conception and genetically screen embryos before transfer to the uterus. In such cases the parents’ argument for whole genome sequencing of embryos rests on claims of their right to decide what kind of child to have. Some parents would argue that such a right follows from their basic right to decide whether or not to reproduce. If they are willing to reproduce only if certain genes are present or absent, they would claim the right to test for those genes in order to decide whether to continue with reproduction (Robertson 1996). Other persons would reject such claims as blatantly eugenic, and ultimately harmful to offspring and society (Kass 2002).

Although rights to avoid or engage in reproduction have been legally recognized, the right of parents to know the genetic characteristics of offspring prior to birth has not yet been established. Still, some right to choose offspring characteristics, if only negatively, must exist, because we recognize the right of prospective parents to engage in prenatal and preimplantation diagnosis to prevent the birth of children with serious genetic disease or susceptibility conditions, for HLA matching for an existing child, and possibly even to obtain gender variety in a family (Robertson 2003). Yet genomic analysis of embryos could lead to intrusions on a child’s privacy that would not be tolerated with genomic testing conducted after birth occurs. Parental interests in making informed reproductive choices will have to be balanced against an offspring’s interest in genomic privacy.

### **Sequencing for All**

In a transition period when information about genes and their function is increasing, only individuals with knowledge and resources will be able to obtain whole genome sequencing. But if whole genome sequencing does become cheaply available, then it should be provided universally regardless of ability to pay, as is now the case with newborn screening. The costs of genotyping should be covered by standard health insurance and public programs such as Medicare and Medicaid, just as other medical care is covered. Coverage of whole genome sequencing for under \$1000 is not likely to be a financial bar to other necessary care, and may be essential in an era of genomic medicine for all persons to receive good care.

The adoption of individual whole genotyping as an essential health care tool in the developed world will draw attention to the need to make such testing available to peoples in less developed countries as well. Genomic science has a great potential to help persons in the less developed, whether through better control of infectious diseases through molecular diagnosis or more rational drug and vaccine development (University of Toronto 2002; World Health Organization 2002). If genotyping itself becomes essential for effective deployment of therapies directed to

diseases in undeveloped countries, then it should also be provided to the extent feasible as part of the health services directed to deal with those conditions.

### **Whole Genotyping and the Criminal Justice System**

An important policy issue with whole genotyping will be its interface with the criminal justice system's use of DNA identification. As discussed earlier, the recognition of a person's right not to provide DNA or have his DNA medically analyzed should not prevent law enforcement agencies or others who lawfully acquire DNA to use it to establish unique personal identifiers. But whole genotyping for medical purposes beyond personal identification should not occur without a person's consent. Given this policy, DNA samples and genetic information collected for criminal justice purposes should not be subject to medical testing or whole genome analysis. By the same token, whole genome information obtained for medical purposes should ordinarily be exempt from law enforcement uses or inquiry.

These lines are important because every state collects DNA samples from persons convicted of sexual and other felonies to establish unique personal identifiers. Proposals exist for extending testing to all persons arrested for any crime, as now occurs in the United Kingdom (Kaye 2001). Some commentators have argued that the fairest approach would be to have a non-criminal justice entity take, process, and hold everyone's DNA fingerprint taken at birth (Williamson and Duncan 2003).

At this stage of experience with DNA databasing, the soundest policy would be to keep DNA fingerprinting for identity purposes entirely separate from whole genotyping for medical purposes. Criminal justice databanks should be limited to non-coding loci that establish personal identity and not be used for tests or markers for medically relevant conditions. The samples from which the DNA is extracted should not be retained. If DNA samples are retained for testing verification or other valid purposes, laws that prohibit using retained samples for whole genotyping or medical testing are essential.

By the same token, DNA samples and whole genotypes sought for medical purposes should not be available for criminal justice or other identity purposes. The strongest policy would forbid criminal justice or other authorities accessing that information without the person's consent even if there is legally adequate probable cause for doing so. If there is probable cause to suspect someone of a crime, a sample could ordinarily be obtained from him directly. Even if a suspect were not available to give another sample, a strong policy against using the results of whole genotyping, whether by SNPs, haplotypes, or the entire genome would inspire confidence in the privacy of such a system. Such a policy would not be costless, but its privacy benefits should make those costs worthwhile.

### **Whole Genotyping and the Human Narrative**

Whole genome sequencing of individuals as an integral part of medical practice will further entrench the impor-

tance of genetics in understanding disease and protecting health. Although environment, nutrition, poverty, and geography will often be more powerful determinants of individual well-being, genetics will be increasingly relevant and not easily ignored. Some ethicists, however, warn of the risks to human dignity of an undue emphasis on genetic factors, which routine whole genotyping would facilitate and reinforce (Lippman 1991; Rothman 1998). The worst fear is that it could lead to a "geneticization" of society that will ultimately harm or diminish human dignity in significant ways. The image of a CD-ROM that contains a person's "genetic identity" and which can be owned, traded, and stolen and used to categorize and discriminate aptly captures that fear.

Yet there is no reason to think that the \$1000 genome poses unique or especially weighty risks in this regard. As with other genetic applications, the important question is how genetic information is used and the meanings that attend that use. Whole genotyping to prevent genetically-based diseases or determine drug responsiveness would appear to have little effect on the meaning of human personhood and the human narrative.<sup>7</sup> Rather than change the essence of our humanity, the \$1000 genome will simply be another development in the meliorist paradigm of modern medicine. The risk of "geneticization" and diminished human dignity is more plausible if germline modifications for therapy, enhancement, or diminishment of offspring became available. But those uses represent quantum leaps beyond whole genotyping for medical purposes, and do not justify discouraging whole genotyping that serves standard medical needs.

### **Conclusion**

The idea of a \$1000 genome is a useful vehicle to identify the ethical, legal, and social issues that will need resolution in a world of genomic medicine. Whole genome sequencing of individuals will greatly increase the ethical, legal, and social risks of genetic testing. If technically feasible, whole genome sequencing will be widely sought only if strong protections are in place for individual control over DNA and its information.

The discussion has shown that the decision of individuals to have their entire genome sequenced or characterized will depend on the medical and social benefits of whole genome scanning compared to the costs of obtaining and maintaining that data and the risks to privacy which doing so entails. Past engagement with the ethical, legal, and social issues raised by genomic information have identified the relevant normative issues. It remains for providers and policymakers to install the rules and procedures necessary for satisfying those norms in future practice. ☺

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#### Notes

- 1 The article assumes that the "\$1000 genome" is sought and used only within the medical care system, but some persons will seek to have their genome sequenced outside of medical settings. Firms will advertise such services over the internet, and some persons will have their own or another person's DNA sequenced outside of a medical context. While some abuses could occur with easy internet access to whole genome sequencing, demand for it may also be quite limited. Having the sequence is useful only if the information it contains is interpreted by knowledgeable persons. For most people medical involvement will be necessary.
- 2 Merely identifying the sequence of an individual may not itself infringe patented segments of DNA. But use of that sequence to test for mutations or polymorphisms is likely to infringe a patent if the patentee has claimed an invention for diagnostic purposes. (I am grateful to Jon Merz for discussion of this point).
- 3 Use of otherwise lawfully acquired DNA to determine whether it came from a particular individual is an exception to a policy of requiring consent for most sequencing of a person's DNA. If a person voluntarily provides material or engages in activities that yields DNA, he may not have a reasonable expectation of privacy in not having that material associated with him. Thus there should be no bar to the police extracting DNA from a cigarette butt that X abandoned on the street to see if it matched DNA taken from a crime scene (Hanley, 2003).
- 4 Law enforcement access to and use of DNA for personal identification is discussed in a later section.
- 5 The protections recommended here leave persons free to donate DNA for banking for current or future research in accordance with the common rule procedures for the ethical conduct of research.
- 6 The right of privacy recognized in *Roe v. Wade's* recognition of a constitutional right to abortion involved a right of autonomy of action, not a right of non-disclosure of information (United Supreme Court, 1973). Indeed, later cases have held that the 14<sup>th</sup> amendment's liberty clause does not create a constitutional right not have private information disclosed (United States Supreme Court, 1976).
- 7 I am indebted to Harold Shapiro for the idea of the "human narrative" as an organizing analytic concept in thinking about reproductive and genetic technologies.

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