



Topic overview

## Human Genome Project

*Bioethics*

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### Human Genome Project

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Without acknowledging reliance on radiographic measurements and structural inferences from Rosalind Franklin and Maurice Wilkins, on February 28, 1953, James D. Watson and Francis H. Crick formally announced the structure of DNA, recognizing at once the potential of the double helical structure for storing and replicating genetic information. A month later—on March 19, 1953—Crick penned in a seven-page handwritten letter to his twelve-year-old son away at boarding school: “We have built a model for the structure of des-oxy-ribose-nucleic-acid, called DNA for short. In other words, we think we have found the basic copying mechanism by which life comes from life” (Watson and Crick 1953; Sivakumaran 2013). In the wake of the rediscovery of Gregor Mendel's basic laws of heredity by Hugo de Vries, Carl Correns, and Erich von Tschermak-Seysenegg in the early 1900s (Roberts 1929), this announcement fueled a spate of groundbreaking research in molecular biology,

bioinformatics, and ethics (Juengst 1996; McCain 2002; Collins et al. 2003; Koski 2005; Gannet 2008; US Department of Energy Genome Research Programs 2008; National Human Genome Research Institute 2013).

## THE HUMAN GENOME PROJECT: A SELECTED HISTORICAL BACKDROP

Stepping-stones toward the Human Genome Project (HGP) included rapid achievements. Frederick Sanger sequenced the first protein (bovine insulin) in 1952 (Sanger 1952), and four years later Arthur Kornberg discovered the polymerase enzyme that synthesizes DNA in *E. coli* bacteria (Kornberg, Lehman, Simms 1956). In 1957 Francis Crick and George Gamov articulated the “Central Dogma” of molecular biology (Crick 1958). Their “sequence hypothesis” posited that the DNA sequence specifies the amino acid sequence in a protein. They also suggested that genetic information flows only in one direction, from DNA to messenger RNA to protein, the central concept of the central dogma. In 1961 the French biologists François Jacob and Jacques Monod isolated DNA sequences

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they dubbed “repressors” and “operons” as the mechanisms behind genetic regulation (Jacob and Monod 1961).

The year 1961 also saw the publication of the Nobel-winning research of Marshall Nirenberg and Heinrich Matthaei, both working in the laboratory of Severo Ochoa, which described the isolation of 20 essential amino acids, each comprising a three-nucleotide base sequence (codon), thus cracking “the genetic code” (Nirenberg and Matthaei 1961).

In 1970 two other eventual Nobel Prize winners, David Baltimore and Howard Temin, independently isolated “reverse transcriptase,” the enzyme that makes DNA from RNA (Baltimore 1970). Two years later, Paul Berg, a biochemist at Stanford, was among the first to produce a recombinant DNA molecule. “rDNA” is “genetically engineered” DNA created by transplanting or splicing genes from one species into the cells of a host organism of a different species using DNA-cutting (restriction) and binding enzymes (ligase). Such (recombinant) DNA becomes part of the host's genetic makeup and is replicated (Jackson, Symons, and Berg 1972). In 1974 Berg and ten colleagues published a letter in the journal *Science* urging the National Institutes of Health to regulate the use of recombinant DNA technology while calling on scientists to halt most recombinant DNA experiments until they better understood whether the technique was safe (Berg et al. 1974). These concerns eventually led to the 1975 Asilomar Conference, where one hundred scientists gathered to discuss the safety of manipulating DNA from different species, resulting in NIH's “Guidelines for Research Involving Recombinant DNA Molecules” (Fredrickson 1977). Also in 1975 Edwin Southern developed his “Southern Blot Technique” for identifying DNA fragments (Southern 1975). Two years later, Allan Maxam and Walter Gilbert, and Frederick Sanger working independently, developed techniques for sequencing DNA methods (Sanger, Nicklen, Coulson 1977; Maxam and Gilbert 1977). Fred Sanger's group subsequently applied that knowledge to deliver the first sequence of the complete 5,368 base-pairs (bp) of the bacteriophage  $\phi$ X174 genome (Sanger et al. 1977).

Major breakthroughs between 1978 and 1988 included engineering of human insulin production via

*E. coli* using recombinant DNA technology, development of the “polymerase chain reaction” technique for exponentially multiplying DNA sequences in vitro, and sequencing of human mitochondrial DNA (16,569 bp) in 1981 and the Lambda phage (48,502 bp) a year later. With such breakthroughs in molecular biology, in 1985 the associate director for Health and Environmental Research at the Department of Energy (DoE), Charles DeLisi—founder of the National Institutes of Health's Section on Theoretical Immunology and former Theoretical Division staff scientist at Los Alamos National Laboratory—began formulating a possible project of unprecedented scale in biology: sequencing the entire human genome. Funding was successfully included in President Ronald Reagan's 1987 budget.

A year later, the National Institutes of Health established the Office of Human Genome Research, subsequently renamed National Center for Human Genome Research. Following DeLisi's policy of reserving budget at DoE for the study of ethical implications, director James Watson pledged to Congress that 5 percent of the fifteen-year, proposed \$3 billion project would be dedicated to exploring “ethical, legal, and social implications” of genomic research, a commitment crucial for garnering overall political support before launching the HGP.

The HGP began in 1989 with the primary goal of first compiling all linked DNA bp sequences (guanine-cytosine, adenine-thymine) of the exemplar genome and then mapping them physically and functionally to specific chromosomes. With three billion units of genetic information sequenced, identifying genetic factors in disease and health would follow, with attendant ethical issues, especially concerning variants that increase risk for highly prevalent diseases such as cancer, heart disease, and diabetes but also for rare disorders, with the ultimate goal of advancing treatment for the full range of human disease. The HGP was officially launched in 1990 by the DoE and National Institutes of Health, employing a “map-first, sequence later” approach involving an international consortium comprising geneticists in the United States, United Kingdom, France, Australia, and Japan, with numerous other scientific relationships worldwide.

The project was well on course until 1992, when James Watson and Craig Venter clashed, opening a legal-ethical-commercial chasm ultimately resolved only by the US Supreme Court in 2013. The differences involved whether to patent functional DNA sequences (“expressed sequence tags”). Venter advocated patenting, and Watson opposed it. As a result of this schism, Venter founded the Institute for Genome Research to commercially exploit gene identification and promote drug discovery, apparently abandoning the global scope of the HGP.

By 1995 the Institute for Genome Research succeeded in sequencing the first whole organism (the bacterium *Haemophilus influenzae*). The following year, Stanford's Patrick Brown presented a “gene chip” containing 6,275 different gene-specific sequences of the 12 millions of base pairs (Mb) in size *Saccharomyces cerevisiae* yeast genome (Goffeau et al. 1996). Between 1996 and 1999 to the list were added a small soil nematode, *Caenorhabditis elegans* (97 Mb); the fruit fly *Drosophila*

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*melanogaster* (175 Mb); *Arabidopsis thaliana*, a small flowering plant widely serving as a model organism in plant biology and genetics (135 Mb); and the pathogenic bacterium causing tuberculosis, *Mycobacterium tuberculosis* (4.4 Mb).

Then, in May 1998, Venter formed a company, Celera Genomics (a name deriving from the Latin

word for “to make haste”), announcing his intention to sequence the entire human genome within three years using his mapless “whole-genome shotgun” approach. This spurred the National Institutes of Health to change strategy midstream and accelerate the public effort. Competition proved beneficial, in a rare moment when “big science” moved with efficiency and purpose (Hood and Rowen 2013).

In December 1999 the HGP was first in completely sequencing a human chromosome, number 22, releasing it to public databases worldwide. Also in 1999 the United Kingdom's Wellcome Trust established a pharmaceutical consortium to identify and map 300,000 common single-nucleotide polymorphisms—variants in a single nucleotide between members of a species or between paired chromosomes in an individual—in coding (gene) and noncoding regions of the human genome as well as their structural relationship to RNA functions.

On June 26, 2000, leading HGP researchers gathered at the White House, among them, Eric Lander (Whitehead Institute), Richard Gibbs (Baylor College of Medicine), Robert Waterston and Richard Wilson (Washington University), Francis Collins (National Human Genome Research Institute), Craig Venter, and DoE's Ari Patrinos, who was instrumental in resolving the hostilities between the public and private sector efforts to create a working collaboration. President Bill Clinton announced completion of an 85 percent working draft of the human genome, heralding “cracking of the genetic code” as a landmark moment and further predicting that “genome science will have a real impact on all our lives and even more on the lives of our children. It will revolutionize the diagnosis, prevention, and treatment of most, if not all, human diseases” (White House 2000).

The HGP draft sequence appeared in February 2001 in both *Nature* and *Science*. Then, on April 14, 2003, the HGP announced the complete sequencing of the reference human genome, officially ending the project two years ahead of projections. In 2004 an assessment indicated that over 92 percent of samples exceeded 99.9 percent accuracy. HGP researchers from the International Human Genome Sequencing Consortium announced that 20,000-25,000 genes were in the human genome compared with the 30,000-40,000 predicted. Agreement on a precise number will take many years.

## **THE HUMAN GENOME PROJECT: THE BIOETHICS IMPACT**

Perhaps the most remarkable thing about the HGP is that it demonstrated explicitly how the needs of biology can lead to transformational new technologies that, in turn, can revolutionize the field and catalyze the emergence of dramatically different aspects of science in general. The biologist Leroy Hood, a key player in the HGP and inventor of four pioneering instruments in molecular biology—including the automated DNA and protein sequencers and synthesizers—cites the “democratization of genes, that is, made all genes accessible to all biologists” as foremost among accomplishments revolutionizing both biology and medicine (Hood 2011, 47). In providing scientists with a publicly accessible reference genome for research, the thirteen-year \$3.8 billion, three billion DNA bp sequencing represents the largest single undertaking in the history of biological science and a signature scientific achievement.

The HGP was also the first federally funded project that dedicated approximately 5 percent of its

annual budget as a set-aside to support multiple external efforts to examine the ethical, legal, and social implications of humankind's producing and possessing this new scientific information (Juengst 1991). The federal Ethical, Legal, and Social Implications (ELSI) Research Program is primarily a grant-funding initiative administered by the National Institutes of Health and the DoE. Its investigator-centered research program is chiefly organized into four critical areas: (1) privacy of genetic information; (2) safe and effective introduction of genetic information in the clinical setting; (3) fairness in the use of genetic information by third parties, including insurance providers, researchers, and employers; and (4) professional and public education involved in educating, informing, and counseling individuals about genetic test results (Fowler and Garland 1999). The HGP is arguably one of the single most influential investments to have been made in modern science. That is, for every \$1 of federal HGP expenditure, \$209 was calculated to have been generated in the economy (\$796 billion) and, in the process, created some 310,000 direct and indirect jobs in 2010 alone and launched the "genomic revolution" (Tripp and Grueber 2011, 14–15).

## THE HUMAN GENOME PROJECT AND PUBLIC HEALTH

In April of 2005, an international expert workshop convened in Bellagio, Italy, settled on the term *public health genomics* to address the challenges of using genome-based research to benefit population health, an effort combining knowledge from genetic and molecular science tempered with insights from population sciences, humanities, and social sciences (Burke et al. 2006). Using tools

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from the information sciences, genomics systematically studies and develops genetic information involving hundreds to thousands of genetic interactions simultaneously in order to better understand the function and structure of the genome, including root causes of disease and ways in which the human organism works in interaction with environmental factors. Public health genomics seeks to understand genetic factors that contribute to individual and group variation of disease risk to translate that knowledge into actions reflected in the core functions of public health and clinical medicine in three key areas: (1) prenatal and newborn screening; (2) genetic testing and privacy; and (3) genome sequencing and personalized medicine, including the intergenerational impact of environment-genomic interactions, described by the emerging field of "epigenetics" (Thornburg et al. 2010).

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### Prenatal and Newborn Screening

Genome sequencing will accelerate the generation of ethical and policy issues concerning prenatal and newborn screening within and outside institutional walls. Specific areas of concern include prenatal testing, preimplantation genetic diagnosis (PID), newborn screening, as well as the locus of testing, institutional control, and regulation given the expansion of direct-to-consumer (DTC) testing.

**Prenatal Testing.** Noninvasive prenatal genetic diagnosis tests are likely to become commercially available by 2018. When they do, estimates predict that the number of fetal genetic tests in the United States will jump from 100,000 to about three million annually. With noninvasive prenatal genetic diagnosis comes the technical ability to analyze thousands of genetic markers with as little as 10 milliliters of the mother's blood. Beyond eliminational assumptions of prenatal screening under

cost-effectiveness rubrics—and the numerous ethical issues raised by the technology (Benn and Chapman 2009)—therapeutic discourse is transitioning from prenatal genomic diagnosis to fetal personalized medicine (Bianchi 2012).

***Preimplantation Genetic Diagnosis.*** For many years, in the context of in vitro fertilization, parents have accepted preimplantation genetic diagnosis to screen embryos for genes certain to cause severe and largely untreatable childhood diseases. Eggs extracted from the mother are fertilized with the father's sperm in a petri dish. When the resulting embryos are three days old, doctors remove a single cell from each to analyze its DNA. Only embryos without the associated variation are considered candidates to implant in the mother's uterus. The others are discarded (Sermon et al. 2004). With the goal of preventing genetic disease in children altogether, the California biotech company Counsyl (Srinivassan et al. 2010) tests the saliva of prospective parents for over 100 Mendelian diseases across all major population groups. How or whether couples who test positive as carriers will use this information to lower or avoid disease risk in their progeny uncertain, but preimplantation genetic diagnosis is clearly one option toward increased control, along with prenatal testing, or use of “donor” gametes after identification of a deleterious allele in the genetic profile of prospective parents.

***Newborn Screening.*** Residual blood spots from newborn screening are a potential source of specimens for population and individualized studies. Guthrie cards (filter paper collection kits) have been used for decades to collect blood in newborn screening programs in the United States, Australia, New Zealand, Japan, and most European and South American countries. This genetic information is valuable for examining risk factors for disease and to potentially diagnose diseases before conditions manifest (Bodurtha and Strauss 2012).

Numerous studies, however, reveal insufficient guidance for health departments and argue for policy recommendations for storage and use of blood spots to help programs address the rights of families and promote potential social goods generated through public health research. State health department newborn screening requirements have occasioned divergent court decisions and legislative remedies on blood-spot retention after initial reporting periods. If retained, blood spots could provide statewide baselines for future genomic research. In such contexts it is difficult to determine what constitutes informed consent. Additional legal and administrative firewalls have been established between health departments and other state functions, such as criminal apprehension, for which at-ready DNA identification of all locally born citizens also has obvious attractions in the context of investigations (Kharaboyan et al. 2004).

## **Genetic Testing and Privacy**

Of all our natural rights, few are guarded more zealously than personal privacy, especially in matters of health. Yet as medical technology advances and public health costs demand action, the boundary between privacy rights and the “common good” is increasingly strained. Genomics—the study of genes and their functional roles in health and disease—offers enormous potential for bettering public health, improving treatment, informing social support, and reducing costs. These are worthy ends, but they require screening a significant number of individuals for predisposition to disease. Similar issues arise in the context of biobanks in which tissues are stored for future research and reference. The confluence of new technologies for data generation and information access, including generally accessible databases—given the desire of the public to benefit from these advances—and the desire of

the public to benefit from these advances pose significant challenges for ensuring the full societal benefits of biomedical research while respecting both individual interests and the communal good (Rodriguez et al. 2013). Many people are afraid to undergo genetic testing, fearing that the results may make it harder for them to get or keep a job or health insurance. After a decade of effort, the Genetic Information Nondiscrimination Act (GINA) was passed in 2008. The act prohibits prospective employment discrimination and forbids insurance companies to use genetic information to deny benefits or raise individual policy premiums (Steck and Eggert 2011).

**Direct-to-Consumer Genetic Testing.** Scores of companies, primarily in the United States and Europe, offer genome-scanning services directly to the public. The proliferation of these services demonstrates a public appetite for such information and may indicate where the future of genomics is headed (Nordgren and Juengst 2009). The availability of these services also demonstrates the need for serious discussion about the regulatory environment, subject patient privacy, and other policy implications of direct-to-consumer genetic testing. Just as questions arise about ease of access to information with respect to one's own DNA, accelerating genetic research has raised questions about the responsibility of researchers to inform individuals about how their DNA may be used in research and what information it may divulge in general (Gutmann and Wagner 2013).

## Genome Sequencing and Personalized Medicine

The term *P4 medicine* (“predictive,” “preventive,” “personalized,” “participatory”) was coined by the biologist Leroy Hood, a key player in the HGP. The premise of P4 medicine is that biotechnology will soon revolutionize medical practice toward managing a person's overall health and not just diseases, using more sophisticated and innovative measurements of health based on an individual's genotype. The end will be truly personalized treatments.

In terms of *prediction*, technologies and tools of “systems biology”—a holistic, interdisciplinary field that focuses on complex interactions in biological systems (Burke and Trinidad 2011)—will provide medical practitioners with two exciting sources of health-related diagnostic data. An individual's complete genetic makeup will enable a physician to generate comprehensive predictions about health prospects, while protein and other markers will allow for determining health status, including the effects of any deleterious alleles or reactions to environmental toxins or infectious pathogens (Green and Guyer 2011). In the area of *prevention*, the new individualized genomic approach promises to individually predict the probability of contracting certain diseases and the ways in which an individual may respond to various treatments, thereby providing guidance for customizing therapeutic drugs, that is, personalized medicine (Tian et al. 2011).

On average, a human differs from another human by less than 1 percent in genetic makeup. Yet these differences, in interaction with the environment, contribute to health differences, including predisposition toward diseases. One's unique genetic makeup and a customized approach to treatment are at the heart of predictive, preventive, and personalized medicine (Juengst et al. 2012). Patients actively participate in choices affecting diagnosis, disease management, and well-being. *Participatory* medicine will require powerful new approaches for securely handling enormous amounts of personal information in “biobanks” (Gatter 2012) and to educate patients and their health care providers.

Achieving the goals of P4 medicine will be technologically daunting, considering the human genetic complexity that lies within the 20,000 or so disease-potential genes once, but no longer, thought to be “junk DNA.” The Encyclopedia of DNA Elements project (ENCODE 2012) aims to identify all functional elements in the human genome sequence. The pilot phase, focusing on 30 megabases (<1% of the genome), involved an international consortium of computational and laboratory-based scientists developing high-throughput approaches for detecting all sequence elements conferring biological function. The pilot results will guide future efforts to analyze the entire human genome (ENCODE 2012).

The potential for personalized medicine lies not in a single genome but in many. Before physicians can discern disease features specific to individuals, researchers need to catalogue the enormous range of genomic and phenotypic variation in human populations, highlighting ethical issues concerning representativeness. The focus of most companies is to look at the ten million most common differences (the single nucleotide polymorphisms, SNPs) in each of us (Lander 2011). In the early stages of the HGP it was thought that those polymorphisms would be at the root of common diseases. That is no longer considered to be true. Instead, it seems that rare differences, harder to identify and accessible only by “whole-exome sequencing”—the 1.7 percent of a human genome that corresponds to protein coding—hold the key to diseases that strike the broadest span of people, among them, heart disease, diabetes, and various cancers (McCarthy 2012). These differences may help identify less common diseases as well (Ng et al. 2010).

**Whole Genome Sequencing.** Whole genome sequencing determines the complete DNA sequence of an organism's genome at a single time, including an organism's chromosomal and mitochondrial DNA

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and, for plants, the chloroplast (Drmanac 2012). In 2000, when President Bill Clinton signaled the completion of the HGP, sequencing a genome cost over \$3 billion. Ordering a personal genome sequence of three billion letters is rapidly approaching \$1,000 (Mardis 2010). The “\$1,000 genome” has long been considered an accessibility tipping point toward population and individual genomic knowledge essential for addressing such difficult questions as these: Which gene variants are associated with Alzheimer's or diabetes, heart disease, or cancers? Which drugs are available for treating various diseases and at what dosage? (Robertson 2003).

**Genomics and Cancer Research.** The Cancer Genome Atlas project attempts to systematically and comprehensively characterize genetic glitches in a long list of tumors in order to provide better information for prevention and cure as well as for other large-scale projects studying healthy and diseased cells. To date, cancer research appears furthest along, in part because cancer is thought to be a disease closely related to DNA. Gene tests are available to identify susceptibility to some types of inherited breast cancer (predicted by the *BRCA1* and *BRCA2* genes), blood cancers such as leukemia and lymphoma, and others (Cancer Genome Atlas Research Network 2008). Cancer diagnostics are heavily dependent upon understanding the relationship to human disease of the millions of genetic variants scattered throughout the human genome (1000 Genomes Project Consortium 2010).

An important ethical issue in the context of cancer and other systematic research projects is how to manage incidental findings in human subjects research—findings concerning individual research participants that have potential health or reproductive importance and are discovered in the course of



conducting research but are beyond the aims of the study. The American College of Medical Genetics and Genomics released the *ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing* (Green et al. 2013) at its 2013 Annual Clinical Genetics Meeting, it was recommended that patients who have their genomes sequenced should automatically be told of incidental genetic findings (Wolf 2012). This raised controversial issues of patient autonomy and distinctions between research and clinical contexts. Additionally, the recommendations contradict the position of the Universal Declaration on the Human Genome and Human Rights which supports a person's choice whether or not to know (UNESCO 1998).

**Genomic Medicine.** “I do think that (next generation) sequencing will be equal to imaging in medicine” (Pollack 2011). These words of Jonathan Rothberg, founder of “Ion Torrent,” a company which has developed a DNA sequencing system that directly translates chemical signals (A, C, G, T) into digital information, reflect a tendency toward maximal claims not uncommon early in emerging disciplines. Clearly, personalized and holistic health care will require knowing what works, knowing why and for whom it may work, and using that knowledge in patient care. Understanding individual genetic profiles will open up opportunities to individualize treatments and provide not only better quality but also better value in health care (Roach et al. 2010; Conti et al. 2010).

The US Department of Health and Human Services lists four overarching goals for personalized medicine: (1) finding relationships between genetics and disease that can be put into practice; (2) preventing insurers or employers from using genetic data to discriminate against individuals with predispositions to disease; (3) ensuring that genetic testing is accurate and useful; and (4) creating standards to enable data sharing. The gulf between genomic discovery and the promise of genomic medicine, however, is rife with ethical and social challenges (Juengst et al. 2012). In practice, information-sharing protections encourage individuals to undergo testing, while better data sharing improves scientific knowledge and speeds research break-throughs (McEwen et al. 2013).

## **THE HUMAN GENOME PROJECT AND HUMAN RIGHTS: GENOMICS FOR ALL?**

In asking how genomics—and discoveries of the HGP as of this writing—can be used to benefit all, it is sobering to consider how poorly and inequitably knowledge and tools have been used in the past. Genomics will certainly expand opportunities but will likely widen disparities, resulting both in astounding advances and astounding inequities.

“Health disparities” are differences in incidence, prevalence, mortality rates, and burdens of diseases and in adverse health conditions or outcomes between identifiable populations regionally, nationally, or globally (Fullerton, Knerr, Burke 2012). Disparities can affect populations according to gender, age, ethnicity, socioeconomic status, geography, sexual orientation, disability, or special health care needs, primarily among groups who persistently experience trauma, social disadvantage, or discrimination and systematically experience worse health or greater health risks than more advantaged social groups. “Disparity” in the context of public health has begun to imply injustice (Jones 2010).

The 1997 UNESCO Universal Declaration on the Human Genome and Human Rights (Harmon 2005)

declared in Article 1 that “the human genome underlies the fundamental unity of all members of the human family, as well as the recognition of their inherent dignity and diversity. In a symbolic sense, it is the heritage of humanity.” The preamble calls for “prohibition of all forms of discrimination based

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on genetic characteristics.” Further, Article 2 affirms the “imperative not to reduce individuals to their genetic characteristics.” Genomics focuses and deflects, allowing finer distinctions that cut across phenotypical and stereotypical classifications, for example, race.

Article 4 declares that “the human genome in its natural state shall not give rise to financial gains.” As the sequencing of the human genome has expanded the ability to test for genetic susceptibility to a broad spectrum of common and rare diseases, the discovery and identification of a functional gene itself was recognized as a patentable invention by the US Patent Office with respect to breast cancer-related genes. In a landmark decision on June 13, 2013, the US Supreme Court rendered a decision on the patents of the *BRCA1* and *BRCA2* mutations predisposing toward breast, ovarian, and uterine cancer held by the molecular diagnostic company Myriad Genetics.

Justice Clarence Thomas wrote the decision for a unanimous court. “Myriad did not create anything. To be sure, it found an important and useful gene, but separating that gene from its surrounding genetic material is not an act of invention” (Liptak 2013). With that decision it now becomes clear that human genes cannot be considered to be intellectual property, that is, DNA is now part of a “Public Commons” instead of being the subject of a patent (Moraia and Kaye 2013).

Article 5 of the Universal Declaration on the Human Genome and Human Rights states that individuals have a right “to decide whether or not to be informed of the results of genetic examination.” Article 7 holds that genetic information must be afforded confidentiality. Article 8 cites the right to compensation in case of breach of confidentiality. Article 12a states further that “benefits from advances in biology, genetics and medicine, concerning the human genome, shall be made available to all,” highlighting global disparities in light of broader threats to health and capacity. The intent of Article 12b to benefit “humankind as a whole” also queries the representativeness of referent genomes and the interest of genetically related communities in their genome. The 2007 UN Declaration on the Rights of Indigenous Peoples includes, in Article 31, “human and genetic resources” under right to “maintain, control, protect and develop.”

Article 15 of the Universal Declaration strikingly breaks the spell of beneficent assumption, stating that scientists “should seek to ensure that research results are not used for non-peaceful purposes.” A background paper for the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction notes “dissemination of knowledge and applications in fields such as genomics means that improvement of biological weapon agents by genetic alteration to enhance properties such as survival, antibiotic resistance, and ability to overcome particular prophylaxis or detection methods, could now be attempted in an increasingly wide range of countries” (Secretariat 2001, 3). The document's technical Annex discusses genomics and proteonomics, bioinformatics, the HGP and human diversity, gene therapy, and virulence and pathogenicity.

This discussion presciently raises the ethics of publication and dissemination. The 2005 artificial reconstruction of the 1918 influenza virus by Centers for Disease Control scientists took place in a

high-containment, Biosafety Level 3 lab with associated manuscripts reviewed by the National Science Advisory Board for Biosecurity. The increasing capabilities of do-it-yourself biology operating outside traditional institutional contexts, with pride of independently achieving significant (functioning) results using reengineered or repurposed technology, have been significant enough to elicit Federal Bureau of Investigation outreach. Besides quasi-anarchical impulses, the intersection of genomics policy and intentionally destructive uses by state or nonstate actors or individuals will likely grow in prominence.

A 2001 UN secretary general's report on Human Rights and Bioethics (United Nations General Assembly 2001) stressed the importance of collaboratively working out application of human rights norms to genomics, giving a particular role to the World Health Organization with respect to the ethical, legal, and social issues of developing countries and related impacts of intellectual property issues in genomics (Séguin et al. 2008). Within a decade many members of relatively affluent nonmarginal populations in the developed world may carry their own genetic code around on a small card to every physician visit. The hope is for a new world of prevention, with each person able to obtain genomically informed care toward being as healthy as possible. The individual use of science to improve one's own health may well blossom. Conversely, it will be much more difficult to apply genomic knowledge for the benefit of everyone. Much time is spent thinking about possible errors—primarily errors of commission. Yet historically, the greatest harm has been through errors of omission: things not done, science not applied, vaccines not given, medications not available given their cost, and water supplies not treated, to name but a few.

In spite of the many calls for “public dialogue” (e.g., Fahey and Nisbet 2013), a striking feature of the history of genetic engineering and biomedical biotechnology, especially in the United States, is the extent to which the genome science policy process has remained largely impervious to the fears, hopes, and concerns of the public to which it is in theory ultimately accountable. Consequently, strategies to integrate prudential social values into the science/public policy-making process remain

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controversial, at best, and inadequate in the extreme, calling for a model for implementing a shift from monologue to substantive public dialogue (Fowler and Allison 2008).

There will always be dilemmas about how to use the tools and power of genomics, but among the greatest will be the equity gap—the failure to use science for the poor, the foreign, the unnoticed and disenfranchised. Tools and infrastructure must be clearly identified and made functionally affordable also within the context of the developing world. If done correctly—and ethically—available technologies can harness the basic tools of genomics not only for the benefit of the rich and powerful but also to provide the poorest people a better chance of optimal health.

As more diverse genomes are sequenced, the molecular data will provide considerable evidence on the genetic similarities and dissimilarities between humans, other primates, and all living things. As the scientific, ethical, legal, social implications of the HGP continue to unfold, will that knowledge change how we view and value ourselves as persons? Can we maintain our individuality and privacy, avoid genetic discrimination, and value diversity? Will we care for persons for whom treatments and cures are still elusive? Can we work to assure the benefits of the HGP are accessible to everyone? The end of the HGP is becoming just the beginning (Bouma 2000). In that context, the words of Leon

Kass, former Chairman of the President's Council on Bioethics (2001–2005), are instructive:

Our hope can only lie in education: in a public educated about the meanings and limits of science and enlightened in its use of technology; in scientists better educated to understand the relationships between science and technology on the one hand and ethics and policy on the other; in human beings who are as wise in the latter as they are clever in the former. (Kass 1985, 42)

**SEE ALSO** *DNA Identification ; Genetic Citizenship ; Genetic Discrimination ; Genetic Testing and Screening ; Genetics and Human Behavior ; Human Genome Analysis/Return of Results ; Human Genome Diversity Project ; Human Rights ; Patenting Organisms and Basic Research ; Personalized Medicine ; Pharmacogenomics ; Privacy in Health Care ; Whole Genome Sequencing*

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