Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Introduction

Genomics is the study of structure and function of deoxyribonucleic acids (DNA) within the gene and genome contexts. It is a branch of genetics, but is less focused on downstream products – studied as proteomics – or correlation to specific heredity traits, as in clinical genetics. It uses Genome-Wide Association Studies (GWAS) and Whole-Genome Sequencing (WGS) approaches to investigate how molecular structure, haplotype variation, and gene–environment complexity affect genotypes and phenotypes, and invokes other life science system studies and -omics. GWAS captures a population-wide picture of health, looking to locate patterns across multiple genes and many people. Thus, genomics refocuses from individual diagnostic and allied services, to initiatives for identifying opportunities to improve health and transform health-care across populations (Church, 2006). Genomic medicine is quantitatively different from genetics, using variants as markers for diagnosis, prognosis, and prevention, as well as targets for treatment. These variants are segregated into non-Mendelian as well as Mendelian patterns, and integrated with the evidence base for gene–environment interactions. Public Health Genomics extends these studies into population-wide variations and their impact on evidence-based policy, health systems, and health delivery and resources. The concurrent sequencing technology developments and large-scale generation of population data uses informatics to collect, store, and analyze genetic combinations, patterns, and networks.

The Human Genome Project (HGP), a landmark in genomics, was an international consortium effort to map the entire human genome. Started in 1990 and completed in 2003, the publication of the human reference genome heralded ‘The Genomic Era’ (Collins et al., 2003), characterized by high-throughput sequencing, high-resolution data, and large-scale bioinformatics. The HGP milestone was significant in the development of efficacious and economical sequencing tools available to researchers, lending to further studies of the population variants within the exome. On completion of the HGP, the future of genomics was set out as three grand challenges (Collins et al. 2003):

1. Genomics to biology: Elucidating the structure and function of genomes.
2. Genomics to health: Translating genome-based knowledge into health benefits.
3. Genomics to society: Promoting the use of genomics to maximize benefits and minimize harms.

Many of these challenges are already being met though the application of everyday sequencing that is efficient, accurate, and analytical. A human genome can be sequenced (with errors) in about 24 hours for what is now less than US $5000. The goal is for genomic sequencing to be accessible for under US $1000, but for clinical purposes, this would have to be at an extremely low error rate, and be comprehensive of relevant variations among genes, exomes, and haplotypes. In terms of public health, the implications of genomics are substantial: extending pre- and neonatal screening to predispositions and susceptibilities in complex disorders; transforming health-care service organization and delivery through creation of vast amounts of data, simultaneously requiring complex systems for storage, access, and analytics; and creating new paradigms for population health care through prevention and treatment. Genomics is driving concurrent IT technologies, commercial and public biobanking initiatives, open access databases like the 1000 Genomes Project (see Relevant Websites listed at the end of the article), and commercial personalized medicine. All of these are contributing to the context of ‘Big Data’: data acquisition and use at a scale that allows new insights or creates new forms of value. The application of genomics to many areas of public health is expanding, such as the study of emerging infectious diseases and how they spread and evolve, to inform future pandemic planning.

These technology advances have significant ethical, legal, and social implications (ELSI) – ELSI was built into the HGP as a parallel and integral research program to anticipate, identify, and develop strategies in respect to the creation and implementation of the vast data sets and information that would be generated. These implications have expanded from the significance to the individual – in terms of concepts like consent and privacy – to the societal impacts of the governance genomic infrastructure, and the use and accessibility of technology in health systems.

The ELSI of Genomics

The Committee to Evaluate the ELSI Program of the Human Genome Project was appointed in 1996 to assess the issues raised by and as a consequence of the HGP, and, in the longer term, raised more generally by research involving human genetics. What followed was a dynamic period of public debate, scholarly work, policy making, and the enactment of national legislation, such as the Genetic Information Nondiscrimination Act (2008) in the United States. The ELSI initiative soon became an applied bioethics approach, concerned with new developments in the diagnosis and treatment of human disease and possibilities for reproductive choice. It became characterized by its ethical, legal, and social scrutiny of the implications of emergent technologies, active outreach to constituencies involved in the development and use of them, and making these issues relevant to policy makers and accessible to publics. In particular, ELSI focused on the design and conduct of genomic research in respect to the production, analysis, and sharing of individual genomic information, the rapid advances in genomic technologies and the availability of increasing amounts of genomic information to affect health care, and the development of new paradigms and regulatory approaches in clinical medicine and public health. In Europe, the ethical, legal, and social aspects, or ELSA, of science has
strengthened contributions from the fields of philosophy, science and technology studies, and sociology in respect to genomic technology governance.

Since the HGP, there have been further consortiums developed, such as the International HapMap Project – a catalog of common genetic variants (see Relevant Websites) – and concurrently, efforts to extend the analysis of the implication of genomics for society. For example, launched in 2012, ELSI 2.0 would catalyze an international ‘collaboratory’ in ethics, science, and policy, and analyze the grand challenges of genomics though a global initiative to develop digital tools, protocols, and infrastructure (Kaye et al., 2012). The Human Genome Organization’s (HUGO) Committee on Ethics, Law and Society has published a number of statements, including proposing a ‘benefit-sharing’ model in respect to the common humanity of the human genome (HUGO, 2000).

**The Impact of Genomic Medicine in Public Health**

Next generation high-throughput and comprehensive sequencing technologies will become an integral feature of future clinical decision making. Genomic sequencing, like targeted genetic tests, may be carried out at the individual level. In clinical medicine, genetic tests are available for a handful of gene or chromosomal variants known to cause or associated with particular diseases; these tests can be highly predictive of penetrance and carrier status. Clinical genomic sequencing raises challenges that, while not unique, are different in scope.

First, the systematic sequencing of an entire genome with clinical correlates, in addition to revealing specific genes, will involve multilevel analysis of complex but more common disorders, such as the variants that indicate probabilities, rather than diagnosis, for multifactorial diseases like Type II diabetes and heart disease. Clinical genomic correlations to common disorders are an evaluation of susceptibility and predisposition; these often create open-ended diagnoses that are different from currently used genetic tests. In these cases, prognosis will be uncertain, treatments for a pathophysiological state might not be available, and often lifestyle changes might be a way of managing or avoiding the onset of etiology.

Secondly, gene discoveries are going to be likely that are not normally tested for, based on informed counseling. These incidental or nontarget findings might be unwanted or unexpected, such as the presence of carrier gene, a presymptomatic allele that lacks effective treatment, or nonmedical information (such as paternity), and therefore, ways to manage these and counsel the patient should be anticipated.

Thirdly, sequencing of an entire genome will reveal many findings potentially ‘all at once,’ and that data might be used across one’s life span. The genome sequence can be queried repeatedly as novel genes are implicated in diseases, new gene targets are identified, and clinically useful diagnostics become possible. Instead of needing a test each time, this might be a once in a life time reading with the clinical information laid out in full (all the information is published in one go as a list of conditions, diseases, predisposition, and risks), or it might be designed for ad hoc inquiries – the physician can go back to the sequences database and submit a query based on present clinical presentation. The data can be installed within a personalized genome chip (carried on one’s person such as an identity document or passport), or located in health repositories covering many people that can be readily accessed.

The challenge would be a model that is cost effective at a population level – systems might permit multifactorial analysis of many markers simultaneously given as a ‘profile’; or access would be requested when indicated, that is, on presentation of symptoms, the physician can call up the relevant information, and would take advantage of IT developments to provide expedient health communications to patients (see section Big Data).

Fourthly, communicating health implications will remain complex, involving interpreting risk, environmental factors, and predictive etiology of the disease progression. This has two implications: one, understanding how postnatal and adult exposure to agents will affect gene expression – so that whether, in fact, some traits are reversible or malleable. Two, whether population-based studies risk underestimating the potential importance of particular development events on individuals. Individuals will experience exposure to environment and other factors in different ways, and these will be difficult to meaningfully measure as part of public health. Assumptions and generalizations may skew how public health reacts to population events, which are different from how the same event impacts on the individual. However, while many of the ethical issues are similar to clinical genetics in this regard, there continue to be shortcomings in clinical education in genomics, uneasiness in interpreting clinical correlates to patients, and a lack of infrastructure to support sequencing, data storage, and access.

Genomic medicine is largely interpretive. Lifestyle and the environment have clinical correlates in the genome, and these effects, in respect to health, will be factors in treatment options and outcomes. That means that lifestyle choices and environments will become more important targets for policies of prevention and health promotion, and therefore will be highly relevant to public health because of the scaling up of individual health susceptibilities and the effects of population-wide social determinants of health. This ignites interest in large-scale population resources, such as biobanks, that meet the demand for information resources adapted for clinical queries, and novel drugs (and other technological interventions) for targeting genomic polymorphisms. The Centres for Disease Control and Prevention Office of Public Health Genomics maintain an online database of genomic tests with the potential to impact on public health called Genomic Applications in Practice and Prevention (GAPP; see Relevant Websites). It includes genomic targets for treatment, risk prediction, prognosis subtyping, and diagnostic aids for clinical use.

In respect to the ethical implications in clinical medicine, population effects will be felt in reproductive health where genomics will create more opportunities for prospective parents. This raises questions with respect to the ‘broadband' screening and testing of embryos, fetuses, and neonates. For example, how many tests will be concurrently offered or simultaneously analyzed, and how these tests may be analogous to indirect screening offered in pregnancies, for instance, to recommend potential invasive testing. This further raises issues with respect to the options for parents and the knowledge of variants as correlating to perceptions of disabilities. Beyond this, WGS will reveal many potential targets for screening – this
raises questions about the expansion of registries of permitted diseases, previously based on the Wilson and Junger criteria (1968, see Further Reading), with each one implicating families and cultures, and also revealing further complex health information such as gene–gene and genome–environment interaction.

Public health applications also include the sequencing of pathogens (see following section) and cancer genomes, that allows for targeted treatments that are more effective and present with fewer side-effects for the individual, and which would scale up to stratified treatment of populations. A number of consortiums are mapping genomes in respect to specific disease variations. For example, the Cancer Genome Atlas (TCGA), a project of the National Cancer Institute set up in 2009, is compiling the genomes of 20 common cancers; in the United Kingdom, the Breast Cancer Somatic Genetics study is creating genomic profiles of 500 breast cancer cases (see Relevant Websites, listed at the end of the article).

**Ethical Implication in Public Health Genomics**

The translation of genome-based knowledge and technologies to improve population health will have significant implications for health systems, impacting on the delivery of health care to populations. Genomic’s clinical utility will depend in part on developing analytics to read, expediently and error-free, vast and complex genotypes. This will be done at different stages, from embryos prior to implantation, through to prenatal and neonatal screening and diagnostics, and upon clinical presentation. It will require investment in data storage systems to handle the large amounts of information, and algorithms that can simultaneously process, synthesize, and interpret the interacting biological and environmental variables to create statistical associations between specific gene sequence patterns.

With the realization of genomic medicine, anxieties about the ELSI of genetics are likely to reemerge in the public discourse. In terms of public health genomics, organized efforts of social change have become allied to the positive reaction to environmental determinants of health, so that, in the sense that gene effects are often not deterministic, identification and functional characterization of concepts like risk and susceptibility are critical to predicting health outcomes. This has applications to pollution and toxicant exposure, population stratification (e.g., in respect to poverty, or drug use), and themes of wellness (healthy, or otherwise, lifestyles). The reemergence of genetic determinism (or essentialism), a feature of early genetics that explained all simple and complex behavior by way of genes, is less likely given acknowledgment of epigenetic and environmental effects known to occur throughout embryonic development and postnatal life. However, geneticization, “an ongoing process by which differences between individuals are reduced to their deoxyribonucleic acid (DNA) codes” (Lippman, 1991), may become more persuasive in medical practice and the ways that genomics shapes medicine, society, and culture. How genomics is engaged with in society might lead to counterproductive ways in which not just diagnosis, prognosis, and treatment, but also social and professional attitudes, are reflected in unpacking health determinants; especially with a concurrent shift from high penetrance tests to less that certain genomic contexts. For example, these kinds of prosaic attitudes may contribute to the increasing ‘medicalization’ of health, using the explanation of “genome for ...” to focus on illness as the result of genomic fate (that is unavoidable) and choice (that is blameworthy). When applied across a population, some of these perhaps imperceptible medico-social changes may have significant implications for public health efforts, such as in health expenditure and allocation, poverty alleviation, or environmental activism. One of the key ethical challenges will be providing an appropriate balance between preventing untimely translation of nonvalidated or potentially harmful technologies and practices, and losing sight of the benefits of genomic technologies if appropriately used (Burke et al., 2010).

**Personalized Genomics**

Personalized genomic medicine uses information about genes (and interactions), proteins, and environment to prevent, diagnose, and treat disease on an individual level. Knowledge of the gene variants potentially allows for more individually responsive and therefore effective clinical treatments; and might avoid unnecessary or hazardous health care, particularly to avert adverse drug reactions. Utilizing reliable variations will allow physicians to prescribe effectively – avoiding potentially ineffective and/or expensive medications – and allow individuals to make informed decisions about managing their lifestyle or to avoid potential environmental triggers.

Pharmacogenomics, the study of how genes affect a person’s response to drugs, may be used to stratify populations according to recommended treatments. For example, Herceptin, a therapeutic antibody that was designed for treatment of metastatic breast cancers, has been shown to be highly effective for those tumors which are HER2-positive (having copies of the HER2 gene), but ineffective for those that are negative for the gene (Ross et al., 2009). This approach might be expanded to screening populations effected by specific cancers for better targeted (and less harmful), and more economical drug management. An example of populations stratification was the use of Isosorbide and hydralazine in a fixed-dose combination (BiDiil), but which provoked controversy when approved by the Food and Drug Administration as the first drug marketed for a single group, African Americans, in the treatment of congestive heart failure (Brodry and Hunt, 2006).

Many cultures, groups, and relationships are characterized by ancestry; sometimes, they are only related by social backgrounds or cultural associations. In addition to the observable customs and traditions a community shares, certain traits may permeate through generations that are not always isolated to close hereditary relations: one’s ancestry or certain social identity will imply certain rights and obligations, and knowledge of genomics may break such hereditary lineages. Close-knit communities may be weary of debunking such hereditary beliefs, and moreover, may object to certain kinds of research – particularly that which delves into traits and behavior with significant social repercussions (Mello and Wolf, 2010). However, while it is also clear that genes predispose some kinds of identity, beyond that are the important family bonds that develop through close relationships such as...
partnerships, friendship, and adoption. In these cases, the stresses (and challenges) that heredity and social bonds are uniformly subjected to are equally likely to offer an explanation of many shared social values, behavioral characteristics, or health traits. When misused and perpetuated, genomic characterizations merely keep alive prejudice or serve as an excuse to do nothing about existing social inequalities.

The current model for personalized medicine has largely been developed as direct-to-consumer products, combining commercial enterprise with clinical care provision. The model has been challenged in respect to opaque protocols for consent and data management, concerns related to interpretation of test results, and absence of, or inappropriate systems for disclosure of clinical results to customers. For example, an investigation by the US Government Accountability Office concluded that test results were often "misleading, and of little or no practical use" (GAO, 2010). The industry has been accused of offering medical advice without appropriate clinical licenses, because they often operate outside of medical regulatory oversight. In particular, it was a concern that consumers had no access to genetic counseling after utilizing these commercial services.

The future of personalized genomic medicine is bound by the current limits of the speed and cost of mapping a single genome that makes clinical use preclusive. Given quick, accurate, and relatively affordable sequencing becoming a reality, personalized medical data may be merged with public data systems for the purposes of public health planning (environmental and pathogen surveillance; disease response), and research alluding to population stratification in respect to medications. Many of the strategies to care just mentioned face logistic challenges in obtaining suitable genomic information in a timely enough fashion to guide diagnosis and prescriptions (including drug and lifestyle modification), and delivering it broadly enough to cover populations. Placing genomic information in an electronic medical record (covering all citizens) would facilitate this kind of personalized medicine. If the patient's entire genome were part of his or her medical record, then the complexities of acquiring a DNA sample, shipping it to a sequencing laboratory and waiting for the readout would be replaced by an electronic query. That data inquiry would still need clinical interpretation. However, the safeguards necessary to maintain the integrity of the model include challenges to access and control of the data medium or repository, the accuracy and long-term stability of the data, and clinical rigor in analysis and interpretation. It is likely that a number of ongoing debates about the application of clinical genetics will reemerge, such as the conceptual targets of screening – where there is a predisposition or risk of a trait – to the application of direct tests for a haplo- or phenotype. Currently, clinical genetics is offered to patients who receive pre- and post-test genetic counseling. Clinical genomics would likely require a substantial infrastructure review to provide this coverage for populations, with access to not just offered to clinical staff, but also those utilizing commercial genomic sequencing. A large burden for interpreting these sequences would likely fall to primary physicians; expanding their repertoire from routine laboratory tests, to the real time scrutiny of a patients' electronic health and genomic records. A report by the UK Human Genomics Strategy Group included recommendations for improved genomics training for health-care professionals and changes to medical education to meet some of these future needs (Human Genomics Strategy Group, 2012).

Big Data

The number of variations, across all the possible sequenced genomes, is going to be in the tens of millions, raising the significant issues of 'Big Data.' The Big Data concept concerns data of a large size, typically to the extent that its manipulation and management present significant logistical challenges, that signifies "... things one can do at a large scale that cannot be done at a smaller one, to extract new insights or create new forms of value" (Mayer-Schönberger and Cukier, 2013). Big Data has become a key component in crime control, social engineering, and disease prediction (infectious disease emergence and spread). Genomics, therefore, is a version of Big Data in its perspective size and application; and, just like other sources of Big Data, it has become a driver of health information investment. Big Data has been associated with a culture of 'open access,' 'open consent,' and 'information altruism.' The opportunity for collecting vast amounts of information about people embraces genomes and medical records as part of the vast networks of cameras and drones, personal tracking (e.g., face recognition software, transport cards, credit cards, and library cards), mapping of habits (purchases, holidays, and interests), and information analytics (such as internet use). This all-encompassing data creation is raising questions about the ownership and use of information generated by not just population-wide health systems, but also diverse intelligence gathering and logistics sources. For example, in the United Kingdom the government's care.data initiative proposed the sale to research institutions, pharmaceutical corporations, and others of data from all visits to National Health Service clinicians. While this is seen by some as a resource to benefit all by collating vast data and making it available for researchers to mine, a UK report observed that, although "Business and government are united in their belief in the potential of 'Big Data' to drive economic growth, scientific innovation and service efficiency," there are a number of potentially less welcome implications for rights, such as privacy (Sciencewise, 2014).

For example, in the sale of health data, it is a concern that no patient explicitly agreed to this sharing (and implied intrusion); and, as such, these new commercial goals diverge from the original consent that was provided during the course of clinical care. This is sometimes compounded by barriers to opting out of such commercial enterprises. On the one hand, it is presupposed that collective interests in economic, social, or public health benefits justifiably override the principles that protect individuals, often captured by consent and privacy norms. On the other hand, as well as it being a violation of rights or a betrayal of the doctor–patient relationship, it has been argued that such assumptions, especially when there are links to commercialization, can diminish public support (Crichtley, 2008). A recent special edition of Science lamented the end of privacy because, along with changing attitudes to making one’s genetic sequences available to the public, it was experimentally confirmed that with some knowhow it is possible to identify persons in closed databases from open genealogy and internet searchers (Gymrek et al., 2013). These are significant challenges to traditional research and clinical
ethics. Big Data is enabled by emerging opportunities (genomics is but one of these), and the volunteers and unaware who provide the data (in this case, the participants of open data, and patients). This is creating novel questions of privacy, consent, participation, and the dynamics (and norms) of clinical relationships, within the networks of the Big Data collectors, users, and generators. This suggests that the more patient-specific information included in centralized databases – crucial to the long-term success of genomic medicine – the harder it will be to ensure patients’ anonymity.

A compelling case has yet to be made for Big Data’s contribution to public health research. There are still questions about the capacity to store and analyze the data usefully; problems of ‘theory free’ methods and statistical ‘gaming’, and the validity of inferences made from vast correlations. Although, it is also the case that the fuzziness of Big Data (among others, e.g., format inconsistencies and measurement artifacts) is the result of a representation of the messiness of reality, globalization of data, and rapid evolution of the technology. Google Flu, an attempt to predict influenza activity, was shown to be flawed in predicting the influenza pandemic of 2009, questioning its usefulness over national and global epidemiological surveillance networks. The growth and emphasis of creating Big Data is challenging ethics within information streams from linked studies, across computers, and around the globe. These concerns, however, should not detract from the useful tools that carefully constructed data sets can provide to health research.

**Biobanks**

Biobanks have been features of public health research for some time now. They are characterized by the data therein (health records and/or lifestyle information) and biological samples from various populations, and are designed to enable potentially vast clinical correlations. Biobank governance models control the kinds of access or uses of the data possible (Capps, 2013). In public health, this might affect how they are used in clinical or research contexts, which, in addition to genetics research, include cord blood banks, banks for storage of gametes and embryos for use in IVF, and stem cell banks.

Biobanks raise specific issues with respect to whether it is necessary for consent when data is appropriated for research purposes. The acquisition of data becomes more acute when located in centralized databases covering many thousands of people who may, or not, want to participate. For example, recently, deCODE Genetics, an Iceland-based company “…determined the sequence of the whole genomes of 2636 Icelanders and imputed the variants found into the rest of the population via over 104,000 genotyped individuals and the pedigrees of the Icelandic people” (Gudbjartsson et al., 2015). It was claimed that some genotypes, such as BRCA-predisposed breast cancer, could be inferred across the population. In an editorial that accompanied a special edition on the ‘Genomes of Icelanders,’ it was stated that the results could provide a strategy for the analysis of the genetic variation in any population and raises questions about how society should implement the knowledge gained (see Relevant Websites, at the end of the article). The deCODE example is contentious in this regard because, although it collected full DNA sequences from just a few thousand volunteers, it is possible to extrapolate genotypic features of all the other Icelanders, including those who never volunteered. This has been presented as a public health interest, because it is possible to detect these mutations in the volunteer population and infer the status of the rest of the population. So, for example, if information about the status of breast cancer e.g., (BRCA) genes is already known, it is now a question as to whether everyone affected should be told. The idea is that nonvolunteers might be compelled to know their status.

UK Biobank represents a different model for public health infrastructure. It was created to support “a diverse range of research intended to improve the provision, diagnosis and treatment of illness and the promotion of health throughout society” (see Relevant Websites, at the end of the article). The Governance Framework creates a mandate for public health by allowing access to any researcher who is willing to give up rights of exclusivity to the data they create as a result, and to provide these back to the Biobank and for other researchers to use. The Governance Framework primarily created conditions for access and use based on the biobank’s purpose for the public good. For example, the biobank would operate a stewardship model in which it “will retain ownership of its rights in the resource (so that it is available to all other approved researchers), while at the same time facilitating the development of clinical advances (e.g., diagnostics and treatments) arising from its use.” Additionally, the public good creates a sui generis obligation to honoring the conditions of the donors’ consent, which is widely construed to accommodate this public health mandate.

With the significant growth in biobanking, it is important to define how such resources can facilitate the responsible and effective translation of genome-based knowledge and technologies for the benefit of population health. One endeavor to this end is the Biobanks and Biomolecular Resources Research Infrastructure Consortium–European Research Infrastructure Consortium (BBMRI-ERIC; see Relevant Websites, at the end of the article), which was established as a pan-European research infrastructure for biobanks and biomolecular resources. Its primary goal is to initiate collaborations between biobanks and to enable the exchange of biological samples and data. In addition to establishing ELSI as a framework for cross-border exchanges of human biological resources and data attached for research uses, it also established the BBMRI-Large Prospective Cohort that includes consideration of WGS in respect to facilitating access to large prospective study sets on human health and disease.

**Benefit Sharing and Patents**

There are about 11,868 gene patents in force, with 5936 patents directed to humans. It is disputed how much of the human genome is already patented. In one paper, it was concluded that patents were claimed on 21–41% of human genes based on long (over 150 nucleotide) fragments, whereas for short fragments nonspecificity meant that 100% of human genes had some portion patented (Rosenfeld and Mason, 2013). At the outset of the HGP, it was proposed that the DNA sequence generated should be freely available to the public. This
principle was codified in the 1997 Bermuda Principles that called for rapid sharing without restrictions on use. However, isolated genomic sequences are still patentable in many jurisdictions often as long as the patent meets certain conditions. Patents are based on the outlay of research and the costs of bringing an invention to market. They are awarded based on general principles of novelty, technical progress, and creative effort (the inventive step), influence of prior patent applications on validity, and scope of description and claims. The interpretation of these principles will differ between jurisdictions. However, with respect to DNA, it is likely that the cost of identifying the function of a gene is a fraction of the cost of turning that into something useful. Making genomic data freely accessible would therefore allow researchers to focus on patenting the innovations that come from them. Nevertheless, gene patents have become central to many genomics companies’ strategies. On 13 June 2013, the US Supreme Court in Association for Molecular Pathology v. Myriad Genetics, Inc. held that a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated (a similar judgment was subsequently made in Australia in 2015). However, the US court did find that cDNA, synthetic DNA molecules that contain only exons, do involve an inventive step and thus remain patent eligible. It is not clear how the decision will affect the claims on other sequences and whether they are still valid. Before the Myriad decision, there were substantial concerns that in order to offer whole genome sequencing, clinical laboratories would have to pay royalties to a long list of gene patent holders.

The Human Genome Organization (HUGO) has taken the lead in advocating for ‘benefit sharing’ as a way to realize genomic opportunities. They elaborated:

A benefit is a good that contributes to the well-being of an individual and/or a given community … Thus, a benefit is not identical with profit in the monetary or economic sense. Determining a benefit depends on values, needs, priorities and cultural expectations … The HUGO Ethics Committee recommends … that all humanity share in, and have access to, the benefits of genetic research. HUGO (2000).

Benefit sharing suggests that genomic research must be preceded by engaging with communities, rather than allowing exclusive interests to run roughshod or become divisive. However, more often it is difficult to pronounce whether such arrangements potentially contribute to or perpetuate inequality.

As pointed out in the context of property in human cells and tissues, research exploitation often leads to one side’s rewards being grossly disproportional and with little fairness for opportunities (Dickenson, 2007). The balance sought by HUGO is not to deny rewards to the artiest of science, but to bring limits on those who brazenly trawl and ring fence the goods that make research possible. When biotech companies engage with research populations but secure disproportionate monopolies, they are accused of inequitable profiteering and exploitation. When they hunt in isolated regions of the world (or unique island populations) to clamber over valuable biodiversity, not just that of people, but fauna and flora too, they are criticized for their lack of respect for culture, tradition, and ecological sustainability; that they are taking (and profiteering from) something that they cannot – or at least should not – own. They are sometimes characterized as ‘bio-pirates,’ rather than ‘bio-prospectors.’ Thus, there are attempts to redress the balance by cultivating a sense of awe in a global genomic heritage, while simultaneously asserting, on behalf of all communities, their rights to be compensated in participating in fair agreements. This has been captured by the idea of genomic solidarity, as one of the pillars of ethical genomic research (along with benefit sharing). Solidarity recognizes the coextensive commitment to sharing expected health and economic benefits. Out of this comes the idea that the conditions of ethical genomics include the opportunities to taking part in research and divesting exclusions to the potential benefits of genomic initiatives. With equal expectations of participation and benefit, solidarity acknowledges and prizes collaborations, and encourages shared imagination in addressing health challenges.

Future of Public Health Genomics

Synthetic Biology and CRISPR

A new method called RNA-programmable CRISPR/Crispr-associated gene (Cas) editing (or CRISPR, which refers to the Clustered Regularly Interspersed Short Palindromic Repeats that are referenced by the system) promises to revolutionize genomics (Doudna and Charpentier, 2014). The technology is derived from the CRISPR system found in bacteria that, among other functions, is used to defend against viruses. The Cas enzyme neutralizes foreign DNA by snipping, and uses a CRISPR DNA sequence to know what and where to snip. CRISPR is like a personal reference collection for acquired resistance to viruses, which is added to each time the organism is infected. Utilizing the system allows researchers to precisely cut DNA at any location on the genome, enabling precise control gene expression by deleting and adding sequences. This can be coupled with systems to read the genetic code, and mechanisms to write synthetic functional code. It can be used to replace or augment genetically diseased tissues, and to insert new material to alter an organism’s function in situ. Uses so far include creating models of human disease in animals; or to introduce environmental tolerance, improve crop yield, and create resistance to pathogens in plants. It may be adapted to synthetic biology to allow natural organisms to be reprogrammed to have novel, useful functions such as making plastic, to treat wastewater, generate electricity, manufacture fuel, and fabricate new drugs. In addition to the basic science it enables, it might be used to target blood circulating parasites, viruses, or cancer genomes, for example. Most controversially, a study used CRISPR to genetically engineer a human embryo (Liang et al., 2015).

In terms of public health, CRISPR raises a number of scientific, ethical, and policy issues associated with gene editing. At the experimental level, the CRISPR technique is not infallible; there are problems of ‘off-target’ hits, where the method alters DNA at other (similar) sites elsewhere in the genome and not just the gene being targeted. This raises the prospect of environmental or population damage previously expressed as the spectre of Genomically Modified Organisms becoming established and being out of control in nature. However, if these
technicalities are solved (for example, mirroring the use of ‘terminator’ technology to ensure GMOs have a limited time in the wild) then CRISPR will be a prospectively powerful tool in the creation of artificial genomes, DNA artifacts, and (model) organisms. The tantalizing prospect is of correcting (editing) point mutations in the germline, gametes, embryos, and patient-derived tissues, which will impact on diseases with Mendelian – single gene – inheritance. CRISPR can also alter expression of multiple genes simultaneously, thus potentially offering an approach to more complex disorders. The study of genomes potentially leads to the dual use of such technologies, for example, to sequence the influenza virus and potentially introduce further threatening characteristics. Moreover, a concern for public health would be the access to the technology by DIY-biologists creating synthetic or modified organisms with potential or accidental pathogenic traits.

**Infectious Diseases**

Infectious diseases, including zoonotic Emerging Infectious Diseases, are a major health burden; often these diseases are unpredictable in patterns of emergence, transmission, and virulence, which is attributable in part to genetic variation. Genomics, or **genomic epidemiology**, promises to not only understand the mechanisms of pathogen exposure and infection, but also the human genetic variation in response to diseases, including susceptibilities and resistance. Additional uses include precise diagnosis of microbial infection, describing transmission patterns, understanding the genomics of emerging drug resistance, and identifying targets for new therapeutics and vaccines. Genomics offers a number of tools for the study of endemic pathogens, diagnostics and surveillance, and the development of new synthetic drugs active against resistant microbes. In respect to emerging infectious diseases, expedient ‘on-site’ sequencing can fingerprint pathogenic microbes to investigate their transmission and mutation within the community and/or from the environment, which might indicate impending pandemics, and thereby inform appropriate responses based on the character of the pathogen. Having sequencing systems in place, and response teams prepared to collect samples across the globe at a moment’s notice, would expedite the development and production of pharmaceutical countermeasures such as vaccines.

**Ecology Genomics**

The emergence of zoonotic pathogens – those that transmit between humans and animals – are not just an ecological risk, but also indicate the shared susceptibility between species to potential endemic and pandemic pathogens. Genomic studies will allude to the complexities of ecosystem interactions between all components of the biosphere. Increasingly, genomics will engage transdisciplinary studies, involving experts in clinical, epidemiological, anthropological, ecological, and veterinary fields, to identify risks and solutions. Many hosts are unaffected by pathogens that they harbor, and these pathogens often affect closely related species, such as human beings and Great Apes. Many endemic pathogens, such as HIV, originate in primates, and those such as Influenza and Coronaviruses like SARS and Middle East Respiratory Syndrome, have animal reservoirs and hosts. Genomic studies promise approaches to pandemic planning and response, such as mapping origins and susceptibilities thought the ecology.

Genomics also will impact on environmental, animal, and plant sciences. The same techniques as mentioned above will enable the creation of genetically modified organisms adapted to anthropocentric climate change, improved food sustainability, disease protection, and nutritional value, as well as to produce chemicals and drugs useful to human beings. The gene editing based on CRISPR promises novel organisms that are adapted to extreme environments or have novel functions such as water purification or pollution clean-up.

**Conclusion**

The clinical significance of public health genomics will grow as sequencing becomes possible with low error rates, using better analytical methods that signal which variants are clinically significant, and the development of technologies that allow long-term stability of data storage. For example, comprehensive analysis of the genome sequence of individual cancers has helped uncover the specific mutations that contribute to the malignant phenotype, identifying new targets for therapy, and increasing the opportunities for choosing the optimal treatment for each patient. The impact of cancer genomics across populations would be substantial. At present, it is likely that the infrastructure is not in place to support both the patient and the physicians who encounter the resultant data. Moreover, even the most promising technologies cannot fully realize their potential if the relevant policy, legal, and regulatory issues are not adequately addressed.

See also: Cancer Screening: Theory and Applications; Ethics of Infectious Disease Control; Ethics of Screening: Foundations in Public Health Ethics; Health Technology Assessment: Ethical, Legal and Social Issues; New Technologies: Ethics of Stem Cell Research.

**References**

Brody, H., Hunt, L., 2006. BDII: assessing a race-based pharmaceutical. Ann. Fam. Med. 4, 596–560.
Burke, W., Burton, H., Hall, A., Karmali, M., Khoury, M., Knoppers, B., Meslin, E., Stanley, F., Wright, C., Zimmern, R., Ickworth Group, 2010. Extending the reach of public health genomics: what should be the agenda for public health in an era of genome-based and “personalized” medicine. Genet. Med. 12, 785–791.
Capps, B., 2013. Defining variables of access to UK biobank: the public interest and the public good. Law Innov. Technol. 5, 113–139.
Church, G., 2006. Genomes for all. Sci. Am. 294, 46–54.
Collins, F., Green, E., Guttmacher, A., Guye, M., 2003. A vision for the future of genomics research. Nature 422, 835–847.
Crichtley, C., 2008. Public opinion and trust in scientists: the role of the research context, and the perceived motivation of stem cell researchers. Public Understand. Sci. 17, 309–327.
Dickens, D., 2007. Consent, commodification and benefit-sharing in genetic research. Dev. World Bioeth. 7, 109–124.
Doudna, J., Charpentier, E., 2014. Review: the new frontier of genome engineering with CRISPR-Cas9. Science 346. http://dx.doi.org/10.1126/science.1258896.
Government Accountability Office (GAO), 2010. Direct-to-Consumer Tests: Misleading Tests Results Are Further Complicated by Deceptive Marketing and Other Questionable Practices. GAO-10–847T.
Gudbjartsson, D., Helgason, H., Guðjónsson, S., et al., 2015. Large-scale whole-genome sequencing of the icelandic population. Nat. Genet. 47, 435–444.
Gymrek, M., McGuire, A., Golan, D., Halperin, E., Erlich, Y., 2013. Identifying personal genomes by surname inference. Science 339, 321–324.

HUGO Ethics Committee, April 9, 2000. Statement on Benefit-Sharing. http://www.hugo-international.org/Resources/Documents/CELS_Statement-BenefitSharing_2000.pdf (accessed February 3, 2016).

Human Genomics Strategy Group, January 2012. Building on Our Inheritance: Genomic Technology in Healthcare. A report by the Human Genomics Strategy Group. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213705/dh_132382.pdf (accessed January 2015).

Kaye, J., Meslin, E., Knoppers, B., et al., 2012. Research priorities: ELSI 2.0 for genomics and society. Science 336, 673–674.

Liang, P., Xu, Y., Zhang, X., et al., 2015. CRISPR/Cas9-mediated gene editing in human tripronuclear zygotes. Protein & Cell 6, 363–372.

Lippman, A., 1991. Prenatal genetic testing and screening: constructing needs and reinforcing inequalities. Am. J. Law Med. 17, 15–50.

Mayer-Schönberger, V., Cukier, K., 2013. Big Data: A Revolution That Will Transform How We Live, Work, and Think. Hodder & Stoughton.

Mello, M., Wolf, L., 2010. The Havasupai Indian tribe case – lessons for research involving stored biologic samples. N. Engl. J. Med. 363, 204–207.

Rosenfeld, J., Mason, C., 2013. Pervasive sequence patents cover the entire human genome. Genome Med. 5, 27.

Ross, J., Stedlowinska, E., Symmans, W., et al., 2009. The HER-2 receptor and breast cancer: ten years of targeted anti-HER-2 therapy and personalized medicine. Oncologist 14, 320–368.

Scientific Expert Resource Centre, April 2014. Big Data: Public Views on the Collection, Sharing and Use of Personal Data by Government and Companies. Version 1.

Further Reading

Caufield, T., McGuire, A., Cho, M., et al., 2008. Research ethics recommendations for whole-genome research: consensus statement. PLoS Biol. http://dx.doi.org/10.1371/journal.pbio.0060073.

Clayton, E., 2003. Ethical, legal, and social implications of genomic medicine. N. Engl. J. Med. 349, 562–569.

The Hinxton Group: An International Consortium on Stem Cells, Ethics and Law, September 9, 2015. Consensus statement on genome editing technologies and human germline genetic modification. Aregenberg.

The International HapMap Consortium. 2003. The International HapMap Project. Nature 426, 789–796.

Kevels, D., 1995. In the Name of Eugenics: Genetics and the Uses of Human Heredity. Harvard University Press.

Mertz, J., Mcgee, G., Sankar, P., 2004. ‘Iceland Inc.’? On the ethics of commercial population genomics. Soc. Sci. Med. 58, 1201–1209.

Nuffield Council on Bioethics, 2002. The Ethics of Patenting DNA. Nuffield Council on Bioethics, London.

Prainsack, B., Buyx, A., 2011. Solidarity: Reflections on an Emerging Concept in Bioethics. Nuffield Council on Bioethics, London.

Wilson, J., Jungner, G., 1968. Principles and Practice of Screening for Disease. World Health Organization.

Zwart, H., Nelis, A., 2009. What is ELSA genomics? Science & society series on convergence research. EMBO Rep. 10, 540–544.

Relevant Websites

http://www.genome.gov/25520385 — 1997: Bermuda Meeting Affirms Principle of Data Release (National Human Genome Research Institute) (Last accessed 28.03.16.).

http://www.bbmri-eric.eu/en/about — Biobanks and Biomolecular Resources Research Infrastructure Consortium — as a European Research Infrastructure Consortium (Last accessed 28.03.16.).

http://www.basisproject.eu/ — The Breast Cancer Somatic Genetics Study (Last accessed 28.03.16.).

http://www.cancergenome.nih.gov/ — The Cancer Genome Atlas (Last accessed 28.03.16.).

http://www.egappreviews.org/ — GAPP Knowledge Base (Genomic Applications in Practice and Prevention) (Last accessed 28.03.16.).

http://www.1000genomes.org/ — The 1000 Genomes Project (Last accessed 28.03.16.).

http://www.hapmap.ncbi.nlm.nih.gov/whatishapmap.html — The International HapMap Project (Last accessed 28.03.16.).

http://www.ukbiobank.ac.uk/ — UK Biobank (Last accessed 28.03.16.).