

# Genomics innovation: transforming healthcare, business, and the global economy<sup>1</sup>

Gerardo Jimenez-Sanchez

**Abstract:** The genomics revolution has generated an unprecedented number of assets to propel innovation. Initial availability of genomics-based applications show a significant potential to contribute addressing global challenges, such as human health, food security, alternative sources of energies, and environmental sustainability. In the last years, most developed and emerging nations have established bioeconomy agendas where genomics plays a major role to meet their local needs. Genomic medicine is one of the most visible areas where genomics innovation is likely to contribute to a more individualized, predictive, and preventive medical practice. Examples in agriculture, dairy and beef, fishery, aquaculture, and forests industries include the effective selection of genetic variants associated to traits of economic value. Some, in addition to producing more and better foods, already represent an important increase in revenues to their respective industries. It is reasonable to predict that genomics applications will lead to a paradigm shift in our ability to ease significant health, economic, and social burdens. However, to successfully benefit from genomics innovations, it is imperative to address a number of hurdles related to generating robust scientific evidence, developing lower-cost sequencing technologies, effective bioinformatics, as well as sensitive ethical, economical, environmental, legal, and social aspects associated with the development and use of genomics innovations.

*Key words:* genomics innovation, precision medicine, genomic medicine, genomic selection, agriculture.

**Résumé :** La révolution génomique a généré un nombre sans précédent d'actifs pour propulser l'innovation. Le développement initial des applications basées sur la génomique montrent un potentiel important de contribuer relever les défis mondiaux, tels que la santé humaine, la sécurité alimentaire, d'autres sources d'énergies, et la durabilité environnementale. Dans les dernières années, les plus développés et les pays émergents ont mis en place des programmes de la bioéconomie où génomique joue un rôle majeur pour répondre à leurs besoins locaux. La médecine génomique est l'une des zones les plus visibles où l'innovation en génomique est susceptible de contribuer à une pratique médicale plus individualisée, prédictive et préventive. Exemples dans l'agriculture, les industries laitières et bovines, la pêche, l'aquaculture, et les forêts comprennent la sélection efficace des variantes génétiques associées à des traits de valeur économique. Certains, en plus de produire plus d'aliments et de meilleure qualité, représentent déjà importante une augmentation des revenus à leurs industries respectives. Il est raisonnable de prévoir que les applications de la génomique seront conduire à un changement de paradigme dans notre capacité à alléger le fardeau important pour la santé, économiques et sociaux. Toutefois, pour bénéficier succès de l'innovation génomique il est impératif de répondre à un certain nombre d'obstacles liés à la production de solides preuves scientifiques, le développement des technologies de séquençage à moindre coût, la bioinformatique efficaces, ainsi que les aspects éthiques, économiques, environnementaux, juridiques et sociaux sensibles associés avec le développement et l'utilisation des produits de l'innovation génomique.

*Mots-clés :* l'innovation en génomique, la médecine de précision, la médecine génomique, la sélection génomique, l'agriculture.

## The cornerstone of a revolution

The genomic revolution driven by the Human Genome Project has significantly advanced our knowledge of the biology on living organisms. The widespread access to

genomic technologies and information resources is transforming multiple fields very quickly, introducing an emerging generation of innovations that offer new opportunities and challenges to contemporary societies.

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**G. Jimenez-Sanchez.** Harvard T.H. Chan School of Public Health, Department of Epidemiology, Boston, MA, USA; Global Biotech Consulting Group, Mexico.

**E-mails for correspondence:** [gjimenez@hsph.harvard.edu](mailto:gjimenez@hsph.harvard.edu); [gerardo.jimenez@gbcbiotech.com](mailto:gerardo.jimenez@gbcbiotech.com).

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Next-generation sequencing technologies are leading a paradigm shift in our ability to generate large-scale sequence data sets. In addition, the significant drop in sequencing costs has made genomics technologies routinely available to a wide range of disciplines on a significant geographical spread. Thus, the ability to produce massive amounts of sequencing data moved from sophisticated academic institutions to diverse environments, including industry.

The availability of sequencing technologies contributed to an unprecedented increase in the number of publicly available genome sequences, which now account for thousands of species. Currently, the Genomes on Line Database (GOLD), under the auspices of the United States Department of Energy and the University of California (<https://gold.jgi-psf.org>), harbors close to 56 000 sequencing projects and 39 400 analysis projects that include prokaryotic and eukaryotic organisms and cover the entire phylogenetic scale (Reddy et al. 2015). The rate at which genomic data are generated has made this field a Big Data science, and its massive production is becoming one of the most demanding areas in terms of acquisition, storage, distribution, and analysis (Stephens et al. 2015).

Genomics has substantially increased our knowledge of the structure and function of coding and non-coding regions of genomes. In addition, it has generated the founding bases for emerging disciplines, such as epigenetics, and their roles in human disease. Our ability to sequence genomes from multiple microorganisms has led to the detailed characterization of the human microbiota, enabling the discovery of numerous biosynthetic gene clusters. The analyses of their structure, function, and interactions offer the potential to discover new molecules and metabolic pathways with important roles in human metabolism during health and disease (Donia and Fischbach 2015). Furthermore, new genome engineering methods are being described, including a powerful class of tools that are redefining the boundaries of biological research and enabling a broad range of genetic modifications with significant potential in science and medicine (Gaj et al. 2013).

Beyond the scientific and technological benefits generated by the Human Genome Project, its economic analysis showed that the \$3.8 billion investment not only launched the genomics and DNA sequencing revolution but also generated close to a trillion dollars in economic return and over 300 000 jobs in the US economy (Battelle Memorial Institute 2011). The return on investment has been estimated at \$178 for every public dollar (Wadman 2013). This indicates the great potential that genomics holds as a transformative agent in the global economy.

### From DNA sequencing to meeting global challenges

The direct relationship between genomics and the vast diversity of living organisms has opened broad horizons

for the development of applications with strong potential for economic growth, social benefits, and cultural enrichment of communities worldwide. Since the Organization for Economic Cooperation and Development (OECD) published a policy agenda for a bioeconomy (OECD 2009), interest has grown among nations to use genomics technologies to meet local and regional challenges. Genomics sciences are expected to decisively drive the economy over the next two decades in areas that include human health, veterinary medicine, agriculture, aquaculture, fisheries and food, industrial biotech, environment, forensics, justice, and security. Thus, the timely and appropriate development of genomics-based innovations offers valuable opportunities to meet global challenges, such as human health, food security, identification of alternative sources of energies, and environmental sustainability (Jimenez-Sanchez and Philp 2015b).

The crystallization of these opportunities requires a virtuous cycle to stimulate innovation based on genomic research. To this end, it is important to connect ideas and individuals across sectors to find new uses and applications for genomics. This needs to be followed by sustained investment in large-scale science and technology to fuel innovation. The cycle progresses by translating discoveries into applications to maximize their impact across all sectors and looping again to continue connecting those who bring ideas to the innovation cycle. This is exemplified below with a description of innovations that have arisen from genomic research in the fields of medicine, agriculture, meat and dairy industries, fisheries, and aquaculture. This article does not pretend to be an exhaustive list of innovations, but is rather a discussion of a few examples that illustrate the transforming power of genomic research.

In medicine, the genomic revolution has significantly increased the identification of genes associated with both Mendelian diseases and the risk to complex ones. In consequence, genomic medicine has emerged as a medical discipline that involves the use of an individual's DNA information as part of their clinical care (Green et al. 2011). Genome-wide association studies (GWAS) have generated valuable contributions to the identification of genes associated with common diseases, including some that represent significant health, economic, and social burdens such as diabetes, obesity, cardiovascular disease, and cancers, among others (Manolio 2013). Although the majority of genes associated to common disease have a limited contribution to their heritability, some have made it possible to identify metabolic pathways with significant roles in the pathophysiology of these conditions. It is foreseeable that genomics will integrate with other current technologies into the medical practice. Currently whole genome- and whole exome-sequencing are becoming part of the armamentum in the search for disease-associated genes. Although there are still a number of limitations before these approaches

can be routinely used in the clinical setting, criteria for specific applications begin to be defined (Biesecker and Green 2014).

Pharmacogenomics identifies variations in the DNA sequences that influence the effects of drugs. Initial applications have allowed a more effective and safer use for a growing number of them. Progress in pharmacogenomics includes the tailored treatment of some cardiovascular and psychiatric diseases, and pain management, among others (Wang et al. 2011). Also, genomics applications in oncology begin to develop effective treatments for cancers carrying specific driver mutations identified by whole-genome sequencing tumor DNA (Jackson and Chester 2014). The Food and Drug Administration (FDA) has issued recommendations to modify the labeling of medications in which pharmacogenomic variations affect the response to them. Currently, the FDA has a list of over 150 FDA-approved drugs for which there is pharmacogenomic information available that must be included in their labeling (<http://www.fda.gov/drugs/science/research/researchareas/pharmacogenetics/ucm083378.htm>). The adoption of these emerging tools in the clinical practice is still limited by the generation of scientific evidence supporting their medical and economic value, which is essential to cover genotyping-related costs. The ultimate integration of pharmacogenomics into clinical practice will require the development of simple clinical algorithms to support the interpretation and use of genomic information by the physician.

Our ability to routinely translate genomics into a more individualized, predictive, and preventive medical practice will require a better understanding of complex interactions between individuals and the environment under different circumstances. To this end, creative and sophisticated strategies have been proposed to determine the detailed interactions between genomes and their variants, and different environmental factors, including lifestyles, nutrition, and microorganisms in the human body. At the beginning of 2015, a research initiative was announced in the United States that aims to accelerate progress towards a new era of precision medicine ([www.whitehouse.gov/precisionmedicine](http://www.whitehouse.gov/precisionmedicine)). This initiative includes a comprehensive approach to prevent and treat human disease taking in account each individual's genetic variations, environmental factors, and lifestyle. The Precision Medicine initiative has the potential of generating scientific evidence required to move the concept of personalized medicine into the routine clinical practice (Collins and Varmus 2015). Short-term goals of this initiative focus on efforts to realize precision medicine in cancer, including the implementation of innovative clinical trials of targeted drugs for adult and pediatric cancers, use of combination therapies, and acquisition of knowledge to overcome drug resistance. Longer-term goals include the creation of a research cohort of over one million American volunteers who will

share genetic data, biological samples, and diet/lifestyle information, all likely to be linked to their electronic health records. This data collection will enable novel models to conduct biomedical science emphasizing an active engagement of participants and responsible data sharing, along with robust methods to protect privacy. It is expected that results from this research cohort data will advance our knowledge on pharmacogenomics, identify new molecular targets for treatment and prevention, and explore strategies where mobile devices can encourage healthy behaviors. In summary, it will set the scientific foundation for precision medicine on a large number of human diseases. Other efforts to this end are in progress elsewhere, such as in the case of The 100 000 Genomes Project initiative under the leadership of Genomics England ([www.genomicsengland.co.uk/the-100000-genomes-project/](http://www.genomicsengland.co.uk/the-100000-genomes-project/)) (Auton et al. 2015; Walter et al. 2015). In contrast to previous attempts, these strategies have the advantage of using recently created data bases such as the human genome sequence and its variants, powerful analytical methods for the molecular characterization of patients, and computer tools that allow the analysis of large amounts of data. Research programs like these have the potential to produce valuable contributions from exploring the association of multiple factors with human health and disease, including the generation of solid evidence to guide the use of genomics in healthcare.

Selection of high economic value traits using genomics has empowered the food-related industries to produce more and better foods. Introduction of these technologies to agriculture, and beef and dairy farms has proven to be valuable to the economy and society at large. This is occurring in developing countries as well as in fully industrialized nations as illustrated by the following examples. The rice industry in Southeast Asia provides close to 20% of the world's caloric intake, and the economies of those countries are significantly dependent on it. Unfortunately, this region of the world frequently needs to contend with floods caused by monsoons and typhoons affecting the fields and destroying large extensions of cultivars since most rice varieties die during the first week of total submersion. These environmental phenomena damage close to 15 million ha of crops yearly, resulting in over one billion dollars in losses that disproportionately affect the poorest farmers in the world. In this context, the identification of the *Sub1* gene in the submergence-tolerant rice FR13A has been of most value (Septiningsih et al. 2009). This trait allows rice plants to tolerate excessive water and survive total submersion for up to two weeks, resuming growth and development once the flood passes. The *Sub1A-1* variety of this gene supplies the plant with the capacity to tolerate immersion by decreasing its sensitivity to ethylene (a plant hormone that promotes its growth), the loss of stored energy, and chlorophyll degradation (Sarkar

and Bhattacharjee 2011). Once the gene responsible for this trait was identified, the use of innovative strategies based on marker-assisted backcrossing made it possible to transform popular varieties of rice to tolerate submergence, while maintaining their original features greatly appreciated by farmers and consumers (Cuc et al. 2012). This and other genomic-based innovation initiatives are reconciling food and industrial needs contributing to the Asian economy (D'Hondt et al. 2015).

The beef and dairy cattle industries are undergoing a significant transformation process based on the progressive introduction of genomics into their production processes to select traits that are valuable to the market. The introduction of these strategies has resulted in significant benefits to those industries. Applications of genomic research are finding creative ways to increase production in the beef, dairy, and swine industries. For example, the Canadian Cattle Genome Project aims to bring genomic technology to Canada's beef industry (Ludu and Plastow 2013). Recently, they completed the sequencing of 315 animals and the genotyping (770K and 50K) of over 10 000. Most of those individuals sequenced and genotyped were key historic bulls that had a major influence on the current Canadian herds (Daetwyler et al. 2014). In addition, new genomics-based methods are contributing to improve product traceability and food safety.

Animal selection based on genomic breeding values is revolutionizing dairy cattle production. The dairy industry has integrated the use of genomics technologies to identify genetic variants associated with traits of economic importance, particularly in industrialized countries in America, Europe, and Oceania. In recent years, the integration of large amounts of genomic data along with statistical tools and computer science has made it possible to successfully introduce genomic-based decision-making algorithms. These emerging strategies allow the selection of animals at early ages by accurately predicting breeding values without requiring information on their performance. These values result from the integration of genetic markers across the entire genome and their potential to capture all of the quantitative trait loci contributing to a given trait. In consequence, the use of genomics begins to allow the design of more robust breeding strategies reducing costs to the industry (Bouquet and Juga 2013). Although challenges related to the selection methods and their routine implementation remain to be addressed, this strategy is expected to at least double the rate of genetic gain in the dairy industry (Hayes et al. 2009). The use of single nucleotide polymorphism low-density assays arrays to predict direct genomic values of traits involved in milk production has demonstrated its ability to generate precise evaluations in bull and cow populations (Moser et al. 2010). Thus, it is reasonable to predict that the use of genomic

technologies will become routine in this industry as costs continue to fall.

The fishery and aquaculture sector constitute an increasingly important source of high-quality protein. Between 1980 and 2012, the world aquaculture production volume raised at an average rate of 8.6% per year. The global production of food fish aquaculture increased dramatically to more than double from 32.4 million t in 2000 to 66.6 million t in 2012 (Food and Agriculture Organization of the United Nations 2014). Considering the rate at which the world population is growing and the resulting demand for fish products, it is essential to ensure the sustainability of this industry. Genomics of aquatic organisms offers numerous opportunities to accelerate genetic gain through the use of genomic technologies, thereby empowering many improvement programs in a large number of species (McAndrew and Napier 2010). Currently, traits under investigation include those related to reproduction capacity, meat features, resistance and tolerance to diseases, pathogens, and other kinds of stress. These programs have been boosted by the availability of high quality reference genome sequences and high density markers for various aquatic species (Yáñez et al. 2015). Genomic research and technologies accelerate the discovery of genetic variants associated with traits with high economic value and their progressive integration into selective breeding programs.

Genomics has proven to be valuable for the development of strategies for environmental sustainability. The detailed characterization of the biodiversity and the interactions within ecosystems contributes to the development of applications designed to tackle specific challenges to the environment. Among the number of areas where genomics contributes to environmental care, those related to an improved understanding of forests are essential. Trees constitute approximately 82% of the continental biomass and harbor more than 50% of the terrestrial biodiversity (Ramawat et al. 2014). They are of key importance in the production of raw materials. In recent years, the integration of genomics into the sustainable use of forest sources of biomass has made it possible to develop forward-looking strategies to maintain and protect the environment. For example, the sequencing of forest trees of economic importance, such as white spruce (*Picea glauca*) (Wegrzyn et al. 2014) and Norway spruce (*Picea abies*) (Nystedt et al. 2013), has contributed to the design of strategies to improve tree breeding and forest management. Moreover, these efforts have generated resources to increase our understanding of commercially valuable traits, such as insect resistance, wood quality, growth rates, and adaptation to changing climates (Neale and Kremer 2011).

Other innovative and pertinent areas that contribute to the mitigation of environmental damage are those related to bioremediation. These include strategies to

improve the extraction of existing hydrocarbon resources by developing more environmentally responsible methods. In Canada, researchers are looking into metagenomics to enable the greener production and extraction of hydrocarbon energy (An et al. 2013). Genomic characterization of the microbial communities inhabiting hydrocarbon deposits aims to develop new bioprocesses and improve existing ones to enhance recovery, reduce water and energy use, and minimize greenhouse gas emissions. This model has the potential to become the foundation for strategies that harness indigenous bioprocesses on a practical time-scale and make hydrocarbon extraction greener ([www.hydrocarbonmetagenomics.com/about-project/](http://www.hydrocarbonmetagenomics.com/about-project/)). Similar strategies are being developed in China to better understand the interactions between microorganisms and local geochemical variables. These efforts aim to define ideal parameters for effective bioremediation strategies to clean major oilfields across different geoclimatic regions (Sun et al. 2015).

### Realization of the promise

Unlike most other major scientific investments, sequencing the human genome is a permanent asset. Not only did this project pave the way for unprecedented understanding of biology, but it also opened up the possibility of better understanding human health. The Human Genome Project potentially enabled the development of preventive strategies and treatments for human disease, the production of more and better crops, the development of effective actions towards bioremediation of air, water, and soils, and the production of clean energy, among other benefits to humanity (Jimenez-Sanchez and Philp 2015a).

Genomics represents a major propeller of the bioeconomy, an economy where the basic building blocks for materials, chemicals, and energy are derived from renewable biological resources, and represents a significant opportunity to meet global challenges. The magnitude of these challenges is unprecedented in the context of an increasingly growing population and particularly burdensome in the wake of a global economic crisis. Moreover, they tend to interact very much like a global ecosystem and thus have created one of the most complex periods in human history. Because these grand challenges are truly international, there is a need to achieve a consensus of action across countries with different starting points and levels of economic development. International organizations including the OECD (<http://www.oecd.org/newsroom/genomicsofferingthepromiseofabetterfuture67decemberatoecdheadquartersinparis.htm>) and the Human Genome Organization ([http://www.hugo-international.org/comm\\_genomicsandbioeconomy.php](http://www.hugo-international.org/comm_genomicsandbioeconomy.php)) have implemented efforts to propel genomics as a major driver of the economy. In 2012, the United States published its bioeconomy blueprint (United States White House Office 2012) and the Euro-

pean Union (Directorate-General for Research and Innovation 2012) launched its own strategy. Several nations have developed similar initiatives (e.g., Belgium, Canada, Denmark, Finland, Germany, Malaysia, the Netherlands, and South Africa). Other countries have important policies consistent with the bioeconomy concept without a formal blueprint (i.e., France, Italy, Japan, Korea, and the UK) (Bioökonomierat 2015). Although each strategy varies in its priorities and approaches, genomics plays a central role in all of them. In addition to these, some countries have put in place specific efforts to translate genomics research into economic outputs and the creation of public welfare, such as Canada (Genome Canada 2015) ([www.genomecanada.ca](http://www.genomecanada.ca)), the United Kingdom ([www.genomicsengland.co.uk](http://www.genomicsengland.co.uk)), Mexico (Jimenez-Sanchez et al. 2008) ([www.genomicaybioeconomia.org](http://www.genomicaybioeconomia.org)), Singapore ([www.a-star.edu.sg/gis](http://www.a-star.edu.sg/gis)), and various Asian countries (D'Hondt et al. 2015). Given the considerable impact of genomics in the economy and its extensive markets of influence, there are an increasing number of industries participating in genomics innovations aiming to make timely investments. Additionally, public-private partnerships are attracting substantial capitals from all over the world to develop specific applications to meet grand challenges. These are expected to grow rapidly, create new markets and jobs, and play a major role in the economy in the years to come.

The potential applications of genomics are powerful and indeed promising. However, it is important to recognize that thoughtful forward-looking public policies are required to effectively benefit from them and avoid unnecessary risks in the early stages and beyond. Moreover, there are other significant challenges that need to be met before the promise becomes a reality. Some are particularly bold. In medicine, there is a need to continue generating solid evidence of their effectiveness in guiding personalized medicine into the routine medical practice. Additionally, cost/benefit studies and other rigorous economic analyses are required to guide policies regarding reimbursement and coverage (Shabaruddin et al. 2015). Appropriate risk analysis and effective communication of results to patients and members of the communities is essential. Other challenges, as important, are related to technology access, report of incidental findings, discrimination, appropriate counseling, and establishing standards for the appropriate use of technologies. These need to be addressed to effectively introduce personalized medicine.

The pace at which genomic data are being produced also poses important technological challenges for data storage, processing capacity, quality control management, and the interpretation of vast amounts of sequence data (Stephens et al. 2015). In addition, the cost of genomics technologies is still a major bottleneck that prevents genomics innovations from more expeditious development. It is reasonable to predict that novel high-

throughput sequencing and analytical technologies will emerge, and given the size of the markets integrating these technologies into their processes, costs will continue to decrease to a level at which global access becomes possible.

The complexity of genomic information and technologies in combination with the diverse nature of their applications requires a permanent update of the educational curricula in medicine and in other areas. Additionally, there is a pressing need for novel training programs that contribute to the generation of professionals in the management of bioeconomy, innovation, and governance to successfully integrate genomics innovation into contemporary societies. These programs have begun to emerge ([www.sps.ed.ac.uk/gradschool/prospective/taught\\_masters/h\\_n/msc\\_management\\_bioeconomy\\_innovation\\_governance](http://www.sps.ed.ac.uk/gradschool/prospective/taught_masters/h_n/msc_management_bioeconomy_innovation_governance)), and others should be on their way.

The rapid evolution of genomics offers optimistic perspectives on potential applications that may emerge from scientific research. However, one must be aware of the different challenges that stand in the way of innovation. Successfully overcoming them will require creative participation of society at large.

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