Chapter 20
Genomics and Potential Downstream Applications in the Developing World

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Introduction: Status of Genomic Research

The genomics revolution has been fueled by an increase in the efficiency of sequencing technologies and the development of high-throughput experimental approaches for generating other types of biological data. Each month, an increasing number of genomes are churned out, and at lower costs. Up to the last decade, DNA was sequenced by the low-throughput Sanger-based chemistries commonly

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known as a "first-generation" sequencing platform. However, since 2008, there has been wide adoption of the "second-generation" or "next-generation" sequencing approaches because of their high-throughput sequence data output at a lower cost. The current generation of machines can produce an estimated 250 billion bases in a week, compared to just about 25,000 in 1990 and 5 million in 2000 (Lander 2011). The cost per base of DNA sequencing has plummeted approximately 100,000-fold over the past decade. As of October 2010 the cost of sequencing a eukaryote genome was USD $29,092 and the cost of sequencing per megabase was USD $0.32 (Wetterstrand 2011).

Genomics studies have primarily been collaborative efforts involving a large number of scientists usually from different parts of the world, with each contributing a unique set of skills ranging from mathematics, biology, computer science, and statistics. This team-driven approach in genome projects and the public distribution of data is transforming the way collaboration in science is done. Open access to genomic data increases the probability of scientific discoveries by having many eyes pouring over the datasets, hence allowing for input from a large number of people with diverse skill set(s) and above all facilitating meta-analysis of the data. Currently, there is a deluge of publicly available data which presents a major challenge in the analysis. Despite the seemingly insurmountable mountain of data, genomics has begun impacting biological research. Genomics has facilitated the investigation of biological phenomena in a comprehensive, unbiased, hypothesis-free manner (Lander 2011). For example, a cancer patient can now have his or her genome sequenced from healthy cells and compared to that of diseased cells. However, despite the great potential of genomics, the benefits will take time, especially in developing countries, to be fully realized due to a number constrains.

Today's inventory of possible applications of genomics can be broadly categorized into human and animal health (personalized medicine, pharmacogenomics, and drug development), agriculture, evolutionary biology, and environmental studies among others. In the near future, an individual's genetic profile will be used not only to define disease status or susceptibility but to treat it as well (Ng et al. 2008). It is anticipated that genomic sequencing will provide doctors with information to treat disease more precisely by using both preventative approaches and customized treatment regimens.

In Africa, researchers have sequenced and participated in the sequencing of many genomes. These include human, livestock, food crops, pest, and parasite genomes. Additionally, the application of genome-wide association studies (GWAS) in Africa, which is less expensive than whole genome sequencing, can be used to identify rare genetic variants that cause diseases in marginalized populations having little or no access to medical care. A notable achievement is the recent sequencing of genomes of South African Bushmen and Bantu individuals with the aim of understanding human genetic variation at the genome level and its effect on human health (Schuster et al. 2010). This interesting study established that there were more genetic differences between any two South African Bushmen than between a European and an Asian. Such information is crucial in the development and treatment of disease within populations.

Genomic information helps researchers identify sets of genes responsible for disease and hence design corresponding drugs to counter the effects of the mutation in the target genes. Whole genome sequencing of cancers, for example, has helped in building genetic maps of the disease. Sequencing genomes of patients with disease such as diabetes can help identify genetic variants that predispose one to disease. So far, many of the genetic variants identified in medicine have a weak link to disease and are not definitive risk factors. The variants increase an individual's chance of getting a disease, but they do not determine whether a person will get sick.

Pharmacogenomics is another important spin-off of the genomics revolution (Please see other chapters on this topic). Pharmacogenomics facilitates the identification of biomarkers that can help physicians optimize drug selection, dose, and treatment duration and predict adverse drug reactions (Wang et al. 2011). Drugs can be designed to suit a patient's genetic profile. However, significant challenges need to be addressed before personalized medicine can become a reality. These include scientific challenges, such as determining which genetic markers have significant clinical significance, limiting the off-target effects of gene-based therapies, and conducting clinical studies to identify genetic variants that are correlated with a drug response. However, as genome sequencing becomes cheaper and more accurate, more clinically significant genetic markers will be identified, making personalized medicine a reality for the multitudes.

Genomics has also started to contribute toward improving animal health. Genomes of a number of organisms that cause livestock diseases have been sequenced. These include *Babesia bovis* (cattle pathogen, genome sequence completed in 2007), *Theileria parva,* and *Theileria annulata* (cattle pathogen, genomes sequenced in 2005). Therefore, traditional research methods in human and livestock pathogens can be augmented using genomic approaches. Many parasites are difficult to culture in the lab. Furthermore, their hosts are often not suitable for lab experiments. The analyses of these parasite genomes give insight into their biology and provide approaches for measuring genetic variation, transcript abundance, and protein or metabolite abundance on a genome-wide scale in ways which would not have been possible using traditional molecular biology methods.

In agricultural development, advances in genomics have made molecular plant breeding feasible on marginal crops including medicinal plants and crops of the developing world (CNAP Artemisia Research Project). The importance of food security in this era of climate change cannot be overstated. Food insecurity brought about by climate change could result in serious social problems, including price inflation, then successively war outbreak, famine, and population decline (Zhang et al. 2007). Africa is uniquely positioned to contribute to food security due to its vast variety of plants that have not been fully exploited as food crops. Genomics is poised to enhance the search for useful traits in uncharacterized plants with potential to be food, fodder, or fuel crops. When scientists and breeders can pinpoint the genetic differences between crop varieties with different traits, they can subsequently develop cultivars that can thrive in a wide variety of conditions. In light of climate change, the accelerated development of cultivars that can thrive in harsh

conditions will improve food security across the globe; hence, there is a need for increased sequencing and genome analyses of important crops in Africa.

Sorghum was the first plants of African origin whose genome was sequenced (Paterson et al. 2009). It is a hardy drought-tolerant crop that can thrive in arid and semiarid regions in Africa unlike other cereals. As the effects of climate change continue to afflict agricultural production on the continent and the world at large, there is an increasing need to develop higher yielding cultivars that are tolerant to both biotic and abiotic stresses. Although marker-assisted selection of crops has been a very useful tool in plant breeding, it has its limitations, which include low heritability and genotype×environment (G×E) interactions, making it useful only for simple traits that are inherited in a Mendelian fashion. As a result, genomic selection will lead to improved breeding strategies that leverage the large amounts of genomic information generated by high-throughput sequencing.

The cocoa industry received a boost after the sequencing of the cacao genome (USDA/Agricultural Research Service). This effort will assist in the development of cacao trees that can resist evolving pests and diseases, tolerate droughts, and produce higher yields. The cacao genome will enable faster identification of genetic markers that produce beneficial traits that are useful in breeding programs. The Global Crop Diversity Trust in collaboration with the Royal Botanic Gardens, Kew, and the Consultative Group on International Agricultural Research (CGIAR) is working to identify wild relatives of about 22 of today's main food crops. Their main objective is to isolate essential traits from the wild plants and introduce them into the modern crops to make them more hardy and versatile in light of climate change (http://www.croptrust.org/main).

Finally, genomics can be applied to the study of evolutionary history and extinct life forms, for example, Neanderthals and woolly mammoths. Mining of genomic information from the different evolutionary time points can establish evolutionary relationships between species.

Despite these advances and a wide range of applications of genomics, there is still a genomics divide between developing and developed countries. In spite of the disparity, developing countries can leverage on the available genomic resources for the improvement of both human and animal health and enhance crop production.

Genomics in the Developing World

Rich nations such as the UK, the USA, and Japan continue to expand and reap the benefits of genomic research and development (Heard et al. 2010), while emerging economies such as Brazil, India, South Africa, and China have intensified their investments into genomic research. For example, China's BGI (formerly Beijing Genomics Institute) sequenced the first Asian diploid genome and is currently involved in a number of population-based variation studies including the 1,000-human genome project. Additionally, it is undertaking a 1,000-plant and animal genomes project with the aim of resequencing 1,000 reference genomes of

significant plant and animal species. However, the majority of poor nations still grapple with the entry points into genomic research (Daar et al. 2007). In spite of the disparity, there are already a number of genomics studies and resources that stand to benefit the sub-Saharan region. The following section expounds on challenges, how genomics may be utilized to overcome them, and the potential drivers of genomics within the region.

Poor countries, a quarter of which are in sub-Saharan Africa (SSA), continue to face insurmountable challenges many of which require biosciences-based solutions. In human health, disease prevalence is rampant. The region bears a double burden of infectious and chronic diseases. The "big three" HIV/AIDS, tuberculosis (TB), and malaria are widespread, and noncommunicable diseases that were previously unheard of are on the rise. For example, baseline projections have predicted ischemic heart disease to become a leading cause of death followed by HIV/AIDS by the year 2030 in low-income countries (Mathers and Loncar 2006), thus exemplifying the epidemiological transformation within the region. With infectious diseases being antecedents to some of the chronic infections (Powanda 1999), the burden posed by both (chronic and infectious) diseases is set to aggravate. Additionally, neglected diseases that are responsible for millions of disability-adjusted life years are endemic in these countries (Boutayeb 2007).

Amidst the extensive disease prevalence, incidents of drug resistance (Noedl et al. 2008; ALKER et al. 2007; Beissner et al. 2010; Beshir et al. 2010; Mir and Zaidi 2010), lack of efficacious vaccines, dearth of medical facilities and expertise to manage chronic diseases, and inefficient and untimely disease diagnosis exacerbate the already dire situation. Agriculture, the mainstay of poor countries economies, faces relentless challenges that reduce yield and consequently food insecurity (Gupta et al. 2010). Severe and unpredictable weather conditions; infestation of crops by pests and weeds; incidents of plant diseases, most of which are understudied; and increased populations are some of the problems afflicting crop production. The orphan/understudied crops, grown in over 250 million ha of land (Nelson et al. 2004), often result in poor yield, and some have meager nutritional value. Infectious animal diseases that are poorly understood, the rise in cases of drug resistance, lack of affordable vaccines and drugs, plus poor conversion rates result in severe yield losses for farmers practicing animal husbandry.

By no means are the aforementioned challenges comprehensive; however, this provides an overview of the key domains that genomics holds great promise of positively transforming in its nascent years with the region.

As of March 1, 2011, a total 111, 1,970, and 264 archeal, bacterial, and eukaryotic genome projects, respectively, had been completed with almost 5,000 either in progress or targeted (http://www.genomesonline.org/cgi-bin/GOLD/bin/sequencing_status_distribution.cgi). Of these genomes, a number are important to developing countries. They include animal and plant pathogens (Heidelberg et al. 2000), disease vectors (Lawniczak et al. 2010), and animals and plants of economic value (Sequencing et al. 2009) among others. Sequencing these genomes has provided the genetic blueprint and insight into the molecular biology of these organisms and above all provided primary genetic information for downstream genome-wide investigations.

With affordable sequencing technologies, complex genomes such those of understudied plants and animal breeds in these countries will be available in due time. Fastidious pathogens that are impossible to culture in the laboratory will also be sequenced, and based on their biology, it may be possible to use them in controlled experiments. With the aforementioned sequences accessible, comparative genomics, molecular phylogenetics, candidate gene studies, and downstream genome-wide experiments will be attainable. Genomes of multiple strains (or isolates) of a given species will be obtainable, making genome-wide variation studies a reality. It is important to mention that some species with significant health implications such as *Plasmodium falciparum* already have multiple genomes from different strains sequenced. With reduced sequencing costs (and an expectation that they will plummet in the near future), genome sequencing will be carried out routinely in biological research. Poor countries will have a chance to resequence the genomes of pathogens causing infectious diseases with the aim of establishing genome-wide variations and evolutionary patterns. These variation studies stand to generate vital information that would guide drug/vaccine design besides explaining subtleties such as host specificity and host–pathogen interaction.

The *-omics* experiments (transcriptomics, proteomics, and metabolomics among others) continue to churn out volumes of data to publicly accessible repositories and concomitantly catalyze the development and improvement of related technologies. For example, ArrayExpress (Parkinson et al. 2011), a database for expression data, had 5,667 experiments constituting 138,864 assays spanning 18,398 biological conditions as of March 2011.

The rise in cases of resistance to existing drugs (Sirinavin and Dowell 2004; Okeke et al. 2005), lack or suboptimal vaccines against important infections, increased prevalence of disease, and emergence of highly infectious agents make the need for novel drug targets and candidates indispensable in poor countries. For diseases whose etiological agents have been sequenced, comparative genomics provide an in silico approach for identifying drug candidates in a rational manner. As a case example, the identification of essential genes without human homologs using essential gene databases (Zhang et al. 2004) has facilitated the identification of candidate gene products and metabolic pathways for drug design in *Leptospira interrogans* (Amineni et al. 2010), *Pseudomonas aeruginosa* (Sakharkar et al. 2004), *Helicobacter pylori* (Dutta et al. 2006), and *Neisseria gonorrhoeae* (Barh and Kumar 2009). This also includes the verification of other properties such as drug ability and subtractive comparative genomics. Using similar approaches, a database archiving human bacterial pathogen targets, Genomic Target Database, (GTB; Barh et al. 2010) has also been established.

In some infectious disease pathogens, such as *Mycobacterium tuberculosis* (Ioerger and Sacchettini 2009), the putative drug candidates have been resolved structurally by the Structural Genomics Consortium, thus enabling identification of potential binding sites and docking of chemical agents. Additionally, the World Health Organization's Special Programme for Research in Tropical Diseases, TDR, has created an integrated repository, http://tdrtargets.org/ (Aguero et al. 2008), that facilitates browsing, querying, customized mining, and ranking of putative drug

targets from the tropical disease causing organisms' genomes such as *Plasmodium* spp., *Cryptosporidium* spp., *Leishmania*, and *Mycobacterium* spp. among others.

In terms of drug response, an individual's genetic makeup is a critical determinant (Wilson et al. 2001). Pharmacogenomics focuses on identifying allelic variants in drug metabolizing enzymes or targets that would adversely affect drug response in individuals and across populations. The International HapMap project (The International HapMap Project 2003; The International HapMap, Consortium 2005) provides genome-wide SNP variation in the form of haplotype maps for samples drawn from European, Asian, and African ethnic background. Additionally, NCBI's dbSNPs (Sherry et al. 2001) provides a comprehensive database for SNPs in several organisms including human. With availability of population genetic variations and high-throughput technologies for genome-wide variation discovery (Ragoussis 2009), it will be possible to develop drugs that do not elicit undesirable responses by selecting candidates whose metabolizing enzymes or targets lack variants, and if they do (have variants), then the variation has no negative effect on response.

Vaccines offer sustained protection against infectious diseases both in animals and humans. Using a reverse vaccinology approach and taking into account population-based genome variation, rational and efficient vaccines that would be efficacious across populations can be developed against the infectious diseases including the neglected animal and human diseases. In agriculture, genomics holds great promise for improving animal breeds and plant cultivars. Though poor in yield and understudied, some animals and plants in sub-Saharan regions harbor rich genetic information in terms of tolerance to both biotic and abiotic stresses. For example, N'Dama cattle, *Bos taurus*, an indigenous cattle breed, is trypanotolerant (Hill et al. 2005), and the crop *Oryza longistaminata* harbors rich information on mechanisms for biotic and abiotic stress tolerance and efficient nitrogen usage. The so-called orphan crops cultivated in poor countries (Nelson et al. 2004) are an important source of livelihood but are staggeringly understudied. These include *Sorghum*, pearl millet, cassava, and yam among others. Sequencing the genomes of such plants would provide molecular knowledge into the biology of the crops, their genetic structures, and the primary genetic information for ascertaining mechanisms for traits such as disease and drought tolerance. Functional genomics holds great promise in unraveling the genetic mechanisms underlying such invaluable traits and ultimately providing a genetic resource base to establish improved crops and animals through genetic engineering.

Bioinformatics and computational biology form an integral part of genomic research. These fields facilitate interoperability, analysis, storage, and mining of genomic data. There is notable bioinformatics capacity in certain parts of the African continent, although this is not as established as in the richer nations. The Centre for Applied Biotechnology, Bioinformatics and Microbiology based in Nigeria has been involved in *P. falciparum* genome analysis. In Tunisia, there has been a strong bioinformatics setup at the Institut Pasteur de Tunis since 2005 whose activities are centered on host–parasite interactions for leishmaniasis, sequence annotation, ab initio gene prediction, and modeling of signal transduction pathways.

The International Livestock Research Institute (ILRI) in partnership with Biosciences eastern and central Africa (BecA) hub is actively undertaking bioinformatics research in livestock pathogens (Gardner et al. 2005; Hill et al. 2005; Bishop et al. 2005), African native crops genome projects, and bioinformatics capacity building in collaboration with the Regional Student Group of Eastern Africa. The hub currently hosts a high-performance computing platform with quad eight-core Xeon processors (32 cores in total), 128 GB of RAM, and 8 TB of disk space. The Google-funded Arbovirus Incidence and Disease project brings together a consortium of health, veterinary, wild, vector biology institutions using computational and genomic technologies to establish a model for the surveillance and diagnostic of emerging zoonotic diseases (http://www.icipe.org/avid/). In the southern region, South Africa has an established and reputable network of institutions undertaking research and capacity building in bioinformatics. South African National Bioinformatics Institute, SANBI, established in 1996, is tackling the intricacies of host–pathogen interactions, cancer biology, HIV, and multifactorial diseases using bioinformatics approaches. University of Cape Town Computational Biology Group, CBIO, is involved in evolutionary and systems biology research of infectious disease agents such as *M. tuberculosis*.

In spite the aforementioned activities, a number of sub-Saharan countries still lack human resources and infrastructural capacity to support bioinformatics research. And even for the regional capacities, challenges such as loss of skilled bioinformaticians for better paying positions in developed countries still poses a bottleneck to the field (Hoal 2011). As SSA grapples with genomic research and development, there are a number of drivers, some even social factors, that will be useful in building genomics capacity in the region.

Scientific collaborations, both South–South and North–South, will be critical in ensuring sustainable technology transfer, effective capacity building, and mobilization of resources to support genomic research. North–South collaborations will provide an entry point into genomics for the poor countries by tapping into the infrastructure, technologies, knowledge, and skills from their richer counterparts. However, these collaborations must be well defined, in terms of role(s) and should have concrete steps for building human and infrastructural capacity for genomics. It is worthy to note that South–South collaborations are already gaining momentum (Osama 2008) and stand to catalyze pooling of the limited resources toward common and mutually beneficial research for participating countries. Nations such as South Africa, Kenya, Namibia, Botswana, and Malawi among others are already involved in collaborative genomic research (Thorsteinsdottir et al. 2010). Community engagement through education on genomics and its products should be carried out. Additionally, appropriate regulatory mechanisms to address issues of ethics in studies involving animal or human genetic resources and genomics products must be in instituted. The profit-driven private sector should also be encouraged to invest in genomic research by creation of domestic and regional markets for the products in addition to a favorable business environment.

Applications of Genomics to Developing Countries

Genomics holds great potential toward alleviating some of Africa's greatest problems such as disease and food insecurity among others. As it were, it may be the much needed "-*omics* revolution" that the region currently needs to address some of the problems that have ominously affected most economies leading to high levels of poverty. However, in order for genomics to deliver, a global approach with "innovative financing machineries" specifically from within the region's coffers is required (Singer and Daar 2001). This section aims to highlight key applications especially in relation to human health and food security.

Integrating genomics in public health is almost seen as a panacea toward some of today's pertinent health issues (Halliday et al. 2004). In Africa, these would include infectious diseases such as HIV/AIDS, malaria, tuberculosis, and noninfectious ones such as diabetes and cancer among others. Previously, public health focused mainly on the former group of diseases and malnutrition, but over the years, there has been a conscientious shift to more complex chronic diseases that are noncommunicable due to their recent high prevalence in Africa. Due to this, the field of genetic counseling that started in the 1940s has blossomed into the new field of genomics medicine (Resta 1997; Duff 2001). This was heralded by the fact that in the 1990s, the Human Genome Project (HGP) had been spearheaded and was completed in the early 2000s (Venter et al. 2001). Consequently, several genomes both human and nonhuman have been sequenced, and the comparison of two genomes to deduce differences that may have important implications in controlling specific and measurable phenotypes is currently possible. These differences often in terms of SNPs may either occur in coding or noncoding regions (A physical map of the human genome 2001) and may determine the disease or nondiseased state. The sequencing of pathogen genomes is important toward understanding their biology and consequently, to identify new antimicrobials. For example, the malaria burden in developing countries could be reduced through the manipulation of the mosquito genome. This should enable the cycle of the parasite transmission to be blocked. There is also a potential to develop vaccines against HIV/AIDS that target specific segments of the HIV virus genome (ThorsteinsdÛttir et al. 2003).

Drug development has also been sped up in the recent past, thanks to genomic approaches used to identify suitable drug targets against pathogens or host cells responsible for disease. The battle against drug resistance in parasites, pests, and vectors has gained a powerful new ally in genomics. Their evolution can be monitored over time using a genomics-based approach in order to develop effective ways of combating them. This is particularly important for Africa as it tries to combat numerous parasitic and vector-based diseases. There have been some interesting developments in the fight against malaria, for example. GWAS have been used to understand how several strains of *P. falciparum* are becoming resistant to a number of currently available antimalarial drugs (Mu et al. 2010). Artemisinin is the most widely used antimalarial, and genomics is aiding in the understanding of the genetic

basis of resistance to artemisinin therapy for malaria and will possibly lead to better therapies. Whole genome analysis of several genetic crosses of artemisinin-resistant malarial parasites has helped in uncovering genes that confer resistance (Hunt et al. 2010). In another recent development, a detailed analysis of the M and S strains of the *Anopheles gambiae* mosquito has revealed that the two strains are evolving into different species (Lawniczak et al. 2010). Understanding how species divergence affects mosquito breeding and development will assist scientists and health officials in creating and implementing effective methods for combating the malarial mosquito and other vectors as well as parasites.

A Footprint to Study Genetic Diversity and Unlock Its Potential

Large-scale genome projects and the capacity building that is associated with them have the potential to accelerate the ability of Africa to deal with public health problems. These include both communicable and noncommunicable diseases such as cancer, diabetes, and heart attack among others. A unique collaboration known as the Human Heredity and Health research (H3 project http://www.h3africa.org) has been formed in Africa with the support of the National Institutes of Health (NIH) and the Wellcome Trust research fund. The focus is to use genomics on a large scale on different African populations in order to study both communicable and noncommunicable diseases. This project is timely since Africa has diverse populations with unique environments and risk factors. Such large studies should be able to examine in detail multiple interacting risk factors in disease. This in time should drive innovation, foster training and enhance local capacity, and provide vital evidence for public health decision-making (Dalal et al. 2010). Furthermore, evidence from studies in Africa could provide insights into disease processes relevant to other populations around the globe besides advancing public health in Africa. With such projects, developing countries can harness human genetic variation to benefit their populations and economies through a better understanding of the correlations between genotype and phenotype. This can be achieved by sequencing select populations followed by large-scale genotyping initiatives in human populations, which stand to address both infectious diseases (host response) as well as chronic diseases (Seguin et al. 2008b). At the very least, such approaches will increase our understanding of disease susceptibility and drug responses in local populations (Daar and Singer 2005).

The industrialized G-8 nations have greatly benefited from using genomics in public health. It is time that genomic centers were set up in Africa in order to address the problems at hand that maybe different from those in developed nations (Singer and Daar 2001). Apart from the elimination of parasitic diseases, efforts are required for a social economic change among the different cultures so that the new technologies can be easily embraced.

Over the years, very few African genomes have been sequenced only until recently when the first individual genome sequences and sequences of protein-coding regions (exomes) from individuals inhabiting southern Africa (Skipper 2010).

This has given new insights of genetic diversity and should help to understand recent human evolution and the future of disease-association studies (Skipper 2010). With the inception of the H3 project, Africa will be in a unique position to sequence samples from several populations as most of the examples in the HapMap project are from Caucasian and Asian origins (McVean et al. 2005). This should lead to the discovery of SNPs that will further enable GWAS. A new era of personalized medicine (i.e., pharmacogenomics) will be ushered, as detailed genomic information will be available from a vast majority of African populations. This should greatly contribute toward understanding human genetic diversity.

Animal Health Research to Ensure Food Safety and Quality

Genomic information from livestock species is becoming abundant, and if the revolution is successfully exploited, this could be used to better understand host–pathogen interactions and therefore develop new control strategies for some of the pertinent livestock diseases within the continent. In order for Africa to benefit from agricultural genomics, it is crucial to tap into the continent's genetic resources rather than the exotic livestock genotypes as sources of useful genes. For example, it is known that the Maasai sheep have genes that encode for resistance to helminths (ILRI, http://www.ilri.org). Therefore, genomic manipulation should increase productivity, without much dependence on agrochemicals, hence improving environmental health and sustainability of the livestock systems (Machuka 2004). Another benefit of genomics would be understanding the tick-borne diseases of livestock that remain major barriers to the improvement of livestock productivity in Africa (Jensen et al. 2007). Diseases such as East Coast Fever (ECF) cause major losses despite many decades of research aimed at producing effective chemical and vaccine-based control strategies (http://www.ilri.org). New approaches are needed if the potential for livestock improvement is to be reflected in the economies of the world. The genomics revolution has great potential to generate new insights, hypotheses, and, ultimately, new methods for disease control.

Metagenomics can be used to investigate the viral flora of healthy and sick animals. Such studies are able to show viruses circulating in nature and the complex interaction between virus and host. It is also possible using such approaches to discover previously unknown viruses (Blomström 2010).

Spiraling a Genomic Revolution for African Crops

In order for Africa to benefit from genomics, the development of new crop varieties with higher yields and increased resistance against biotic (diseases, pests) and abiotic (drought, frost, soil toxicity) stresses is of paramount importance (Delmer 2005). Molecular breeding (MB) is the generic term used to describe several modern breeding strategies including marker-assisted selection (MAS) which is the

selection of specific alleles for traits conditioned by a few loci. There is also marker-assisted backcrossing (MABC) which is the transfer of a limited number of loci from one genetic background to another, including transgene. More recently, marker-assisted recurrent selection (MARS) has become popular which is the identification and selection of several genomic regions involved in the expression of complex traits (Ribaut et al. 2010). The emergence of affordable large-scale marker technologies and the sharp decline of sequencing costs have boosted marker development based on sequence information. International initiatives such as the CGIAR generation challenge program (GCP, http://www.generationcp.org) in developing countries have also increased the number of genomic resources for less-studied crops. As a result, a number of key crops in developing countries have adequate genomic resources for meaningful genetic studies and most MB applications. Improving phenotyping infrastructure in developing countries must thus be a top priority to promote modern breeding.

Nutritional genomics is the field that aims to apply genomics to fortify food staples to enhance levels of essential and nonessential micronutrients and macronutrients, such as vitamins (e.g., A, C, E, folate), minerals (e.g., iron and zinc), and proteins (Machuka 2004). This is especially important to vulnerable groups such as pregnant women, children, and the elderly who are faced with the risk of malnourishment. Examples of biofortification include cereals and sweet potato with enhanced levels of vitamins and/or proteins in their seeds and tubers, respectively. This field takes advantage of the many genes that have been cloned for vitamin pathways and for the synthesis of many other "nonessential" compounds and macronutrients. In the future, it should be possible to directly manipulate the content and composition of many nutrients in staple African food crops such as cassava, sweet potato, banana, cowpea, maize, millets, and *Sorghum* (Machuka 2004).

Challenges and Opportunities for Genomic Research

The advancement and use of genomic technologies has taken root in many developed countries. However, the story is different in the developing countries that face various challenges in the development and application of these technologies. Researchers in many developing countries have not fully participated in genomic research mainly due to technological isolation, limited resources, and capacity for genomic research combined with competition for the meager resources from other priorities such as health. Challenges for applications of genomics in developing countries include but are not limited to lack of sustainable funding and lack of infrastructure and highly trained genomics experts. In contrast to developing countries, advances in genomics in the developed countries have led to the development of many genomics tools. While the tools can be used for the benefit of the scientific community in many developing countries, there exists a severe lack of well-established scientific infrastructure and research platforms. Most developing countries especially in SSA face major challenges to implementation of genomic tools with minimal or nonexistent infrastructures. Some developing world countries

have national laboratory systems that mostly contain rudimentary facilities and lack competent staff. However, in certain countries, some of the National Research Centers, International Research Organizations, and nongovernmental organizations have good facilities that complement the work of the government institutions in addressing genomic and health challenges.

Cost of Infrastructure

Most genomic and genetic analysis procedures require expensive tools, equipment, and consumables that many laboratories in resource-poor developing countries cannot afford. Even in their availability, the use of genomic tools may be impractical for many underequipped laboratories in developing countries. Many in-country and remote research facilities lack basic amenities such as constantly running water, electricity, and refrigeration. This challenge therefore makes it impractical to use genomic tools that depend on thermo-sensitive reagents. These shortcomings of in-country scientific infrastructure have however been addressed in some areas by strategic placement of genomic tools in centralized clinical laboratories that have the necessary resources for their maintenance. Well-equipped laboratories also act as reference for other underequipped labs locally and regionally. Such was the initiative of the African Biosciences initiative (http://www.nepad.org/foodsecurity/africa-biosciences-initiative-abi/about), and this has been facilitated by NEPAD in order to create centers of excellence in terms of research in different African regions.

Lack of Access to Genomic Analysis Tools

Despite the advancement in genomics technology and development of new tools for manipulation of genomic data, the biggest challenge is that much of the advanced knowledge is concentrated in individuals and in a few research centers, companies, and not in academia. Therefore, this has restricted knowledge dissemination even though massive amounts of genomic data and software are openly accessible through the Internet. To strengthen genomics in developing countries and globally, the tools necessary for analysis of genomics data are urgently needed where they are currently underutilized (Coloma and Harris 2009). Consequently, developed nations need to be encouraged to make a conscious effort to transfer knowledge on the use and analysis of genomic resources so as to empower developing countries to manage data pertaining to issues within the continent.

Lack of a Regulatory Framework

One of the major challenges in the application of genomic technologies in emerging economies and developing countries involves the limited, or even absent, regulatory

framework. Some of the countries may have limited capacity to regulate drugs and diagnostics, and will need to build capacity for these and the emerging genomic products. Furthermore, regulatory capacity in many developing countries will need to encompass the work of ministries of health, science and technology, industry, commerce, natural resources, and legislative bodies, as well as of drug licensing agencies. In developed countries, international ethical and scientific guidelines for genomic research have been created and are being adopted by nations participating in the field as it evolves. A critical problem faced by developing countries is the lack of national guidelines for genomic research and its ethical ramifications. Thus, the countries need to draw up the necessary rules and legislation on genomics and to generate procedures for their implementation (Conley 2010).

Infringement of Intellectual Property Rights

Lack of advanced research infrastructure and stringent regulatory framework has necessitated biological samples to be taken out of developing countries for research that does not benefit the local populations. This has been possible due to lack of proper informed consent and privacy protocols between research participants protecting them against the potential discrimination that might emerge from genetic information and ensuring that any benefit that comes to fruition from the research reaches them. This experience has prompted some middle-income countries such as Mexico, India, and Brazil to draw up legislation governing "sovereignty" over genomics material and data that restricts the export of biological materials for studies abroad and prioritizes national interests. Poor countries currently lacking their own genomics initiatives could benefit from similar legislation balancing the protection of "genomic sovereignty" while fostering international collaborations that bring much needed resources and increase local scientific capacity (Coloma and Harris 2009).

Needing a Skilled Human Resource Capacity

While some developing world laboratories might have acquired the genomic tools, for them to be properly utilized, personnel need to be trained. Genomic tools, data, and resources may be useless if developing countries have limited research and human resource capacity to receive such technology. Insufficient training that plagues national research laboratories becomes an obstacle for effective use of genetic tools and resources. Therefore, training on technology platforms and laboratory techniques designed to help local scientists and researchers to strengthen their knowledge on scientific infrastructure is needed. Trained local researchers within Africa are better able to address indigenous challenges faster and more cost-effectively. This is because the local researchers are able to understand the cultural

contexts of disease, food security, and the sociopolitical conditions that influence how these problems manifest in communities.

Training young scientists by sponsoring scholarships abroad in relevant areas related to genomics in which developing countries lacks expertise is a viable model for developing countries. To avoid brain drain, beneficiaries should be required to return home for some years and must have a committed position at a research institution or local university as well as research funds for local human resource capacity building. This model has been applied successfully in Brazil, thus providing both an important contribution to genomics and a benefit to Brazil's economy and scientific endeavor (Acharya et al. 2004).

Access to Scientific Information

For genomic tools and technologies to be useful in laboratories in the developing world, another challenge to address would be to ensure that the laboratories have access to scientific information, which has often proved expensive to access for many developing world institutions. There exist initiatives that help laboratories and researchers in the developing world to access such information. These include publication of research papers on publicly accessible websites and open access journals, which often have subsidized subscription for third world research and academic institutions. Initiatives such as HINARI (http://www.who.int/hinari/en/) and AGORA (http://www.aginternetwork.org/en/) have proven to be invaluable resources for accessing literature in developing countries. Online resources on websites such as NCBI, PlasmoDB, and Gramene among others which host genomic and proteomic data and other publicly available genomic information and resources for different species of organisms and open access journals such as PubMed, PLoS, and BMC Genomics for publications may help to stimulate research and encourage more local scientists to be involved in targeted research.

Establishment of "North–South" and "South–South" Collaborations

North–South collaborative efforts with the developed world countries as well as South–South collaborations within public research sector and with the private sector are both essential. This will bridge the "genomics divide," enhance information and data exchange, facilitate sample sharing, as well as catalyze research and capacity in developing countries in terms of infrastructure and human resources (Coloma and Harris 2009). North–South collaborations, starting with capacity building in genomic research, need to be strengthened so that developing countries that are currently excluded from the genomics revolution find an entry point for participation. South–South collaborations must be encouraged to allow countries with limited

resources to pool their human and financial capital, learn from each other's experience, and share in the benefits of genomics. Current and future collaborative initiatives and investments in research and development capacity should ensure that countries in the developing world participate, as equal research and development partners, with the developed counterparts instead of merely facilitating access to local biological resources.

Opportunities to Harness Genomic Research in Africa

Although developing countries are faced with myriad of challenges in terms of the development and uptake of genomics technologies, these technologies proffer opportunities that can be harnessed for their benefits. Several mechanisms can be used (and have been used) to tackle the challenges and empower developing countries toward strengthening their capacity for genomic technologies and research. Below is an outline some of the initiatives that could be employed to achieve this goal.

The resource-poor developing countries can enter the genomics era by creating partnerships with regional centers for technology and resources. DNA sequencing technology is, for example, still unaffordable for many researchers and public laboratories in developing countries due to low-use volume and high costs of equipment, reagents, and maintenance. This can be affordable if a regional center provides services to a pool of laboratories and researchers within a country or a geographical region. For instance, using Brazilian infrastructure, Peru and Chile joined the global potato sequencing consortium, which is sequencing different varieties of potato (Consortium 2011). Brazil has also generated several open-source bioinformatics tools for the annotation of bacterial and protozoan genomes that can be used by any researcher worldwide (Coloma and Harris 2009).

Emerging economies in the developing world, such as India, China, and Brazil, are investing heavily in innovative science and technology (S&T) and making significant progress in the life sciences arena, where they are increasingly protecting intellectual property. Mexico's National Institute for Genomic Medicine (INMEGEN) has established a strategy for the adoption of genomic medicine that includes, among other things, conducting research and development in genomic medicine, application of genomic technology to common health problems, and excellence in teaching and training programs. This has in turn enabled support of academic programs in genomic medicine addressing ethical, social, and legal issues and translating genomic knowledge into products and services (Jimenez-Sanchez et al. 2008).

As training and knowledge translation remains a major challenge across developing countries, human resources and local capacity in genomics are thus central to development as countries with these skills could participate in the potential benefits of the field with respect to health, food security, natural resource management, and other critical areas (Hardy et al. 2008). A WHO conference on health research recommended that emphasis should be made on the importance of developing

countries in investing in their own PhD training programs and in the use of more developing countries' regional centers and networks for PhD studies, instead of institutions in developed countries. In the case of training programs in the North, the implementation of postdoctoral fellowships and reentry projects was seen to be very important (Calva et al. 2002). To equitably share the benefits of this technology worldwide, some have advocated that developed and developing countries alike should participate in genomic research to prevent widening of the already large gap in global health resources (Acharya et al. 2004).

In terms of the benefits of science and technology generally, it has been discovered that the trend to develop knowledge, skills, and products in the economically and scientifically more developed countries and then struggle to make these available to the less scientifically developed and poorer countries is not sustainable in the long run. Thus, many developing countries, especially the emerging economies, are focusing more on local innovation, invention, and commercialization to break the cycle of dependency (Masum et al. 2007). Because science and technology are increasingly recognized as vital components for national development, emerging economies and some developing countries are building their infrastructures to promote local innovation and to retain the value of their human, plant, and microbial genomic diversity and research. India, Thailand, South Africa, Indonesia, Brazil, and Mexico, for example, have devoted considerable resources to large-scale population genotyping projects that explore human genetic variation (Seguin et al. 2008a).

In order to boost human resource capacity regionally in genomics, the Center for Training in Functional Genomics of Insect Vectors of Human Disease (AFRO VECTGEN) was initiated by TDR and WHO. This is a special program in Research and Training in Tropical Diseases at the Department of Medical Entomology and Vector Ecology of the Malaria Research and Training Center in Mali. The aim is to train young scientists in functional genomics who will ultimately use genome sequence data for research on insect vectors of human disease. The program triggers collaborative research with neighboring nations and the vector biology network in Mali, which was built around research grants funded by the US NIH and TDR/WHO (Hardy et al. 2008).

To bridge the "the genomics divide," successful ""North–South" partnerships should involve scientific participation in projects of mutual interest. Currently, there is a North–South collaborative trend where countries in the developing world participate in research and development with more developed nations. An example is the common effort of ILRI in Nairobi and The Institute for Genome Research (TIGR; now the J. Craig Ventner Institute) to sequence and annotate the genome of *T. parva*, a cattle parasite that causes significant economic losses to small-scale farmers in Africa and elsewhere. This effort has generated local human resource capacity in genomics and infrastructure for the future (Gardner et al. 2005). The Human Genome Organization (HUGO) Pan-Asian SNP Consortium provides another example of recent North–South research and development collaboration between Asian countries.

There is also a trend toward South–South collaborations, enabling developing countries to pool their limited resources; this has enabled them to work and learn

from each other's experiences (Osama 2008). An example is the New Partnership for Africa's Development (NEPAD)/African Union African Biosciences Initiative to come up with the BecA hub presently at ILRI (BecA Hub@ILRI website: http://hub.africabiosciences.org/). BecA is a NEPAD African Biosciences Initiative within Africa that is a center of excellence enabling a research platform for researchers in the region on African agricultural improvement. In terms of knowledge dissemination, ILRI, BecA, and the Regional Student Group Eastern Africa (RSG-EA) have organized several bioinformatics introductory courses and workshops and conferences, some of which have been held remotely via Internet (http://hpc.ilri.cgiar.org/training.html; Gichora et al. 2010; Ommeh et al. 2011). Other useful avenues for knowledge dissemination have been the Wellcome Trust Sanger Institute training courses on bioinformatics and genomic analysis held in Africa, the Sustainable Sciences Institute – Broad Institute bioinformatics workshops, and the TDR/WHO – South African Bioinformatics Institute (SANBI) regional training center. Online training like the S-star alliance bioinformatics courses with remote participation are becoming more widespread and are an excellent option for countries with limited resources.

Conclusion

As exemplified by the success of some developing countries such as Brazil, Mexico, and several African countries, it is possible to turn challenges and problems that hinder genomics in developing countries into opportunities for unique scientific and economic growth. However, access to scientific facilities, scientific information, human and infrastructural capacity, North–South and South–South collaborations, elaborate regulatory framework, and harmonized methodologies for genomic analysis among others remains essential for the future of genomics in the developing world.

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