SCIENCE AND SOCIETY

Genomic medicine and developing countries: creating a room of their own

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Abstract | The notion that developing countries must wait for the developed world to make advances in science and technology that they later import at great cost is being challenged. We have previously argued that developing countries can harness human genetic variation to benefit their populations and economies. Based on our empirical studies of large-scale population genotyping projects in Mexico, India and Thailand, we describe how these resources are being adopted to improve public health and create knowledge-based economies. A significant additional benefit is building the capacity for scientific research and internalizing advances in technology, whatever their source.

In 2003 Collins et al.1 described the future of genomics research as a house and the Human Genome Project as its foundation. The question this raises is who will live in that house? Will it be only those lucky few in the industrialized economies, or will all people be able to find a room, no matter where they come from? The use of genomic information to develop therapeutics is growing in industrialized countries². In the developing world, however, advances in genomics are perceived to be out of reach; critics question why countries would invest in genomic research when they face other more pressing health needs such as poverty, infectious diseases and the lack of basic infrastructure. In addition, the high cost that is associated with genomic research and the inadequacy of existing regulatory and intellectual property regimes are seen as significant obstacles3. We too have argued that developing countries are the ones that can least afford to waste their limited health resources on ineffective diagnostics and therapies^{4,5}.

Until now, the more immediate health applications resulting from investing in genomic sciences, in developing countries and globally, have been attained through the sequencing of genomes of microorganisms and viruses such as the severe acute respiratory syndrome (SARS) coronavirus and the influenza virus⁶⁻¹⁰. But infectious diseases are not the only major cause of morbidity and mortality in developing countries; the rates of non-communicable disease are also increasing¹¹. Currently, one-third of all deaths in the world are caused by cardiovascular diseases. Of these, nearly 80% occur in developing nations. By the year 2020, the number of new cancer cases will increase by a staggering 73% in developing countries as opposed to only 29% in developed countries¹². Wanting to assess the resources that the developing countries already possess to improve public health we chose to focus our case studies on large-scale genotyping initiatives in human populations, which stand to address both infectious diseases (host response) as well as chronic diseases through a better understanding of the correlations between genotype and phenotype. Investing in this field, identifying niche areas within it and within areas of local interest, and building life sciences-based capacity around such knowledge in developing countries might not only contribute to improving local health but also potentially stimulate economic development. At the very least, such approaches will help understand disease susceptibility and drug responses in the local population¹³.

There is increasing realization that science and technology are vital to human development, and that the life sciences are particularly relevant to developing countries. To break the cycle of dependence, emerging economies14,15 and other developing countries¹⁶ are beginning to build infrastructures for local innovation and capture the value of their scientific research. The concept of genomic sovereignty that we describe in this article is linked to the wish of the three countries described here — Mexico, India and Thailand — to capture the value of their investments in these large-scale genotyping projects. A crucial outcome of investments in these projects and related life-science technologies is the acceleration of the capacity to build scientific research and the ability to internalize new technologies, whether spawned locally or imported.

Despite the perception that the benefits of genomics are unattainable outside the industrialized world, large-scale genotyping efforts exploring human genomic variation have been initiated in several emerging markets. Here, we discuss the results of a cross-comparison of three case studies of genotyping initiatives taking place in Mexico, India and Thailand. Using previously described methods (BOX 1), we conducted 56 in-depth interviews to develop case studies of the Mexican National Genomic Medicine Institute (INMEGEN) (BOX 2), the Indian Genome Variation database Consortium (IGVdb Consortium) (BOX 3) and two smaller initiatives in Thailand, the Thailand SNP Discovery Project, and the Pharmacogenomics Project at the Thailand Centre for Excellence in Life Sciences (TCELS) (BOX 4). We explored the motivations for undertaking these largescale genotyping initiatives, the adoption of genomic medicine in each country, the mechanisms that the three countries are envisioning or implementing to develop genomic medicine appropriate to their own circumstances, and the potential ethical, legal, social and cultural issues that have arisen or might arise as a result. Here, we define genomic medicine as health applications derived from genomic approaches and research, manifested, amongst others, in

Box 1 | Research methodology

Qualitative case study methods were used for this research^{39,40}. The case studies of the following genotyping initiatives were selected for three reasons: first, to our knowledge, these initiatives were the most advanced with respect to planning or implementation; second, the countries the initiatives were housed in give a good regional representation; and third, access to key informants was facilitated by existing contacts with individuals involved in these initiatives.

We collected data between June 2006 and January 2008. We performed 56 in-depth, face-toface (or by teleconference call), semi-structured interviews with key informants representing scientists and managers from the Mexican National Institute of Genomic Medicine (INMEGEN), the Indian Genome Variation Database (IGVdb) Consortium, the Thai SNP Initiative, the National Center for Genetic Engineering and Biotechnology in Thailand (BIOTEC), the Thai Centre of Excellence for Life Sciences (TCELS) as well as key informants from diverse backgrounds such as the media, non-governmental organizations, regulatory agencies, ministries of health, and experts in the area of genomics, pharmacogenetics and/or ethics from developed and developing countries. We also collected data from documents such as publicly available materials that were relevant to the study questions. Interviews lasted approximately one hour and were audio-taped and transcribed.

Data were analysed in several phases. Theme categories were identified by analysing the interview transcripts by generative or open coding (analysis of words repetitions, key terms and key words). The next phase of data analysis consisted of axial coding of the data to build connections within and between theme categories. In the final phase, core concepts were identified using selective coding. We ensured authenticity of the study by having other members of our research group cross-validate the coding^{39,40}.

The study was approved by the committee on use of human subjects of the University of Toronto, Canada. Each interviewee provided written consent.

both boutique personalized medicine and population or sub-population level pharmacogenomics and theragnostics^{17,18}.

Until now there has been little data based on empirical studies that describe how the emerging knowledge of human genomic variation can be practically applied to improving health in the developing world. Our findings provide a snapshot that will be of interest to other emerging and developing economies that are interested in the evolution of genomic studies, particularly their intersection with public health and as potential sources of economic activity. In this respect, the findings are relevant to the private sector in both industrialized and developing countries, and to those international organizations that are interested in how science and technology can be used to achieve and accelerate health security and human development in general.

Roadmap to genomic medicine

Our cross-comparison analysis of the above cases has generated a roadmap that will help readers better understand the ways in which these three countries are harnessing human genomic variation studies. The roadmap is made up of several common themes that emerged from the data. It represents the key factors contributing to the establishment and potential future success of the initiatives we studied. These include political will, institutional leadership, local health benefits, genomic sovereignty and the aspiration to create knowledge-based economies. Political will. In all three countries, government leadership, political support and/or government legislation were crucial to the establishment of the genotyping projects discussed here. In Thailand, TCELS, which oversees the Thai Pharmacogenomics Project, was established by Royal Decree of the King of Thailand in June 2004. Similarly, in Mexico, INMEGEN was the first department of the Mexican National Institute of Health (M-NIH) to be legislated with the support of all political parties in Congress, thus providing a strong message that genomic medicine is a priority for the Mexican people. Subsequently, INMEGEN received an initial investment of US\$120 million from the Mexican government.

In 2001, the Ministry of Health in India pledged \$20 million towards research in medical genomics¹⁹. More recently, the Indian government's <u>National</u> <u>Biotechnology Development Strategy</u> and the Thai government's <u>National</u> <u>Biotechnology Policy Framework</u> identified genomic medicine as an investment opportunity. Accordingly, the IGVdb Consortium received public funding for its genotyping initiative through the federal government's Council for Scientific and Industrial Research.

Undoubtedly, political will was instrumental to the initial development stages of these initiatives — it enabled them to access the necessary public funding. Nevertheless, given that genomic medicine and these initiatives are still in their infancy, objective criteria by which to measure their success have yet to be agreed upon. Importantly, in developed countries, critics suggest that the promise of the Human Genome Project was overhyped and that it has failed to deliver on its potential²⁰. In this context, the definition of success will probably pose a challenge as the initiatives in Mexico, Thailand and India are seeking continued political support, and healthy scepticism is called for. With this narrow understanding of the potential of genomics, the criticism is indeed valid, and we did encounter sceptic voices; for example, some key informants worried that INMEGEN is superfluous and expensive to maintain. However, if we consider genomics more widely, especially including its capacity to improve public health, the picture is different. For example, we are much better able to track SARS now that we have its genomic sequence than when the disease surfaced just a few years ago. Nevertheless, the genotyping initiatives discussed here

Box 2 | Mexican National Institute of Genomic Medicine

The Mexican National Institute of Genomic Medicine (INMEGEN) is one of twelve national institutes of health in Mexico. Created in 2004, it aims to develop a national platform in genomic medicine that is focused on national health problems and is based on the genomic structure of Mexican populations. It received an initial investment of US\$120 million from the Mexican government.

Most of Mexico's population is considered Mestizo resulting from a dynamic admixture of over 65 ethnic groups, Spaniards and, to a lesser extent, Africans, within the last 500 years. INMEGEN has genotyped over 1,200 Mestizos from different regions of Mexico, analysing 500,000 to 600,000 SNPs. This information is triggering a series of disease-related genomic studies in Mexico that will be used to improve health care for the Mexican population, and is likely to be useful to other Latin American countries with similar population profiles.

INMEGEN's first step focused on generating the Mexican HapMap in order to facilitate the next phase of research, which will concentrate on relating genomic information of the Mexican population to significant causes of morbidity and mortality in Mexico, including macular degeneration, diabetes mellitus, hypertension and obesity, cancer, infectious diseases and cardiovascular diseases. will need to anticipate scepticism and, as such, establish strategic plans outlining criteria that can be used to measure success.

Institutional leadership. Our key informants pointed to INMEGEN's and TCELS's leadership in establishing communication strategies to engage the public on matters of genomics. For instance, in an effort to engage the young Mexican public on issues of genomic medicine, INMEGEN has developed a comic book series entitled 'La Medicina Genómica, El Genoma Humano' describing the human genome, potential applications, and ethical, legal and social issues that arise out of human genomics. In addition, the institute promoted understanding of the Mexican HapMap project through radio appearances and publications for the general public. Similarly, TCELS, in conjunction with local scientists, is preparing a book on 'Pharmacogenomics for layman' to be released in June 2008. Each of these initiatives is publicly funded, hence their dependence upon public support. Investing in public engagement programmes will help raise the level of understanding of the public, possibly increasing the likelihood of public support. However, in Mexico and Thailand, some key informants told us that local critics consider some of the genomics public engagement activities as propaganda. Although public understanding will ensure public demand of genomic products and services, and encourage physicians to implement genomic medicine in their practice, genomics institutes will have to strike a balance between public relation activities and proper public engagement activities to avoid hype. Despite this concern, increased public understanding of genomics can ensure that the public have realistic expectations as to the benefits associated with genomic medicine as well as the length of time it will take to reap these benefits.

Institutional leadership in all three countries has also led to international collaborations. For example, INMEGEN is engaged in several strategic collaborations in industrialized countries, including Nestlé International Headquarters, Genóma Spain, the Pharmacogenetics for Every Nation Initiative (PGENI), the Translational Genomics Research Institute (TGen), John Hopkins University, the Broad Institute and the Public Population Project in Genomics (P3G). These collaborations enable INMEGEN to participate in research and policy decisions on the international level that are frequently led by industrialized

Box 3 | The Indian Genome Variation database (IGVdb) Consortium

Initiated in 2003, the Indian Genome Variation database (IGVdb) Consortium is a collaborative network between the Institute of Genomics and Integrative Biology (IGIB), the Centre for Cellular and Molecular Biology (CCMB), the Indian Institute of Chemical Biology (IICB), the Central Drug Research Institute (CDRI), the Industrial Toxicological Research Centre (ITRC) and the Institute of Microbial Technology (IMTECH). The aim of the consortium is to construct a public DNA-variation database with 15,000 samples from unrelated Indian sub-populations that are selected on the basis of their geographical locality and linguistic categories. This aim will further research on disease predisposition, adverse drug reactions and population migration, with the ultimate goal of improving both local and global health. Linguistic categories include Tibeto-Burman, Dravidian, Indo-European, and Austro-Asiatic from northern, southern, eastern, western, central and northeastern India. Thus far for phase 1, analysis has been carried out on, and validation is ongoing for, both reported and novel SNPs located within 75 disease genes that are thought to be prevalent in both the Indian and the global population.

Although the IGVdb Consortium is providing their data to be used by the academic community, research conducted by the IGVdb Consortium that results in discoveries and/or potential commercialization opportunities will be protected by intellectual property and will need to be licensed through them.

countries, indicating that investment in genomic medicine is providing INMEGEN with the opportunity to participate in the global economy.

Likewise, some of the same researchers leading the genotyping initiatives in India and Thailand are collaborators on the Human Genome Organisation (HUGO) Pan-Asian SNP Consortium - an international genotyping project that focuses on anthropology and human migration (BOX 5). The consortium has required scientific groups from different geopolitical environments and varying levels of scientific infrastructure to work together towards a common goal. According to key informants, several crucial factors contributed to its success, including leadership, equal partnerships, good intentions, stewardship and consensus. As a result, the HUGO Pan-Asian SNP Consortium has generated goodwill between the member countries, which in turn might act as a foundation for future Pan-Asian collaborative studies with a focus upon health as opposed to anthropology.

These north-south and south-south collaborations are valuable as they leverage the infrastructure available in host countries for the benefit of less well-developed countries; enabling them to participate as equal contributors to genomics and increasing the likelihood that they will reap benefits from it.

Our previous work has shown that political will and institutional leadership are necessary to promote a successful biotechnology sector in developing countries²¹. These case studies provide evidence of how developing countries are leveraging these two characteristics in order to coordinate the necessary policy and public requirements for the establishment of genotyping initiatives and the eventual adoption of genomic medicine. *Local health benefits.* Investing in genotyping projects can provide these countries with the necessary tools to better understand drug response, disease mechanisms and disease susceptibility in their own populations¹³. However, translation of evidence-based population allelic frequencies into targeted health interventions for local populations is seen as a challenge globally^{22,23}.

In Mexico, these challenges are being addressed and the integration of INMEGEN within the Mexican Ministry of Health facilitates more effective translation of genomic findings into public health applications. Specifically, key informants thought the results of INMEGEN's studies could inform local health decision making — for example, by focusing health promotion campaigns at Mexican sub-populations that might be at higher risk of certain chronic diseases. The 2004-2009 INMEGEN work plan is supportive of this model for public health genomics, as it reports that genomic medicine has the potential to reduce Mexican health-care costs related to diabetes management by 36% between 2010 and 2025 (REF. 24). We found this feature of INMEGEN to be unique in the developing world.

According to one key informant, largescale genotyping projects, and the capacity building that is associated with them, have already accelerated the ability of the country to deal with public health problems in India. The tools of genomic analysis have, for example, been used to genotype polio and Japanese encephalitis viruses, and have enabled public health officials and researchers to identify the evolution and spread of different strains. Thus, public health officials are able to track and manage infectious disease outbreaks more effectively.

Other downstream applications are likely to emerge from basic research being conducted in India. For example, researchers at the IGVdb Consortium have recently demonstrated an association between a haplotype at the ADRB2 locus (encoding a beta-2-adrenergic receptor) and the response to salbutamol in asthma patients in the Indian population^{25,26}. Others have found a possible link between tardive dyskinesia and specific polymorphisms located within the catechol-*O*-methyltransferase (COMT) genes²⁷. Data from these studies could lead to improved diagnostics for treatment of patients in India.

In contrast to INMEGEN, the IGVdb Consortium, the TCELS Pharmacogenomics Project and the Thai SNP Discovery Project are not incorporated within their respective health ministries. Consequently, although key informants emphasized that these initiatives would be used to better understand the biological determinants of disease, to address local prevalent health concerns, and to reduce health-care costs through improved use of therapeutics and reduced adverse drug reactions, it is not yet clear how quickly this knowledge will be adopted into public health interventions. This will pose a particular challenge in the context of Thailand's health system, which offers universal health coverage. The government will have to decide where genomic medicine ranks in terms of resource allocation.

Achieving local health benefits through genomic medicine is a lofty challenge but one that many key informants described as a key motivator and maintained is achievable in the long term. If health applications are developed from these initiatives, widescale adoption of genomic medicine and delivery of products and services will vary depending on each country's local health care and delivery systems. For instance, unlike Mexico and India, Thailand has implemented universal health care that could serve as a driver for the adoption of genomic medicine as it could, in turn, promote public health savings. One application that two Thai key informants cited as amenable to public health interventions is the screening of patients with human immunodeficiency virus (HIV) for susceptibility to nevirapine-induced skin rash; nevirapine is an antiretroviral treatment that we were told is commonly used in Thailand. Nevertheless, there were a number of concerns raised by interviewees regarding the capacity within rural communities of developing countries to take up these technologies; concerns ranged from aspects regarding public and physician understanding to the ability to deliver the services. These concerns further raise issues of who in developing countries will benefit from these new technologies and they will need to be addressed through appropriate governance methods in order to ensure equitable delivery and access.

Box 4 | Thai SNP Discovery Project and TCELS Pharmacogenomic Project

The Thai SNP Discovery Project is a collaboration between Mahidol University's Faculty of Medicine, Ramathibodi Hospital and Oracle Co. Ltd (Thailand), the National Center for Genetic Engineering and Biotechnology (BIOTEC, Thailand) and Centre National de Genotypage (CNG, France)^{41,42}.

A SNP database will contain allele frequency and linkage disequilibrium (LD) block patterns for all genes identified in the human genome and their regulatory regions in Thai and other populations (French, Japanese and African). The database will also contain other information, such as genomic sequences, genomic structure, primer sequences and functional genomic information. The information from this database will be used to identify disease-associated genes, for the candidate gene approach, for systematic genome screening and for pharmacogenomic research. It will also form the Thai contribution to the Human Genome Organisation (HUGO) Pan–Asian SNP consortium.

The Thailand Centre of Excellence in Life Sciences (TCELS) Pharmacogenomics Project has performed SNP genotyping of genes involved in drug response. For example, it has collected 1,500 samples for five pharmacogenomics projects: the human immunodeficiency virus (HIV) pharmacogenomics project (nevirapine-induced skin rash, see main text); drug allergy to allopurinol and carbamazepine; pharmacogenomics in childhood acute lymphoblastic leukaemia; pharmacogenomics in oncology chemotherapy (using fluorouracil); and pharmacogenomics in thalassaemia.

In addition, TCELS is collaborating with the RIKEN institute in Japan, which has collected 3,000 samples of patients with post-traumatic stress disorder in the attempt to understand any genomic contributions to this syndrome. Other disease areas that will be investigated by the TCELS Pharmacogenomics Project include diabetes, cardiovascular diseases, rheumatoid arthritis, HIV/AIDS, lupus, childhood leukaemia and dihydropyrimidine dehydrogenase (DPD) deficiency.

Genomic sovereignty. In 1997, the United Nations Educational, Scientific and Cultural Organization (UNESCO) declared the human genome 'the heritage of humanity' in the Records of the 29th session of the General Conference (volume 1; resolutions). But critics suggested that this stance could result in 'bio-colonialism' or 'genetic piracy' of human samples in developing countries that do not have the resources to carry out the research themselves²⁸. Several key informants in Mexico maintained that the unique patterns of variation that might exist in subpopulations have implications for the development of genomic diagnostics and genomic medicine, and as such are the equivalent of sovereign resources. Similarly, in India, there is a history of lobbying to protect the Indian genome from foreign exploitation as a response to the export of human samples by foreign researchers who often failed to acknowledge Indian collaborators or participants²⁹⁻³¹.

Consistent with the idea that unique patterns of genomic variation are sovereign resources and should be protected from foreign prospectors, Mexico has recently enacted an amendment to Mexico's General Health Law that aims to protect the national genomic sovereignty of Mexicans³². In India, although there is no specific legislation concerning genomic sovereignty, the country has made an effort to prevent the wholesale export of human biological material without prior arrangements through the government in their Guidelines for Exchange of Human Biological Material for Biomedical Research Purposes, last revised in November 1997.

By contrast, in Thailand, the concept of genomic sovereignty did not appear as explicitly in our key informant interviews, although there was recognition of the need to protect Thai DNA samples through clear regulation or legislation. It was noted that, although there are institutional guidelines within universities and hospitals, there is no central national legislation on the export of human DNA samples. However, other Thai researchers expressed concerns that guidelines and/or legislation pertaining to genomic sovereignty might impede international collaborations and partnerships.

The ability to implement genomic sovereignty legislation and to protect their resources from foreign exploitation seems to be key for each country to ensure that they can leverage the genomic variation data to encourage local innovation and participate as equal partners in the global knowledge-based economy.

Box 5 | The HUGO Pacific Pan-Asian SNP Initiative

This international collaboration between China, India, Indonesia, Japan, Korea, Malaysia, Nepal, the Philippines, Singapore, Thailand and Taiwan aims to study the genetic diversity in Asian populations. The results from the study will be made available to the public. Although this initiative is not focused on health applications, its goal is to uncover the breadth of genetic diversity and the extent of genetic similarity in Asia. The Human Genome Organization (HUGO) is an international organization of scientists originally involved in the Human Genome Project. HUGO Pacific, which is sponsoring the Pan–Asian SNP Initiative, is a chapter of HUGO and is based at the University of Tokyo, Japan. The study began in the middle of 2005 and was completed in late 2007 (REF. 42).

Knowledge-based economy. Key informants in our study indicated that stimulating the economy through innovation is a desired outcome. This seemed to be particularly relevant for key informants at INMEGEN, who stressed this outcome as a major motivator to the creation of a genomic medicine platform; they saw investment in genomic medicine as a potential entry point for Mexico into the global knowledge-based economy.

Although intellectual property protection does not guarantee the development of a commercial product, many still suggest that, in health biotechnology, intellectual property protection remains a vital factor towards the establishment of a private sector and the commercialization of products in developing countries^{21,33,34}. An early example from 1997 is Shantha Biotechnics Private, a spin-out company from the Osmania University in Hyderabad, India, that leveraged its patented innovative manufacturing process in the Pichia pastoris expression system to produce a recombinant hepatitis B vaccine¹⁴. As a result, they were subsequently able to drive down the cost of the hepatitis B vaccine within India¹⁴. Although this example is specific to health biotechnology, the model is also applicable to genomic medicine. Given the criticisms of the inadequacy of intellectual property protection systems in developing countries, we decided to focus on how each of these initiatives chose to approach this challenge. Mechanisms for intellectual property protection exist in Mexico, India and Thailand. In Mexico and Thailand, INMEGEN and TCELS are actively engaging in specific intellectual property and commercialization activities, which will hopefully offset the general opinion that these countries have traditionally weak patenting cultures, especially among academic and hospital researchers. However, establishing such intellectual property protection systems seems to involve different strategies. We found that INMEGEN, some members of the IGVdb Consortium, and the TCELS Pharmacogenomics Project were developing and exploring models to facilitate the translation of early stage research to commercialized products.

INMEGEN has a comprehensive plan for intellectual property protection: it has entered into a collaborative relationship with the Mexican Institute of Intellectual Property (IMPI) to share expertise. Currently, IMPI and INMEGEN are in negotiations for a \$5 million grant, which would enable them to maintain an in-house intellectual property office through which INMEGEN could provide Mexican researchers with the infrastructure and expertise needed to acquire patents on their research. INMEGEN also intends to use the IMPI grant to kick-start an in-house business incubator — a key factor in technological innovation³⁴, which will offer support and consulting services in business planning, commercialization, marketing, operations and information technology. Key informants at INMEGEN argued that because the institute is integrated within the M-NIH system, having intellectual property over its discoveries will also help to integrate the generated knowledge into the public health system.

Similarly, in Thailand, the TCELS Pharmacogenomics Project — by virtue of its association with TCELS — has the ability to use the available in-house lawyers to manage its own intellectual property needs. TCELS also works closely with the Department of Intellectual Property at the Ministry of Commerce. For example, TCELS assists in filing for intellectual property protection, coordinating researchers and external organizations, analysing the maturing of innovations, finding potential investors and licensing opportunities, and negotiating royalties and terms of agreement.

Although the genotyping projects, at least in Mexico and Thailand, seem to aspire to foster the development of commercial products through intellectual property protection, we are not aware of any concrete products or services in the short-term pipeline. Furthermore, such products or services are unlikely to be developed soon, considering the complexity of these

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research initiatives. We therefore searched for evidence of current small-to-medium enterprises that have, or are actively developing, human genomic medicine products and services. We did not find any specific firms in Mexico, although both Thailand (two start-up companies offering personal genotyping and wellness services were identified) and India (Avesthagen has announced it is initiating a large-scale genotyping project of the Parsi genome) show evidence of burgeoning local private-sector involvement in human genomic variation studies and genomic medicine. Despite the existence of a few companies, it is too early in their development to provide a detailed analysis of their capabilities, business models and economic benefit. However, key informants from the private sector did tell us that interfacing with public research centres is often a challenge. Creating and maintaining bridges between the public and commercial sector is thought by some to be necessary for knowledge translation and commercialization.

Despite the existing scepticism around the adoption of genomic medicine in emerging markets and developing countries, the above examples are indicative of an effort to increase the likelihood that the knowledge they generate will provide them with a competitive edge in a knowledge-based economy.

Concluding remarks

If the Human Genome Project is the foundation of a house representing the future of genomics, Mexico, India and Thailand are already claiming and building their rooms in that house. They are not the only

Glossary

Admixture

The pattern of genetic variation that results when a population is derived from founders that originated from more than one ancestral population.

Linkage disequilibrium block

A DNA segment that contains markers that are in significant linkage disequilibrium with each other, which implies that there is low recombination activity within the block.

Linkage disequilibrium

(LD). A measure of genetic associations between alleles at different loci, which indicates whether allelic or marker associations on the same chromosome are more common than expected.

Theragnostic

The union of a therapy with a diagnostic that can determine the presence of a series of predictive biomarkers, including genomic, metabolomic and proteomic markers. Theragnostics will enable clinicians and physicians to limit the number of adverse drug reactions and refine treatments for their patients.

ones; China's Beijing Genomics Institute is preparing to sequence the entire genome of one hundred Chinese individuals, and South Africa's Africa Genome Education Institute is devoted to educating the public about the structure and function of genomes, and plans to study the genetic basis of diseases relevant to the South African population. Brazil, which has long been considered a leader in genomic sciences in the developing world, has invested in cancer genomics (see genomics advances in Brazil at the World Health Organization web site) and the sequencing of parasite³⁵ and plant genomes³⁶. Specifically, in 2001, the Organization of Nucleotide Sequencing and Analysis (ONSA), in Sao Paulo, Brazil, completed the first published sequence of the Xylella fastidiosa bacterium, a plant pathogen responsible for disease in economically important crops such as citrus³⁷. This effort was in large part responsible for establishing the subsequent capacity in genomic sciences in Brazil and it has brought moderate economic benefits³⁸. <u>Alellyx</u>, for instance, is a biotechnology company that spun out of the ONSA network and focuses on crops that are of economic importance to Brazil. Alellyx also holds, amongst others, the US patent on the whole genome and gene sequences for disease diagnostics of X. fastidiosa, which they are currently using to develop disease resistance and pesticide research³⁸. In addition to our case studies, these examples indicate that emerging economies are beginning to establish footholds in genomic sciences.

The findings we report here suggest that a clear motive for the genotyping and associated life-sciences initiatives is to improve health and capture the value of research to help create knowledge economies. We found that political will and institutional leadership were crucial in developing a vision and a plan, and in the implementation of large-scale population genotyping initiatives in Mexico, India and Thailand. In contrast to many developed countries, we found these three countries to be more focused on practical applications of genomics rather than solely on advanced basic research. Another difference between these three developing countries and other developed countries is the extent to which industry (for example, GlaxoSmithKline) drives genomics research and development in developed countries. Also, INMEGEN in Mexico is unique in the extent of its integration with public health needs, partly owing to its relationship from its inception to the Mexican Ministry of Health.

The large-scale human genotyping projects described in this article are not unlike the early sequencing efforts in Brazil — they are helping to build scientific capacity, which is in line with the increased focus on innovation in science and technology as the engines of economic growth in developing countries. They are setting the scene for local discovery, development, commercialization and delivery of affordable health products. They might allow these countries to be more competitive in the global economy and perhaps, in niche areas, to leap-frog ahead of some advanced economies.

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Competing interests statement

The authors declare <u>competing financial interests</u>; see web version for details.

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India's Guidelines for Exchange of Human Biological Material for Biomedical Research Purposes:

http://icmr.nic.in/min.htm

Indian Genome Variation database Consortium (IGVdb Consortium): http://www.igvdb.res.in

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South Africa's Africa Genome Education Institute:

http://www.africagenome.co.za

Thai government's National Biotechnology Policy Framework: http://www.biotec.or.th/document/W-Eng/ FrameWork9-11-2548.pdf

Thailand Centre for Excellence in Life Sciences (TCELS):

http://www.tcels.or.th/en/index.asp Thailand SNP Discovery Project: http://thaisnp.biotec.or.th

The Organization of Nucleotide Sequencing and Analysis (ONSA): <u>http://watson.fapesp.br/genoma.htm</u> UNESCO's Records of the 29th session of the General

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