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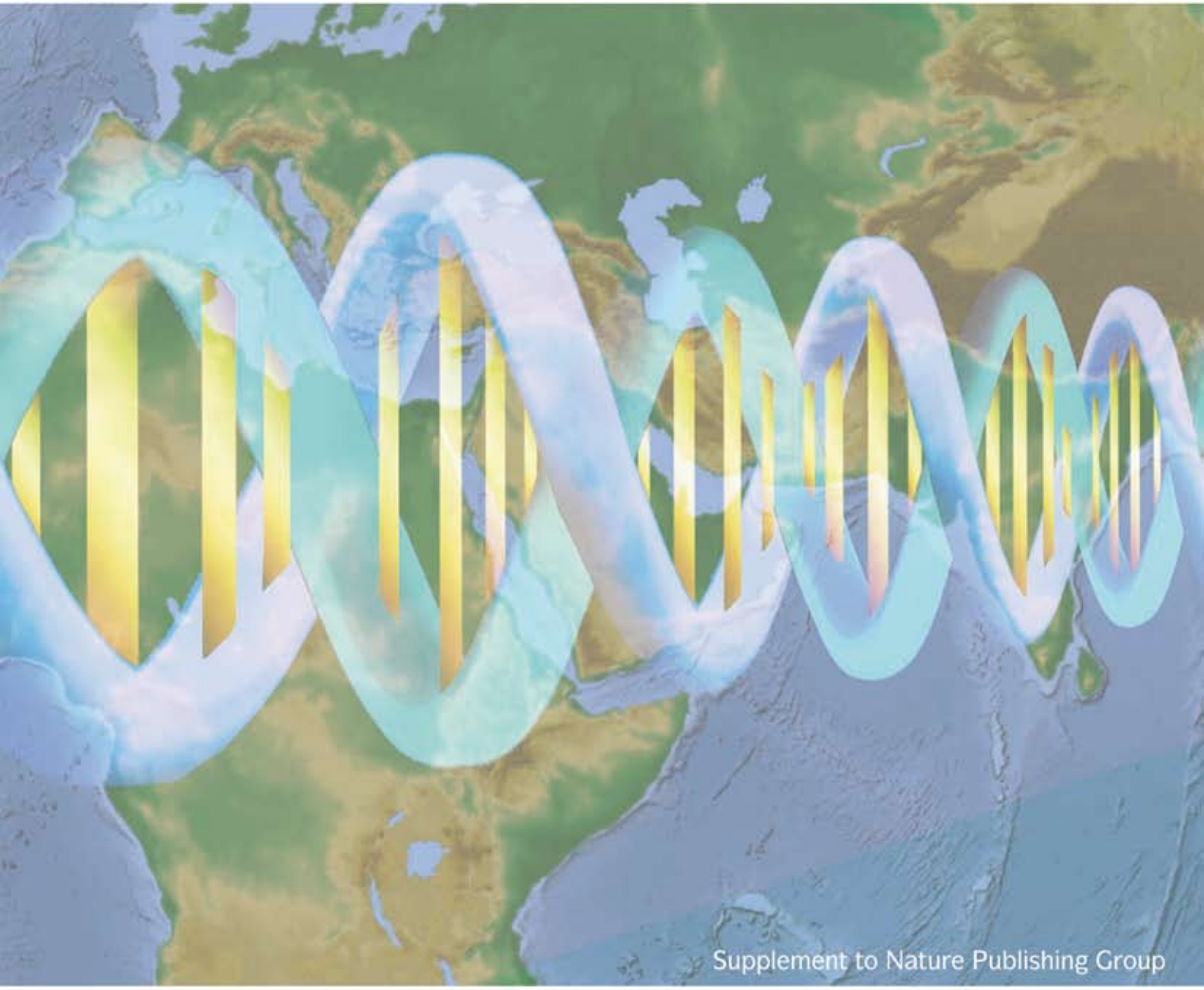
Genomic medicine
in developing countries



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SCIENCE AND SOCIETY

Genomics, public health and developing countries: the case of the Mexican National Institute of Genomic Medicine (INMEGEN)

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Abstract | In 2004, the government of Mexico established the National Institute of Genomic Medicine (INMEGEN), to carry out disease-related genomic studies that will address national health problems and stimulate scientific and technological development by generating new commercial products and services in genomic medicine. Towards this end, INMEGEN is carrying out a large-scale genotyping project to map genomic variation within its own population. The initiative is expected to generate a key resource for local researchers to understand disease susceptibility and variation in drug responses, which will contribute to Mexico's goal of developing public health genomics — a field in which Mexico is proving to be a leader amongst emerging economies.

Mexico recently joined the global community in investing in human genomic variation studies through the formation of the National Institute of Genomic Medicine (INMEGEN), the first Mexican institute to systematically describe the genomic diversity of the Mexican population. INMEGEN will provide an opportunity for Mexico to create innovative solutions to its own health challenges as it will focus on the link between genomic variation in the Mexican population, disease susceptibility and drug-response variability. This initiative is of particular relevance as recent statistics show that in addition to the rising rates of infectious diseases in developing countries, the rates of non-communicable diseases are also on the increase[1]. Any tool, including genomics, that can address these health burdens will be of great value in a country like Mexico. INMEGEN will also play a part in economic development. Mexico's recent draft proposal for the new Law on Science, Technology and Innovation[2] cites several challenges to Mexico's innovation system that INMEGEN will help address: Mexico has a slow economic growth amounting to only 2.8% per year between 1980 and 2004; there are only 0.80 researchers per 1000 labour force; only 0.33% of Mexico's gross domestic product (GDP) was spent on science and technology (S&T) in 2006; and linkages between the knowledge-based public sector and the private sector have been weak or insufficient[2].

Using previously described qualitative methods[3,4] we performed 19 in-depth semi-structured interviews with key informants representing scientists and managers at INMEGEN and key informants from diverse backgrounds, such as the media, one non-governmental organization, scientists from other Latin-American countries, as well as experts in the areas of genomics/pharmacogenetics and ethics from developed and developing countries. Here, we discuss the analysis of the INMEGEN case study; uniquely, it aims to develop public health genomics in Mexico.

Adoption of genomic medicine in Mexico

Political will. In 2000, the consortium for the creation of INMEGEN, which included representatives from the Ministry of Health (SSA), the Mexican Health Foundation (FUNSALUD), the National Council for Science and Technology (CONACYT) and the National Autonomous University of Mexico (UNAM)[5,6], commissioned a feasibility study that concluded that developing genomic medicine in Mexico would lead to significant improvements in the diagnosis, treatment and prevention of disease, thereby enabling a reduction in health-care costs. The study also indicated that a Mexican genomic-medicine platform would stimulate local S&T, particularly in the field of pharmacogenomics, and promote the development of goods and services[7]. The report was crucial for gaining social and political support in the Mexican Congress.

In 2004, INMEGEN became the eleventh member of the Mexican National Institutes of Health (M-NIH), which is composed of the government's main medical research entities and provides the highest level of medical care in Mexico. The creation of INMEGEN is of particular historical importance in Mexico because it is the first member of the M-NIH to be created with the support of all political parties in Congress; providing a strong message that genomic medicine is a priority for the Mexican people and also legitimizing its creation.

Genomic sovereignty. Our key informants agreed that, although the human genome is a public good, there are unique patterns of variation that might exist in sub-populations that have implications for the development of genomic diagnostics and therapeutics in Mexico. This concept is further reinforced by recent advances in whole-genome scanning techniques, which have revealed that large-scale copy number variants and other structural genomic variants are a more frequent source of human variation than nucleotide-level variation[8–10]. As one key informant explained, "surely others have commented on genomic sovereignty […] we believe that if we do not carry out studies to understand our genomic patrimony that we possess, well, no one else will because they will be interested in their own populations. Secondly, should the interest exist and they [other countries] come to get this information, they make us

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dependent on this information and then it will cost us. We have to develop our own genomic information." In this context, the term 'genomic sovereignty' was described to us by several informants as the central motivator behind the creation of INMEGEN.

An amendment to Mexico's General Health Law that aims to protect the national genomic sovereignty of Mexicans has recently been enacted[11]. As a result, the sampling of genetic material and its transport outside of Mexico without prior approval from the SSA is illegal. The legislation also stipulates that the SSA will reserve the right to consult INMEGEN for opinions pertaining to requests to transport any human genetic material outside of Mexico. This law was initiated in response to reports of 'safari research', in which foreign researchers attempted to obtain blood samples from Mexican subjects, including indigenous groups, without the approval of the SSA and local Mexican ethics committees[12]. These reports fuelled concerns that neither the research participants nor the general Mexican population would benefit from such research. The new law, although specific to the transport of human genetic material, is part of a broader desire to ensure that any benefit resulting from genomic medicine will be made accessible to the Mexican public. Towards this end, INMEGEN also plays the part of the national reference centre for genomic medicine, enabling the Institute to oversee any future product or service derived from human genomic research carried out on the Mexican population.

Local health benefits. The Mexican government spends about 6.4% of its GDP on health care[13], and its health system consists of public and private entities. As part of the public health sector, INMEGEN is tasked with addressing the health-care needs of a nation faced with an increasing burden of chronic diseases, which often require ongoing drug therapy. INMEGEN has genotyped over 1,200 Mestizos from different regions of Mexico, analysing 500,000 to 600,000 SNPs. This information has triggered a series of disease-related genomic studies in Mexico that will be used to improve health care for the Mexican population. These studies will in turn facilitate research that will focus on relating genomic information of the Mexican population to significant causes of morbidity and mortality in Mexico, such as macular degeneration, diabetes mellitus, hypertension and obesity, cancer, infectious diseases, and cardiovascular diseases. The Institute's strategy is to use evidence-based population allelic frequencies to inform public health decision-making and target health interventions accordingly.

Given that the top three causes of mortality in Mexico are cardiovascular disease, diabetes and cancer[14], INMEGEN's contribution to improving public health could be through health promotion campaigns aimed at those Mexican sub-populations that have a higher risk of developing these chronic diseases, based on the results of INMEGEN's genomic and clinical studies. For instance, the 2004–2009 INMEGEN work plan reports that genomic medicine has the potential to reduce health-care costs related to diabetes management by 36% between 2010 and 2025 (REF. 5). Another contribution highlighted by INMEGEN is the potential that pharmacogenomics can offer towards the treatment of paediatric leukaemia with 6-mercaptopurine, an effective drug known for its narrow therapeutic index (the ratio of therapeutic benefit to side effects) and risk of severe toxic events.

So far, INMEGEN has focused its genotyping initiative on the Mestizo population (~80% of Mexico's population) and not the indigenous populations. INMEGEN proceeded with phase one of its haplotyping project by sampling the Mestizo population across all geographic states of the country. Obtaining their consent was consistent with the Mexican Federal Law and included eight guidelines from the HapMap ethical, legal, and social issues (ELSI) project[15]. INMEGEN's decision to defer sampling of Mexico's indigenous populations was motivated by the reported local and international incidents of safari research and well known cases of indigenous DNA sample use without consent[16–19]. Consequently, phase two, the haplotyping of Mexico's indigenous populations, has only recently begun, and INMEGEN is working with the communities to help them understand the goals as well as the benefits and risks of the study. Towards this end, INMEGEN has been working with the Institute of Anthropological Research at the UNAM, the Ministry of Health in each state, and with indigenous community leaders and social scientists to translate the informed consent forms into local indigenous languages.

How will INMEGEN translate its discoveries to products that benefit the population? Although INMEGEN's focus is public health genomics, it also aims to promote private sector development as part of a broader desire to increase Mexico's competitiveness in a global market. The Institute recognizes that the private sector is essential for the efficient delivery of safe and effective diagnostics and therapeutics. Consequently, it intends to foster the growth of the local small to medium enterprises (SMEs) in the private sector through government initiatives, such as investment in local research and development (R&D), which addresses local health needs and can secure a competitive advantage in a knowledge-based economy. Engaging in the knowledge-based economy is crucial for Mexico in the face of the slow economic growth it has recently experienced[2,20].

Knowledge-based economy. According to our key informants, Mexican researchers and academics have generally not adopted a commercialization culture. Between 1980 and 2001, 96% of biotechnology patents were filed in Mexico by foreigners[21]. Accordingly, INMEGEN's strategic vision includes the development of a strong intellectual property platform[4]. Moreover, because INMEGEN is integrated within the M-NIH system, owning intellectual property over its discoveries will help to integrate the generated knowledge into the public health system. Hence, access to products that are related to discoveries made at INMEGEN is guaranteed to Mexican citizens because the Institute's intellectual property strategy provides the leverage to negotiate affordability and access to therapeutics resulting from its patents.

Currently, INMEGEN and the Mexican Institute of Intellectual Property (IMPI) are sharing expertise in genomic sciences and intellectual property rights. In addition, INMEGEN is in negotiations for a US$5 million grant from IMPI to establish and maintain an in-house intellectual property office and Business Incubator. These facilities would enable INMEGEN to provide Mexican researchers with the infrastructure and expertise required to translate basic research into commercial applications. Additionally, INMEGEN's board of trustees is made up of local business leaders from companies such as Nestlé Mexico, Apasco Cement and the Mexican Association of Banks that advise the Director General and the Board of Governors of INMEGEN on key areas of business development. Although INMEGEN has secured $125 million in initial government funding over 5 years[6], the Board of Trustees is also active in fundraising initiatives, thereby diversifying funding sources and increasing the probability of long-term sustainability of INMEGEN.

INMEGEN encourages genomic researchers to develop spin-off companies that can translate the acquired knowledge

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into health products. It will foster the development of local SMEs in the area of genomic medicine. As one key informant highlighted, "if we want these [potential therapeutics and diagnostics] to reach pharmacies and bedsides and doctors' offices, there's no question we need to create a product and commercialize it. We need to do it." These SMEs could, in the future, initiate partnerships with Mexican pharmaceutical companies or larger multinationals in order to develop diagnostics and therapeutics that will better meet local health needs. Promoting a commercialization culture will also require market receptivity of future genomics health products. INMEGEN, however, is aware that genomics products might not be well received unless an adequate public engagement strategy is developed.

Institutional Leadership. INMEGEN has demonstrated institutional leadership in developing public engagement programmes and tools, placing emphasis on education and training, developing an ELSI unit, and engaging in both north-to-south (between developed and developing economies) and south-to-south (among developing economies) collaborations.

INMEGEN has engaged with the public since its inception. The Institute's efforts to promote understanding of the Mexican HapMap project resulted in radio appearances and publications for the general public[22]. To engage the young on issues of genomic medicine, the Institute has developed a comic book series titled 'La Medicina Genómica, El Genoma Humano', describing the human genome, potential applications and ELSIs that arise from the study and application of human genomics. Intended for students 10 to 12 years of age, the series is printed and distributed in schools nationwide with the help of the Ministry of Education and can be accessed from the INMEGEN comic book web page. The goal of the comic book is to engage the public and develop a 'genomics culture' that includes public understanding and acceptability of future products of genomic medicine. In the words of one key informant, "why it is so important to create this genomic culture is because if we find something and we develop a product and there is no culture, but myths on cloning and some other issues, and we put this first product out — that won't be well received." As a follow-up to the release of the first comic book, INMEGEN held a focus group with a sample group (15 students and 14 adults) to obtain feedback on how to make improvements to future issues. This process of self-evaluation is crucial to ensuring that its public engagement tools are effective. The impact of this comic book series as a public engagement tool extends beyond Mexico. For instance, INMEGEN has been collaborating with the Translational Genomics Institute in Phoenix, Arizona, to develop an English version. In addition, INMEGEN participates in public presentations at local science museums to discuss the human genome. All of these efforts are aimed towards creating a generation of well informed citizens that can be engaged in public policy.

The Institute participates in the multi-institutional undergraduate degree programme in genomic sciences — the first of its kind in Latin America. INMEGEN offers several courses at the undergraduate level, not only in genomics and genomic medicine but also in areas such as public administration, communications, health sciences, law, design, technological development, economics, information technology and supercomputers. For health professionals, INMEGEN organizes courses on genomic medicine in Mexico City's top medical schools, such as 'Introduction to Genomic Medicine', 'Genomic Applications in Pediatrics' and 'Genomic Applications in Internal Medicine'. Graduate courses for masters and doctoral students in biomedical sciences are also offered, and topics include polymorphism sequencing and identification, genotyping and expression analysis, population genomics, and multifactorial diseases. INMEGEN has also organized the first two National Congresses on Genomic Medicine, which have attracted world-renowned speakers.

In addition to developing a human resource base in genomic sciences and genomic medicine, INMEGEN is developing its ELSI research and education capabilities. This includes creating a research centre for ethical, legal, and social implications of genomic medicine. The proposed centre is part of a collaboration with the Pan American Health Organization and the World Health Organization, and includes training human resources in bioethics, carrying out research projects that examine bioethics in the context of genomic medicine, and overseeing all ethical, legal and social aspects of the research carried out at INMEGEN[7].

INMEGEN is establishing collaborations between Mexico and other Latin-American countries, a natural extension given the shared cultural history and language. The creation of INMEGEN has sparked interest in domestic genomic platforms in other countries of the region that currently might not have the resources to establish such programmes but might have enough funding to contract INMEGEN to develop a map of their genomic diversity. According to our key informants at INMEGEN, several Latin-American countries are keen to form governmental partnerships with services provided by INMEGEN. INMEGEN could then act as a hub for various human genomic medicine networks that can be very beneficial as they will enable other Latin-American countries to understand their public health needs and develop genomic therapies without needing to duplicate the initial investment already made by Mexico.

INMEGEN also collaborates with institutions, organizations and individuals in industrialized countries, consistent with its strategy to create long-term links with institutions that also share the goal of developing genomic applications to improve human health. These partnerships are strategic because they enable the Institute to actively participate in research and policy decisions that are frequently led by developed countries on the international stage. INMEGEN recognizes that this is an ideal opportunity to act as a bridge for north-to-south collaborations on behalf of all of Latin America. Its current collaborators include Nestlé (International Headquarters), Genoma Spain, the Pharmacogenetics for Every Nation Initiative, the Translational Genomics Research Institute, Johns Hopkins University, The Broad Institute, the Human Genome Organisation Pan-Asian SNP Consortium, and Public Population Projects in Genomics.

Challenges for INMEGEN

The long-term sustainability of INMEGEN will depend on the way that the Institute addresses challenges in several areas.

Human resources. A shortage of trained professionals who can work in R&D in genomic medicine and in pharmacogenomics and ethics will continue to be a challenge as INMEGEN ramps up its capacity. In an era in which the importance of human capital is widely recognized, the ability to retain local talent and possibly repatriate Mexican scientists living abroad to reverse the brain drain[23,24] is crucial. We were told by INMEGEN that they would be making efforts to engage the Mexican scientific diaspora by tapping into repatriation packages offered through CONACYT. INMEGEN receives support from the Mexican Health Foundation to offer recruitment bonuses, and it has recently signed an agreement with Nestlé to establish the Nestlé Chair in Nutrigenomics, which offers a competitive salary and relocation expenses. The

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INMEGEN–Nestlé agreement also includes funding for two fellowships for Mexican graduate or postdoctoral candidates to receive training abroad with the intention of returning to INMEGEN. Currently at 120 employees, INMEGEN is slated to grow to 400 employees by 2012.

The need for measures of success. Given that genomic medicine is still in its early stages, no criteria have been agreed upon by which to measure the success of an institution like INMEGEN. It takes a long time for the results of a large-scale genotyping effort to translate into health interventions or products. In the context of Mexican science, INMEGEN received a substantial sum of money ($125 million) from the Mexican government. Such an investment into one institution when R&D spending in Mexico represents only 0.33% of its total GDP[2] has been perceived as hoarding limited R&D funding resources. In addition, there is a clear conflict between classically trained human geneticists in academia who understand success in terms of peer-reviewed scientific publications and citations, and the new generation of genomic scientists who have additional parameters in mind, such as building infrastructure and training human resources. Not surprisingly, the realities of a long-term investment provide fertile ground for scepticism and misunderstandings, which leads to the perception by some of the key informants that it might not be possible to deliver on all the objectives. However, INMEGEN's strategic plan also reflects a more global shift in thinking from a purely academic approach in human genetic research to a broader approach that includes public–private partnerships and technology transfer. Therefore, solutions will require validation of novel criteria for success — substantially increasing the number of INMEGEN's high-impact peer-reviewed publications and demonstrating that an increase in patents and business incubators result in tangible benefits for the Mexican population.

Political will. The Mexican government's policies can change every 6 years following the inauguration of new regimes, which can make achieving the country's long-term goals challenging. In addition, the broader innovation system in which INMEGEN exists presents several challenges to ensuring that genomics and S&T in general can improve health and development in Mexico. In January 2007, Filipe Calderon's newly elected government announced a budget cut of 6.7% (including inflation) for S&T funding[25], bringing Mexico's investment in S&T to a 20-year low. In light of reports on the part that S&T plays as a tool for national[26] and economic development[26–28], this type of controversial budget cut is a barrier to the creation of an environment that fosters the development and the adoption of health-related technologies that can help solve problems relevant to developing-world populations. Although INMEGEN does not seem to be affected by these policies in the short term, achieving its long-term deliverables will require that the Institute secures long-term sustainable funding by maintaining open communication with all political parties, promoting partnerships and collaborations with those individuals and institutions who object to the budget being redirected towards INMEGEN, and carrying on the fight for an increase to the S&T federal budget.

The need for regulatory frameworks. Mexico has enacted legislation to protect its genomic resources[12], however, enforcing this law will require manpower and the development of specific mechanisms. For instance, as the national reference centre on genomic medicine, INMEGEN will need to continue to build on the current Genomic Sovereignty Law mentioned earlier in this article so that it includes a regulatory framework that specifically addresses guidance on importation of future foreign products derived from genomic medicine. Will INMEGEN require that these products be tested on Mexicans during Phase II and III clinical trials? Currently, there are no formal guidelines set by the M-NIH that require collection of genomic and pharmacogenomic data during clinical studies.

Scientific literacy among the public. Although literacy rates in Mexico have reached 91%[29], the level of scientific literacy required for outreach, public engagement and public education will remain a challenge, despite the available tools. As an example, the creation of INMEGEN took place at a time when the world media was reporting claims that scientists in Italy[30] and Korea[31] were cloning humans. These media reports, along with the amendment of laws governing the Mexican Health Institutes to allow embryonic stem-cell research and therapeutic cloning[32], fuelled concerns and misconceptions, including among followers of the Roman Catholic Church, that INMEGEN was going to conduct research involving embryonic stem cells and cloning. We also noted that environmental activists, along with advocates of indigenous rights, distrust the government and are sceptical of S&T advances, considering them yet another form of Western imposition aimed at destroying the indigenous way of life. Although INMEGEN successfully dispelled the concerns of the Church, the Institute will have to continue developing a more robust public engagement strategy focused on educating the public and showing that genomic medicine provides concrete benefits to indigenous populations.

Concluding remarks

In 2005, a group of experts from industrialized nations convened in Bellagio, Italy, to develop a consensus on the structure needed for the "effective translation of genome-based science and technology into improved population health" — often referred to as public health genomics[33]. The group concluded that four core activities are necessary: informing public policy, developing and evaluating preventive and clinical health services, communication and stakeholder engagement, and education and training. INMEGEN is active in each of these areas and illustrates Mexico's leadership as an innovative emerging economy that is committed to developing and delivering public health genomics. The Mexican government's initial investment of $125 million in INMEGEN signifies its commitment towards this effort. However, as a result, INMEGEN is largely government driven, thus sustaining this commitment will be crucial — as INMEGEN will remain costly to maintain in the long term.

INMEGEN's real strength lies in demonstrating how to link a well resourced, vertically integrated genomic medicine R&D facility (with a business incubator and ELSI unit) to a national health-care system to provide public health genomics. Within this model, they provide numerous lessons: the importance of political will and leadership; generating knowledge that is relevant to local health needs; working with the private sector to ensure that translation of genomics knowledge can be converted to products and services; engaging with the public early on to create a genomics culture and acceptability of future products and services; fostering north–south and south–south collaborations; and integrating ELSI into the development of genomics from the beginning. INMEGEN has only just begun and, so far, has met its initial objectives. The next few years will be crucial for INMEGEN as it attempts to illustrate how public health, economic development and global competitiveness can be achieved in tandem.

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Competing interests statement
The authors declare competing financial interests; see web version for details.

FURTHER INFORMATION
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INMEGEN comic book web page: http://www.inmegen.gob.mx/index.php?option=com_content&task=view&id=663&Itemid=0
INMEGEN's Business Incubator: http://www.inmegen.gob.mx/index.php?option=com_content&task=view&id=405&Itemid=275
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SCIENCE AND SOCIETY

From diversity to delivery: the case of the Indian Genome Variation initiative

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Abstract | India currently has the world's second-largest population along with a fast-growing economy and significant economic disparity. It also continues to experience a high rate of infectious disease and increasingly higher rates of chronic diseases. However, India cannot afford to import expensive technologies and therapeutics nor can it, as an emerging economy, emulate the health-delivery systems of the developed world. Instead, to address these challenges it is looking to biotechnology-based innovation in the field of genomics. The Indian Genome Variation (IGV) consortium, a government-funded collaborative network among seven local institutions, is a reflection of these efforts. The IGV has recently developed the first large-scale database of genomic diversity in the Indian population that will facilitate research on disease predisposition, adverse drug reactions and population migration.

With one of the world's largest populations, a high burden of infectious disease and an increasing rate of chronic disease[1], India cannot afford to adopt existing and expensive Western health-care models to address its local health needs. Instead, India needs to look to innovative, cost-effective models, including adopting emerging health technologies. Genomic sciences and related technologies can add value to India's

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knowledge-based economy, and to harnessing life-sciences research for health and economic development. Although the relevant policies are in place, what remains to be seen is to what extent they will be translated into concrete support for research, development and delivery of products and services in the human genomics field. Identifying the needs, encouraging local collaborations and helping to form R&D networks will go a long way towards establishing South Africa in this field.

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FURTHER INFORMATION
African Genome Education Institute (AGEI): http://www.africagenome.com
African Institute of Biomedical Science and Technology (AiBST): http://www.aibst.com
African Society of Human Genetics (AfSHG): http://www.afshg.org
Biodiversity Act: http://www.info.gov.za/gazette/acts/2004/a10-04.pdf
Burden of Disease Research Unit FAQs, Medical Research Council: http://www.mrc.ac.za/bod/faqdeath.htm
Centre for Proteomic and Genomic Research (CPGR): http://www.cpgr.org.za
Freedom to Innovate report by the African Union High Level Panel on Modern Biotechnology: http://www.nepadst.org/doclibrary/pdfs/biotech_africa_2007.pdf
Gknowmix: http://www.gknowmix.com
Lifelabs: http://www.lifelab.co.za
McLaughlin–Rotman Centre for Global Health: http://www.mrcglobal.org
National Institute of Genomic Medicine (INMEGEN), Mexico: http://www.inmegen.gob.mx
The Division of Human Genetics, University of Cape Town: http://web.uct.ac.za/depts/genetics
The Living History Project: http://www.africagenome.com/index.php?option=com_content&task=category&sectionid=4&id=13&Itemid=43
The Public Understanding of Biotechnology programme: http://www.pub.ac.za
The Skin Colour Education Project: http://www.africagenome.com/index.php?option=com_content&task=view&id=17&Itemid=39
The World Health Organisation's South Africa overview: http://www.who.int/countries/zaf/en

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SCIENCE AND SOCIETY

The next steps for genomic medicine: challenges and opportunities for the developing world

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Abstract | This is a historical moment on the path to genomic medicine — the point at which theory is about to be translated into practice. We have previously described human genome variation studies taking place in Mexico, India, Thailand, and South Africa. Such investments into science and technology will enable these countries to embark on the path to the medical and health applications of genomics, and to benefit economically. Here we provide a perspective on the challenges and opportunities facing these and other countries in the developing world as they begin to harness genomics for the benefit of their populations.

Thanks to rapid economic development, two-thirds of the entire global economic growth last year was from the so-called emerging economies, which are predicted to grow at an average of 6.7% in 2008 compared with 1.3% in the United States, Japan and European Union[1]. In addition, 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 the subsequent intellectual property[2–4]. The situation in the poorer parts of the developing world, especially in sub-Saharan Africa, has so far been different. The proportion of gross domestic product (GPD) spent on research and development (R&D) is extremely low in sub-Saharan Africa[5], and health expenditure is less than

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US$30 per capita annually[6] compared with more than $6,000 in the United States[7]. However, in terms of understanding the value of S&T for development, of investing in S&T, and of realizing the need to spend more on health, the situation might be changing. For example, African Union countries have endorsed the call to spend 1% of their GDP on S&T and have undertaken to spend more on health[8,9].

We have described several case studies in Mexico, India, Thailand and South Africa, which demonstrate how emerging economies in the developing world are investing in large-scale human genomic variation studies[10–13]. The most comprehensive programme is Mexico's National Institute for Genomic Medicine (INMEGEN), which has described in a recent publication a nine-point strategy for the adoption of genomic medicine, including: building an innovative organizational design; establishing the initial infrastructure; initiating nationwide strategic alliances; conducting R&D in genomic medicine; applying genomic technology to common health problems; reaching excellence in teaching and training programmes; supporting academic programmes in genomic medicine; addressing ethical, social and legal issues; and translating genomic knowledge into products and services[14]. For these countries that have already embarked on major genomics initiatives, establishing research institutes and conducting the research are the first steps on the path to genomic medicine. For them the major question now is how they will go from this early-phase investment towards the hoped-for health-oriented applications, and the economic benefits. For other countries that have not started genomics initiatives, the question is: what are the potential entry points? And for all developing countries, with or without current genomics initiatives, the question is: what are the challenges and opportunities along the way to the adoption of genomic medicine and to deriving economic benefit from genomics? Some challenges are common to all countries, whether economically developed or developing. Other challenges will be more specific to developing countries. Here we present a perspective on the challenges and opportunities associated with the adoption of genomic medicine, particularly in the developing world, and the need to understand the interdependent nature of efforts to develop genomic medicine globally.

Projects in the developing world

The large-scale human genomic variation projects that we have described are not the only projects of their kind taking place in emerging economies and the developing world. China was the only developing country that participated in the sequencing of the human genome. Several years later, it has a number of important initiatives related to genomics. For example, China's Beijing Institute of Genomics plans to sequence the entire genome of 100 Chinese individuals. Some relatively wealthy countries, previously unknown for their involvement in human genomics, are also investing in this field. Researchers in the Al-Mulla molecular pathology laboratory at the University of Kuwait, for example, are using haplotype mapping to study the Arab genome and to identify genomic sites linked to colorectal cancer and type II diabetes. Iran has initiated the Human Genome Diversity Project of Iran (HGDPI), with the main objective of documenting genomic diversity in the populations of Iran for anthropological purposes, and generating a database towards furthering the understanding of disease predisposition. Finally, sub-Saharan African countries other than South Africa are also investing in this field. In the year 2000, a national DNA data bank was initiated in The Gambia containing samples from ~57,000 West Africans[15,16]. More recently, a biobank and pharmacogenetics database was established in Harare, Zimbabwe, containing 1,488 samples from several ethnic sub-Saharan African populations (Nigeria, Kenya, Tanzania, Zimbabwe and South Africa)[17].

Finally, the Pharmacogenetics for Every Nation Initiative (PGENI) is also worth noting in this context as its goals include: enhancing the understanding of pharmacogenetics; building local infrastructure for pharmacogenetic studies; providing guidelines for medical prioritization; and promoting the integration of genetic information in the developing world.

Exploring potential opportunities

Countries in the developed world, such as the United Kingdom, the United States and Japan have made tremendous investments in R&D towards genomic medicine[18,19] (the UK Biobank and the US National Office of Public Health Genomics, for example). Emerging economies in the developing world that have made a similar commitment will need to consider how best to identify their next steps into genomic medicine. Thinking of these next steps might also help them identify unique niches that would give them commercial advantages. For other countries that have not yet started genomics initiatives, their entry points will depend, to some degree, on their respective life-sciences innovation infrastructure. Such entry points (see below) would need to be appropriate for their level of investment in genomics R&D and their existing health-care delivery systems.

The current trend in terms of both next steps and entry points is for countries in the developing world to collaborate in R&D with more developed nations (north–south collaborations). The Human Genome Organisation (HUGO) Pan-Asian SNP Consortium provides an example of a recent north–south R&D collaboration between Asian countries[20,21]. Lessons learned from such collaborations have contributed to the further development of international ethical guidelines for benefit sharing, ownership and R&D capacity building in human genomic research. However, increasingly there is a trend towards south–south collaborations[22], in which developing countries pool their limited resources, help each other and learn from each other's experience. For example, Mexico's significant investment in genomic research infrastructure provides other Latin-American countries lacking genomic R&D capacity the opportunity to pool their resources with Mexico, as opposed to the United States or Europe, towards the development of genomic medicine and innovative genomic medicine products for this region.

Next steps and entry points will need to be cost effective. Pharmacogenomic approaches, including diagnostics, can reduce adverse drug reactions in countries that can least afford to waste money on drugs that might not have the expected therapeutic effect. Diagnostics might be easier to develop than new drugs and vaccines, as they bypass the costly clinical trial stage and tend to have a shorter regulatory review schedule. In this respect, once the cost drops significantly, pharmacogenomic diagnostics might be an early next step or even an entry point for some developing countries. Given their access to large populations exposed to multiple infections (for example, HIV/AIDS, malaria and tuberculosis), another viable option for developing countries could be to focus genomics R&D on the host–pathogen responses for these infections.

Bioinformatics provides another potential option. The South African National Bioinformatics Institute (SANBI), for example, has developed eVOC — a software program that unifies gene expression data by facilitating a link between the genome sequence and expression phenotype information[23]. The World Health Organization-based Special Program on Tropical Diseases Research and Training runs training

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programmes on bioinformatics for scientists in the developing world[24].

National genotyping projects are useful for establishing base-line profiles, which might have great benefit for subsequent studies. For example, INMEGEN has revealed significant ancestral components between populations from different regions of Mexico. Moreover, identification of unique SNPs and significant differences of functional variations related to drug metabolism suggest the need for regional approaches for the study and applications of genomic medicine in Mexico. The Indian Genome Variation (IGV) consortium recently uncovered high levels of genetic divergence between groups of Indian populations that cluster largely on the basis of ethnicity and language[25]. The study of such population groups will be useful for addressing stratification and complex study design issues[25]. Here, large collaborative efforts on R&D in fields such as pharmacogenomics, vaccinogenomics and toxicogenomics could serve as entry points for developing countries. Examples include pharmacovigilance programmes and detailed analyses of data from vaccine trials in which some but not all the human subjects respond to a particular vaccine. A well known example demonstrating that genetic factors can have a strong effect on the immune response to certain vaccines is the response to hepatitis B surface antigen (HBsAg). Up to 10% of people do not respond to HBsAg vaccination. Recent evidence suggests that although genes encoded within the major histocompatibility complex are important for this immune unresponsiveness, more than half the heritability is determined outside of this complex. Identification of these genes will help us to understand regulation of immune responses to viral proteins[26].

A potential to improve the understanding of genomics and traditional medicines through fields such as nutrigenomics provides another possible entry point that offers these countries an intellectual property advantage. Traditional medicine is well established in China and India, where a memorandum has recently been signed to further the understanding of their respective traditional medicine sectors[27]. Whether genomics can add any value to such endeavours remains to be seen.

Although limited, private sector firms in developing countries have also begun to leverage the opportunities in genomic medicine, identifying possible entry points and using unique resources. Avesthagen Ltd, an Indian-owned life-sciences company, has a large-scale genotyping project of the Parsi population in India[28]. They predict an initial market in translational medicine, such as genomic medicine, with an eventual foray into early diagnosis, pre-symptomatic and life-long treatment through a combined offering of wellness products (for example, nutrigenomics) and personalized health care. In other countries, such as South Africa and Thailand, a few innovative firms are considering targeting the medical tourism market[12,13].

Finally, additional possible entry points might involve anthropology or human history and migration studies, as part of establishing a base-line of data for possible health applications. This, for example, was the original impetus for the HUGO Pan-Asian SNP Consortium[20,21]. Other countries might become involved as a result of participating in the HapMap project, as did Nigeria[29,30].

Challenges

Genomic research platforms in emerging economies and developing countries will be faced by a number of similar challenges as they become established and proceed towards the adoption of genomic medicine in their respective countries. These challenges are: the current lack of skilled human resources; ensuring sustainable funding and political will; sourcing alternative funding; improving collaboration within the public research sector as well as between the public research sector and the private sector; developing opportunities for south–south and north–south collaboration; improving the commercialization infrastructure in both the public and private sector; developing and improving the existing regulatory infrastructure; developing a health-care infrastructure that can address access and delivery issues of genomic medicine; training health-care workers; and engaging with the public to improve awareness and participation[10–14]. A number of these challenges are local and can be addressed as such by and in individual countries. Others, such as establishing international R&D collaborations in genomics research and the need to address the lack of harmonized regulatory infrastructure for genomic medicine, require collaborative efforts on an international scale to address them.

Internationally, issues that rapidly need to be addressed for productive and equitable collaborations include data and sample sharing, research capacity building in developing countries, and rules and guidelines for building and using international repositories containing long-term treatment outcomes in both developed and developing nations. These issues are often not straightforward to address. For example, data and sample sharing in many developed countries have traditionally focused upon consent and the concerns associated with privacy and confidentiality[31]. But in international collaborations, in addition to these concerns, considerations will also have to be given to the sovereign nature of the data and of samples sourced in emerging economies and developing countries[32]. The Public Population Project in Genomics (P3G), an international consortium that aims to build the necessary collaborative infrastructure between institutes in order to foster interoperability on the research level[33], provides one example of how international consortia can contribute to addressing these challenges. It is important to think about such issues early because the need for large-scale collaborative research is becoming more pressing as R&D in genomic medicine advances. These studies will require data comparisons and validation in large sample sets across different populations[34], which is one reason the European Science Foundation has recommended that European biobanking initiatives harmonize their efforts to achieve maximal benefit[35].

Collaborative efforts will also be necessary to address policy issues related to translation of genomic research and applications for population health. An example is the Genome-based Research and Population Health International Network (GRaPH-Int), a global collaborative network that fosters dialogue, research, education and training, and communication and stakeholder engagement, with the aim of establishing public policies, programmes and services in public health genomics. These types of consortia will be necessary for integrating approaches to genomic medicine and accelerating global consensus-building towards the development of international standards, the regulation of genetic testing and consumer genomics, and accessibility of genetic data and associated information.

Broader issues that require consideration include the integration of genetic information into public health decision-making, guidelines for medical prioritization, intellectual property regimes, and the association between regulatory bodies and health technology assessment bodies. For instance, forward-looking intellectual property regimes will need to be developed that can be used by countries, depending on the stage of economic and scientific development, to facilitate access to health products, scientific capacity building or economic profit. There is also a great need to build capacity in

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technology transfer in many developing countries.

One of the major challenges in the application of genomic medicine in emerging economies and developing countries involves the limited, or even absent, regulatory infrastructure. Some of these countries may have limited capacity to regulate traditional drugs and diagnostics, and will need to build capacity for these and for emerging genomic medicine 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, the judiciary and legislative bodies, as well as of drug licensing agencies. Developing countries might benefit from the experience of developed countries that are currently drafting the necessary guidelines to address unique emerging issues associated with the regulation of genomic medicine products[36]. In the developed world, these issues are being addressed on a national scale by their regulatory agencies and on an international scale through the International Conference on Harmonization (ICH)[37]. The inclusion of emerging or developing countries in the ICH harmonization of guidelines associated with genomic medicine, as well as in other consortia that can help to improve regulatory capacity, will provide a concrete opportunity to improve the application of genomic medicine to global health.

Genomic medicine is redefining how both developed and developing countries need to work together in the application of new knowledge to improve public health. The intrinsic value of information in the human genome is associated less with national boundaries and income than with how comprehensive this information is, and is strongly dependent on the information from many individual genomes and from many individual countries. Data acquired from the genotyping and sequencing projects in emerging and developing countries summarized above help to bridge the gaps in the application of genomic medicine between developing and developed countries. Access to these data throughout the world will be crucial for the identification of novel biomarkers of drug safety and efficacy. Whereas the generation of information from the human genome requires a global effort, its application will require development of therapeutic, diagnostic and other applications and products aimed at sub-populations and individuals. The most important benefits will probably be in the use of genomics knowledge to prevent diseases and promote health. At an individual level, and perhaps a sub-population level, the benefits will depend on how genomics is integrated in health systems. To achieve these aims of genomic medicine on a larger scale, public health systems in countries throughout the world will need to integrate pharmacogenomic data from their citizens and will need to use these data effectively for the optimal allocation of diagnostic and therapeutic resources, to improve health education of their publics. This will help their public to change their health-related behaviour, to educate health professionals, and to re-engineer health-care systems more towards prevention and health promotion.

In terms of the benefits of S&T generally, the current 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. This is why so many developing countries, especially the emerging economies, are focusing more on local innovation, invention and commercialization to break the cycle of dependency. To go 'from the lab to the village' through discovery to product development to commercialization by, and in, developing countries will require that science, business and capital be brought together creatively. One proposal involves creating 'convergence centres', which are an evolution beyond science parks and incubators, aimed specifically at enhancing opportunities for knowledge sharing and rapid innovation, and have a focus on product development and commercialization[38].

Conclusions

The existing initiatives in emerging economies in the developing world, which range from databases run by research networks to comprehensive national institutes with public health mandates, serve as models for how to invest in innovative S&T towards development. Such initiatives can strengthen local research infrastructure and local intellectual property regimes, address local health needs and reduce health-care costs, thus improving local health equity. How these countries choose to capture these benefits early on will depend, in part, on the type of entry points they opt for, which in turn will depend on the level of development of their research and health infrastructure. There is much to be learnt from the experience and examples of India, Mexico, Thailand and South Africa.

There are, however, significant challenges to be addressed before the adoption of genomic medicine, and although these are for the most part being experienced by all countries, the challenges are more pronounced for developing countries. There is therefore a need to strengthen existing collaborative efforts, especially south–south collaborations, which in the long run might be more sustainable. Current and future initiatives and investments in R&D capacity will further enable countries in the developing world to participate as equal R&D partners with more developed countries, instead of merely facilitating access to local biological resources.

In terms of international collaborations that would add value to all countries, at a recent workshop in Mexico City (see Emerging Regulatory Issues in Genomic Medicine conference overview) experts in the emerging issues in genomic medicine from both the developed and developing world discussed a number of ways forward. They included the creation of an information clearing-house, a virtual network of interested parties, phenotypic and genotypic databases associated with drug development, an international consortium for biomarker development with real involvement of emerging economies and developing countries, and methods of international harmonization of genomic product regulation. Many in the developing world are excited with the prospects of genomic medicine. We are at the crossroads between theory and practice. It is important now that we all think seriously about the challenges and opportunities lying ahead.

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