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## Human Genomics in Asia

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### Abstract

In the past decade, Asia has been actively engaged in human genomic studies and has made great contributions to the field. There is an increase in the number of genomics institutes, consortiums, and initiatives across the continent to study the association between genetic variation and disease. Despite these laudable efforts, Asia faces tremendous challenges in terms of funding, regulation, collaboration, and ethical, legal, and social issues related to genomics. These need to be addressed in the near future to promote the development of genomic medicine.

### Introduction

The past decade has seen the advancement of human genetics and genomics worldwide. Various countries have invested seriously in this field, with the expectation of gaining a better understanding of human health and disease. Biobanks and genetic databases have been built to facilitate interdisciplinary clinical research. Regional and international efforts have also been made to promote the success of genomic medicine. For example, in Europe, the Biobanking and Biomolecular Resources Research Infrastructure has been constructed to secure global competitiveness of research and industry of the European Union, and benefit the health of European citizens. International genomic research collaborations, such as the Human Genome Project (HGP), the International HapMap Project, and the International Cancer Genome Consortium, have produced open-access genetic databases for researchers around the globe (Kaye, 2011; Vaught et al., 2009). The completion of the sequencing of the human genome, the mathematical analysis of DNA variants called single nucleotide polymorphisms (SNPs), and the progress in genome-wide association studies have contributed dramatically to biomedical research. Yet the majority of medical genomics research has mainly focused on people of European descent, the results of which will not be beneficial to the greatest segment of the world's population. Given that the lack of diversity in these studies will bias our understanding of the association between genetic variants and diseases, researchers have recognized the importance of inclusion of populational diversity in pharmacogenomic and genome-wide disease studies (Bustamante et al., 2011).

The geopolitical continent of Asia contains almost two-thirds of the world population, with rich cultural, ethnic, linguistic, and genetic diversity. Asian nations, particularly those still developing, are often depicted as the epicenter of pandemics, e.g., severe acute respiratory syndrome (SARS) and avian influenza outbreaks (Tan et al., 2012). At the same time, these countries also face growing chronic disease burdens, but the causes of diseases in Asian populations remain unknown (Jemal et al., 2011). Thus, genomic research on Asian populations is essential to further enhance our knowledge of the genetic basis of complex chronic and infectious diseases, and to cope with Asian and global public health challenges. In this article, we first give a brief introduction to the contributions of Asian nations to human genomics, placing greater focus on the

genomics consortiums and initiatives in the region: Asian Cohort Consortium (ACC), Human Genome Organization (HUGO) Pan-Asia SNP consortium (PASNP 1.0) and HUGO Pan-Asia Population Genomics Initiative (PASNP 2.0). We then discuss the challenges that Asia faces in bringing genomic science and technology to bear on applications of genomic medicine. Finally, we outline several future perspectives for the advancement of genomics in Asia.

### Asia's Contribution

The world's largest geopolitical continent, Asia, exhibits heterogeneous geographical, cultural, and socioeconomic characteristics. The investment and progress of genomic science and technology of each country across the continent are uneven. Wealthy countries, such as Singapore and Japan, have made tremendous investments in genomics research and development (R&D) toward efficient diagnosis tools and personalized medicine. The Genome Institute of Singapore (GIS), located at Singapore's biomedical hub, Biopolis, is one of the centers of excellence in genomics in Asia and indeed the world. GIS gained world recognition through its rapid response to SARS and identification of five strains of SARS coronavirus in 2003 to effectively contain a pandemic. The strength of GIS's research lies in three milestone arenas: "infectious diseases, cross-national science diplomacy, and regenerative medicine" (Fischer, 2013). Japan has established several research institutions, e.g., RIKEN Center for Genomic Medicine, and research infrastructures, e.g., Biobank Japan, which are steering the nation ahead on the path toward genomic applications in medicine and health (Yoshizawa et al., 2014).

Emerging economies, such as China and India, are the rising powers in the global biomedicine field and are now challenging the developed economies (Salter and Faulkner, 2011). China was the sole developing country to participate in the HGP, contributing toward sequencing of 1% of the human genome. The Beijing Genomics Institute (BGI) has become a global sequencing powerhouse that sequenced the first Asian human genome, and a number of plant and animal genomes, such as rice, silkworm, chicken, and panda (Normile, 2012). India is endeavoring to foster economic development and address local health needs through investment in genomics-based innovation. The Indian Genome Variation Consortium, a government-funded collaborative network of

several local institutions, is one of the examples that reflect these efforts (Hardy et al., 2012). Still other Asian countries, such as Indonesia and Philippines, have emerged in recent years as active actors in the field of genomics, partly due to their ethnic and linguistic diversity (Liu, 2008). Such efforts by nations across the continent are crucial for Asia's genomic research collaboration networks, such as ACC, APSNP 1.0 and 2.0. We introduce these networks in detail below.

### Asia Cohort Consortium

First proposed in November 2004, in Seoul, the ACC is a collaborative cancer cohort research project, involving more than one million healthy people across Asia who will be followed over time until various disease endpoints are reached. The ACC seeks to understand the relationship between genetics, environmental exposures, and the etiology of disease, and to discover early detection biomarkers. The ACC has two missions: "(i) to serve as a platform for cross-cohort collaborative projects and combined analysis and (ii) to act as an incubator for new cohorts" (Song et al., 2012). The ACC has approximately 50 active members from Bangladesh, China, India, Iran, Japan, South Korea, Malaysia, Singapore, Taiwan, and the United States, among others. It is cochaired by John Potter of the Fred Hutchinson Cancer Research Center, Seattle, Washington, USA, and Daehee Kang of Seoul National University College of Medicine, South Korea. Its coordinating center is located at the Fred Hutchinson Cancer Research Center to provide support for scientific collaboration, coordination and communication, data operations, and statistical consultation (Rolland et al., 2011).

As most studies on the associations between body mass index (BMI) and the risk of death have been conducted on North American and European populations, and less is known about these associations in Asian populations, the focus of ACC's projects is on BMI in Asian populations. To date, the cross-cohort collaborative projects of ACC have yielded about seven articles, showing the association between BMI and risk of death; BMI and diabetes; BMI, tobacco smoking, alcohol consumption, and risk of cancer of the small intestine; BMI and risk of death from pancreatic cancer; meat consumption and cause-specific mortality; and BMI and cardiovascular disease mortality in Asian populations (<https://www.asiacohort.org/index.html> (accessed 03.07.14.)).

### PASNP 1.0 and 2.0

The SNP consortium was established in early 1999 through a collaborative effort among major pharmaceutical companies, the Wellcome Trust, and five leading academic centers to provide a resource pool for clinical genomic research and for the discovery of novel diagnosis and personalized therapies (Holden, 2002). This consortium largely focused on Caucasian populations, while genomic variation among Asian peoples remained unexplored. In 2007, HUGO Pan-Asia SNP Consortium (PASNP 1.0) was set up with 93 researchers from 40 institutions in 11 Asian countries to map human genetic diversity in Asia. Coordinated from the GIS, the PASNP took the first steps toward collaboration among Asian scientists.

Based on strong bioinformatics teams from China, India, Japan, Singapore, etc., diverse ethnicities from Indonesia, Malaysia, Philippines, and Taiwan, and the scientists' common interests, the consortium used samples from more than 1900 individuals representing 73 populations to conduct migration studies (Normile, 2004, 2009). The PASNP consortium's first report, published in *Science* in December 2009, provided a physical map of human variation in Southeast Asian, East Asian (EA), and Central South Asian populations, and showed strong evidence for the southern migration route to Asia, though it did not completely rule out a two-wave model of migration (Abdulla et al., 2009).

In order to advance the work of PASNP, the HUGO Pan-Asia Population Genomics Initiative was launched in 2011 as a version 2.0 of PASNP 1.0. It established a larger network with hundreds of researchers, and constructed a gene pool with diverse people, data, and cultures, including those from mainland Central Asia and the Pacific Islands. The goal of PASNP 2.0 is to further explore Asian migration patterns, Asian genetic diversity, and local adaptation, and eventually to translate genomics knowledge to the practice of genomic medicine. The data collected by PASNP 2.0 will be open to the worldwide scientific community for further genomic studies ([http://papgi.org/index.php/About\\_Us](http://papgi.org/index.php/About_Us) (accessed 03.07.14.)).

Despite the achievements that Asian countries and consortiums have made, they still face formidable challenges in terms of funding, regulation, collaboration, and the ethical, legal, and social issues (ELSI) of genomics in Asia. As we show in the next section, the development of human genomics in Asia faces not only similar issues as do other national and transnational endeavors, such as funding, standardization of data and samples, harmonization of ELSI practices and regulations, and gaining public trust, but also some Asia-specific issues and local concerns in the practice of Asian science and collaboration.

## Current Challenges

### Funding

Funding for genomic science is becoming more competitive and more difficult to obtain, both from the government and from industry sources. For this reason, ensuring sustainable funding is one of the major challenges for genomic studies (Vaught et al., 2009). Even in Singapore, where the government had attracted many top scientists from the West with substantial funds, after two 5-year periods of multibillion dollar investments, with little or no warning the core budgets for bioscience institutes under the Agency for Science, Technology and Research (A\*STAR) was cut in the third-year period beginning in 2011. A\*STAR bioscientists, including those from GIS, had to compete for grants from the new Industry Alignment Fund, and collaborate with clinicians on industrial and clinical applications (Fischer, 2013; Normile, 2011).

Elsewhere, BGI took an entrepreneurial approach to fuel its growth of sequencing and bioinformatics capabilities. It borrowed 1.5 billion U.S. dollars from a government-owned bank and must begin to pay back the principal within 10 years. Since sequences do not make money, BGI established subsidiary

companies to expand the application of genomic science and technology in order to pay off the debt and generate more income (Normile, 2012). For example, BGI Diagnostics offers health services, such as noninvasive prenatal test and tests for various genetic disorders; BGI Ark Biotechnology Co. LTD has set up a transgenic platform, a cloning platform, an experimental farm, and an animal model department (see BGI's website). In addition to the challenges of funding, some Asian countries also find regulation a problem.

### Regulation

When appointed as the first director of the HGP, James Watson resolved that the U.S. National Institutes of Health should allocate part of its funds to study the ELSI of genomics in the face of unprecedented challenges posed by genomics and its future application. Research into the ELSI of genomics was initiated first in the USA, thence spreading to Canada and Europe (Zwart and Nelis, 2009). Awareness of the issues in the East happened much later, but such research was supposed to study similar issues as those in the West for the purpose of some outcomes leading to better regulation of genomics. More recently, Yoshizawa et al. identified heterogeneous regulatory frameworks and ELSI practice among EA countries. They found that EA countries' regulation of genomics had a relatively inconsistent and mixed character. Consider the aspect of privacy as an example: Japan, Singapore, South Korea, and Taiwan have regulations and oversights to protect personal information, while China and Indonesia exert little or no control over privacy issues. A similar situation is seen with ethics review. Even though there are ethics review committees in nearly all of these countries, discrepancies in ethics review capacities and the implementation of oversight between different countries are noticeable (Yoshizawa et al., 2014).

What is perhaps of greater concern is that, in overall terms, there are limited or even absent regulations in many developing countries. Some of these countries may have no or limited capacity to regulate innovative genomic medicine. This could be a major barrier to the application of emerging genomic medicine products to improve global health. Therefore, it is significant to include the developing countries in the International Conference on Harmonization, as well as other international consortia, so that developed countries can help improve the regulatory capacity of developing countries (Hardy et al., 2008). Yet international health research collaboration between developed and developing countries in the field of human genetics is often a sensitive issue.

### Biopiracy

There are concerns about possible exploitation of the populations in the developing countries in the commercialization of human tissues, and unfairness in benefit sharing and ownership between developed and developing countries (Schulz-Baldes et al., 2007). Biodiversity-rich countries like China, India, and Indonesia are concerned about the exploitation of genetic resources by more developed countries. They have been uneasy about equitable benefit sharing, ownership, and intellectual property rights in international research collaboration. As a consequence, China

promulgated the Interim Measures for the Administration of Human Genetic Resources, issued by its Ministry of Science and Technology and the Ministry of Health in 1998. This directive stipulates that only through collaboration with Chinese parties can foreign researchers get access to Chinese genetic resources (Chen, 2013).

Fearing that Indonesia may not benefit from vaccines developed by international scientists and multinational pharmaceutical companies, the Indonesian government stopped sending H5N1 virus specimens to the World Health Organization in 2006. This stance was supported by Malaysia, Thailand, and other developing countries to communicate their desire for mutual trust, transparency, and equity between the developed and developing nations in the virus sharing mechanism. Moreover, Indonesia revised its health law and enacted the Ministry of Health Regulation on Material Transfer Agreement in 2009 in order to safeguard national sovereignty over its biological materials (Sedyaningsih et al., 2008). Although India has ethical guidelines and regulations in place to prevent biopiracy, there is a lack of adherence to regulations and an absence of strict implementation of measures to monitor the misuse of genetic samples (Kumar, 2009). China faces similar problems. To protect the use of Chinese genetic resources in research collaboration, the Office of Legislative Affairs of the State Council, People's Republic of China, published the exposure draft of Measures for the Administration of Human Genetic Resources online in 2012 to solicit advice from the public. As of this writing, the official measures have still not been issued ([http://www.gov.cn/gzdt/2012-10/31/content\\_2254379.htm](http://www.gov.cn/gzdt/2012-10/31/content_2254379.htm) (accessed 09.07.14.)). The biopiracy issue reflects complexities in cross-border collaboration as well as the importance of mutual trust and equity among scientists in using human genetics.

### Collaboration

Although there are potential dangers of biopiracy and unfair benefit sharing in collaboration between developing countries and more developed countries (north-south collaborations), collaboration should nevertheless be promoted as a strategy to help build developing nations' research and translational capacities (Schulz-Baldes et al., 2007). Increasingly, there is also a trend toward collaboration among developing countries (south-south collaborations) in building human resource capacity (Ivers et al., 2010). In the case of the PASNP consortium, Edison Liu, one of the key organizers of the consortium, found it challenging to coordinate science collaboration among Asian scientists. As he pointed out:

Scientists in Asia have a tendency to look past each other and focus on collaborations with the United States or Europe, partly because these collaborations get them more credit from their school administrations. Also, in Asia, most countries see each other as competitors. Just getting people together is an accomplishment.

Liu, 2008

The science culture in Asia is different from that among scientists in the West and tends to be more hierarchical and bureaucratic. Another challenge rests with the disparity in research capacities and research infrastructures between Asian

countries (Liu, 2008). Besides these challenges, Asian genomic research collaborations face similar challenges as those of the international science communities more generally. As large-scale genomic research collaborations require data comparisons and validations across different populations, the lack of harmonized ELSI and lack of a regulatory infrastructure for genomic research and application are major hurdles. It is also difficult but crucial to ensure the quality of samples and the interoperability of data for collaboration (Song et al., 2012; Vaught et al., 2009). Finally, the translation of genomics knowledge to genomic medicine and innovative medicine products necessitates the interaction and collaboration of all stakeholders. They are not only scientists, clinicians, policy-makers, and industry people, but also patients, consumers, and healthy individuals.

### Publics

Engaging the public in biobank and genomic studies is of great importance because researchers need access to patients' and to the public's biological samples. There are a good number of qualitative and quantitative studies about public perception of biobanks and genetic databases in Western countries to explore the public's reasons for participating and not participating in biobank studies; their views of issues such as informed consent, benefit sharing, commercialization, and internationalization; and their concerns over privacy, discrimination, ownership, and the return of results. However, except for a few limited studies in Asian countries, among them China, Japan, and Singapore, little is known about the Asian public's perception of biobanks (Gottweis et al., 2011).

Investigation of public perceptions of biobanks reveals several factors that affect the public's willingness to donate their samples for research and to participate in the studies. These factors include the public's understanding of biobanks, its trust in research institutions and the scientists running those institutions, and its consideration of privacy, discrimination, and commercialization (Gottweis et al., 2011). In Asia, there is tendency for the public to distrust science. For example, Singapore's growing emphasis on commercialization of science discourages the public's participation in research. In Japan, public trust in expertise was eroded following the earthquake, tsunami, and nuclear accident in 2011 (Arimoto and Sato, 2012). There are cases reporting public distrust of experts, and public concerns over the misuse of genetic information and genetic discrimination after genetic testing in China and South Korea. In Taiwan, tensions and distrust arose between the public and authorities of the Taiwan Biobank due to a lack of open science communication (Yoshizawa et al., 2014). Well-known cases of scientific fraud in South Korea (Bonetta, 2006), Japan (Tsurimoto et al., 2009), and China (Lin, 2013) have also contributed to the lack of trust between the public and scientists. All of these signal a call for an interface of science and society to actively interact with the public.

### Future Perspectives

As a result of rich and diverse genetic resources, together with political will of various countries, and the great efforts that

scientists have made, Asia is rising in the field of human genomics in the postgenomic era. Building regional collaborative genomics networks, such as ACC and PASNP 1.0 and 2.0, is the first and vital step toward better science, medicine, and health in Asia. The research conducted by these networks is competitive in the global arena and bridges the gaps between Asia and Western countries. However, compared with research collaboration in Europe and North America, Asian genomics networks face more challenges than their counterparts in the West. The emerging economies and the developing countries in Asia have not established consistent and robust regulatory frameworks to govern the conduct of genomic research. Furthermore, their ELSI practice and regulation is often influenced by local sociopolitical and cultural concerns and tends to be heterogeneous. This has been a disincentive to regional collaboration on genomic science and technology, which requires the harmonization of ELSI practice and regulation across Asia. Therefore, in the future, it will be helpful to place more emphasis on research into ELSI of genomics and develop regulatory infrastructures, which could become a tool to secure the public's trust in science. It is also important to encourage both north-south collaborations and south-south collaborations. Experience gained from PASNP could contribute to further collaboration on the basis of previous networks and research collaboration.

### Editor's Note

Relevant aspects of genomics research in other countries on the Asian continent are covered in other articles of this Encyclopedia (see cross references). See also e.g. (Najmabadi, et al., 2003; Kumar, 2012; Prainsack, 2007).

*See also:* Anthropology, Genomics, and Human Variation: National Roots; Biobanking: Ethical Issues; Bioethics in the Post-genomic Era; Bioethics: Genetics and Genomics; Ethical, Legal, and Social Implications Program at the National Human Genome Research Institute; Gene-Environment Interactions in Health and Well-Being; Genetics and Indigenous Communities: Ethical Issues; Genetics and Society; Genetics: Legal Aspects; Genetics: The New Genetics; Genomics, Ethical Issues in; Human Genome Diversity Project: History; Human Genome Project: History and Assessment.

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## Relevant Websites

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- <http://www.genomics.cn/en/index> – Beijing Genome Institute.
- <http://biobankjp.org/index.html> – Biobank Japan.
- <http://www.gis.a-star.edu.sg/internet/site/> – Genome Institute of Singapore.
- <http://www.igvdb.res.in> – Indian Genome Variation Consortium.
- [http://papi.org/index.php/Main\\_Page](http://papi.org/index.php/Main_Page) – Pan-Asian Population Genomics Initiative.
- <http://www4a.biotech.or.th/PASNP> – Pan-Asian SNP Consortium.