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RESEARCH REVIEW

Precision medicine in Thailand

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Extraordinary advances in high throughput next generation sequencing (NGS) technology and bioinformatics are the main thrust that transforms the current state of healthcare into the era of precision medicine where clinical practice takes individual variability into account. Here, we summarize the current status of the infrastructure we have and the adoption of precision medicine in Thailand in four spheres: rare diseases, oncology, pharmacogenomics, and noncommunicable diseases. Moreover, we provide our perspectives to the future of precision medicine in Thailand, especially the manpower and ethical, legal, and social issues. We believe that with decreasing costs of NGS, increasing ability to interpret the genomic data, a greater number of actionable and available treatments, implementation of precision medicine at the public health level is not a matter of if but when.

KEYWORDS

noncommunicable diseases, pharmacogenomics, precision medicine, precision oncology, rare diseases, Thailand

1 | PRECISION MEDICINE IN THAILAND: CURRENT STATUS AND APPLICATIONS

Recent advances in next generation sequencing (NGS) technology have driven whole genome sequencing from the territory of fundamental research in laboratories to real practice of healthcare. In the era of genomic medicine, clinicians utilize genomic information as an important contributing factor to medical care of an individual. Combining personal genome and other large-scale biological databases with behavior and environmental exposure, genomic medicine transforms to precision medicine when clinical practice takes individual variability into account.

Precision medicine started to boom when the then US president Barack Obama announced the initiative in January 2015 (Collins & Varmus, 2015). It has rapidly spread all over the world. Several countries have started to incorporate genomic sequencing into their health systems (Stark et al., 2019). With a strong foundation in human genetics due to the burden of thalassemia, Southeast Asian countries especially the two largest economies: Singapore and Malaysia, have significant advancements in genomic medicine. Singapore, led by Genome Institute of Singapore, has finished the SG10K project to do whole genome sequencing at 12–15× coverage for 10,000 Singaporean individuals (https://www.a-star.edu.sg/Portals/100/38.%20BELLIS_ASHG_2016_approved.pdf). Malaysia has established Genom Malaysia, a network based nonprofit organization to implement the genomic technology (http://www.nibm.my/index.php/institutes/genom-malaysia), and the Malaysian Human Variome Project, collecting variations through various platforms including SNP array and NGS (http://hvpmalaysia.kk.usm.my).

Thailand, a middle income country, also sees the potential of genomics to provide everyone the best chance at good health. To maximize the opportunity, we have acquired sequencers with long-read, short-read and linked-read technologies, established high-performance computer at National Science and Technology Development Agency (NSTDA) and Chulalongkorn University, developed programs to manage and analyze genomics data, and created exome and genome databases of Thai populations (manuscripts under preparation). Nonetheless, a shortage of man power in all relevant fields has made the realization of precision medicine in our country challenging (Shotelersuk, Limwongse, & Mahasirimongkol, 2014). Here, we summarize the current status of the adoption of precision medicine in various spheres and provide our perspectives on its future in Thailand.

2 | RARE AND UNDIAGNOSED DISEASES

A rare disease can arbitrarily be defined as a disease that affects less than 1 in 2,000 citizens (Eurordis, 2005). Although individually rare, with more than 7,000 different entities, they collectively account for as many as 8% of the population (Eurordis, 2005). In addition to their rarity, a broad diversity of symptoms and ages of onsets makes the diagnosis of rare disease very challenging. It could take decades before the right diagnosis is established. Since 80% of rare diseases have identified genetic origins, the advent of NGS technology is a real boon for this sphere. One of the most tangible near-term benefits of clinical exome or genome sequencing is for care of these rare diseases. For an increasing number of diseases, recommendations for diagnostic investigations have progressed from complicated algorithm to whole genome first (Raymond, Horvath, & Chinnery, 2018).

We have established the Thailand's Rare and Undiagnosed Disease Network (T-RUN) with nine institutes from every part of Thailand. After a patient with a rare or undiagnosed disease is found and written informed consent is obtained, blood samples are taken and sent to the center at Chulalongkorn University for clinical NGS. The usual practice has moved from whole exome sequencing (WES) of singleton to trio, and started to shift to whole genome sequencing (WGS) of trio, for which there is evidence of a higher yield. So far, we have performed of more than 2,000 WES and 300 WGS. Recently, V.S. won a Newton Prize together with Professor Phil Beales of the University College London. We have successfully launched a rapid WES in the King Chulalongkorn Memorial Hospital with only 9 days from consultation to result delivery to help diagnose and improve care of patients with an acute and severe neurometabolic symptoms admitted to the ICU. The cost of these tests is mainly covered by research grants with some by the patients' pockets and donations.

Patients consulted for diagnosis by NGS are from all specialties, including neurologists (Veeravigrom et al., 2015), dentists (Intarak, Theerapanon, Ittiwut, et al., 2018a; Nowwarote et al., 2018; Porntaveetus, Nowwarote, et al., 2018b; Porntaveetus, Osathanon, et al., 2018), orthopedists, endocrinologists (Sangsin, Srichomthong, Pongpanich, Suphapeetiporn, & Shotelersuk, 2016a, 2016b), hematologists (Ittiwut et al., 2018; Ittiwut et al., 2017), dermatologists (Intarak, Theerapanon, Srijunbarl, et al., 2018; Panmontha et al., 2015; Panmontha et al., 2016), immunologists (Suratannon et al., 2016), syndromologists (Porntaveetus, Abid, et al., 2018; Porntaveetus, Srichomthong, Ohazama, Suphapeetiporn, & Shotelersuk, 2017; Porntaveetus, Theerapanon, Srichomthong, & Shotelersuk, 2018), biochemical geneticists (Chaiyasap et al., 2017; Phowthongkum, Ittiwut, & Shotelersuk, 2018; Porntaveetus, Srichomthong, Suphapeetiporn, & Shotelersuk, 2015), oncologists (Sahakitrungruang et al., 2014), and radiologists (Yeetong, Phewplung, Kamolvisit, Suphapeetiporn, & Shotelersuk, 2018). We have observed a wide range of yields depending on disease groups, recruitment criteria and, very importantly the cooperation of the clinicians and the bioinformaticians. The yield of trio WES ranges from 20% observed in intellectual disability to 60% in early infantile encephalopathic epilepsy. NGS allows us to identify patients with more than one disorders (Porntaveetus, Srichomthong, Suphapeetiporn, & Shotelersuk, 2017). The definite diagnoses have ended the patients' diagnostic odysseys and provided information about the disease, more accurate recurrence risks and more reproductive options. However, although specific treatments are devised for an increasing number of rare diseases, their availability, accessibility and affordability are limited in Thailand.

Besides the immediate benefits to the patients and families, NGS of rare diseases has led to discoveries of many new human disease genes at a more rapid pace. Before the NGS era, we found few new disease genes including *SATB2* for SATB2-associated syndrome (Leoyklang et al., 2007; Leoyklang et al., 2013), *p63* and *PDGFRA* for isolated oral clefts (Leoyklang, Siriwan, & Shotelersuk, 2006; Rattanasopha et al., 2012). Since 2012 when we started clinical WES at Chulalongkorn University, we have found at least 10 candidate new disease genes including *MBTPS2* for X-linked osteogenesis imperfecta (Lindert et al., 2016) and *KIF6* for intellectual disability (Konjikusic et al., 2018). The rate limiting steps are identifying other families with the same disorder and a mutation in the same gene and the experimentation to verify the pathogenicity of the detected mutations and ascertain the pathogenesis of the disease. Identification of disease genes for rare diseases and elucidating their pathogenesis has a potential to generalize the knowledge for care of common diseases (Gahl, 2012).

3 | PRECISION ONCOLOGY

Cancer is one of the best examples to demonstrate the benefit of precision medicine. It has been universally accepted that oncogenic genome alteration is the major drive that propels normal cells to acquire several cancerous phenotypes including abnormal cell growth, invasiveness and metastasis. Better understanding in cancer genomics leads to new types of cancer diagnostic tests and several novel drugs which are designed to target specific genetic abnormalities in cancer. Several genetic tests for cancer are available in Thailand. Unlike other conditions, genetic testing for cancer consists of germline testing to determine which patients are affected with hereditary cancer syndromes, and somatic testing to identify specific cancer genome alterations for accurate diagnosis and treatment selection. The frequency of heritable forms varies greatly by cancer type but together account for 8–12% of cancer patients (Huang et al., 2018). Many somatic tests

become companion diagnostics for various cancer types such as *BCR-ABL* for chronic myeloid leukemia, *EGFR* for nonsmall cell lung cancer, *RAS* for colorectal cancer, *IDH1* for glioblastoma and *BRAF* for melanoma. Clinical tests in most hospitals are limited to single gene or single allele tests.

Many studies have shown that genetic diversity plays role in phenotypic differences among various ethnic groups with the same diseases. Some cancer types are significantly more prevalent in Asian than in Western population (Ferlay et al., 2015). Same cancers display differences in subtypes among countries. Similar cancers from various ethnic groups also have different treatment outcome and prognosis (Banegas & Li, 2012). To be able to determine the role of genetic diversity in Thai cancer, as well as development and implementation of precision medicine to clinical care for cancer patients, Thai Cancer Precision Medicine project has been established in the Research University Network (RUN), the collaborative consortium of Thailand's eight universities. The initial phase of the project focuses on breast cancer, head and neck cancer, and glioma. Eligible Thai cancer patients are invited to participate in the project through various member institutes, in which clinical data, blood and tumor samples will be collected. Tumor genome testing is done either by WES or targeted gene panel sequencing. Germline multigene panel testing for hereditary cancer syndrome is performed and further testing for family members can be done when pathogenic mutations are identified in probands. Furthermore, the research team has also developed Thailand's first-ever three-dimensional model of primary cancer cell lines, also known as "cancer organoids", and use these cancer organoids for high-throughput cancer drug screening. In the past year, more than 300 tumor genome sequencing and 160 germline multigene panel testing have been done. More than 35 primary cancer cell lines have been established. The test results are also provided to the physicians taking care of those patients. Many patients are able to take advantage of their test results for treatment selection and screening of their family members. Although available novel cancer drugs are still limited in Thailand, dramatic clinical response is observed in some patients whose actionable mutations are matched with those agents. This is particularly true in glioma which has minimal current standard treatment options. Majority of those diagnostic and treatment costs are supported through research grants and clinical trials. In addition to direct clinical benefits from genetic testing and precision medicine approach for cancer care, cancer genome and other cancer biological data generated from Thai cohorts are used to investigate roles of genomic and biological differences between cancers in Thai and other populations that could translate to new insight on carcinogenesis and clinical application.

4 | PHARMACOGENOMICS

Pharmacogenomics is the use of the genetic information to prioritize the most suitable drugs (Manolio et al., 2015). The most obvious example of the genetically mediated adverse drug reactions is drug-induced Steven Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) (Manolio et al., 2018). The most common drugs that caused SJS/TEN are carbamazepine, allopurinol, sulfamethoxazone, and NSAIDs (Mockenhaupt & Schöpf, 1996). HLA-B*15:02 was found to be a genetic risk of carbamazepine induced SJS/TEN (Chung et al., 2004). Clinical studies showed the effectiveness of HLA-B*15:02 screening prior to carbamazepine prescription to prevent SJS/TEN (Chen et al., 2011). Later on, the HLA-B*15:02 testing has become a reimbursable pharmacogenetic test in Taiwan since 2011 and in Singapore since 2013 (Dong, Sung, & Finkelstein, 2012; Tan-Koi et al., 2017).

For the Thai population, HLA-B*15:02 has also been found to be a risk for drug-induced SJS/TEN (Locharernkul et al., 2008; Locharernkul, Shotelersuk, & Hirankarn, 2010; Tassaneeyakul et al., 2010). A health economic study indicated a positive cost-utility of HLA-B*15:02 testing (Rattanavipapong, Koopitakkajorn, Praditsitthikorn, Mahasirimongkol, & Teerawattananon, 2013); subsequently, in 2018, it was announced to be reimbursable from the national universal healthcare scheme.

Another effort of implementing pharmacogenetics in Thailand is to prevent allopurinol induced SJS/TEN. HLA-B*58:01 is known to be a risk with a high sensitivity (Hung et al., 2005). 5 to 10% of the Thai population carry the HLA-B*58:01. Patients who carry HLA-B*58:01 are recommended to be prescribed febuxostat as an alternative effective drug (Kamatani et al., 2011). However, febuxostat is significantly more expensive and poses a burden to the health system. A prioritization approach is needed for the public health implementation of this test.

Clinical Pharmacogenetics Implementation Consortium (CPIC) Guidelines are recommendations to translate research of pharmacogenomics to healthcare, developed by international experts (Relling & Klein, 2011). They are often used in the clinical decision support system with the electronic medical records (Clancy et al., 2014; Luzum et al., 2017; Martin et al., 2014). Thailand is working closely with Southeast Asian countries in the Southeast Asian Pharmacogenomics Research Network to develop a CPIC guideline which is suitable for Southeast Asian populations (SEAPHARM, www.seapharm.org). During 2018–2020, at least four guidelines will be made available by SEAPHARM. One is the guideline for pharmacogenetics of antituberculosis. Asian populations have a unique distribution of drug metabolizing enzymes contributed to higher rates of antituberculosis induced liver injury (Azuma et al., 2013). In addition, a higher rate of alcohol abuse in tuberculosis patients was observed (Dalton et al., 2012). With the combination of genetics, drug exposures and lifestyles, the one size fits all dosage recommendations from international organizations inevitably pose a risk to a group of patients with rapid acetylators to a lower efficacy and another group of patients with slow acetylators to a higher rate of adverse drug reactions. Hoping to increase tuberculosis treatment success rate in Thailand, we are conducting a clinical trial to determine the benefit of genotype-guided dosage adjustment of isoniazid and the prevention of its adverse events (Azuma et al., 2013).

The benefit of pharmacogenomics will be realized only when the clinical and pharmacological practices are designed to incorporate these genetics information into the healthcare system. The healthcare delivery includes the development of specific health informatics system, the training of the health professionals, and the continuous monitoring and evaluation of the large-scale implementation program. The endpoints are the reduction of the avoidable genetically determined adverse drug reactions, the increase in the proportion of populations with adequate dosages, and the improvement of overall efficacy of the drug prescription.

5 | NONCOMMUNICABLE DISEASES (NCDS)

NCDs are leading causes of death and disability worldwide, affecting both developed and developing countries. Although traditionally regarded as the diseases of the rich, the increase in NCD burden is at present disproportionately large in low- and lower-middle-income countries (World Health Organization, 2017). One reason could be the shorter time available for these population to evolutionarily adapt to the more affluent living conditions, resulting in larger genetic, epigenetic and cultural ("triple evolutionary") mismatches to the new environment, thereby disproportionately increasing their susceptibility to NCDs compared with people from more developed, affluent nations (Koopman, van Bodegom, Ziem, & Westendorp, 2016). Furthermore, even the variants of smaller effect which are less susceptible to natural selection could also differ among the populations solely because of the difference in ancestry. It is therefore important for precision medicine program and for NCDs in developing countries to recognize these divergences from developed countries, and to gain understanding in their own genetic risks and the interaction of their genes with their environmental risk factors.

Genetic studies of noncommunicable diseases generally require a large number of population-based participants due to the smaller genetic effect and larger contribution from the environmental risk components. With this in mind, a collaborative project between the Ministry of Public Health's Department of Medical Science and the Faculty of Medicine Ramathibodi Hospital under the Genomics Thailand initiative is currently genotyping 10,000 individuals using Illumina's Asian Screening Array (ASA), and is due to be completed in the mid 2019.

Samples for this genotyping project come from two well-established previous studies. One of these is the Electricity Generating Authority of Thailand (EGAT) cohort (Vathesatogkit et al., 2012), which has been following workers of EGAT from as early as 1985 with the initial aim to establish cardiovascular risk factors as well as to assess their nutritional and toxicological status. The study has since been expanded to include a wide range of risk factors and outcomes such as cancers, liver diseases, kidney diseases, respiratory problems, allergies and gynecological problems, and include a detailed mortality assessment. It is currently one of the most feature-rich long-term cohorts in Thailand. The other study is the National Health Examination Survey (Aekplakorn et al., 2011). This is a series of cross-sectional population-wide surveys conducted approximately every 5 years, focusing on common NCDs and epidemiological risk factors. As the sampling for this study was done at the whole population level by the National Statistical Office, this will inherently be highly representative of the country's general population.

Genotyping data from this project will serve three main purposes: they will provide more accurate national reference SNPs information; will enable studies of the genetic and environmental risks of relatively common NCDs from within the data set, as well as their risk stratification/prediction models; and will serve as a large common control group for further genomic studies of less common conditions. At the time of writing, several projects that will use the common control from this project in conjunction with the genotyping data from their own disease groups are in various stages of planning.

Several WGS projects have also been initiated this year with the primary aim to establish reference sequencing for the Thai population (Table 1). The combined sample size is currently modest, but they can serve as the basis for the imputation of whole genome variants of the Genomics Thailand SNP array project above, and will allow more detailed study of NCDs in the intermediate term. In the longer term, it is expected that the majority of the data used in NCD studies will come from the sequencing projects once the later phases are completed.

6 | BIOINFORMATICS, DATABASE AND COMPUTATIONAL INFRASTRUCTURE

Success in the pursuit of precision medicine implementation in Thailand majorly relies on interpretation of genomics big data to facilitate the proper intervention of a patient. The success of a high throughput sequencing technology triggered a service-cost competition to slash the sequencing cost to be under $1,000 (Service, 2006). With such a lower sequencing cost, the time is right to run a national precision medicine program. Several countries that early adopted precision medicine have sequenced large number of volunteers representing their countries, for example, the 100,000 Genomics England sequencing project (Barwell, O'Sullivan, Mansbridge, Lowry, & Dorkins, 2018; Samuel & Farsides, 2017) following, All of Us project from the united states (Collins & Varmus, 2015) and the announcement of one million human genome sequencing in China (Wang, 2016). To meet the high demand, high throughput deep sequencing infrastructures from the two leading companies namely Illumina and BGI have been deployed in these countries. The large volume of sequencing data of a national sequencing project requires high-performance computing infrastructure (HPC) with large storage and a good backup system. A file containing WGS raw data is approximately 100 gigabytes and takes many hours to perform variant calling from the sample. These called variants lay the underlying genomic landscape of the country population which is fundamental to determining susceptible genetic factors.

To help transform the economic structure of Thailand to an innovation driven economy, the Ministry of Science and Technology (MoST) granted large funding to the National Center of Genetic Engineering and Biotechnology (BIOTEC), National Science and Technology Development Agency (NSTDA). Major part of this funding is concentrated on building a *national biobank* that also includes cataloging of biodata and bioinformation of living plants, animals, microbes and humans. The funding was used to procure large HPC infrastructure with big data storage and a backup system. In the context of Thailand Precision Medicine, the underlying computational infrastructure will be utilized to accommodate any analyses of human genomic big data (Figure 1). With the conception of Genomics Thailand consortium, the very first groundwork project is to capture genetic variants and their distribution among Thais by constructing a Thai variation reference database.

Building a reference database for Thai genetic variations is an important task because the reference information can be used to test a hypothesis if a candidate mutation should be further validated. The

TABLE 1 Current whole genome sequencing projects in Thailand

Leading team	Type of subjects	Sample size in current phase	Target sample size in final phase
MoST/TCELS/ Ramathibodi hospital	Generally healthy family trios (initial phase) or individuals (later phases)	120	10,000
MoPH/DMSc	Disease groups or individuals	300	10,000
NSTDA/BIOTEC	Disease groups	450	450
Chulalongkorn University	Sudden unexplained death syndrome (initial phase) and other rare diseases	750	2,000
Ramathibodi hospital	General population	1,000	1,000

Note. BIOTEC = National Center for Genetic Engineering and Biotechnology; DMSc = Department of Medical Science; MoPH = Ministry of Public Health; MoST = Ministry of Science and Technology; NSTDA = National Science and Technology Development Agency; TCELS = Thailand Center of Excellence for Life Sciences.

very first project to achieve this was done through collaborative contribution of sequencing data by the members of Genomics Thailand. The first aggregated Thai variant database is from more than 1000 WES of patients recruited for various studies of rare and undiagnosed diseases. At the time of writing, almost 1,000 Thai individual samples will be whole genome sequenced. HPC facility at NSTDA will be primarily stored in the HPC infrastructure operated by NSTDA. The sequencing data will be processed using GATK best practices (DePristo et al., 2011; Poplin et al., 2018; Van der Auwera et al., 2013) to identify variants and INDELs that represent a genome landscape of Thai population. Another reference project followed the above NCD activity is to collect more than 10,000 genotyping data from several large cohorts to perform genome wide association studies (GWAS) that are set to identify polygenic risk scores of various complex diseases. Such collected common variations are also useful not only as a reference but also as a control cohort for future studies (Bennett et al., 2011).

BIOTEC/NSTDA partakes in the Genomics Thailand consortium activities by offering bioinformatics services as well as hosting genomics big data. Due to highly competitive of NGS service, high volume of sequencing data is to be expected. Thus, to help foster upcoming omics-related research, BIOTEC/NSTDA prepares a high-performance system focusing on efficiently preprocessing, for example, quality control and variant calling, NGS sequencing data. The deidentified sequencing data with informed consent as well as other processed information are to be stored securely on the HPC system. At the moment, only aggregated genomic data can be used to avoid potential ethical violation.

7 | FUTURE DIRECTION AND CHALLENGES

The utmost benefit of genomic medicine would depend upon how to successfully implement these knowledge and technology to healthcare and society. Thailand has many strengths and uniqueness that could achieve the very challenging objectives. First, almost all Thai people are covered by three publicly funded healthcare coverages; government employee health benefit scheme, social security health benefit scheme, and the universal healthcare scheme. Thai government provides majority of healthcare, including primary care, inpatient care, health promotion and disease prevention, through countrywide public hospitals and referral networks. So, major healthcare policies could be effectively and uniformly enacted. Thailand has previously shown success stories on national implementation such as thalassemia screening and universal HIV treatment programs (Reich et al., 2016). Second, healthcare service at private hospitals is a major business sector in the country. Thailand is considered one of the leading destinations of medical tourism due to high quality medical care and lower cost of service comparing to other countries. Precision medicine is one of the health agenda that conform with the government's "Thailand 4.0" policy on healthcare industry to create a regional medical hub consisting of pharmaceutical and medical device industries and world-class medical service providers. Third, population in Thailand is comprised of many ethnic groups that are closely related to population from surrounding nations as well as

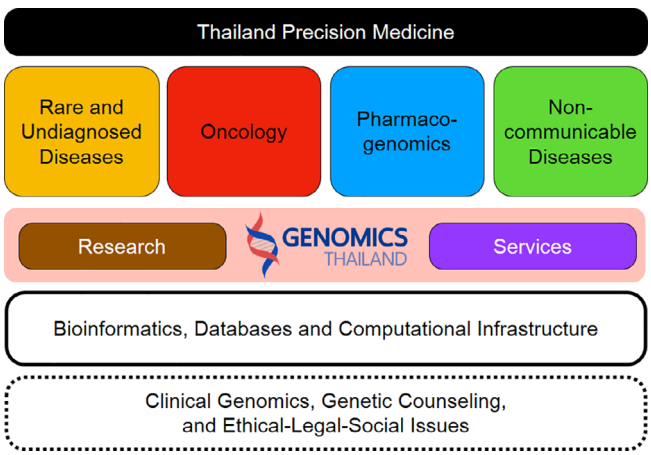

FIGURE 1 Schematic concept of Thailand Precision Medicine. Based on burden of healthcare costs in Thailand, we will be beneficial from the implementation of precision medicine if these four main focuses are to be addressed, namely, (a) rare and undiagnosed diseases, (b) oncology, (c) pharmacogenomics, and (d) noncommunicable diseases. As a major part of precision medicine implementation will rely on analyses of personal genomic big data, researchers and governmental sectors are working closely together to establish computational platforms and ethnic specific variation reference databases as well as securing more funding to foster stronger bioinformatician community. Furthermore, clinical genomicists and genetic counselors will be indispensable, practiced under an evolving ethical, legal and social issues

Chinese immigrants (Wangkumhang et al., 2013). The large scale genome data from population in Thailand would be valuable to diverse areas of research across different subpopulation. To facilitate the precision medicine in the country, Genomics Thailand Initiative is established with the support from the ministries of education, science and technology and public health. This collaborative effort has brought several leading medical schools, health authorities, funding agencies and policy makers together to set up the national framework for strengthening genomic research, integrating genomics in the healthcare system and promoting precision medicine in health industry.

With current improvement in high throughput technology and reduction in costs, large-scale NGS sequencing service is now technically feasible in our country. However, to do so for precision medicine implementation in clinical practice without causing serious ethical, legal or social complications requires that several issues be addressed. Successful implementation of precision medicine program requires adequate workforce of many advance-skilled professionals including clinical geneticists, genetic counselors, molecular scientists and computational bioscientists including bioinformaticians and genetic epidemiologists. As is common to many low-middle income countries, one key challenge in Thailand at present is the large gap between the existing workforce and those required for research and implementation of the program, as outlined in Table 2. This is recognized in the Genomics Thailand initiative, which attempts to build up the workforce and also create an appropriate referral system that can efficiently utilize this limited workforce at the national level. To serve a population of 65 million people of Thailand, there are currently 24 clinical geneticists, no genetic counselor and approximately 20 well-versed bioinformaticians who can handle large sequencing data in the country. Apart from the obvious limitation to service capacity, this limited manpower also puts a constraint on the potential size of prospective population-based sequencing project as there will be limited capacity for consenting and pretest counseling, bioinformatic analysis, and reporting back and handling actionable incidental findings. To address this issue, training courses for relevant professions have been initiated: clinical geneticists with the first trainee just graduated in 2018; genetic counselors with the first trainee recruited in 2018, and bioinformaticians started in 2003, with a program focusing specifically on human in 2016.

Precision medicine services also rely not only on the reference variants for Thai people, but also software that assists physicians to better their understanding of their patients. To do so, a new information technology infrastructure for precision medicine capable of managing and making use of both genotype and phenotype data is demanded in order to give support for clinical decision support systems (CDSS) that help medical practitioners make recommendations for patients based on their genetic profiles. To make sustainable services, more precision medicine research projects must be initiated by conducting data science on existing genotype–phenotype data. An electronic consent and reconsent system must be implemented so that researchers can ethically request proper data from patients to do other research.

TABLE 2 Current and projected core precision medicine workforce in Thailand

Profession	Current numbers	Projected additional requirement in 5 years
Clinical geneticists	24	30
Genetic counselors	0	100
Molecular geneticists, biologists, pathologists	NA	100
Computational bioscientists, bioinformaticians, genetic epidemiologists	20	500

Note. NA = not available.

It is foreseeable that the genotyping capacities could come from many players in the near future. This will increase the service availability, but will have to be properly regulated to avoid potential misuse or abuse and to assure the quality of the tests. Thailand still lacks law or regulation that adequately addresses the quality assurance of genetic testing, advertisement of genetic testing, proper use of genetic testing, and prevention of misuse of genetic information. These topics will need to be addressed as a matter of urgency. Raising awareness and continued educational programs for the public might be able to minimize the misuse of the technology.

There are some other concerns, including cost effectiveness of precision medicine at the population level and the accessibility and affordability of drugs and specific treatments to patients with rare diseases in low to middle income countries, although they are available in the world. Some experts opine that the ability to diagnose these patients may be opening a can of worms. With decreasing costs of NGS, increasing ability to interpret the genomic data, more actionable and available of specific treatments, we believe that implementation of precision medicine at the public health level is not a matter of if but when.

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CONFLICT OF INTEREST

None of the authors have conflict of interest to declare.

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REFERENCES

Aekplakorn, W., Kessomboon, P., Sangthong, R., Chariyalertsak, S., Putwatana, P., Inthawong, R., … NHES IV study group. (2011). Urban and rural variation in clustering of metabolic syndrome components in the Thai population: Results from the fourth national health examination survey 2009. *BMC Public Health*, *11*, 854. https://doi.org/10.1186/1471-2458-11-854

Azuma, J., Ohno, M., Kubota, R., Yokota, S., Nagai, T., Tsuyuguchi, K., … Kawase, I. (2013). NAT2 genotype guided regimen reduces isoniazid-induced liver injury and early treatment failure in the 6-month four-drug standard treatment of tuberculosis: A randomized controlled trial for pharmacogenetics-based therapy. *European Journal of Clinical Pharmacology*, *69*, 1091–1101. https://doi.org/10.1007/s00228-012-1429-9

Banegas, M. P., & Li, C. I. (2012). Breast cancer characteristics and outcomes among hispanic black and hispanic white women. *Breast Cancer Research and Treatment*, *134*, 1297–1304. https://doi.org/10.1007/s10549-012-2142-1

Barwell, J., O'Sullivan, R., Mansbridge, L., Lowry, J., & Dorkins, H. (2018). Challenges in implementing genomic medicine: The 100,000 genomes project. *Journal of Translational Genetics and Genomics*, *2*, 13.

Bennett, S. N., Caporaso, N., Fitzpatrick, A. L., Agrawal, A., Barnes, K., Boyd, H. A., … Consortium, G. (2011). Phenotype harmonization and cross-study collaboration in GWAS consortia: The GENEVA experience. *Genetic Epidemiology*, *35*, 159–173. https://doi.org/10.1002/gepi.20564

Chaiyasap, P., Ittiwut, C., Srichomthong, C., Sangsin, A., Suphapeetiporn, K., & Shotelersuk, V. (2017). Massive parallel sequencing as a new diagnostic approach for phenylketonuria and tetrahydrobiopterin-deficiency in Thailand. *BMC Medical Genetics*, *18*, 102. https://doi.org/10.1186/s12881-017-0464-x

Chen, P., Lin, J.-J., Lu, C.-S., Ong, C.-T., Hsieh, P. F., Yang, C.-C., … Consortium, T. S. (2011). Carbamazepine-induced toxic effects and HLA-B*1502 screening in Taiwan. *The New England Journal of Medicine*, *364*, 1126–1133. https://doi.org/10.1056/NEJMoa1009717

Chung, W.-H., Hung, S.-I., Hong, H.-S., Hsih, M.-S., Yang, L.-C., Ho, H.-C., … Chen, Y.-T. (2004). Medical genetics: A marker for Stevens-Johnson syndrome. *Nature*, *428*, 486. https://doi.org/10.1038/428486a

Clancy, J. P., Johnson, S. G., Yee, S. W., McDonagh, E. M., Caudle, K. E., Klein, T. E., … Giacomini, K. M. (2014). Clinical pharmacogenetics implementation consortium (CPIC) guidelines for ivacaftor therapy in the context of CFTR genotype. *Clinical Pharmacology and Therapeutics*, *95*, 592–597. https://doi.org/10.1038/clpt.2014.54

Collins, F. S., & Varmus, H. (2015). A new initiative on precision medicine. *The New England Journal of Medicine*, *372*, 793–795. https://doi.org/10.1056/NEJMp1500523

Dalton, T., Cegielski, P., Akksilp, S., Asencios, L., Caoili, J. C., Cho, S.-N., … Viiklepp, P. (2012). Prevalence of and risk factors for resistance to second-line drugs in people with multidrug-resistant tuberculosis in eight countries: A prospective cohort study. *The Lancet*, *380*, 1406–1417. https://doi.org/10.1016/S0140-6736(12)60734-X

DePristo, M. A., Banks, E., Poplin, R., Garimella, K. V., Maguire, J. R., Hartl, C., … Daly, M. J. (2011). A framework for variation discovery and genotyping using next-generation DNA sequencing data. *Nature Genetics*, *43*, 491–498. https://doi.org/10.1038/ng.806

Dong, D., Sung, C., & Finkelstein, E. A. (2012). Cost-effectiveness of HLA-B*1502 genotyping in adult patients with newly diagnosed epilepsy in Singapore. *Neurology*, *79*, 1259–1267. https://doi.org/10.1212/WNL.0b013e31826aac73

Eurordis. (2005). *Rare diseases: Understanding this public health priority*. Plateforme Maladies Rares. 102 rue Didot, 75014 Paris, France. www.eurordis.org.

Ferlay, J., Soerjomataram, I., Dikshit, R., Eser, S., Mathers, C., Rebelo, M., … Bray, F. (2015). Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. *International Journal of Cancer*, *136*, E359–E386. https://doi.org/10.1002/ijc.29210

Gahl, W. A. (2012). The battlefield of rare diseases: Where uncommon insights are common. *Science Translational Medicine*, *4*, 154ed157. https://doi.org/10.1126/scitranslmed.3004980

Huang, K. L., Mashl, R. J., Wu, Y., Ritter, D. I., Wang, J., Oh, C., … Ding, L. (2018). Pathogenic germline variants in 10,389 adult cancers. *Cell*, *173*, 355–370 e314. https://doi.org/10.1016/j.cell.2018.03.039

Hung, S.-I., Chung, W.-H., Liou, L.-B., Chu, C.-C., Lin, M., Huang, H.-P., … Chen, Y.-T. (2005). HLA-B*5801 allele as a genetic marker for severe cutaneous adverse reactions caused by allopurinol. *Proceedings of the National Academy of Sciences*, *102*, 4134–4139. https://doi.org/10.1073/pnas.0409500102

Intarak, N., Theerapanon, T., Ittiwut, C., Suphapeetiporn, K., Porntaveetus, T., & Shotelersuk, V. (2018). A novel PITX2 mutation in non-syndromic orodental anomalies. *Oral Diseases*, *24*, 611–618. https://doi.org/10.1111/odi.12804

Intarak, N., Theerapanon, T., Srijunbarl, A., Suphapeetiporn, K., Porntaveetus, T., & Shotelersuk, V. (2018). Novel compound heterozygous mutations in KREMEN1 confirm it as a disease gene for ectodermal dysplasia. *The British Journal of Dermatology*, *179*, 758–760. https://doi.org/10.1111/bjd.16541

Ittiwut, C., Natesirinilkul, R., Tongprasert, F., Sathitsamitphong, L., Choed-Amphai, C., Fanhchaksai, K., … Shotelersuk, V. (2018). Novel mutations in SPTA1 and SPTB identified by whole exome sequencing in eight Thai families with hereditary pyropoikilocytosis presenting with severe fetal and neonatal anaemia. *British Journal of Haematology*. https://doi.org/10.1111/bjh.15559

Ittiwut, R., Suchartlikitwong, P., Kittikalayawong, Y., Ittiwut, C., Prasopsanti, K., Sosothikul, D., … Suphapeetiporn, K. (2017). Novel mutations in Thai patients with glanzmann thrombasthenia. *European Journal of Haematology*, *99*, 520–524. https://doi.org/10.1111/ejh.12965

Kamatani, N., Fujimori, S., Hada, T., Hosoya, T., Kohri, K., Nakamura, T., … Matsuzawa, Y. (2011). Multicenter, open-label study of long-term administration of febuxostat (tmx-67) in Japanese patients with hyperuricemia including gout. *Journal of Clinical Rheumatology: Practical Reports on Rheumatic & Musculoskeletal Diseases*, *17*, S50–S56. https://doi.org/10.1097/RHU.0b013e31822541d0

Konjikusic, M. J., Yeetong, P., Boswell, C. W., Lee, C., Roberson, E. C., Ittiwut, R., … Gray, R. S. (2018). Mutations in kinesin family member 6 reveal specific role in ependymal cell ciliogenesis and human neurological development. *PLoS Genetics*, *14*, e1007817. https://doi.org/10.1371/journal.pgen.1007817

Koopman, J. J. E., van Bodegom, D., Ziem, J. B., & Westendorp, R. G. J. (2016). An emerging epidemic of noncommunicable diseases in developing populations due to a triple evolutionary mismatch. *The American Journal of Tropical Medicine and Hygiene*, *94*, 1189–1192. https://doi.org/10.4269/ajtmh.15-0715

Leoyklang, P., Siriwan, P., & Shotelersuk, V. (2006). A mutation of the p63 gene in non-syndromic cleft lip. *Journal of Medical Genetics*, *43*, e28. https://doi.org/10.1136/jmg.2005.036442

Leoyklang, P., Suphapeetiporn, K., Siriwan, P., Desudchit, T., Chaowanapanja, P., Gahl, W. A., & Shotelersuk, V. (2007). Heterozygous nonsense mutation SATB2 associated with cleft palate, osteoporosis, and cognitive defects. *Human Mutation*, *28*, 732–738. https://doi.org/10.1002/humu.20515

Leoyklang, P., Suphapeetiporn, K., Srichomthong, C., Tongkobpetch, S., Fietze, S., Dorward, H., … Shotelersuk, V. (2013). Disorders with similar clinical phenotypes reveal underlying genetic interaction: SATB2 acts as an activator of the UPF3B gene. *Human Genetics*, *132*, 1383–1393. https://doi.org/10.1007/s00439-013-1345-9

Lindert, U., Cabral, W. A., Ausavarat, S., Tongkobpetch, S., Ludin, K., Barnes, A. M., … Shotelersuk, V. (2016). MBTPS2 mutations cause defective regulated intramembrane proteolysis in X-linked osteogenesis imperfecta. *Nature Communications*, *7*, 11920. https://doi.org/10.1038/ncomms11920

Locharernkul, C., Loplumlert, J., Limotai, C., Korkij, W., Desudchit, T., Tongkobpetch, S., … Shotelersuk, V. (2008). Carbamazepine and phenytoin induced Stevens-Johnson syndrome is associated with HLA-B*1502 allele in Thai population. *Epilepsia*, *49*, 2087–2091. https://doi.org/10.1111/j.1528-1167.2008.01719.x

Locharernkul, C., Shotelersuk, V., & Hirankarn, N. (2010). HLA-B* 1502 screening: Time to clinical practice. *Epilepsia*, *51*, 936–938. https://doi.org/10.1111/j.1528-1167.2010.02549.x

Luzum, J. A., Pakyz, R. E., Elsey, A. R., Haidar, C. E., Peterson, J. F., Whirl-Carrillo, M., … Freimuth, R. R. (2017). The pharmacogenomics research network translational pharmacogenetics program: Outcomes and metrics of pharmacogenetic implementations across diverse healthcare systems. *Clinical Pharmacology and Therapeutics*, *102*, 502–510. https://doi.org/10.1002/cpt.630

Manolio, T. A., Abramowicz, M., Al-Mulla, F., Anderson, W., Balling, R., Berger, A. C., … Ginsburg, G. S. (2015). Global implementation of genomic medicine: We are not alone. *Science Translational Medicine*, *7*, 290ps213. https://doi.org/10.1126/scitranslmed.aab0194

Manolio, T. A., Hutter, C. M., Avigan, M., Cibotti, R., Davis, R. L., Denny, J. C., … Shear, N. H. (2018). Research directions in genetic predispositions to Stevens-Johnson syndrome/toxic epidermal necrolysis. *Clinical Pharmacology and Therapeutics*, *103*, 390–394. https://doi.org/10.1002/cpt.890

Martin, M. A., Hoffman, J. M., Freimuth, R. R., Klein, T. E., Dong, B. J., Pirmohamed, M., … Kroetz, D. L. (2014). Clinical pharmacogenetics implementation consortium guidelines for HLA-B genotype and abacavir dosing: 2014 update. *Clinical Pharmacology and Therapeutics*, *95*, 499–500. https://doi.org/10.1038/clpt.2014.38

Mockenhaupt, M., & Schöpf, E. (1996). Epidemiology of drug-induced severe skin reactions. *Seminars in Cutaneous Medicine and Surgery*, *15*, 236–243.

Nowwarote, N., Theerapanon, T., Osathanon, T., Pavasant, P., Porntaveetus, T., & Shotelersuk, V. (2018). Amelogenesis imperfecta: A novel fam83h mutation and characteristics of periodontal ligament cells. *Oral Diseases*, *24*, 1522–1531. https://doi.org/10.1111/odi.12926

Panmontha, W., Amarinthnukrowh, P., Damrongphol, P., Desudchit, T., Suphapeetiporn, K., & Shotelersuk, V. (2016). Novel mutations in the fuca1 gene that cause fucosidosis. *Genetics and Molecular Research*, *15*, 1–6. https://doi.org/10.4238/gmr.15038733

Panmontha, W., Rerknimitr, P., Yeetong, P., Srichomthong, C., Suphapeetiporn, K., & Shotelersuk, V. (2015). A frameshift mutation in pen-2 causes familial comedones syndrome. *Dermatology*, *231*, 77–81. https://doi.org/10.1159/000382122

Phowthongkum, P., Ittiwut, C., & Shotelersuk, V. (2018). Severe hyperammonemic encephalopathy requiring dialysis aggravated by prolonged fasting and intermittent high fat load in a Ramadan fasting month in a patient with CPTII homozygous mutation. *JIMD Reports*, *41*, 11–16. https://doi.org/10.1007/8904_2017_74

Poplin R, V. Ruano-Rubio., DePristo MA, Fennell TJ, Carneiro MO, Van der Auwera GA, . (2018). *Scaling accurate genetic variant discovery to tens of thousands of samples*. Biorxiv: Cold Spring Harbor Laboratory.

Porntaveetus, T., Abid, M. F., Theerapanon, T., Srichomthong, C., Ohazama, A., Kawasaki, K., … Shotelersuk, V. (2018). Expanding the oro-dental and mutational spectra of kabuki syndrome and expression of KMT2D and KDM6A in human tooth germs. *International Journal of Biological Sciences*, *14*, 381–389. https://doi.org/10.7150/ijbs.23517

Porntaveetus, T., Nowwarote, N., Osathanon, T., Theerapanon, T., Pavasant, P., Boonprakong, L., … Shotelersuk, V. (2018). Compromised alveolar bone cells in a patient with dentinogenesis imperfecta caused by DSPP mutation. *Clinical Oral Investigations*, *23*, 303–313. https://doi.org/10.1007/s00784-018-2437-7

Porntaveetus, T., Osathanon, T., Nowwarote, N., Pavasant, P., Srichomthong, C., Suphapeetiporn, K., & Shotelersuk, V. (2018). Dental properties, ultrastructure, and pulp cells associated with a novel DSPP mutation. *Oral Diseases*, *24*, 619–627. https://doi.org/10.1111/odi.12801

Porntaveetus, T., Srichomthong, C., Ohazama, A., Suphapeetiporn, K., & Shotelersuk, V. (2017). A novel gja1 mutation in oculodentodigital dysplasia with extensive loss of enamel. *Oral Diseases*, *23*, 795–800. https://doi.org/10.1111/odi.12663

Porntaveetus, T., Srichomthong, C., Suphapeetiporn, K., & Shotelersuk, V. (2015). A novel PCCB mutation in a Thai patient with propionic acidemia identified by exome sequencing. *Human Genome Variation*, *2*, 15033. https://doi.org/10.1038/hgv.2015.33

Porntaveetus, T., Srichomthong, C., Suphapeetiporn, K., & Shotelersuk, V. (2017). Monoallelic FGFR3 and biallelic ALPL mutations in a Thai girl with hypochondroplasia and hypophosphatasia. *American Journal of Medical Genetics. Part A*, *173*, 2747–2752. https://doi.org/10.1002/ajmg.a.38370

Porntaveetus, T., Theerapanon, T., Srichomthong, C., & Shotelersuk, V. (2018). Cole-carpenter syndrome in a patient from Thailand. *American Journal of Medical Genetics. Part A*, *176*, 1706–1710. https://doi.org/10.1002/ajmg.a.40358

Rattanasopha, S., Tongkobpetch, S., Srichomthong, C., Siriwan, P., Suphapeetiporn, K., & Shotelersuk, V. (2012). Pdgfra mutations in humans with isolated cleft palate. *European Journal of Human Genetics*, *20*, 1058–1062. https://doi.org/10.1038/ejhg.2012.55

Rattanavipapong, W., Koopitakkajorn, T., Praditsitthikorn, N., Mahasirimongkol, S., & Teerawattananon, Y. (2013). Economic evaluation of HLA-B*15:02 screening for carbamazepine-induced severe adverse drug reactions in Thailand. *Epilepsia*, *54*, 1628–1638. https://doi.org/10.1111/epi.12325

Raymond, F. L., Horvath, R., & Chinnery, P. F. (2018). First-line genomic diagnosis of mitochondrial disorders. *Nature Reviews. Genetics*, *19*, 399–400. https://doi.org/10.1038/s41576-018-0022-1

Reich, M. R., Harris, J., Ikegami, N., Maeda, A., Cashin, C., Araujo, E. C., … Evans, T. G. (2016). Moving towards universal health coverage: Lessons from 11 country studies. *The Lancet*, *387*, 811–816. https://doi.org/10.1016/S0140-6736(15)60002-2

Relling, M. V., & Klein, T. E. (2011). CPIC: Clinical pharmacogenetics implementation consortium of the pharmacogenomics research network. *Clinical Pharmacology & Therapeutics*, *89*, 464–467. https://doi.org/10.1038/clpt.2010.279

Sahakitrungruang, T., Srichomthong, C., Pornkunwilai, S., Amornfa, J., Shuangshoti, S., Kulawonganunchai, S., … Shotelersuk, V. (2014). Germline and somatic dicer1 mutations in a pituitary blastoma causing infantile-onset Cushing's disease. *The Journal of Clinical Endocrinology and Metabolism*, *99*, E1487–E1492. https://doi.org/10.1210/jc.2014-1016

Samuel, G. N., & Farsides, B. (2017). The UK's 100,000 Genomes Project: Manifesting policymakers' expectations. *New Genetics Society*, *36*, 336–353. https://doi.org/10.1080/14636778.2017.1370671

Sangsin, A., Srichomthong, C., Pongpanich, M., Suphapeetiporn, K., & Shotelersuk, V. (2016a). Short stature, platyspondyly, hip dysplasia, and retinal detachment: An atypical type II collagenopathy caused by a novel mutation in the C-propeptide region of COL2A1: A case report. *BMC Medical Genetics*, *17*, 96. https://doi.org/10.1186/s12881-016-0357-4

Sangsin, A., Srichomthong, C., Pongpanich, M., Suphapeetiporn, K., & Shotelersuk, V. (2016b). Whole-exome sequencing reveals a novel COL2A1 mutation in a patient with spondylo-epiphyseal dysplasia congenita. *Genetics and Molecular Research*, *15*, 15017624. https://doi.org/10.4238/gmr.15017624

Service, R. F. (2006). Gene sequencing. The race for the $1000 genome. *Science*, *311*, 1544–1546. https://doi.org/10.1126/science.311.5767.1544

Shotelersuk, V., Limwongse, C., & Mahasirimongkol, S. (2014). Genetics and genomics in Thailand: Challenges and opportunities. *Molecular Genetics & Genomic Medicine*, *2*, 210–216. https://doi.org/10.1002/mgg3.83

Stark, Z., Dolman, L., Manolio, T. A., Ozenberger, B., Hill, S. L., Caulfied, M. J., … North, K. N. (2019). Integrating genomics into healthcare: A global responsibility. *American Journal of Human Genetics*, *104*, 13–20. https://doi.org/10.1016/j.ajhg.2018.11.014

Suratannon, N., Yeetong, P., Srichomthong, C., Amarinthnukrowh, P., Chatchatee, P., Sosothikul, D., … Shotelersuk, V. (2016). Adaptive immune defects in a patient with leukocyte adhesion deficiency type iii with a novel mutation in fermt3. *Pediatric Allergy and Immunology*, *27*, 214–217. https://doi.org/10.1111/pai.12485

Tan-Koi, W. C., Sung, C., Chong, Y. Y., Lateef, A., Pang, S. M., Vasudevan, A., … Chan, C. L. (2017). Tailoring of recommendations to reduce serious cutaneous adverse drug reactions: A pharmacogenomics approach. *Pharmacogenomics*, *18*, 881–890. https://doi.org/10.2217/pgs-2017-0016

Tassaneeyakul, W., Tiamkao, S., Jantararoungtong, T., Chen, P., Lin, S.-Y., Chen, W.-H., … Yodnopaglaw, P. (2010). Association between HLA-B*1502 and carbamazepine-induced severe cutaneous adverse drug

reactions in a Thai population. *Epilepsia*, *51*, 926–930. https://doi.org/10.1111/j.1528-1167.2010.02533.x

Van der Auwera, G. A., Carneiro, M. O., Hartl, C., Poplin, R., Del Angel, G., Levy-Moonshine, A., … DePristo, M. A. (2013). From FastQ data to high confidence variant calls: The genome analysis toolkit best practices pipeline. *Current Protocols in Bioinformatics*, *43*(11), 10 11–10 33. https://doi.org/10.1002/0471250953.bi1110s43

Vathesatogkit, P., Woodward, M., Tanomsup, S., Ratanachaiwong, W., Vanavanan, S., Yamwong, S., & Sritara, P. (2012). Cohort profile: The electricity generating authority of Thailand study. *International Journal of Epidemiology*, *41*, 359–365. https://doi.org/10.1093/ije/dyq218

Veeravigrom, M., Damrongphol, P., Ittiwut, R., Ittiwut, C., Suphapeetiporn, K., & Shotelersuk, V. (2015). Pyridoxal 5-phosphate-responsive epilepsy with novel mutations in the PNPO gene: A case report. *Genetics and Molecular Research*, *14*, 14130–14135. https://doi.org/10.4238/2015.October.29.34

Wang, B. (2016). China's $9.2 billion precision medicine initiative could see about 100 million whole human genomes sequenced by 2030 and more if sequencing costs drop. *Next big future*.

Wangkumhang, P., Shaw, P. J., Chaichoompu, K., Ngamphiw, C., Assawamakin, A., Nuinoon, M., … Tongsima, S. (2013). Insight into the peopling of mainland southeast Asia from Thai population genetic structure. *PLoS One*, *8*, e79522. https://doi.org/10.1371/journal.pone.0079522

World Health Organization. (2017). *Noncommunicable diseases progress monitor 2017*. Geneva: World Health Organization.

Yeetong, P., Phewplung, T., Kamolvisit, W., Suphapeetiporn, K., & Shotelersuk, V. (2018). Widespread and debilitating hemangiomas in a patient with enchondromatosis and d-2-hydroxyglutaric aciduria. *Skeletal Radiology*, *47*, 1577–1582. https://doi.org/10.1007/s00256-018-2963-z

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