



Building capacity for human genetics and genomics research in Trinidad and Tobago

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ABSTRACT

Advances in human genetics and genomic sciences and the corresponding explosion of biomedical technologies have deepened current understanding of human health and revolutionized medicine. In developed nations, this has led to marked improvements in disease risk stratification and diagnosis. These advances have also led to targeted intervention strategies aimed at promoting disease prevention, prolonging disease onset, and mitigating symptoms, as in the well-known case of breast cancer and the BRCA1 gene. In contrast, in the developing nation of Trinidad and Tobago, this scientific revolution has not translated into the development and application of effective genomics-based interventions for improving public health. While the reasons for this are multifactorial, the underlying basis may be rooted in the lack of pertinence of internationally driven genomics research to the local public health needs in the country, as well as a lack of relevance of internationally conducted genetics research to the genetic and environmental contexts of the population. Indeed, if Trinidad and Tobago is able to harness substantial public health benefit from genetics/genomics research, then there is a dire need, in the near future, to build local capacity for the conduct and translation of such research. Specifically, it is essential to establish a national human genetics/genomics research agenda in order to build sustainable human capacity through education and knowledge transfer and to generate public policies that will provide the basis for the creation of a mutually beneficial framework (including partnerships with more developed nations)

that is informed by public health needs and contextual realities of the nation.

Key words: ethics, research; genetics; genomics; policy; research; Trinidad and Tobago; West Indies.

NEED FOR GENETICS/GENOMICS RESEARCH IN TRINIDAD AND TOBAGO

Over the past decade, advancements in human genetics/genomics research and the parallel explosion in sequencing technologies and computational tools necessary for downstream analysis have deepened understanding of human health and revolutionized the biomedical field. There have been marked improvements in disease diagnosis and prognosis as well as patient risk and outcome stratification. These have led to novel therapeutic strategies that prolong disease onset, and mitigate symptoms, as in the well-known case where mutations in the *BRCA1* gene suggests increased risk for breast cancer and the less familiar case of using liquid biopsies to diagnose prostate and breast cancer. The advancement of human genetics/genomics research has also had a profound impact on how people see themselves as individuals and as members of families; affected how they define what it means to be human; and challenged long-held normative beliefs about nature versus nurture. Indeed, these conceptual shifts, among others, have had considerable impact on many aspects of medicine and society and have led to the implementation of new legal and regulatory policies to help guide the conduct of human genetics/genomics research as well as its translation and integration in the clinic and in the community.

In Trinidad and Tobago (TT), researchers at The University of the West Indies (UWI) and other institutions have been contributing to the field of genetics/genomics sciences since as early as the 1970s. A search of PubMed reveals at least 60 human genetics publications involving TT covering subjects including patterns of inheritance, identification of candidate genes for common diseases, genetic epidemiology, and genetic variation. Findings from these research studies have not only provided country-specific baseline data but have also contributed to the understanding of the genetic factors underlying a variety of conditions including diabetes, hypertension, and cancer.

Unfortunately, unlike more developed nations, this contribution has not been matched with significant translation of the results to the benefit of the TT community. For example, with the exception of testing

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for familial relationships or for diagnosis of hemoglobinopathies, biospecimens are generally shipped abroad for analysis, making genetic testing an expensive option, largely unavailable to the average citizen. The lack of integration of genomics into public health in TT is a reminder that a major concern about this field of research is its potential to exacerbate health disparities through the inequitable distribution of benefits between populations (1).

The lack of meaningful integration of genetics/genomics technologies in the health system is compounded by the paucity of relevant public policies. The Administration of Justice (Deoxyribonucleic Acid) Act of 2012 (2), which governs the collection and use of deoxyribonucleic acid (DNA) for forensics, allows access to DNA by government agencies and educational institutions for research. This Act allows DNA data sharing without personal health identifying information and lists the minister designated to oversee forensics and solely responsible for approving research. It does not take into account other ethical considerations, such as the objectives of the studies to be conducted. In addition, even though the Data Protection Act of 2011 (3) recognizes DNA as personal information that should be protected, a more relevant regulatory framework guiding the conduct and translation of genetic/genomic research, and policies protecting against genetic discrimination, are still lacking.

In 2013, collaboration was launched between UWI and renowned universities in the United States and United Kingdom to conduct a nationwide genomics study that would provide evidence for the construction of a policy for the prevention and treatment of degenerative eye diseases in TT. This pioneering initiative was the first national genomics research study and was met with great trepidation by both laypersons and professionals (4). Opponents of the project cited distrust of foreign collaborators and a hidden foreign agenda; the lack of local expertise in the area of genomics; and the dearth of local public policy to protect study participants and prevent discrimination as areas for concern. Although this study had undergone ethics review from three universities and the local Ministry of Health, the outcry substantially delayed and almost derailed the entire project.

Given the failure to meaningfully integrate genetics/genomics into the health system, and the paucity of national public policy in this area, coupled with the challenges associated with the implementation of the first genomics study in TT, this article 1) addresses the urgent need to comprehensively build capacity for human genetics/genomics research in TT and 2) proposes a framework to guide the endeavor.

NEED FOR INVESTMENT

TT is the most southern Caribbean nation and is in close proximity to South America. It is the most industrialized Caribbean nation and has low unemployment rates, high literacy rates, and sustained economic growth. It offers comprehensive, no-cost health care

to all citizens at five Regional Health Authorities (RHAs)—Eastern Regional, North Central, North West, South West, and Tobago—that manage nine hospitals, nine district health facilities, and over 95 health centers. Health care is a national priority, with 15% of the total national budget expenditure of 2015 dedicated to health care—third highest, after education and training, and national security (5).

Despite this investment, TT has a high burden of chronic, noncommunicable diseases. A study conducted between 2008 and 2009 reported a disease prevalence of 19.5% for diabetes mellitus, 30.2% for hypertension, and 8.2% for cardiovascular disease (6). In addition, in 2009, it was reported that diabetes-related mortality is 10 times higher than in the United States, and mortality rates from heart and cardiovascular diseases rank among the highest in the Caribbean (7). More than 50% of the nation's adult population and a frightening proportion of children are reportedly overweight/obese and at risk for diabetes and hypertension (8). Furthermore, breast cancer mortality rates are among the highest in the world (9).

Many of the complex disorders in TT require the integration of genetics/genomics and clinical and epidemiological data to undergird efforts aimed at developing effective public health policy and the delivery of health services. This integrated approach is standard best practice in most developed countries for paving the way for the new emphasis on precision medicine. In fact, as illustrated in Table 1, international genetics/genomics research on the diseases that create substantial public burden in TT have led to the development of genetic tests with proven clinical utility, none of which are currently readily available for use in TT. In addition, there is a growing body of literature reporting that greater investment in biomedical research is associated with better health outcomes for populations in the long term (10, 11).

In TT, one option might be to invest in direct measures that address more immediate infrastructural and resource needs, such as hiring more hospital staff to reduce wait times; training customer service and management personnel; or purchasing more medicines, ambulances and medical equipment. While these direct measures are important, they should be balanced with investments in locally relevant genetics/genomics research aiming to identify and address the etiology underlying the most prevalent diseases in TT.

ENGAGEMENT OF INTERNATIONAL EXPERTISE AND EXTERNAL FUNDING SOURCES

Currently, research in human genetics/genomics conducted in TT is predominantly driven by international agencies and/or involves the purchase of external expertise that contribute their knowledge of genetics/genomics, and the use of technologies/infrastructure from abroad. The reasons for this include the short-term cost-effectiveness of this approach and, more importantly, the alignment with eligibility criteria and priority

TABLE 1. Examples of genetic tests available for leading causes of death, Trinidad and Tobago, 2006

Disease	2006 mortality distribution (%) ^a	Genetic test	Clinical implications
Cardiovascular disease	24.6	Cardiovascular disease risk factor test ^b Factor V Leiden Kit ^{c,d}	Identify mutations in eleven risk inducing genes Diagnose suspected hereditary thrombophilia
Cancer	13.7		
Prostate		NADiA® ProsVue™ ^{e,g} PROGENSA® PCA3 Assay ^{c,f}	Determine risk of cancer reoccurrence post prostatectomy Diagnose prostate cancer
Breast		Prosigna™ Breast Cancer Prognostic Gene Signature Assay ^{c,g} GeneSearch™ Breast Lymph Node (BLN) Test Kit ^{c,h}	Determine likelihood of breast cancer recurrence Detect lymph node metastases
Colon		Cologuard™ hereditary colon cancer panel ^{c,i}	Detect markers associated with early non-invasive cancer Identify mutations in risk inducing genes
Diabetes	13.6	MODY ^j sequencing panel ^l Comprehensive neonatal diabetes mutation analysis ^b	Diagnose maturity-onset diabetes of the young Identify mutations in 11 risk-inducing genes
Cerebrovascular disease	< 10	Factor II (Prothrombin) G20210A Kit ^{c,d}	Determine risk for thrombotic events (e.g., stroke)
Respiratory disease	< 10	Comprehensive diffuse lung disease NGS ^k panel ^l Comprehensive sequencing panel ^l (for pulmonary disease)	Analyze genes associated with inherited forms of diffuse lung disease Diagnose suspected hereditary respiratory disease

Source: authors' compilation using published data.

^a 2011 Health Report Card for Trinidad and Tobago (www.health.gov.tt).

^b Genetic tests (www.genetests.org).

^c FDA-approved genetic tests (www.fda.gov).

^d Roche Molecular Diagnostics (Branchburg, NJ, USA).

^e Iris International, Inc. (Chatsworth, CA, USA).

^f Hologic, Inc. (Bedford, MA, USA).

^g NanoString Technologies, Inc. (Seattle, WA, USA).

^h Janssen Diagnostics, LLC (Raritan, NJ, USA).

ⁱ Exact Sciences Corporation (Madison, WI, USA).

^j MODY: Maturity-onset diabetes of the young.

^k NGS: Next generation sequencing.

research areas for international funding bodies. As a developing country, this is a valid pathway to promote capacity building for genetics/genomics research, but relying solely on external agencies is not an ideal long-term, sustainable solution, and may be a potential source of unintentional harm.

A major challenge of externally driven and focused genetics/genomics research is the tendency to represent the interests of the international community. Usually, there is limited integration into a national research agenda and little relevance to the needs of the host country. This may result in findings and conclusions that are unlikely to have a meaningful, measurable impact/outcome for the host country. Another limitation of externally driven research is the risk of overlooking the social and cultural realities of the host country. This may manifest, for example, in a failure to identify and engage key stakeholders, insufficient procurement, and inadequate sensitization of the population, which may affect local participation and sustainability. An additional risk is that the host country can become a potential field site for scientists (local and foreign) who are motivated by personal benefit rather than national interest. These legitimate sources of ethical concern may lead one to surmise that one of the reasons that TT has not realized a substantial benefit in the areas of genetics/genomics is related to the lack of a national, context-specific genetic/genomics agenda.

In addition, prior research has shown that, in heterogeneous populations, significant variations in genetic

response to diseases within the population can be observed and used to inform more targeted clinical approaches (12). The genetic composition of TT may therefore pose a distinct challenge, as the genetic diversity on each of the sister islands may vary substantially. The populace of Trinidad is generally borne out of the mixing of individuals of Amerindian, African, East Asian, and European ancestry. Therefore, the genetic variation in Trinidad may be similar to that identified in a study of Caribbean nations demonstrating substantial genetic heterogeneity and distinct ancestral lines (13). In contrast, the populace of Tobago is generally of African ancestry. It is thus possible that the genetic composition of Tobago resembles that of the Bahamas, which has > 90% African ancestry (14), and therefore the African founder mutations identified in the hereditary gene for breast cancer in the Bahamian population may be more relevant to Tobago (14). To date, the genetic diversity of TT is uncharacterized and an intimate investigation of the genetic variation within TT will be necessary to determine if there are subgroup-specific disease variants within the population. Theoretically, such insight will enable researchers to determine which imported technologies may lead to more accurate diagnosis (e.g., genetic spectrum analysis in breast cancer); more effective treatment (e.g., variability in diabetic patients' responses to metformin treatment); improved disease prognosis; and the potential identification and development of novel therapeutics.

SYSTEMATIC CAPACITY BUILDING

One way to address these concerns is to systematically build national capacity for human genetics/genomics research (1). Undeniably, this is a challenging endeavor, requiring a combination of short- and long-term strategies directed at the individual, institutional, and national levels. In addition, it cannot occur in a vacuum; rather, it must be embedded with a national effort for health system reform, which, as the World Health Organization (WHO) Genomics and World Health Report (15) suggests, is aimed at producing more functional approaches to clinical practice, public health, and the more traditional clinical and epidemiological research.

This paradigm shift will first require a situational assessment of the nation's health system aimed at generating a national health research agenda. Given the existence of the Health Research Agenda for the Caribbean developed by the Caribbean Public Health Agency (CARPHA) (Port of Spain) (16), TT must decide whether to adopt this regional agenda or create their own country-specific research agenda. This TT research agenda will serve as a foundation to promote the formation of mutually beneficial partnerships with investigators from more developed nations. It will guide the studies that the country agrees to participate in and ensure that local interests are aligned with the research interests of international funders and investigators. It will also facilitate the establishment of capacity-building programs with institutions abroad for training, recruitment, and mobilization of researchers while facilitating access to genetic resources, and information technologies.

While the financial resources required to build capacity for genetic/genomic research will be difficult to estimate, it must be acknowledged that this will be a costly endeavor. Funds will be required to build physical infrastructure, develop human resources, and fund research studies. Resources will also be needed to 1) create public education/awareness campaigns that will ensure national buy-in and 2) retool science and math education so that genetics, genomics, statistics, and computer programming are woven into the education infrastructure at the earliest stages. The government will have to demonstrate commitment to this purpose through the redirection of funds, and innovative ways of generating new financing opportunities for research will be required. One example is the model used in Kenya and elsewhere (17), which involves earmarking a negligible percentage of value-added taxes for health research. These financial outputs will eventually be balanced by revenue gained from reduced long-term health care costs incurred from offering targeted therapies, and increased productivity of patients who are treated with precision therapeutics, which, in turn reduces recovery time. In addition, positioning TT at the forefront of technologies in the field creates another potential revenue stream through the provision of sequencing services and training opportunities to others in the Caribbean.

Finally, government support may attract international funders and key researchers as they discern that genetics/genomics research is now a national priority and a potential growth industry.

Meanwhile, through agencies like CARPHA and universities in TT (and elsewhere in the Caribbean), networks can be developed to provide a forum for scientific exchange and to amalgamate expertise from foreign nationals or nationals living abroad who are knowledgeable in the field. These institutions will also have to develop the human resource capacity in genetics/genomics as well as complementary expertise in epidemiology, health informatics, health finance, health management, and health policy through the creation of new or expanded academic/training programs. Such initiatives will have far-reaching benefits not only on the health of the nation but also on biomedical research as a whole, and may lead to a proliferation of career opportunities in genetic counseling, medical genetics, psychosocial genetics, molecular genetics, policy, and "genethics."⁴ These agencies can also help to identify and support researchers who are knowledgeable and capable of attracting funding and negotiating mutually beneficial international partnerships.

Conclusions

Capacity building for genetics/genomics research will require the construction of national policies developed by the government to 1) protect research study participants and consumers of genetic/genomic technologies; 2) monitor the implications of genetics/genomics on health and society; and 3) guide the integration of genetic/genomics in a manner that does not exacerbate health disparities. Given that some genetic variations are associated with greater health risks than others, and will require different clinical approaches and types of interventions, integrating genetics/genomics policies into existing health-related policies may be appropriate. An integrative approach may be more valuable, as policies that focus on key issues, including privacy, confidentiality, use of tissue samples, and nondiscrimination, will affect multiple sectors.

It must be underscored that while capacity building in genetics/genomics research is a costly endeavor that may not yield immediate benefit, an investment in this area is crucial for health and the sustainable future of biomedical research in TT. The time has come for TT to indigenize human genetics/genomics research systems that will lead to evidence-based, translatable outcomes as part of a comprehensive strategy to strengthen the health system. In order to harness the benefits of genetics/genomics technologies for improvements in the public health of the nation, TT must build local capacity for human genetics/genomics research.

⁴ Genetics ethical issues (e.g., the use of archived tissue specimens for research).

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RESUMEN

Aumento de la capacidad de investigación en genética y genómica humanas en Trinidad y Tabago

Los avances en materia de ciencias genéticas y genómicas humanas y la correspondiente expansión de las tecnologías biomédicas han ampliado la comprensión actual de la salud humana y han revolucionado la medicina. En las naciones desarrolladas, ello ha

conducido a intensas mejoras en la estratificación del riesgo y el diagnóstico de las enfermedades. Estos avances también han conducido a estrategias de intervención dirigidas a promover la prevención de las enfermedades, retardar su aparición, y atenuar sus síntomas, como en el caso del cáncer de mama y el gen *BRCA1*. Por el contrario, en Trinidad y Tabago, nación en desarrollo, esta revolución científica no se ha traducido en la elaboración y aplicación de intervenciones eficaces basadas en la genómica para mejorar la salud pública. Aunque las razones de ello son multifactoriales, el motivo subyacente puede radicar en la falta de adecuación de la investigación genómica a escala internacional a las necesidades locales de salud pública del país, así como a la escasa relevancia de la investigación en genética realizada internacionalmente para los contextos genéticos y ambientales de la población. En efecto, para que Trinidad y Tabago pueda aprovechar los sustanciales beneficios en materia de salud pública de la investigación en genética y genómica, es extremadamente necesario, en un futuro próximo, desarrollar la capacidad local para la realización y traducción de ese tipo de investigación. En concreto, es esencial establecer un programa nacional de investigación en genética y genómica humanas con objeto de desarrollar una capacidad humana sostenible mediante la educación y la transferencia de conocimientos, y generar políticas públicas que proporcionen la base para la creación de un marco mutuamente beneficioso (incluidas las alianzas con naciones más desarrolladas) fundamentado en las necesidades de salud pública y en las realidades contextuales del país.

Palabras clave: ética en investigación; genética; genómica; políticas; investigación; Trinidad y Tabago; Indias Occidentales.

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