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Cancer Genomic Resources and Present Needs in the Latin American Region

Ángela Torres[a] Javier Oliver[b, c] Cecilia Frecha[c] Ana Lorena Montealegre[a] Rosalía Quezada-Urbán[d] Clara Estela Díaz-Velásquez[d] Felipe Vaca-Paniagua[d, e] Sandra Perdomo[a, f]

[a]Institute of Nutrition, Genetics, and Metabolism Research, Faculty of Medicine, Universidad El Bosque, Bogotá, Colombia; [b]Laboratorio de Secuenciación, Servicio de Biología Molecular Diagnostica, Hospital Italiano de Buenos Aires, and [c]ICBME Instituto Universitario, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; [d]Laboratorio Nacional en Salud: Diagnóstico Molecular y Efecto Ambiental en Enfermedades Crónico-Degenerativas, Facultad de Estudios Superiores Iztacala, Universidad Nacional Autónoma de México, and [e]Instituto Nacional de Cancerología, Mexico City, Mexico; [f]Department of Pathology and Laboratories, Hospital Universitario Fundación Santa Fe de Bogotá, Bogotá, Colombia

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Abstract
In Latin America (LA), cancer is the second leading cause of death, and little is known about the capacities and needs for the development of research in the field of cancer genomics. In order to evaluate the current capacity for and development of cancer genomics in LA, we collected the available information on genomics, including the number of next-generation sequencing (NGS) platforms, the number of cancer research institutions and research groups, publications in the last 10 years, educational programs, and related national cancer control policies. Currently, there are 221 NGS platforms and 118 research groups in LA developing cancer genomics projects. A total of 272 articles in the field of cancer genetics/genomics were published by authors affiliated to Latin American institutions. Educational programs in genomics are scarce, almost exclusive of graduate programs, and only few are concerning cancer. Only 14 countries have national cancer control plans, but all of them consider secondary prevention strategies for early diagnosis, opportune treatment, and decreasing mortality, where genomic analyses could be implemented. Despite recent advances in introducing knowledge about cancer genomics and its application to LA, the region lacks development of integrated genomic research projects, improved use of NGS platforms, implementation of associated educational programs, and health policies that could have an impact on cancer care.

Á.T. and J.O. contributed equally to this work.

Sandra Perdomo
Institute of Nutrition, Genetics, and Metabolism Research
Faculty of Medicine, Universidad El Bosque
Av. Cra 9 No. 131 A – 02, Bogotá 110121 (Colombia)
E-Mail perdomosandra@unbosque.edu.co

Felipe Vaca-Paniagua
Laboratorio Nacional en Salud: Diagnóstico Molecular y Efecto Ambiental en Enfermedades Crónico-Degenerativas
Av. De Los Barrios 1, Los Reyes Iztacala, Tlalnepantla, Mexico 54090 (Mexico)
E-Mail felipe.vaca@gmail.com

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E-Mail karger@karger.com
www.karger.com/phg

Background

In Latin America (LA), cancer represents the second most frequent cause of death, after cardiovascular disease. In 2012, 1,005,255 new cancer cases and 550,164 deaths from cancer occurred among both sexes in the Latin American region [1]. The region is highly diverse in terms of ethnicity, diet, culture, and economic factors, augmenting the variation in cancer incidence across countries. The types of cancer with a higher incidence in LA include breast, prostate, cervical, stomach, colorectal, and lung cancer, with the last being the leading cause of death from cancer. Breast cancer is the leading cause of cancer incidence and mortality among women in the majority of countries [2]. Infection-related cancers such as cervical and stomach cancers remain the leading incident types in countries with a medium Human Development Index (HDI) [3]. In contrast, westernization changes in diet and physical activity, as well as increased obesity, are the main risk factors for colorectal cancer, the third most prevalent cancer type in LA [3]. Overall, cancer mortality rates in LA are high, mainly due to deficiencies in prevention, early detection, and disease management [4, 5].

Genomic technologies have offered new perspectives to expand and improve human health. In the field of cancer, large multicenter consortia [4] have analyzed thousands of cancer samples with integrated genomic technologies, which has profoundly changed cancer management, altogether reformulating cancer diagnosis, prognosis, and treatment [6, 7]. However, major advances in cancer science have been mainly concentrated in nations with a high HDI, and most genomic studies have preferentially included populations of European origin. Currently, the global contribution of populations with Latin American ethnicities to GWAS studies is 0.54%, versus 81% for those with European ancestry [8]. Even if only a few large genomic studies have been developed in the LA region, they still show sufficient evidence of important differences from high-HDI nations, both in terms of genomic findings and their clinical applications to mixed populations: a breast cancer GWAS study identified a variant at the 6q25 locus (*ESR1* gene) that represents an important protective factor for Latin women with indigenous American ancestry [9]. Moreover, studies on hereditary breast-ovarian cancer (HBOC) syndrome have reported that both the presence of population-specific germline founder mutations and the frequency of large rearrangements in *BRCA1* and *BRCA2* among Latin women vary according to ancestry [10, 11]. These differences have important implications in terms of diagnostic techniques, genetic counseling, and risk assessment. A recent study described that the frequency of EGFR mutations in non-small cell lung cancer in LA is independently associated with mestizo or indigenous ethnicity [12, 13]. Moreover, Lou et al. [14] described that in Latin women, cervical invasive tumors have a high frequency of mutation in *PIK3CA*, with important implications for the development of therapeutic agents targeting PI3K.

In this study, we investigate the current level of development of cancer genomics in LA in terms of the existing technology, cancer research capacities, educational programs, and national cancer care and control policies and discuss the current necessities for further progress and clinical implementation.

Methods

To assess the current regional capacities in cancer genomics, we reviewed previously identified criteria for the implementation of genomic medicine programs [15–17]. We selected parameters for which we could retrieve the available information from most Latin American countries: technology and infrastructure (next-generation sequencing [NGS] platforms), specialized training and education (educational programs), research capacity (research groups and publications), and public policies (national cancer control plans [NCCPs]).

Scientific articles were searched using the following criterion: whether the first two authors or the corresponding authors were affiliated to a Latin American institute. The databases used to get the information were PubMed, LILACS, BIREME, and SciELO. The search terms applied were "genetic," "genomics," "cancer," "Latin America," "Central America," "South America," and an additional term with the name of any of the 20 countries of Central and South America as well as Cuba. The time period searched was from 2006 to 2016. The impact factor was calculated using the SCImago portal [18]. The articles were classified by title, database, author name, journal type, language, publication year, impact factor, and institution, according to the country of affiliation of the first or last author.

Information regarding research groups with major work on genetics/genomics and cancer was obtained through databases from the national science and technology government agencies of each country (see online suppl. Table 2; for all online suppl. material, see www.karger.com/doi/10.1159/000479291).

NGS platforms in LA were identified by compiling information from all institutions by direct communication with the platform providers in each country and from the publications reviewed.

The NCCPs were searched and retrieved using the International Cancer Control Partnership (ICCP) portal (http://www.iccp-portal.org/map).

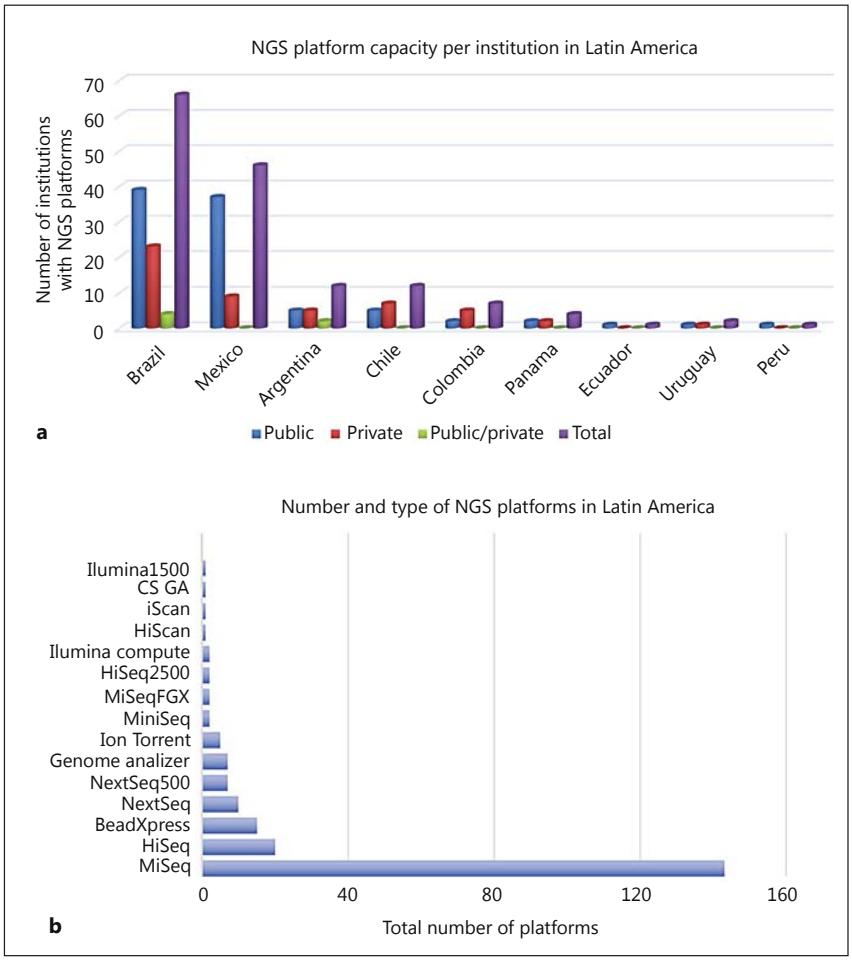

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Fig. 1. Distribution of genomics platforms in the Latin American region. **a** Total number of platforms per institution and country. **b** Genomics platforms dedicated to cancer in Latin America. The absolute number of each platform is shown. NGS, next-generation sequencing.

Results

NGS Platforms in the Latin American Region

Currently, there are 221 NGS platforms distributed in public (89), private (46), and both private and public (5) institutions in LA (Fig. 1a). Sixteen different types of platform are available: MiSeq is the platform with most users in LA, with a total of 143 instruments in 9 countries (Fig. 1b). Brazil and Mexico are the principal users of genomic sequencing systems, while Peru and Ecuador have the lowest numbers of sequencers (see online suppl. Table 1). A distinction of the platforms by intended use (either research or diagnostic) was not included due to lack of information. No information was available regarding NGS resources from Bolivia, Paraguay, and Venezuela. Finally, Panama was the only country in Central America, currently using 4 NGS platforms.

Cancer Genomic Resources for Research and Education

We found 118 research groups working on cancer genetics and genomics. Mexico (34), Argentina (28), Colombia (24), and Brazil (19) have the highest numbers of research groups developing cancer genomics projects (see online suppl. Table 2).

A total of 272 articles addressing cancer genetics/genomics-related studies were published by authors affiliated to institutions in 12 countries during the past decade; 137 articles were published in Spanish, 116 in English, and 19 in Portuguese (see online suppl. Table 3). Mexico and Brazil have the largest numbers of publications in the past decade (Fig. 2a). During this period, the average impact factor per year increased steadily, showing maximum productivity in 2016 (Fig. 2b).

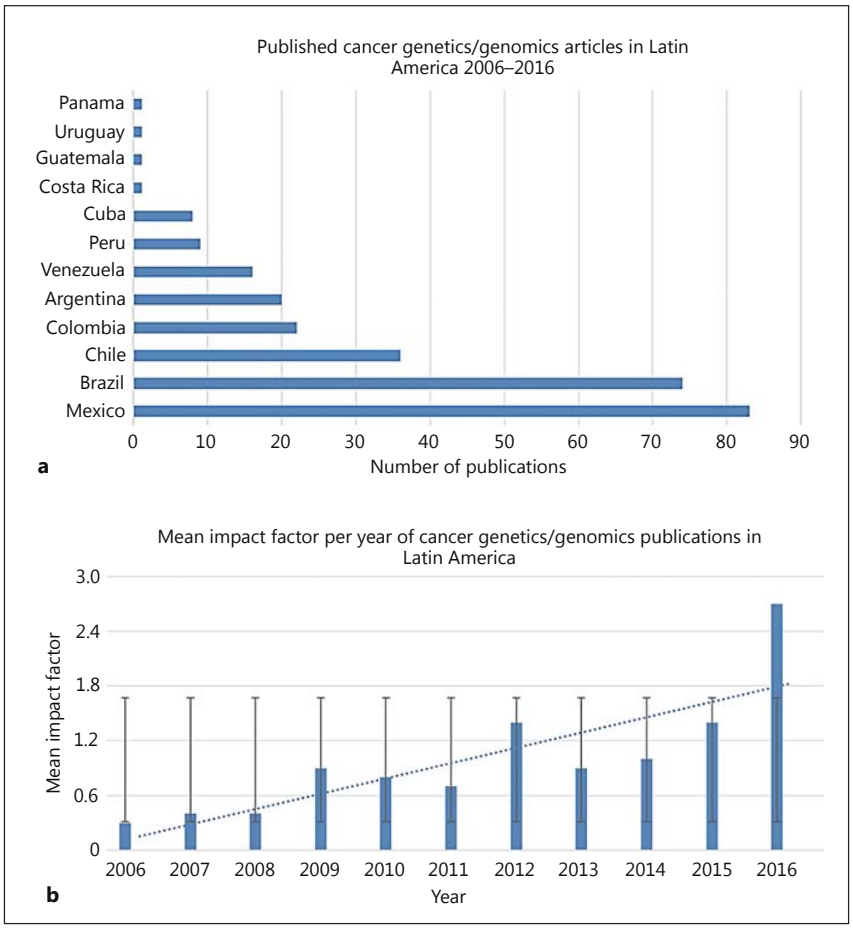

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Fig. 2. Publications on cancer genetics and cancer genomics in Latin America. **a** The absolute number of publications by Latin American authors is shown. **b** Mean cancer genetics and cancer genomics publication impact factor per year. The mean impact factor of all published papers by Latin American authors is shown. The average impact factor trend and standard deviation per year are depicted. Time period: January 2006 to December 2016.

Ten educational programs focusing on genomics have been implemented, mainly in graduate schools, in Mexico (4), Brazil (3), Argentina (2), and Chile (1), but none of them had a special focus on cancer genomics (see online suppl. Table 4).

Cancer Control Policies and Genomics in LA

According to information reviewed from the National Cancer Control Program Capacity Assessment [19], there are 14 countries in LA that have NCCPs [20–29]. In Table 1, we summarized the main objectives and strategies included in the NCCPs and identified those areas where cancer genomic applications could be included. Only 3 NCCPs mention genetic testing as a strategy for early detection, and 4 included a plan to increase research support for the development of cancer prevention and control programs. All national plans incorporate strategies for increasing the economic investment in technology and specialized treatment with the final goal of improving cancer diagnosis and care, but specific mention of investment in infrastructure for genomic analyses is lacking.

Discussion

Cancer is the second leading cause of death in LA, after cardiovascular disease [30]. This is explained by the generalized shift in trend for disease burden from infectious to chronic in the majority of Latin American countries. The populations are increasing and becoming elderly, and the countries lack proper preparation to respond adequately to this epidemiological and sociodemographic transition [30].

In the past 10 years, the development and increased use of NGS technologies has allowed a comprehensive characterization of the genomic landscape of tumors [3].

Table 1. List of NCCPs in Latin America by country and identified areas in which cancer genomics can be implemented

Country	NCCP	Time period	Are genetic tests for early diagnosis mentioned?	Has included research as a plan of action?	NCCP objectives where genetic/genomic analyses could be implemented
Brazil	"Oncological attention plan, a model for Brazil"	2013	Yes	Yes	Includes research programs to define the genetic profile of the Brazilian population with the most prevalent cancer types in order to guarantee early diagnosis and treatment
Bolivia	"Plan nacional de prevención, control y seguimiento de cáncer de cuello uterino y mama"	2009	No	No	Contemplates the implementation of specific tests only for patients with risk factors, genetic predispositions, and other specific characteristics as a strategy to avoid overspending of resources
Colombia	"Plan decenal para el control del cáncer en Colombia"	2012–2021	No	Yes	Focuses on early detection strategies for high-incidence cancers and includes engagement in reinforcing cancer research and increasing the number of professionals with expertise in the different fields
Costa Rica	"Plan nacional para la prevención y control del cáncer"	2011–2017	No	Yes	Aims to reduce the cancer incidence through strategies at the community, educational, and environmental levels; increases the cancer research capacity by integrating different areas and promoting the use of new technologies
Cuba	"Programa integral para el control del cáncer en Cuba; control del cáncer en la atención primaria en salud"	2010	No	No	Conceives the patient via a holistic approach; this includes the integration of multidisciplinary methods for diagnosis and treatment
Guatemala Nicaragua Belize Dominican Republic	"Plan subregional para la prevención y control del cáncer en Centroamérica y república dominicana"	2008	No	No	Provides a subregional plan to establish a network for cancer prevention and control, including information exchange, technical cooperation between countries, multicenter research, and optimization of resources
Honduras	"Plan estratégico nacional para la prevención y el control del cáncer"	2009–2013	No	No	Emphasizes that oncology research could identify and evaluate means of reducing cancer morbidity and mortality
Panama	"Plan nacional para la prevención y control del cáncer"	2010–2015	No	No	Genetic predispositions are recognized for different cancer sites; promotion of research activities focused on early detection, diagnosis, and effective treatment is suggested
Peru	"Plan Esperanza"	2012	Yes	Yes	Includes the implementation of genetic testing for high-incidence cancer types and specific studies that could offer better treatment options
Salvador	"Política nacional de atención integral a las personas con cáncer"	2015	Yes	No	Indicates the need to develop economic strategies that allow the implementation of more specialized clinical studies and early detection strategies
Uruguay	"Programa nacional de control del cáncer, plan estratégico pronaccan"	2005–2010	No	Yes	Offers screening strategies for breast, cervical, and colorectal cancer; the authorities in health policy are creating guidelines to develop more specific tests and providing specialized treatment according to patients' needs

The published NCCPs cover a time period between 2005 and 2021. NCCP, national cancer control plan.

Countries in LA have started to develop the foundations for achieving the integration of cancer genomics into the clinical scenario. We identified 221 NGS platforms that are currently available in the region. However, the actual number is expected to be larger, as we only used freely available information reported by individual institutions and some platform providers in the region. Mexico, Brazil, Chile, Argentina, and Colombia are the leading countries in terms of installed facilities, cancer genetic research groups, educational programs in genomics, and medium-impact publications in the field. Meanwhile, the countries in Central America were shown to be underrepresented in all areas of ongoing cancer genomic development and implementation. These disparities are of great concern, especially when looking at the increasing cancer burden in the region for breast, colorectal, and lung cancer [31]. These particular cancer types currently benefit from genomic testing and analysis in different clinical scenarios: cancer prevention (the identification of high-risk *BRCA1*, *BCRA2*, *MLH1*, *MSH2*, *MSH6*, *PMS2*, or *EPCAM* in carriers to control for hereditary breast and colon cancer) [3], tumor genomic profiling for diagnosis and prognosis (gene expression profile in breast cancer; DNA methylation and microsatellite instability in colorectal cancer) [11], and personalized treatment (molecule-guided targeted therapy for lung, breast, and colorectal cancer) [32].

The efforts to increase the necessary capacities and resources for the implementation of cancer genomics in LA will only be successful if guided by cancer control programs and public health policies. Currently, 14 countries in LA have NCCPs, and all of them contemplate secondary prevention strategies with emphasis on prevention, early detection, opportune treatment, and decreasing mortality. These are areas where genomic analysis could significantly contribute to the identification of cancer population-specific predisposition genes, and lead to the development of screening programs to identify patients "at risk" [33]. The information derived from risk assessment and/or genetic testing will allow health care providers to offer a personalized approach for health promotion and optimize health outcomes long before cancer develops [34]. In addition, genomic analysis of highly suspicious lesions will improve early detection through the identification of localized tumors and the distinction between biologically indolent and aggressive tumors. The benefits from this approach will be reflected in less intensive, less toxic, and less expensive treatments, along with the requirement of fewer medical, nursing, and pharmacologic services [35].

The NCCPs in LA acknowledge the deficiencies in cancer care and control. However, only few recognize cancer research as an action plan. Additional strategies might extend these plans to cancer genomics research and personalized medicine if included as key components of cancer prevention, early diagnosis, and treatment. In order to have a real impact on cancer control, government agencies and health authorities must assign a significant budget to improve cancer services, research capacities, and funds to support genomic studies [36]. Some countries are developing plans to improve research opportunities. Brazil, for example, has created a government plan for "investment in the future" which is committed to increase funding for research groups at universities [37]. In 2015, Peru showed a 3-fold increase in the cancer control budget compared to 2009 [38]. More comprehensive initiatives should be developed in LA to increase research funding in cancer genomics. These efforts need to consider the creation of international consortia with the vision to address the specific needs of the region.

Finally, the implementation of cancer genomics in clinical settings requires the concerted development of technical, academic, and economic resources to guarantee that the application of cancer genomic strategies is not only cost-effective but certainly also beneficial for cancer care and control. As an example, we propose an integrated genomic program for the diagnosis of HBOC syndrome. HBOC syndrome has become a relevant public health issue, as the majority of genetic tests in LA are sent abroad, incurring in higher costs. Still, the currently installed sequencing platforms in LA are suitable for HBOC syndrome targeted sequencing tests already validated in the market. Tests should be performed in centralized facilities with certified laboratories to both ensure their cost-effectiveness and increase the technical and bioinformatic expertise. Cancer prevention programs will then benefit by the identification of potential cancer cases to direct prompt intervention. Moreover, new research opportunities focused on HBOC syndrome germline variants and modifiable risk factors relevant to LA will fill scientific gaps in that area, increase research funding, and support educational programs focused on population-specific genomic analyses and clinical interpretation. Increasing information on the genomics of HBOC syndrome in LA could encourage the creation of a first LA cancer genomic consortium to share genomic, epidemiological, and clinical information.

Conclusions

The increasing cancer burden in LA urges the implementation of more effective diagnostic technologies and specialized treatments at a faster pace. Recent advances in cancer genomics technology and knowledge have been introduced in a limited number of countries of the region. The acquisition of NGS platforms, development of cancer genomic research programs, and scientific publications have increased principally in Brazil, Mexico, Argentina, and Colombia. Only 14 countries in LA have NCCPs, including programs in which cancer genomics could be implemented and provide great benefit. Overall, the region lacks development of integrated genomic research projects, improved use of NGS platforms, expansion of associated educational programs, and health policies that could impact cancer care.

Disclosure Statement

The authors declare no conflict of interests.

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Author Contributions

S.P., F.V.-P., and J.O. conceived and designed the study. Á.T., J.O., R.Q.-U., A.L.M., C.E.D.-V., F.V.-P., and S.P. searched and retrieved all information. Á.T., S.P., F.V.-P., and J.O. analyzed and interpreted the data. Á.T., J.O., C.F., F.V.-P., and S.P. wrote the manuscript. All authors reviewed and approved the final version for publication.

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