The Establishment of the First Cancer Tissue Biobank at a Hispanic-Serving Institution: A National Cancer Institute–Funded Initiative between Moffitt Cancer Center in Florida and the Ponce School of Medicine and Health Sciences in Puerto Rico

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Population-based studies are important to address emerging issues in health disparities among populations. The Partnership between the Moffitt Cancer Center (MCC) in Florida and the Ponce School of Medicine and Health Sciences (PSMHS) in Puerto Rico (the PSMHS-MCC Partnership) was developed to facilitate high-quality research, training, and community outreach focusing on the Puerto Rican population in the island and in the mainland, with funding from the National Cancer Institute. We report here the establishment of a Tissue Biobank at PSMHS, modeled after the MCC tissue biorepository, to support translational research projects on this minority population. This facility, the Puerto Rico Tissue Biobank, was jointly developed by a team of basic and clinical scientists from both institutions in close collaboration with the administrators and clinical faculty of the tissue accrual sites. The efforts required and challenges that needed to be overcome to establish the first functional, centralized cancer-related biobank in Puerto Rico, and to ensure that it continuously evolves to address new needs of this underserved Hispanic population, are described. As a result of the collaborative efforts between PSMHS and MCC, a tissue procurement algorithm was successfully established to acquire, process, store, and conduct pathological analyses of cancer-related biospecimens and their associated clinical-pathological data from Puerto Rican patients with cancer recruited at a tertiary hospital setting. All protocols in place are in accordance with standard operational procedures that ensure high quality of biological materials and patient confidentiality. The processes described here provide a model that can be applied to achieve the establishment of a functional biobank in similar settings.

Introduction

THE PARTNERSHIP BETWEEN the Moffitt Cancer Center (MCC) in Tampa, Florida and the Ponce School of Medicine and Health Sciences (PSMHS) in Puerto Rico was developed in a collaborative way to support high-quality basic, clinical, and community outreach research as well as medical education in cancer-related health disparities. PSMHS is a privately funded, nonprofit postgraduate university con-

sisting of a medical school and graduate programs in Biomedical Sciences, Clinical Psychology, and Public Health. PSMHS is located in Ponce (pop. >200,000 for the city and ~350,000 for the municipality of Ponce) in Southern Puerto Rico, which is considered the second most important city of the island. With 724 staff, 607 students, and 341 faculty members, PSMHS is a medium-sized medical and health-related professional university. For the past decade, PSMHS faculty has developed a thriving independent research

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infrastructure to study cancers of high prevalence in the Puerto Rican population. MCC, on the other hand, is a large National Cancer Institute (NCI) designated Comprehensive Cancer Center that conducts cancer-related research and training in the basic, clinical, and population sciences. The PSMHS-MCC Partnership, funded through an NCI MI-CCP grant, was designed to foster health disparities-related research by using a collaborative approach between investigative teams at both institutions, and also to increase MCC's access to minority and underserved patients. As a result, more faculty and students are participating in cancer research, outreach, training, and clinical trials at both institutions. Since human specimen biobanking plays a central role in the development of basic and translational research projects and personalized medicine,^{1,2} a cancer tissue biobank, the Puerto Rico Tissue Biobank (PRTB), was developed to facilitate the collection, processing, storage, and distribution of well-annotated human biospecimens from Puerto Rican patients with cancer.

Hispanics are currently the most prevalent (and fastest growing) minority population in the United States, representing ~15% of the total population (www.census.org). Similar to other minority populations in the country, Hispanics suffer disproportionately from health disparities in major public health issues such as heart disease, diabetes, and cancer.³⁻⁵ Although most Hispanic populations are expected to be a mix of 3 ancestral populations (African, European, and Native American), the relative proportion of each ancestral genetic background has been shown to vary within and across Hispanic populations.⁶ Previous studies using Ancestry Informative Markers have shown that Puerto Ricans carry more European and African ancestry, but significantly less Native American ancestry when compared with Mexicans.⁷ The relative contribution of each ancestral genetic background explains, at least in part, discrepancies in disease susceptibility between different ethnic groups. Since most tissue banking initiatives currently developed in the United States accrue tissues that are mostly derived from the Mexican-American population,⁸ there is a great need to expand tissue collection to other Hispanic ethnicities to be able to dissect the contribution of ancestry to the development of cancer and other diseases.

One of the major goals of the PSMHS-MCC Partnership was, therefore, to establish a tissue biobank at PSMHS to collect biospecimens from Puerto Rican patients with cancer that would be readily available to investigative teams studying emerging issues in health disparities among Hispanic populations, including Puerto Ricans living in the island and in the mainland. Here, we describe the efforts required and the challenges that had to be overcome to establish the first functional, centralized cancer-related biobank in Puerto Rico, and to ensure its continuous evolution to address the needs of this underserved population. The processes described here provide a model to follow to establish a functional biobank fully in compliance with human subject research regulations in similar settings.

Materials and Methods

Establishment of a leadership team, the PRTB Administrative Core

The process to establish the first biobank collecting cancer-related tissues in Puerto Rico initially required the establishment of an administrative core (the PRTB Admin) including

expertise in pathology, tissue banking, and regulatory aspects, as well as basic cancer research. The functions of this committee were defined by its members, and possible strategies to implement tissue banking were discussed throughout several teleconferences spanning a period of ~1 year. The first steps in this process was for the PRTB Admin to initiate communications with hospitals' administrative officials and clinical faculty to discuss the possibility of broadening the scope of existing affiliations to include this initiative and to assess the available infrastructure and resources during on-site visits.

Assessment of available tissue accrual infrastructure and resources

The PRTB Admin conducted a detailed evaluation of the available resources needed to support biobanking activities at PSMHS and at potential accrual sites. PSMHS had (1) basic scientists with expertise on cancer research; (2) technical staff with training in histopathology and human subject research, and administrative support; (3) a well-developed Information Technology (IT) Department with trained professionals and appropriate infrastructure; (4) available space to be developed into laboratory, storage, and office areas. At the clinical sites, the availability of the following was evaluated: (1) areas for patient consenting; (2) on-site pathology department consisting of gross room for the processing of specimens; (3) space for the collection and storage of fresh biospecimens; (4) histology laboratory for the preparation and storage of formalin-fixed paraffin-embedded (FFPE) tissue blocks, etc.; and (5) a high volume of cancer specimens per year.

Key personnel recruitment and training

The PRTB Admin identified 2 immediate needs necessary to ensure the success of this project: recruitment of an in-house pathologist and technical support. Due to the critical role of the pathologist in tissue procurement activities, since the initial phase of this project an in-house pathologist was hired at PSMHS to oversee all tissue accrual, handling, and processing protocols; provide expert pathological analysis of the tissues; and evaluate results of quality assurance and quality control (QA/QC) analyses. Although this position is budgeted at 0.4 time and effort, as the tissue banking activities continue to evolve, we foresee that a full-time pathologist would be required in the future.

A new position was created for a liaison who is responsible for the coordination of meetings and presentations to administrators and medical faculty of the affiliated hospitals and the community. The PRTB liaison's role also includes supervision of the recruiters (responsible for explaining the project and obtaining consent to patients) and runners [individuals in charge of collecting the tissues during surgery following standard operating procedures (SOPs)] to ensure smooth function of the patient consenting and tissue accrual processes, and to coordinate the collection of information and documentation for each tissue collected. The PRTB liaison is also responsible for adequate tissue transport, storage, and processing, as well as for tissue data entry into caTissue, Suite 1.1.2, a caBIG® biorepository management tool designed for biospecimen inventory, tracking, and annotation.⁹

Both the liaison and in-house pathologist received training at MCC, where they were exposed to all tissue banking activities including patient consent, intake, and acquisition;

solid section; liquid section; histology services; microarray; and shared resources (Molecular Core, Microarray Core, Pathology Core, Bioinformatics Core). This experience provided a complete overview of the MCC-TC activities, and knowledge of the most relevant MCC SOPs.

Regulatory permits and development of SOPs

The PRTB Admin evaluated protocols and procedures established at MCC-TC for patient consenting, the informed consent forms, and the tissue banking questionnaire. The protocols were customized for implementation at the PRTB, taking into consideration the existing facilities, resources, and procedures. All forms were already available in Spanish at MCC, and minimal changes to the language of the informed consent form and to the questionnaire were made to ensure their cultural competency. All forms were reviewed and approved by the PSMHS Institutional Review Board (IRB) Committee.

Tissue collection, processing, and storage SOPs were evaluated by the pathologists who were members of the PRTB Admin (M.G., S.G., and D.C.) to ensure that they mirrored those proved to be successful at MCC. All the SOPs at MCC were established by following the ISBER Best Practices for Repositories Collection, Storage, Retrieval, and Distribution of Biological Materials for Research.¹⁰ The PRTB Admin reviewed the SOPs and provided final approval before implementation. In addition, instruments were developed to document the number of patients approached for tissue donation, the reasons for refusing to donate, and the details of the tissue collection process (ischemia time, time of transport from operating room (OR) to pathology lab). A binder with copies of all SOPs and guidelines is available to all personnel involved in tissue accrual to allow for revision and referencing as needed.

Development of a tissue collection algorithm

A general plan for the tissue acquisition process was drafted to mirror that available at MCC for its affiliated hospitals. The human and technical resources needed at the tissue collection sites and various operational constraints were also identified, which turned out to be different and unique to each hospital. In general, it was felt that the initiative to establish a biobank was of high priority to hospital administrations, but it was also evident that a single-tissue accrual algorithm will probably not fit all the sites.

The following steps were defined as being critical for the establishment of a centralized tissue collection algorithm in a hospital setting: (1) creation of a position for a liaison who would function as the link between the PRTB admin and the medical/hospital community; (2) definition of the patient consenting process, which needed to occur in a private area within an environment conducive to communicate with the patients in a respectful and sensitive manner; (3) development of a plan for communicating the consented status of a patient to the runner, including information about surgery time and day; and (4) design of a plan to ensure data collection, data entry, and permanent tissue storage at a centralized facility to be supervised by the liaison.

Data acquisition and storage

An IBM System x3650 Quad-core Intel Xeon processor server with 2 terabytes of data storage space was purchased

to be located at PSMHS. The server was configured by using RAID5 for data redundancy, and caTissue Suite was installed by the MCC Biomedical Informatics Shared Resource Facility. The server was shipped to PSMHS to be fully integrated into its network infrastructure. The server will also be used to create the caGrid node and to deliver electronic surveys by using web-based technologies and taking advantage of the portability and ease of use of the Apple iPad.

Results

Establishment of the PRTB Administrative Core

The PRTB Administrative Core (PRTB Admin) was formed to be responsible for the appropriate assessment and evaluation of the available resources for tissue accrual. The first step in such evaluation was to conduct a site visit to the proposed tissue collecting sites and to provide a summary of findings and final recommendation to the Partnership Administrative Core. The functions of the members of the PRTB Admin were defined (Table 1), which included overseeing the management and distribution of resources, defining roles and responsibilities at each accruing site, ensuring that all regulatory permits were in place, and evaluation and approval of SOPs.

Meetings were held between the PRTB admin members and key officials at each targeted hospital (eg, Medical Directors, Hospital Administrators, and Directors of OR, Admissions, Cancer Registry, and Legal/Ethical/Policy Departments) to present the goals and objectives of the PRTB, describe the facilities and human resources required for tissue accrual, and discuss the advantages and benefits of this collaboration for the hospitals and the served patient population. Some of the benefits viewed with interest included opportunities for pathologists' specialized training and education in tissue banking processes at MCC; the option to have interns, residents, and fellows rotate at both PSMHS and MCC, thereby acquiring translational research experience; and the clinicians' participation in MCC Tumor Boards, multidisciplinary conferences where cancer patient management is discussed, via teleconferencing. For the administrators, the opportunity to establish and/or expand their Cancer Registries and to have access to a state-of-the-art IT grid node connecting to caBIG/caTissue were a great incentive.

TABLE 1. U56 TPC ADMINISTRATION:
DEFINITIONS OF ROLES

<i>Tasks related to the establishment of a Tissue Procurement Core in a Minority-Serving Institution</i>	
1. Oversight of SOPs	D. Coppola/J. Matta
2. Training of personnel	D. Coppola/J. Matta
3. Cancer Registry	R. Sutphen
4. IT- caBIG- Bioinformatics	D. Fersteinmacher/R. Espada
5. Personnel recruitment/ supervision	I. Flores/J. Matta
6. Tissue Q&C	D. Coppola/M. Garcia
7. Legal issues (IP, Honest Broker, MTA)	T. Antonia/I. Flores
8. Tissue release policy	Chair: T. Antonia
9. Progress reports/ documentation	All Co-leaders

IT, Information Technology; SOP, standard operating procedure.

During this process, the PRTB admin also identified the need to educate the PSMHS physician/faculty network, as well as community physicians serving the patient population of Southwest Puerto Rico, about biobanking initiatives and their important role in translational research and personalized medicine. Therefore, a series of visits to medical offices was set in motion as well as presentations during existing Tumor Boards, and regularly scheduled departmental meetings to describe the opportunities to collaborate in cancer tissue collection.

Evaluation of available tissue accrual infrastructure and resources and selection of accrual sites

Infrastructure at PSMHS. Before the establishment of the PRTB, tissue collection at PSMHS was being conducted by a few individual investigators using their own personnel and resources. The first step in the development of this biobank was to unify and centralize existing efforts; to evaluate the available space, equipment, and human resources; and to assess the personnel training needs. Detailed budgets and timelines were developed, and efforts were directed toward the optimization of the existent infrastructure. PSMHS allocated space for the processing and evaluation of the specimens and for the QA/QC activities related to the PRTB initiative. Laboratory and office space were designated to this effort, and partnership and institutional funds from both MCC and PSMHS were used to purchase basic office and laboratory equipment (eg, microscope, -80°C freezer, liquid nitrogen tanks) and supplies required for tissue collection, processing, and storage.

Infrastructure at the selected tissue accrual site. Although PSMHS lacks its own hospital, academic affiliations are in place with 3 teaching hospitals in Southwest Puerto Rico: Saint Luke's Hospital (SLH), Damas Hospital (DH) (both in Ponce, South), and Mayagüez Medical Center (in Mayagüez, West). As a result of the evaluation of existing resources, the PRTB admin identified SLH and DH in Ponce as the targeted hospitals. At both hospitals, tissue collection for investigator-initiated research projects was already taking place; however, tissue accrual was neither centralized nor was it being conducted by using standardized protocols. In addition, the PRTB admin identified the Auxilio Mutuo Hospital (AMH) as an alternate or future tissue accrual site based on its recognition by the community as a state-of-the-art cancer center serving the population of San Juan, the capital of Puerto Rico. These hospitals are located within 50 miles driving distance from PSMHS, where tissues are stored long term and processed, and all receive a high number of cancer patients per year.

Due to the inherent complexity of establishing a tissue banking initiative where none existed, it was deemed important to focus initial efforts in the development of a tissue collection algorithm that worked in a single facility. For the initial tissue accrual, SLH was selected, as it is the most important tertiary-level medical center and postgraduate medical education institution in the area. SLH residency programs in Emergency Medicine, Internal Medicine, Ob-Gyn, and Pediatrics have received accreditation by Accreditation Council for Continuing Medical Education. A Surgery Residency Program is currently under development and expected to be functional by Fall 2011. Its Surgery and Pathology Clinical Departments consist of well-known and respected physicians

who are also faculty of PSMHS. In addition, SLH is located at a reasonable distance from PSMHS, and, importantly, the clinical and administrative staff demonstrated a willingness to undertake this type of collaboration. SLH has a high volume of cancer patients/year, >98% of which are Puerto Rican, mainly breast, prostate, and colon cancer cases.

Tissue collection process

Tissue acquisition at a tertiary hospital algorithm. Figure 1 depicts the tissue collection process that can be summarized as follows: during preadmission, the patient undergoes a preliminary interview; informed consent is discussed; and if agreement is obtained, then a questionnaire is completed. The consent process is a function of the recruiter (in this model, a preadmissions official), who informs the Liaison of the consented status of each patient. A green label is added to the record to notify operating room (OR) personnel that the patient has consented to tissue donation. The day of the surgery, the OR staff notifies the runner who collects the tissue(s)

FIG. 1. Schematic representation of the PRTB Tissue Collection Algorithms. To work within the structure of the collaborating institutions, 2 alternative tissue acquisition procedures were developed, targeting either tertiary hospitals or community hospitals. These 2 algorithms differ in the location of the initial steps (preliminary interview; informed consent; and completion of questionnaire), but converge at the time of tissue accrual, processing, analysis, and storage. PRTB, Puerto Rico Tissue Biobank.

from the OR, records warm ischemia time, and transports it/ them to the pathology gross room. After the clinical (diagnostic) sample is accrued, the runner (under the supervision of the pathologist) selects a section representative of the tumor and a section of adjacent uninvolved tissue. Tissues are flash frozen in liquid nitrogen and stored short term in the tank until future transportation to the PRTB facilities. Time is recorded for each of these steps. Optimally, for preservation of genetic material and proteins, the entire accrual process is expected to be completed within 15–20 min.

Accrued tissues transported by the liaison to the PRTB facilities are identified and stored initially in liquid nitrogen and then transferred to -80°C . Tissues are quarantined until the pathologic diagnosis is finalized, and a copy of the final pathology diagnosis is archived at the PRTB office for reference. Once the pathological information is obtained, the tissue is released from quarantine, processed by a contracted histotechnician, and stored. Slides are microscopically evaluated by the PRTB pathologist who completes a report of findings to be recorded in caTissue. A representative number of samples are sent twice a year to MCC for QA/QC that includes independent pathological assessment, nucleic acid extraction, and analysis.

The time from the initial visit to the target hospitals and the establishment of a fully functional algorithm was ~ 3 years. Using this algorithm, the PRTB has accrued the following between January 2010 and April 2011: 107 cancer, 14 abnormal tissues (eg, premalignant and inflammatory tissues), and 81 non-neoplastic tissues (histologically normal, uninvolved tissues mostly accrued from areas adjacent to the resected tumors). Figure 2 shows the site distribution of the collected biospecimens and shows that the highest accrual included breast, endometrium, uterine, and colon cancers.

FIG. 2. Specimen Collection in the first 15 months at the PRTB. The site distribution of the collected biospecimens shows that the highest accrual sites are breast, uterine, and colon cancers. It is of interest to note that breast cancer is the most commonly diagnosed cancer among women in Puerto Rico; and colorectal cancer is the second most commonly diagnosed cancer among men and women in Puerto Rico.

Histological QA was separately conducted at PSMHS and MCC on selected tissues. The analysis revealed a concordance between institutions of $\sim 95\%$. The evaluation of RNA extracted from the collected frozen samples revealed good-quality RNA, as indicated by the presence of 28S and 18S ribosomal bands, and a high RNA integrity number values (Fig. 3). It was noted that up to 30% of the samples collected were not large enough to yield sufficient amount of DNA/RNA for further analysis (Table 2). Measures to improve tissue accrual quality include selectively accruing tumor specimens of size >0.5 cm whenever possible and continued education and training of the staff involved to underline the importance of following SOPs and completing the accrual process within 15–20 min. At this time, all the patients approached favorably consented for tissue donation, which is a unique, positive finding that provides this PRTB with an exceptional advantage.

Tissue release and utilization in research

The release of tissue to investigators includes evaluation of the tissue request by the Tissue Release Committee, composed of a pathologist from each institution, PRTB admin representatives, and the honest brokers from both institutions. Tissue release is prioritized taking into consideration, among other criteria, the relevance of the study to the goals of the PSMHS-MCC Partnership, the funding status, and the scientific validity of the project (Table 3). In addition, the tissue request should specifically detail and define how much tissue is required, per aliquot, to perform the proposed experiments. This information allows the biobank to accurately track usage and how much tissue is left in caTissue or in the current biospecimen inventory management system. Release of biospecimen and associated clinical data are bound by the provisions approved by the investigator's respective IRB. Moreover, honest brokers evaluate the request to ensure that it complies with all federal, local, and institutional requirements. RNA collected from biospecimens

FIG. 3. Biospecimen RNA Quality. Representative RNA gel electrophoresis obtained by running RNA from samples submitted from the second QA/QC set. The presence of 2 distinct 28S and 18S ribosomal RNA bands is indicative of the quality of the RNA. Total RNA electrophoretic profile was analyzed by an Agilent Nano Chip kit using the software provided by the manufacturer for determination of RIN (RNA integrity number). An RIN value greater than 5 signifies that the RNA is not degraded and is of good quality for subsequent molecular experiments. N/A is not available.

TABLE 2. BIOSPECIMEN QUALITY CHECK

QA/QC set	Submitted	Included in analysis	28s and 18S Bands	RIN values
1	38	28 (74%)	26 (93%)	6.0–9.3
2	42	28 (66%)	21 (75%)	6.0–9.7

A representative number of samples are periodically subject to rigorous pathological and molecular analysis to ensure the quality of the stored biospecimens. In the first 2 sets submitted for analysis, of the samples submitted, 70% were included in the analysis; the rest (30%) did not produce enough RNA due to small size of the tissue sample and were excluded from subsequent RNA QC analyses.

by the PRTB has already been released for research. One set of samples was used to derive breast cancer microarray data in women; the first such data from the Puerto Rican population. This data was used to support 2 breast cancer translational projects; one at PSMHS and the other a joint project between PSMHS and MCC investigators. The list of candidate genes generated will be validated by RT-PCR and submitted for publication in 2011.

PRTB activities also include the collection of FFPE tissues and the preparation of tissues microarrays (TMAs) to be used by investigators for immunohistochemical and *in situ* hybridization analyses. The availability of TMAs containing tissues derived from Puerto Rican patients is important to identify possible differences in the expression of biomarkers among Hispanic populations. A TMA exclusively composed of endometrial and endometriosis tissues (160 cores) from

TABLE 3. PRTB POLICIES FOR TISSUE DISTRIBUTION BY THE TISSUE RELEASE COMMITTEE

Criteria used for evaluation of tissue requests:

1. Project should be IRB approved
2. Tissue should be for research purposes only
3. Tissue cannot be sold or in any way distributed to a third party without previous consent
4. Research should be cancer related, and relevant to one or more of the objectives of the PSM-MCC Partnership
5. No ethical or legal issues
6. No interference with the operation of the TPC
7. Priority order: PSM-MCC Partnership investigators, funded projects, PSM and MCC investigators, and then to other parties
8. Projects should include a co-PI from each institution (PSM and MCC), unless the tissue was accrued under the investigators specific accruing protocol
9. Additional special provisions for release of tissue to non PSM-MCC Partnership investigators/projects include level of interference with current or future PSM-MCC Partnership projects, cost, and relevance to the objectives of the partnership; this release of tissue is subject to a written agreement
10. The PSM-MCC Partnership should be acknowledged in any resulting publications

Policies and criteria used by the PSM-MCC Partnership TPC Tissue Distribution Committee for the release of tissue for research. These policies are in accordance with federal, local, and institutional requirements, as well as with the objectives of the PSM-MCC Partnership.

MCC, Moffitt Cancer Center; PRTB, Puerto Rico Tissue Biobank; IRB, Institutional Review Board.

Puerto Rican patients is already available to the partnership investigators, and a manuscript describing some of the results obtained is currently undergoing revision.

Data management, integration, and maintenance

The PRTB has deployed caTissue Suite 1.1.2, a caBIG biorepository management tool that allows standardized biospecimen inventory, tracking, and annotation.⁹ This tool provides users with a web-based interface for data entry by using caBIG semantics that standardizes biospecimen vocabularies for quality assurance and query interfaces which allow scientists to search the collection of stored samples to request distribution of samples for scientific investigations.¹¹ One of the primary benefits of caTissue is the ability of multiple sites throughout Puerto Rico to enter biospecimens preliminary data before their shipment to Ponce for acquisition and storage, whereas the maintenance of the software and hardware are centralized at PSMHS. The final step of deployment will be connecting caTissue Suite to caGrid and establish the grid node to permit data sharing with the caBIG network and allow MCC to query and extract data from the PSMHS instance.¹² Once this occurs, then PSMHS will be the first cancer research center in Puerto Rico, the Caribbean, and Latin America to be connected to caBIG/caTissue.

In addition to caTissue, the PRTB is developing a web-based survey tool that will allow consented study participants to complete a questionnaire by using the iPad technology through the 3G network using secure SSL connections to the host server at PSMHS. iPads have already been acquired and are being tested at the tissue collection off-sites. The questionnaire tool, web interfaces, and database were designed and programmed by the Department of Biomedical Informatics (DBI) at MCC. The DBI works closely with the PSMHS IT Department to maintain the central data management system and software tools through the life of each research project. Tools developed using open source standards are released to the scientific community through a Wiki established at MCC.

Clinical data, biospecimen records, and assay results locally stored at PSMHS on a single server are properly integrated for easy data curation, retrieval, and analysis. In addition, a centralized data dictionary was created while incorporating all data elements from caTissue and the patient questionnaire that is based on caBIG standards, thus making the data usable by researchers.¹² IT personnel at PSMHS and MCC work together to assure that a full range of encryption, monitoring, and auditing technology solutions are in place to support HIPAA (Health Insurance Portability and Accountability Act) security requirements and data protection. All data are backed up by using an incremental strategy to minimize the chance of data loss for the project.

Discussion

With the rise of individualized/personalized medicine and biomarker discovery efforts, establishing a biobank represents a tremendous opportunity to create a resource that can be used to further our understanding of the molecular and genetic factors that predispose to or protect certain populations from cancer.^{2,13} Population-based molecular studies that address emerging issues in health disparity among Hispanic populations are an important focus of the PSMHS-MCC Partnership. The establishment of a biobank in

Puerto Rico was essential to ensure the optimal collection of specimens that are indispensable for this purpose. The genetic basis of known disparities in Puerto Rican Hispanics, which include different prevalence rates of certain types of cancer,^{2,13,14} can only be uncovered through access to these unique biospecimens. In this article, we describe the process of establishing the first algorithm for collecting annotated biospecimens from a predominantly Puerto Rican population. Our article provides an accurate view of the challenges and opportunities that such endeavor entailed and the many lessons learned in the process.

The purpose of establishing the PRTB was to facilitate collection, processing, and storage of well-annotated human biospecimens for use in collaborative translational research efforts jointly developed by investigators at PSMHS, MCC, and at the Partnership affiliated hospitals. Through the current PSMHS-MCC Partnership and with strong support from the NCI through an MI-CCP grant mechanism, a solid infrastructure was put in place to develop the first tumor tissue bank in Puerto Rico, which is capable of optimal accrual and distribution of biological materials derived from this Hispanic population. Through this unique and invaluable resource, cancer tissues are already available to support studies focusing on Puerto Rican Hispanics living in Puerto Rico and those living in the United States, thus enhancing the capacity of both institutions to conduct research that focuses on the molecular aspects of cancers specific to these populations. Availability of Puerto Rican-derived human tissues and biospecimens (paired tumor/uninvolved tissue, plasma/DNA), collected in accordance with standardized protocols, will support much needed research on cancer health disparities and will facilitate future questions on gene-environment-culture interactions involving Puerto Ricans and other Hispanics.

The establishment of the PRTB required a thorough evaluation of the existing infrastructure and resources, including human resources (eg, expertise, training), IT facilities and expertise, and, importantly, of the openness and commitment of private hospital administrators and clinical faculty, which were all essential to undertake this complex endeavor. In our experience, once the infrastructure and physician network were built and personnel were trained, then the attention could be focused on the expansion of the collection to other tissue types (eg, preneoplastic lesions and inflammatory tissues) and biological materials (eg, blood, saliva, serum, plasma, and urine). Since the newest molecular techniques require the availability of adequate amounts of high-quality specimens,^{15,16} standardized SOPs for the accrual, processing, and storage of tissues had to be established. One of the most important outcomes of the NCI-funded Partnership between PSMHS and MCC is that it allowed the implementation of biobank-related guidelines already proved to be effective at MCC, and the training of staff in tissue biobanking by MCC co-leaders with that expertise.

It is also important to underline that the *de novo* establishment of the PRTB required the inclusion of administrators and faculty at the local hospitals as integral members of this initiative. Without their full support for these activities, significant barriers to tissue accrual could not have been overcome. Tissue banking is a complex initiative that will succeed only if the invited hospitals agree to invest by providing access to physical space and, in some instances, human resources. It is, therefore, of critical nature that hospital

administrators understand and welcome the many advantages that participation in biobanking would offer. These include, but are not limited to, increased research opportunities for interns, residents, and clinical faculty; access of the tissues and resources needed to generate preliminary data for grant applications; and opportunities for advanced training in molecular testing and personalized medicine.

A low patient consent rate for tissue banking has been documented, which may be due to a variety of reasons including not only culture and language but also lengthy and difficult-to-read consent forms.¹⁷ However, during this experience, we observed a high rate of patient consenting for tissue donation for biobanking purposes. It is important to acknowledge that the Puerto Rican patients were very receptive to this initiative and to date, all the individuals approached and consented for tissue donation. This is a remarkable finding that provides this biobank with an exceptional advantage. Whether the observed high rates of willingness to donate tissues for research respond to a cultural phenomenon will be investigated by a study under development involving faculty from the Outreach Program of the PSMHS-MCC MI-CCP Partnership.

Critical to the conduction of well-designed studies from which valid conclusions can be drawn is the availability of clinical annotations to the tissues accrued, and the means to store and share health-related information, while keeping the confidentiality of the study subjects.^{10–12,18} To this end, we describe here the development of IT infrastructure to allow the collection and storage of important clinical-pathological data in a database easily accessible to the investigators within the partnership. The IT systems developed allow critical information to be correlated with research results while preserving patient confidentiality. The systems in place allow accurate interfacing with demographic, staging, treatment, and outcome data, which is vital to the quality of scientific conclusions drawn from patient samples. Recently, the US Department of Health and Human Services designated PSMHS as the institution in charge of providing continued medical education on the use of electronic medical records for Puerto Rico and the US Virgin Islands (ie, Regional Extension Center or REC). The future availability of electronic health data will allow real-time documentation of the incidence and outcomes of cancer in Puerto Rico, undoubtedly an important resource that will lead to the further development of the PRTB.

Biobanks should continue to evolve as new technologies emerge, and the needs of the population that we want to serve change. For instance, novel studies on the role of ancestry in cancer susceptibility^{19–22} has prompted the need for centralized collection of DNA from blood of consented individuals, an activity that will be added onto the current procedures but which would require additional infrastructure to be developed. Other future plans of the PRTB include increased research collaborations among investigators from the partnering institutions and from other institutions; continued development of IT technologies to ensure appropriate and secure management of the data; expansion on the current use of the many caTissue and caBIG capabilities; development of a disaster recovery plan including regular data transfers to the MCC for redundancy in case of natural disasters; increased number of hospitals and community physicians involved in tissue accrual; and extension of the accrual process to liquid biospecimens. The latter plan will

require additional laboratory and sample storage space, and the recruitment of additional personnel involved in patient consenting and tissue accrual. The collection of samples from multiple Puerto Rican hospitals, and the extension of this practice to multiple tumor types, normal tissues, and liquid biospecimens, would represent a leap to the next level of sophistication. In addition, workshops on tissue biobanking will be developed for health professionals and communities in Southwest Puerto Rico. Finally, the science of biobanking and its benefits to society need to be taught to the future generation of medical doctors and researchers. Therefore, we are currently developing a core curriculum to expose and engage students from M.D., Ph.D., M.P.H., and Psychology doctorate programs during their formative years.

A retrospective analysis of the process of establishing the PRTB has helped identify the most important challenges encountered and the most important lessons learned. Some of the initial challenges to the establishment of a tissue bank concerned a limited understanding of the medical and hospital communities about the benefits of this research activity to the patients as well as the society. Continuing education to these professionals and presentations in various forums (departmental meetings, office visits by appointment) proved to be key to solve this initial hurdle. Engaging the hospital administration early on and working together with them was found to be of utmost importance to be successful. Each hospital has a different setting, logistics for patient contact, and even vision and mission with regard to research, which have to be assessed early on before a decision to invest time and effort in the development of a tissue bank is made. Issues regarding granting permission to nonemployees to access the preadmission, OR, and pathology laboratory areas need to be clearly defined *a priori*. The specific resources and investments that the hospital has to make to develop a functional tissue accrual algorithm should be clearly defined. Presenting the key officials of the targeted hospitals with a clear plan for the development of faculty, residents, and students in biobanking is very important. It is also useful to define the opportunities to market the hospital as a research-driven institution. The opportunity for the institution to develop a translational research program was critical to gain the full support of the institution's officials. Finally, success strongly depends on appropriate communication, constant supervision, and training. All personnel involved should communicate in a constant and transparent manner, using all the media available (phone, email, and text messages); all staff should have a clear understanding of the importance of using each other's expertise to the maximal potential; and the Admin Core should undertake regular supervision and provide constant feedback and additional training as needed for all staff involved.

In conclusion, we report the establishment of the first cancer-related tissue biobank in Puerto Rico that collects well-annotated human biospecimens derived from this population. For similar initiatives to be successful, it is critical that the institutions involved (medical schools, research centers, and hospitals) fully understand and appreciate the value of biobanking and, thus, show strong commitment to facilitate the multiple tasks that are needed to set these activities in motion. Importantly, the time and effort that should be dedicated to the development of these initiatives cannot be underestimated, for which the members of the Admin Core should receive protected time from the institu-

tion to be able to engage in the many meetings and teleconferences that are a part of this process, in particular during the planning stages. PRTB exemplifies how full commitment and significant investments made by partnering institutions and the NCI ensure that barriers are promptly detected and addressed, and opportunities are seized to ensure the accrual of cancer-related biospecimens. These unique samples are being used in investigator-initiated basic science and in translational and clinical trials research activities designed to address emerging issues in health disparity among Hispanic and Puerto Rican populations.

Acknowledgments

The authors would like to thank PSMHS, MCC, SLH, DH, and AMH administrators and officials for supporting this project and investing time and effort into its development (PSMHS: Ricardo Espada, MIS department; Saint Luke's Memorial Hospital: Guillermo J. Martin, M.H.S., Chief Executive Officer; Jenaro Scarano, M.D., Medical Director; Norma Torres, MHSA, CPHQ, Associate Executive Director; Luz Nereida Rivas, Pathology Lab Supervisor; and Drs. Víctor Carlo, Miguel Echenique, AMH). They are grateful to the PRTB staff members (Mrs. Michelle Colón, Dr. Madeline González, and Dr. Mónica Rivera) and the MCC-TPC staff members (Dr. Alex Lopez, Marek Wloch, and Herman Hernandez). They also acknowledge the leadership of collaborating pathology laboratories (Drs. Cristina Nery and Eliud López of Centro Citopatológico del Caribe; Dr. Adalberto Mendoza, Southern Pathology, Inc; and Dr. Axel Arroyo, DH Pathology Department) for their cooperation and commitment to the goals of this tissue bank.

These studies were supported by grants number U56CA-126379 and U56-CA118809 (PI: J.T.R. and J.P.).

Author Disclosure Statement

No competing financial interests exist.

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Received 22 June, 2011 / Accepted 30 August, 2011