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The Establishment of an ISO Compliant Cancer Biobank for Jordan and its Neighboring Countries Through Knowledge Transfer and Training

Martin Barr,[1*] Lina Souan,[2*] Peadar MacGabhann,[3] Jeanette Müller,[4] Maxim Al Ashhab,[2] Mohammed Jasser,[2] Khetam Hamza,[2] Sallam Al Hassoon,[2] Uwe Kuhn,[3] Daniela Infante,[3] Denise Lawlor,[1] Kathy Gately,[1] Eyad Amireh,[2] Kenneth O'Byrne,[1,5] and Maher A. Sughayer[2]

Research studies aimed at advancing cancer prevention, diagnosis, and treatment depend on a number of key resources, including a ready supply of high-quality annotated biospecimens from diverse ethnic populations that can be used to test new drugs, assess the validity of prognostic biomarkers, and develop tailor-made therapies. In November 2011, KHCCBIO was established at the King Hussein Cancer Center (KHCC) with the support of Seventh Framework Programme (FP7) funding from the European Union (khccbio.khcc.jo). KHCCBIO was developed for the purpose of achieving an ISO accredited cancer biobank through the collection, processing, and preservation of high-quality, clinically annotated biospecimens from consenting cancer patients, making it the first cancer biobank of its kind in Jordan. The establishment of a state-of-the-art, standardized biospecimen repository of matched normal and lung tumor tissue, in addition to blood components such as serum, plasma, and white blood cells, was achieved through the support and experience of its European partners, Trinity College Dublin, Biostór Ireland, and accelopment AG. To date, KHCCBIO along with its partners, have worked closely in establishing an ISO Quality Management System (QMS) under which the biobank will operate. A Quality Policy Manual, Validation, and Training plan have been developed in addition to the development of standard operating procedures (SOPs) for consenting policies on ethical issues, data privacy, confidentiality, and biobanking bylaws. SOPs have also been drafted according to best international practices and implemented for the donation, procurement, processing, testing, preservation, storage, and distribution of tissues and blood samples from lung cancer patients, which will form the basis for the procurement of other cancer types. KHCCBIO will be the first ISO accredited cancer biobank from a diverse ethnic Middle Eastern and North African population. It will provide a unique and valuable resource of high-quality human biospecimens and anonymized clinicopathological data to the cancer research communities world-wide.

Introduction

The development of more effective interventions against cancer requires a better understanding of its molecular basis and a more rapid translation of laboratory findings into improved patient care. One of the most precious resources for patient-directed cancer research is the collection of normal and tumor tissue samples, and blood or other biological fluids that are appropriately stored in a biobank or biorepository. When donated with informed consent, thereby respecting patient confidentiality and privacy, such samples enable examination of the molecular basis of disease. In order to achieve essential added value, sample data must be complemented by clinicopathological data. Although specific patient benefits arising from such research may take many years, biobanked samples are the basis for the identification of biomarkers and drug targets, the testing of new drugs and the identification of patients who are likely to benefit from specific treatments.[1,2] Advancements in bioinformatics and biotechnology have also made it possible to store biospecimens and data on an unprecedented scale and, with globalization and growing

[1]Thoracic Oncology Research Group, Institute of Molecular Medicine, St James's Hospital & Trinity College Dublin, Ireland.
[2]Department of Pathology and Laboratory Medicine, King Hussein Cancer Center, Amman, Jordan.
[3]Biostór Ireland, Wexford, Ireland.
[4]accelopment AG, Zürich, Switzerland.
[5]Cancer and Ageing Research Program, Queensland University of Technology, Brisbane, Australia.
*Authors contributed equally to this manuscript.

interest in transnational sharing of biobank resources, there is an increasing demand to harmonize the biobanking process and its regulation. This emerging trend towards the establishment of biobanks, however, also poses a number of legal, ethical, and regulatory challenges. Regardless of their size, biobanks inherently involve some degree of risk due to the sensitivity of the data they contain. Their success also depends on community support and willingness to participate. For this reason, in order to establish a successful biobank, maximizing public trust is critically important in this process.[3] With a greater reliance on sample-derived data for research in molecular medicine and clinical care, improved standards and informatics for sample procurement, storage, and analysis are necessary to maximize the value of tissue collection for research participants, investigators, academic and medical institutions worldwide.

In November 2011, the King Hussein Cancer Center (KHCC) announced the launch of a European Commission (EU)-funded Seventh Framework Programme (FP7) project (INCO.2011-6.2) to support the establishment of a cancer biobank (KHCCBIO) for Jordan and its neighboring countries through knowledge transfer and training. This would be accomplished through the joint efforts of KHCC and three European partners, Trinity College Dublin (TCD), Biostór Ireland, and accelopment AG. With the goal of establishing a standardized, ISO compliant collection of biological samples for patient-oriented research for the ultimate improvement in the diagnosis, prognosis, and treatment of cancer patients, the KHCCBIO national biorepository in the Hashemite Kingdom of Jordan will be the first of its kind in the region. The KHCCBIO cancer biobank will increase the visibility of the King Hussein Cancer Centre within Jordan, its neighboring countries, and throughout the world, facilitating communication between centers of scientific and clinical excellence. KHCCBIO will disseminate scientific information based on its sample repository in addition to results arising from research, and will result in enhanced networking opportunities for KHCC researchers with other research institutes in the EU and internationally. Moreover, it will encourage the next generation of researchers from Jordan and the region to initiate collaborations at a much earlier stage in their careers, provide better job opportunities and greater access to research infrastructures for young scientists in Jordan. Furthermore the establishment of such a bioresource represents a major investment in Jordan's knowledge economy as it will facilitate cutting-edge academic and industrial research and development.

This article will discuss the efforts and procedures addressed in the establishment of KHCCBIO, in compliance with standard international guidelines and regulations, in order to ensure its evolution as an ISO compliant cancer biobank involving the procurement, processing and preservation of biospecimens in an internationally recognized cancer center in the Hashemite Kingdom of Jordan.

Materials and Methods

Establishing the KHCCBIO Consortium

One of the first stages in the process of establishing a cancer biobank at the KHCC in Jordan was to establish a consortium of partners involved in this project initiative granted by the European Commission (FP7-INCO-2011-6). The KHCCBIO consortium consisted of a unique partnership of four distinctive organizations with complementary and diverse skills and containing all the key prerequisites to establish a first-of-its-kind, state-of-the-art cancer biobank in Jordan. Included in the consortium was the cancer biobank project coordinator, KHCC, in Amman, Jordan, Trinity College Dublin, Biostór Ireland, and accelopment AG. Taken together, the consortium had the necessary skills, experience and expertise in pathology, tissue biobanking (both medical and commercial), regulatory processes, quality management systems, and accreditation and project management. The functions of the consortium were defined by its members and strategies to implement the cancer biobank, KHCCBIO, that were first proposed at the initial kick-off meeting held at the KHCC in November 2011, and brought forward and developed through regular teleconferences and webinars over a period of one year. KHCCBIO envisages the collection of 10,000 biospecimens over a period of 10 years, from its target population of cancer patients in Jordan and its neighboring countries, including Egypt, Iraq, Lebanon, Syria, the Gulf countries, and North Africa. The King Hussein Cancer Center (KHCC) is the only specialized cancer center in the Middle East that treats both adult and pediatric cancer patients, where over 3500 new cancer patients are treated annually.

Generation of Standard Operating Procedures for tissue procurement, processing and preservation

International standardization in biobanking remains to be implemented for biobanks worldwide. Several organizations have produced guidelines that may be used in practice (Table 1). As a contribution towards a more strategic approach to biobanking, and building on the work undertaken in the Design Phase of GeneLibrary Ireland, Molecular Medicine Ireland (MMI) developed guidelines to standardize the collection, processing, and storage of biological materials donated for use in research.[4] In line with these Guidelines for Standardised Biobanking, in addition to those adopted by the lung cancer biobank in St James's Hospital and Trinity College Dublin, standard operating procedures were generated in conjunction with KHCCBIO. The aim of these guidelines was to ensure sample quality, consistency, and integrity of bio-collections at different clinical and research centers. In addition, the use of standardized protocols for sample collection, processing, and storage will help to ensure consistency and harmonization across different institutions. These guidelines were drafted with reference to international best practice in biobanking and approved by the Board of MMI following a consultation phase by those in the research community engaged in biobanking prior to publication.

Consenting procedures, data privacy, and policies

The development of KHCCBIO policies on ethics, data privacy, and sample ownership were developed and approved by a KHCC special task force with assistance from TCD. Assistance in the development of training programs for KHCCBIO staff was provided by consortium partners, TCD and Biostór, based on those implemented and adapted at the latter institutions. The Institutional Review Board (IRB) at KHCC, which was established in 2002, will be acting as the research ethics committee for KHCCBIO. It

Table 1. Current Guidelines in Tissue Biobanking

Guideline	*Reference*
National Cancer Institute (**NCI**) 2007	Best Practices for Biospecimen Resources. http://biospecimens.cancer.gov/global/pdfs/NCI_Best_Practices_060507.pdf
Organisation for Economic Cooperation & Development (**OECD**) 2007	Best Practice Guidelines for Biological Resource Centers. http://www.oecd.org/dataoecd/7/13/38777417.pdf
World Health Organisation (**WHO**) 2007	Common Minimum Technical Standards and Protocols for Biological Resource Centres Dedicated to Cancer Research. http://www.iarc.fr/en/publications/pdfs-online/wrk/wrk2/Standards_ProtocolsBRC.pdf
International Society for Biological and Environmental Repositories (**ISBER**) 2008	Collection, Storage, Retrieval and Distribution of Biological Materials for Research. Cell Preservation Technology. Spring 2008, 6(1): 3–58.
NF S96-900 July 2008	Qualité des centres de ressources biologiques (CRB) - Système de management d'un CRB et qualité des ressources biologiques d'origine humaine et microbienne. http://www.boutique.afnor.org/NEL5DetailNormeEnLigne.aspx?CLEART=FA156209&nivCtx=NELZNELZ1A10A101A107&aff=1&ts=8311666
MMI Guidelines for Standardised Biobanking March 2010	Biopreservation and Biobanking Journal 2010. 8:1:3–63 www.liebertonline.com/toc/bio/8/1

The need for harmonization and standardization in biobanking is widely recognized. Despite the availability of such guidelines, international standards, against which biobanks can be assessed, do not currently exist. Several organizations however, have produced guidelines based on their own biobank experiences and may be used as a guide in establishing best practices in Biobanking (KHCCBIO:Supporting the establishment of a cancer biobank for Jordan and its neighboring countries through knowledge transfer and training. Description of Work. Project number FP7-INCO-2011-6).

will be responsible for approving all ethics-related policies and for all future research projects in which the biobank resources will be utilized. The development of local SOPs and forms that will cover all aspects of the tissue consenting process will then be incorporated in the Quality Management System (QMS). These were reviewed and modified to KHCC requirements. In addition, template patient information and consent forms were provided for inclusion in the ethics review process. Biostór provided templates covering policies on Data Privacy and Confidentiality. All relevant staff were subsequently trained in the above policies and procedures with assistance from TCD and Biostór. Templates based on EU Directives for Data Privacy Policies were established by Biostór which outline how confidential information should be managed at KHCCBIO. These were subsequently reviewed, adapted to KHCCBIO local requirements, approved, and incorporated into KHCCBIO bylaws. Such documents will be used to help define rules for access to the bioresource, its associated data and sample ownership, ensuring the highest standards of ethical approval and governance.

Development of ISO quality management systems

To guarantee sample quality, quality management systems (QMS) standards were based on the EU Tissue & Cells Directives (EUTCD) that specify quality requirements for the donation, procurement, testing, processing, preservation, storage, and distribution of human tissues and cells for human application incorporating best practices from international guidelines.[5] The established QMS will be in compliance with ISO standards and ready for accreditation at the end of the two and a half year project. Collection of relevant patient data is an essential part of biobanking and therefore, personal data privacy and confidentiality must be controlled. This was implemented through the use of secure password-protected access to such data and accessible to dedicated Biobanking staff only. To maximize control and standardization from the onset, KHCCBIO will implement an ISO 9000 QMS that will ensure that KHCCBIO services meet customer requirements and any potential future regulatory requirements. Biospecimens and associated clinical data will be obtained from cancer patients and used in the research and development of biomarkers and potentially, in future diagnostic products.

Qualification and validation of equipment and systems infrastructure

During the course of establishing KHCCBIO, the installation of essential biobanking equipment and systems was required, in addition to performing a documented Installation Qualification (IQ) and Operational Qualification (OQ) to verify that the biobanking equipment and systems meet user and ISO requirements. Based on the Validation Plan defined within the project, Biostór provided KHCC with draft User Requirement Specifications, IQ and OQ protocols, and Report formats for the identified equipment and systems based on the existing Biostór QMS. KHCC was subsequently responsible for revising, adapting, and approving the drafts and performing the equipment testing required. A Master Project Plan of document deliverables was developed for the infrastructure qualification in addition to a validation report following qualification of the biobanking cryoshipping equipment and -80°C storage systems.

Procedures for the collection and storage of tissues

SOPs that were generated for the storage and distribution of human tissue and blood were used in the training of two

KHCCBIO medical technologists and one pathologist. SOPs were reviewed by TCD, modified, and approved by KHCCBIO Quality Management. Such SOPs were then used in the collection and processing of fresh and frozen normal and tumor tissue, formalin-fixed paraffin-embedded tissue (FFPE), blood plasma, serum, and white cells/buffy coats.

Following the acquisition of the tumor resection, the KHCCBIO pathologist selected an appropriate amount of both normal and tumor tissue from the resected specimen.[6] Each of the tissues was then further divided into four additional pieces and either (i) flash frozen in a cryotube in liquid nitrogen and subsequently stored at −80°C, (ii) preserved in RNAlater™ or AllProtect® and stored overnight at 4°C, after which time the tissues were removed from the stabilization solutions and subsequently stored at −80°C, (iii) cryomolds were prepared in Optimum Cutting Temperature (OCT) cryoprotective embedding media, flash frozen in liquid nitrogen, and stored at −80°C. DNA and RNA extractions from tissues were carried out using commercially available kits (Qiagen). For tissue samples, appropriate quality control consisted of traditional Hematoxylin and Eosin (H&E) staining of sections for each specimen collected. DNA and RNA integrity following extraction from blood or tissue samples was tested, in line with recommendations set out by other established cancer biobanks, such as the Spanish National Tumor Bank Network and the Wales Cancer Bank.[7,8] Gel electrophoresis was used for quality control analysis of nucleic acids and proteins and included agarose-, formaldehyde-, and SDS-PAGE electrophoresis, respectively. In addition, yields and purity of nucleic acids isolated from all biospecimens were determined using NanoDrop spectrophotometry. At KHCCBIO, a unique identifier, or a combination of identifiers, is assigned to each biospecimen using a barcode system.

Dissemination of knowledge to society

As the ultimate aim of a cancer biobank is to improve patient care, it is essential that patients as well as the public in general understand the function of a biobank and the role both patients and the public alike can play in making it a success. KHCCBIO developed a dissemination and exploitation plan with the support of its partners, TCD, Biostór, and accelopment AG, in creating awareness of cancer biobanks, in particular KHCCBIO, in a manner that engages the enthusiasm of the Jordanian public and its neighbors (http://www.accelopment.com/en/projects/khccbio). Such dissemination has involved a KHCCBIO project website, printed communications, presentations at national and international meetings, and will continue to include a KHCCBIO branding and advertising campaign in the Middle East with on-going media awareness, and campaigning by advocacy groups. While a policy is currently being addressed and under review by the coordinator, KHCCBIO will continue to ensure that the continued progression and expansion of the biobank and informational material associated with it will be updated and maintained on a regular basis for the benefit of both patients and the wider public. In addition, sustainability of KHCCBIO through worldwide exploitation of pharmaceutical companies dedicated to the development of novel biomarkers and targeted therapies for personalized medicine will be maintained.

Results

KHCCBIO Consortium

The King Hussein Cancer Centre (KHCC) is one of the most prominent, comprehensive cancer centers in the Middle East.[9]It treats more than 3500 new cancer patients each year, from Jordan and its neighboring countries. It is equipped with state-of-the-art medical equipment and services including eight operating rooms and 180 beds and a specialized intensive care facility for pediatric care. KHCC employs highly qualified oncologists and other healthcare professionals trained specifically in oncology, ensuring that all patients receive the latest in comprehensive cancer care. In addition, it is committed to continuous research and education, making KHCC a world-class institution. Its specialities include cancer treatment and care, multidisciplinary services, research training and education, public awareness, and bone marrow transplantation.

The University of Dublin, Trinity College, was founded in 1592. Trinity College Dublin is recognized internationally as Ireland's premier university and is ranked in 61st position in the top 100 world universities by the QS World University Rankings 2013. With almost 17,000 registered students, TCD is committed to excellence in both research and teaching. The Institute of Molecular Medicine, based on the St James's Hospital campus, is one of TCD's major research institutes. It is a center of excellence that drives researchers towards creative thought, descriptive knowledge, integrity, and flexibility of innovation, thus permitting the rapid translation of bioscience from the lab bench to the patient's bedside.[10]

Based in Zurich and established in 2008, accelopment AG is a competent service provider in the project funding sector and assists universities, companies, and other organizations which benefit from public funding programs, European funding schemes for innovation and, in particular, EU Seventh Framework Programme (FP7) for Research and Technological Development. The focus is primarily on projects in the life sciences, information and communication technologies, and the environment and energy sectors. Moreover, accelopment AG supports projects when negotiating contracts with the European Commission, is a partner in publicly funded projects and carries out the administrative aspects of the project management. At present, accelopment AG is involved in several FP7 projects and has strong links and expertise in project communication and marketing (www.accelopment.com).

Biostór Ireland is an independent tissue establishment, licensed by the Irish Medicines Board under the EU Tissues and Cells Directives 2004/23/EU for the storage and distribution of human tissues and cells for human application throughout the 27 countries of the EU (www.biostór.eu). Biostór is one of the main commercial biorepositories of bone marrow, peripheral stem cells, and donor lymphocytes for Ireland's largest transplant centers. The company also stores and transports human reproductive cells, clinical trial samples, master cell banks, and working cell banks under validated cold-chain distribution processes. The company has been audited and approved by several multi-national pharmaceutical companies for Good Manufacturing Practice (GMP) compliance. Biostór also complies with the principals of current GMP, FDA requirements 21 CFR Part 1271,

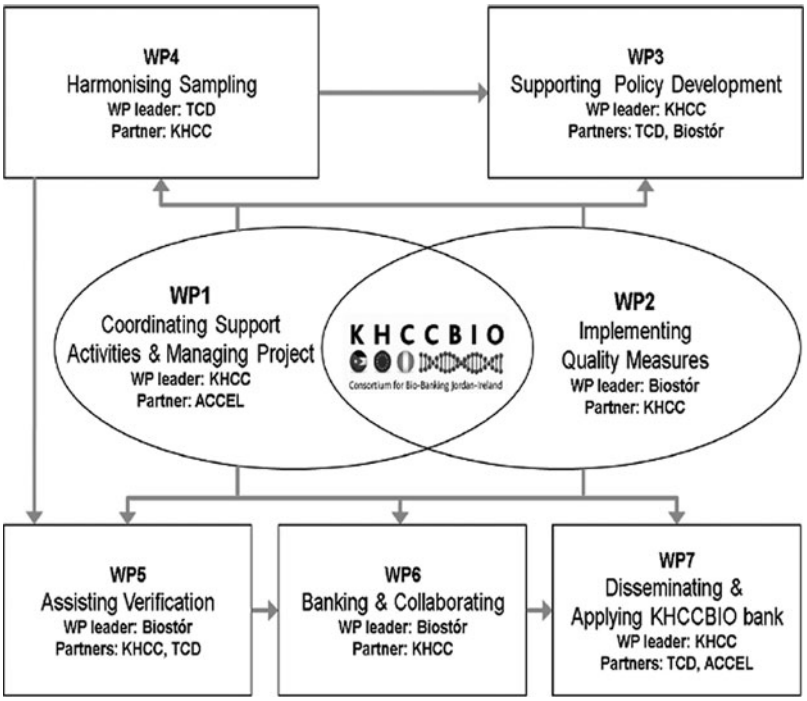

FIG. 1. Workplan structure implemented in establishing KHCCBIO. The overall strategy of the KHCCBIO consortium was set out in the form of various work packages (WP1-WP7), with each partner allocated specific tasks based on their expertise in biobanking and/or project management. Over a 2-year period of the project, a range of support activities were required in order to establish, operate, and maintain a successful cancer biobank at KHCC. (KHCCBIO: Supporting the establishment of a cancer biobank for Jordan and its neighboring countries through knowledge transfer and training. Description of Work. Project number FP7-INCO-2011-6).

and ISBER (International Society of Biological and Environmental Repositories). Together, with KHCC as the project co-ordinator, a KHCCBIO consortium was formed in bringing this biobanking initiative forward.

Coordinating support activities and KHCCBIO project management

From the onset, following the initiation meeting of all partners with the coordinator, KHCC, in Amman, Jordan in November 2011, a work plan of deliverables was established for all involved in this cancer biobank project (Fig. 1). To facilitate communication activities within the consortium, webinar software as well as a dedicated SFTP server was purchased for regular teleconferences and safe exchange of documents. In order to facilitate the collaboration between KHCC and the project partners from one EU Member State and each associated country, a simple but effective organizational structure has been set up (Fig. 2). As part of this organizational structure, all partners agreed to abide by all decisions of the Steering Committee, assembling annually to discuss the progress of the project. The coordinator (KHCC) and legal entity acting as the intermediary between the consortium partners and the European Commission, oversee the overall coordination of KHCCBIO. In particular, responsibilities of the coordinator include: monitoring compliance of partners with their obligations concerning the collection, review and submission of information on the progress of KHCCBIO, in addition to reports and other deliverables (including financial statements and related certifications) to the European Commission, preparing meetings, proposing decisions, and preparing the agenda of the Steering Committee meetings, chairing meetings between partners, preparing minutes of such meetings, monitoring the implementation of decisions taken at meetings, transmitting documents and information connected with KHCCBIO including copies of accession documents and changes of contact information to the partners. The Coordinator was assisted and trained in FP7 project management by accelopement AG. An Advisory Panel composed of international experts in the field of biobanking was developed from three different regions, namely Europe (Professor Keith Kerr, Aberdeen University Medical School, Scotland), USA (Professor Stanley R. Hamilton, University of Texas M D Anderson Cancer Center), and Middle East (Dr. Khawla S. Al-Kuraya, King Faisal Specialist Hospital and Research Centre, Saudi Arabia). The role of the Advisory Panel is to assist the Steering Committee on strategic decision making by providing expert advice whenever sought by the Steering Committee on an ad-hoc basis.

Policy development and training

Protecting the privacy and confidentiality of patients is crucial. While there is currently a lack of legislation relating to biobanking, it is recommended that in line with other European countries, practices such as the use of broad consent and anonymization should be used. KHCC has a well established and functional IRB with approved IRB Policies and Procedures. The KHCCBIO bylaws manual defines, in detail, policies regarding the use of data or tissue repositories for research purposes and sets conditions whereby data and specimens may be accepted and shared through the use of material transfer agreements (MTAs), to define rules for access to the bio-resource, ownership of biological samples, and to ensure the highest standards of ethics and governance. Some of the key principles used to guide biobank governance are outlined in the OECD Draft Guidelines for Human Biobanks and Genetic Research Databases.[11,12] The KHCCBIO bylaws manual addresses many of the issues that need to be addressed before a biobank can be established and has paved the way for identifying many of the ethical issues arising during the development of a cancer biobank (publication pending). However, it was agreed that

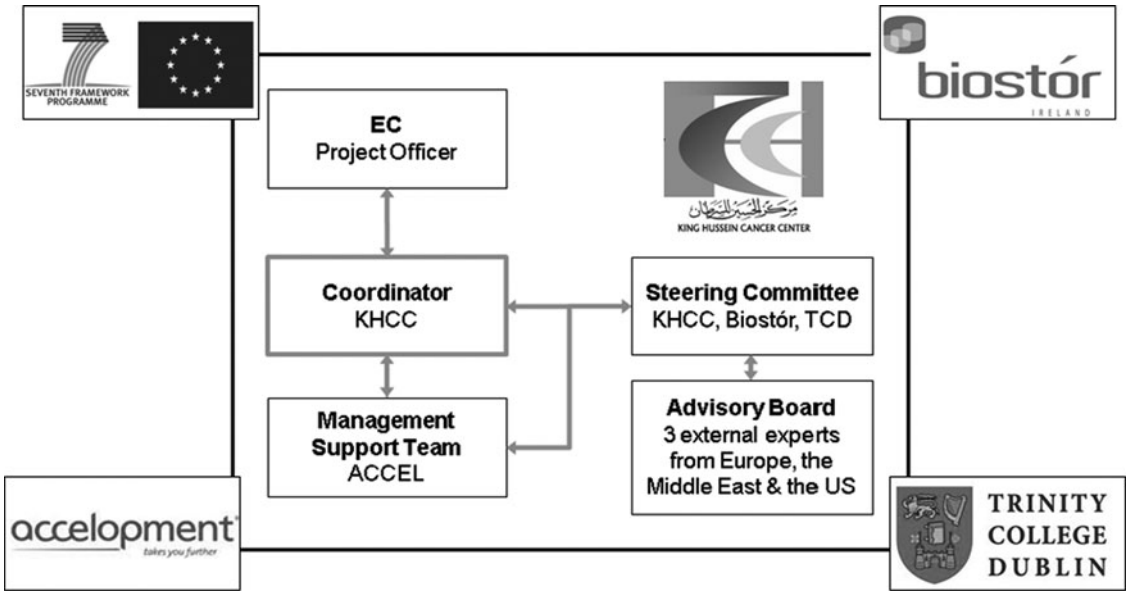

FIG. 2. Organizational structure of the KHCCBIO biobank consortium. In addition to KHCC and its three consortium partners, a Steering Committee was composed consisting of one representative from each partner organization that forms the basis of the decision-making body. The coordinator is the legal entity acting as an intermediary between all partners and the European Commission, and is responsible for the overall coordination of KHCCBIO. An Advisory Panel was also formed that assists the Steering Committee on strategic decisions by providing expert advice whenever sought on an ad-hoc basis. This is composed of biobanking experts from three regions, namely Europe, USA and the Middle East.

European partners could only advise and provide support with this, but that it was necessary for KHCCBIO to develop such policies in their own setting. An independent Ethics Advisor was appointed by TCD from the St. James's Hospital and Federated Dublin Voluntary Hospitals Joint Research Ethics Committee. Activities by the Ethics Advisor to date have consisted of approving KHCCBIO ethics, policies relating to donor confidentiality and SOPs. Moreover, KHCCBIO has established biobanking bylaws that will oversee this set-up and ensure that a competent ethical review has been conducted for all research proposals by the previously established KHCC IRB.

Four core staff will be involved in the operational core of KHCCBIO. To date, 4 weeks training and development have been devoted to KHCCBIO personnel at the host institutions, TCD and Biostór Ireland. Previous to this initiative, however, some personnel had trained for 12 weeks at the MD Anderson Cancer Center in Texas, USA. KHCCBIO personnel were trained in numerous biobanking techniques and policies involved with the procurement, processing, preservation, and storage of patient blood and tissues from lung cancer patients. This was accomplished within the Thoracic Oncology Research Group, St James's Hospital and Trinity College Dublin, where a lung cancer biobank was established in 2004. In addition to biospecimen harmonization, KHCCBIO staff were also introduced to, and trained, in the patient consenting process under the guidance of nurses from the St James's Hospital Oncology Clinical Trials Unit. Sample collection of blood and tissues was demonstrated, in addition to hands-on techniques in the preservation and processing of blood plasma, serum, and white blood cells. A number of preservation approaches were used, such as snap freezing of tissues in liquid nitrogen, cryogenic molds using tissue freezing medium such as OCT, RNA stabilization reagents such as RNAlater™ and AllProtect® for the preservation of RNA, DNA and protein. SOPs drafted for this technical part of the KHCCBIO project were implemented in the isolation of RNA, DNA, and protein from normal and tumor lung cancer tissues, while RNA and DNA were also extracted from white blood cell buffy coats collected from patient blood samples. Biobanking personnel were also trained in a number of practical sessions in the quantification and quality control of proteins and nucleic acids isolated using the appropriate SOPs. A Document Controller assigned to this project at KHCCBIO spent 1 week at Biostór Ireland drafting User Requirement Specifications (URS), Installation Qualification (IQ), and Operation Qualification (OQ) protocols and report formats for the identified equipment and systems at KHCCBIO, using those already existing as part of Biostórs QMS.

Development of a Quality Management System

Prior to the successful FP7 funding awarded to the KHCC for the establishment of KHCCBIO, KHCC had a strong appreciation for Quality Management Systems. In 2006, KHCC was awarded the Joint Commission International (JCI) accreditation, the international arm of the Joint Commission on Accreditation of Health Care Organizations (JCAHO), which was subsequently re-accredited in 2009. In December 2007, KHCC was awarded Disease or Condition-Specific Care (DCSC) accreditation for its Oncology program, while in 2009, the Department of Pathology and Laboratory Medicine (DPLM) was accredited by The College of American Pathologists (CAP). In the same year, the entire KHCC facility was awarded local accreditation from the Health Care Accreditation Council of Jordan (HCAC). A Systems Manual for all laboratory operations (version 1.0, January 2009) was therefore in place at the start of this project. The manual identified 56 SOPs that formed the

basis of the QMS for the cancer biobank, KHCCBIO. As part of the on-going work of the KHCCBIO consortium, an ISO standard Quality Management System (QMS) was designed to prevent, detect, and correct deficiencies that affect the quality of procured, and processed biospecimens and result in consistently more uniform samples. This resulting QMS required, among other things, procedures for appropriate handling, labeling, and record keeping for the procurement, processing, preservation, extraction, storage, distribution, and disposal of human specimens. As such, KHCCBIO was required to retain records concurrently with the performance of each significant step in this process. A records management system was established and records were maintained both electronically, as original paper records or as true copies, 10 years after their creation and for contracts, agreements, and other arrangements with other facilities. Procedures were also maintained for the prompt review, evaluation, and documentation of all adverse occurrences and complaints, and the investigation of these as appropriate.

Strategies implemented to date in sample collection, storage, and distribution

Recommendations for standardization and quality assurance based on best practice guidelines, as outlined in the National Cancer Institute Best Practices for Biospecimen Resources[13] and ISBER's 2008 Best Practices for Repositories document[14] sets out guidelines for sample collection, handling, and storage. Taking these guidelines into account, the timing incurred at each stage of specimen collection and processing, up to the point of storage, was evaluated by KHCCBIO. An appropriate inventory system for sample retrieval together with checklists and other forms that are specifically designed to document the process was implemented.

Best practices in the safety, security, and back-up of biobank samples are crucial when assessing the Biobank's safety and security requirements outlined in ISBER 2008 Best Practices for Repositories. As the purpose of the biobank is the safekeeping of the biospecimens collected, many aspects of facility design that may affect the quality of the samples were carefully considered, such as protection against fire, storage temperature, and air flow. In addition, monitored security systems were employed and provision was made for alarms to be responded to on a continuous basis. These systems were designed in such a way that a number of biobanking personnel were made available to respond to an alarm in a timeframe that either prevented or minimized loss or damage to the biospecimens. All biobank biospecimens were housed in a restricted area, using key-coded access only. As power outages are inevitable, it was essential that a back-up power supply was in place for all freezers. Best practice recommends that computer systems and electronic systems such as freezer controllers should be protected by an uninterruptible power supply (UPS) system.[15] Freezers and refrigerators were monitored daily. For liquid nitrogen storage, a continuous supply was readily available, while the room containing the liquid nitrogen freezers is monitored and alarmed for potential fluctuations in temperature and oxygen levels. All relevant personnel safety measures have also been adopted. Protective clothing, gloves, and face protection, in addition to oxygen sensors have been installed. Procedures for maintenance, repair, and calibration of equipment are also in place. For personnel safety, it is imperative that national guidelines for health and safety in the workplace are adhered to at all times by KHCCBIO staff.[16]

We have validated the distribution of RNA isolated from patient tissues between the lung cancer biobank at St James's Hospital and Trinity College Dublin and KHCCBIO, using a liquid nitrogen dry shipper. Prior to the shipment of samples from Dublin, RNA concentrations and integrity were validated by NanoDrop Spectrophotometry. Upon arrival of the dry shipper containing the RNA samples in Amman, Jordan, such measurements were repeated as part of a blinded sample validation cross-study between the two institutions. A comparison of RNA yield together with 260:280 and 260:230 ratios was made on the same normal and tumor tissue samples, and demonstrated a high level of consistency in RNA readings between both biobanks (Fig. 3). This preliminary validation study further highlighted the use of the liquid nitrogen dry shipper as a way forward in the transport of biospecimens, in particular, nucleic acid components from patient tissues, between Europe and the Middle East. Furthermore, the shipper is validated to maintain the required temperature for up to 2 weeks, which helps avoid any potential issues in delays between the donor and recipient institution.

Data management and protection

To obtain maximum information from each consented sample, the means by which the data is obtained, classified, and stored must be clearly defined in order to protect the privacy of the patient. Data are obtained using appropriate consent, and are recorded in such a way that enables it to be compared with other data. Data collection, including follow-up information, will be coordinated between centers, and a minimum clinical dataset clearly defined. Importantly, the security of the data obtained in relation to coding patient information is also critical in this process. It is essential that the biobanked samples can be tracked at all times. While several documents produced by international experts outline best practices for data collection and management, standards for biobanking data collection have been used, based on the guidelines set out in the National Cancer Institute Best Practices for Biospecimen Resources.[13] Where possible, all relevant clinical data associated with samples is collected in a manner that is in keeping with the relevant regulations. It was critical that the informatics system underlying the data management system in place at KHCCBIO was robust, secure, and reliable, and had the ability to support all biobank operations. Furthermore, in compliance with guidelines,[17] the system, moving forward, will have the capacity to track all aspects of collection, processing and distribution.

Dissemination and impact on health and society

The proposed KHCCBIO project has been conceived to create a world-class, ISO accredited biobank in the King Hussein Cancer Centre (KHCC) in Amman, Jordan, to be used for research into new treatments for cancer. To date, a project website has been developed by KHCC (khccbio.khcc.jo) consisting of a public and private area. Parts of the website that are accessible to the general public contain relevant information on KHCCBIO, ongoing developments

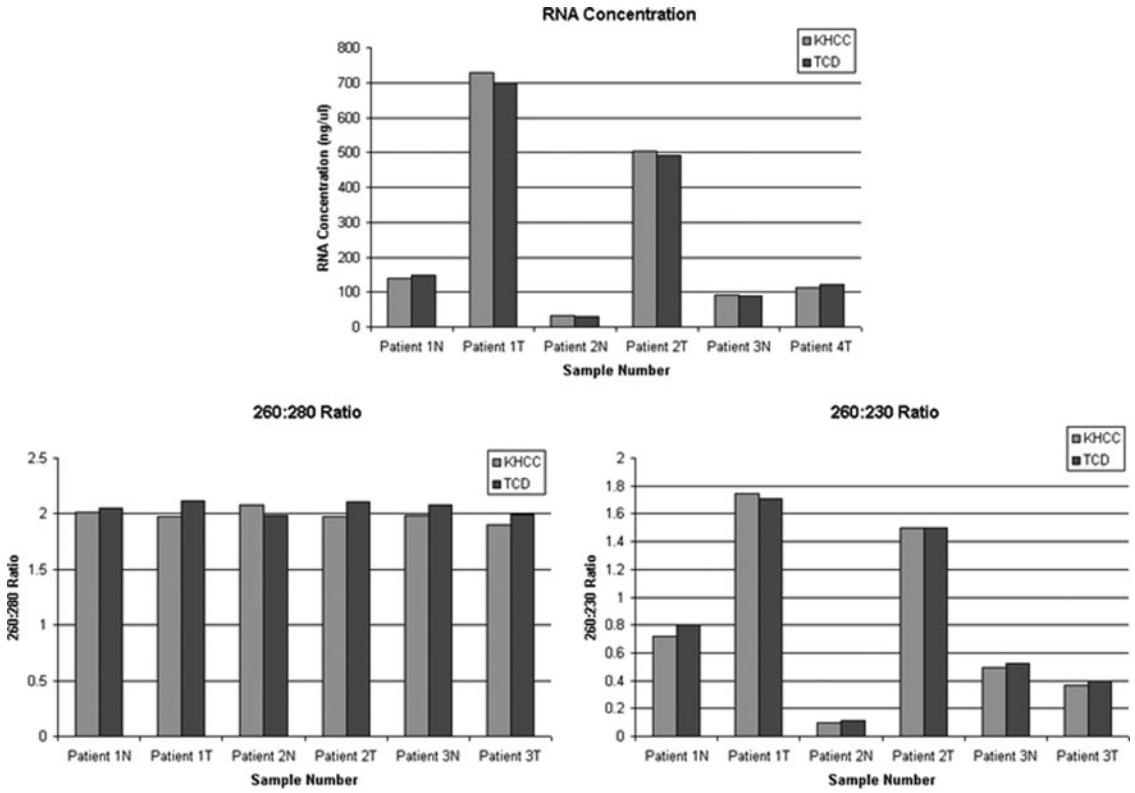

FIG. 3. Validation of tissue RNA. Transport of RNA samples extracted from normal and tumor tissues was validated using a liquid nitrogen dry shipper between Europe (Ireland) and the Middle East (Jordan). Various parameters such as RNA concentration and 260:280 and 260:230 ratios were measured using Nanodrop Spectrophotometry at TCD prior to shipment, and upon receipt of samples at KHCC.

of the biobank, in addition to general educational information on the biobanking of cancer tissues and other biospecimens targeted to tissue donors and their families, media, stakeholders, and project ambassadors. Secured areas (extranet) on the other hand are restricted so that current and future project partners can share and disseminate related knowledge and data. While KHCC's Information Technology Department currently oversees the technical maintenance and development of the website, all partners can contribute updates through an active Content Management System. A media and data center will be available on the website in due course. By creating a publicly accessible KHCCBIO website, we envisage this will lead to higher awareness on the importance of tissue biobanking in Middle Eastern society and will provide an update to researchers in both the scientific and medical communities on the progress of KHCCBIO and its implications in the development of improved treatments for cancer patients.

Once the core message of KHCCBIO is developed, the brand identity will be delivered in a consistent and transparent fashion. The campaign will be delivered across local and national media including radio, television, and press, as well as online media. All audiovisual media advertising will be strongly supported by web and/or printed information leaflets. A well-planned and well-promoted launch of KHCCBIO will generate momentum behind the project and establish contact with the public and press, both at a national and international level. All written materials, especially recruitment material (leaflets, consent forms, questionnaires) will be fully transparent and reflect the goal of KHCCBIO and contain the recognizable KHCCBIO brand identity, in addition to information on the KHCCBIO website and contact information. Information posters, leaflets and newsletters will be targeted to hospitals, library stands, and will also be available for download through the website.

In the long-term, KHCCBIO will have an impact on the health of Jordan and the Middle East through the availability of biospecimens from cancer patients. In the short term, the initiative will add value to, and increase the scope of clinical trials, which may directly benefit all patients. While the ultimate strategy in developing biobank resources worldwide is to improve prevention, diagnosis, and treatment of cancer and other diseases, and to promote the health of society,[18] the establishment of KHCCBIO will represent an important economic investment for Jordan. In order to ensure that research efforts are not duplicated, collaboration not only within Jordan, but internationally, will be promoted.

Discussion

In order for a biobank to be a valuable reservoir of genetic information, large numbers of participants from all racial and ethnic backgrounds need to be recruited. The Middle East and North Africa (MENA) is an economically diverse region that includes both the oil-rich economies in the Gulf and countries that are resource-scarce in relation to population, such as Egypt, Morocco, and Yemen. The region's economic fortunes over much of the past quarter century have been heavily influenced by two factors, the price of

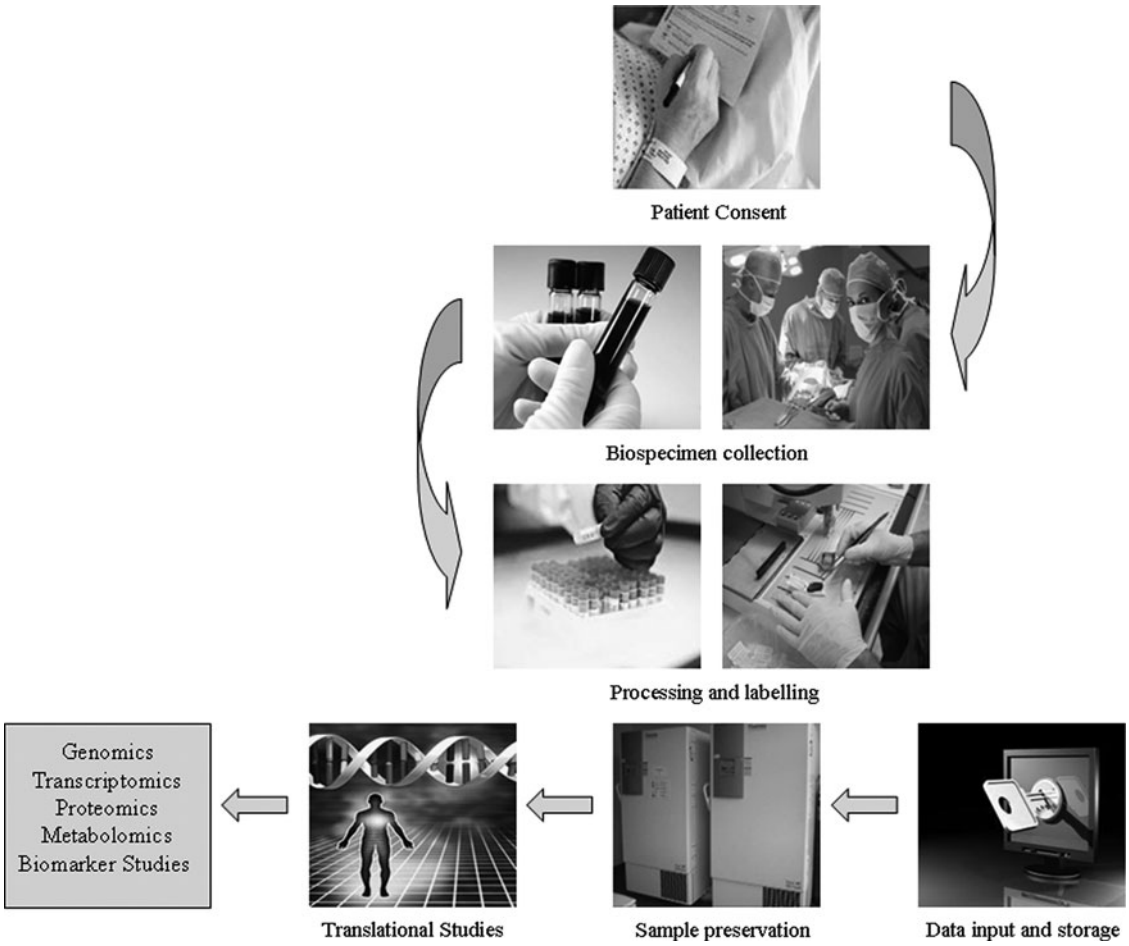

FIG. 4. Workflow of the various stages involved in the procurement, processing, and preservation of biobank samples. Following initial patient consent, blood and tissue samples are procured and processed following surgical resection of the tumor. Specimens are appropriately labeled and stored under tightly regulated storage conditions. Patient clinicopathological data are retained in a password-protected, secure database within the biobanking facility. These biobanked samples may ultimately be used in translational studies, such as the identification and validation of novel biomarkers and as a bioresource for genomic, transcriptomic, proteomic, and metabolomic studies.

oil and the legacy of economic policies and structures that had emphasized a leading role for the state. While an increasing number of cancer biobanks have been established, or are in the process of development across Europe, KHCCBIO is unique in that it represents an ideal opportunity to create a bioresource from a diverse ethnic Middle Eastern and North African population that can be used to further our understanding of the molecular and genetic factors that predispose this population to cancer. As part of sustaining KHCCBIO, a number of marketing strategies are envisaged. These will include the availability of a biospecimen resource of materials from cancer patients from the MENA regions for academic and industrial collaborations. This will be particularly focused on future investments with the pharmaceutical industries and biomarker discovery companies. Joint efforts for further funding will also be a priority from international parties such as the NIH and the EU.

We have described the procedures, challenges, and outcomes of establishing the first cancer biobank in Jordan. KHCCBIO was established to facilitate a biorepository of blood and tissue from cancer patients, through the collection, processing, testing, and preservation of appropriately-annotated samples for subsequent use in translational research efforts, both in the Middle East and Europe (Fig. 4). In collaboration with its partners, TCD, Biostór, and accelopment AG, a solid infrastructure has been put in place for KHCCBIO. This collaborative effort not only involved KHCCBIO and its partners, but also the relevant ethics and advisory committees, IT personnel, and financial administrators. KHCCBIO covers a range of support activities that are currently in place in order to continue to operate and maintain a cancer biobank sustainably. The biobank-related activities will continue to incorporate all current international guidelines and best-in-class practices under an approved Quality Management System to procure, process, and store biospecimens for the benefit of researchers in Jordan, its neighboring countries, and researchers throughout the rest of the world.

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Author Disclosure Statement

No competing financial interests exist.

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Address correspondence to:
Dr Maher A. Sughayer
Department of Pathology and Laboratory Medicine
King Hussein Cancer Center
P.O Box 1269
Amman 11941
Jordan

E-mail: msughayer@khcc.jo