Study Title: Wilmot Biobank Pan-Cancer Biospecimen and Data Collection
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1. Purpose of the Study

The Wilmot Biobank (WBB) is a shared resource that will procure, process, store, and disburse biospecimens and subject data from consenting subjects undergoing a cancer screening or treatment at URMC. University of Rochester investigators will be eligible to request de-identified data/biospecimens through a formal application process involving peer review. This resource will also support peripheral study protocols by offering enrollment, procurement, processing, and storage services. The mission of WBB is to sponsor thoughtful and innovative cancer research on human tissues by providing both technical support and access to collections that were assembled following university, state, federal, and international best practices.

2. Background

Tremendous advances in biomedical technologies over the past several years have greatly increased the quantity and quality of assays available to researchers. For the field of oncology, this advent has accelerated the emergence of personalized medicine, leading to an increased demand for human cancer specimens in research. Human tissues are a critical resource for these research approaches as they provide a primary source of molecular and cellular information through which aberrant factors can be identified, characterized, and targeted[1]. Valuable data can only be generated from high-quality inputs, requiring standardized and consistent biospecimen procurement, processing, and storage methods[2]. Bench researchers are often unfamiliar with clinical workflows and key personnel, making it difficult to coordinate collections that consistently maintain high sample quality. Accordingly, the WBB will serve as a resource dedicated to increasing the accessibility of subject-derived data/specimens to preclinical researchers and meeting the increased demand for high-quality cancer biospecimens by implementing operational best practices.

3. Description of the Repository

The repository will be named Wilmot Biobank and located in the 6-6000 unit of URMC. Room 6-6536 will be used for biospecimen storage following renovation. Updates will include the installation of up-to-date swipe card access and electrical systems to ensure secure access and consistent storage conditions for biospecimens, respectively. Additionally, rooms 6-6715 and 6-6718 are also undergoing renovation and will serve as a tissue processing wet lab and dry workspace for staff, respectively. Repository governance, infrastructure, standard operating procedures, and data/biospecimen management will be developed and maintained by the WBB Director, Bradley Mills, Ph.D. A technical staff (trained by Dr. Mills) will be responsible for the routine recruitment, procurement, banking, and quality assurance of all data/specimen reposits. It is anticipated that the WBB will function indefinitely and within the capacity of its current infrastructure by implementing a regularly scheduled review and destruction of outdated or surplus inventory based on criteria established by the Biobank Advisory Committee (BAC).

Tissue and fluid samples will be collected from enrolled subjects during their cancer surgery, non-surgical treatment, or screening procedures. For subjects undergoing a non-surgical treatment or screening, blood will be collected via a venous catheter draw by point-of-care nurses. Tissue, blood, and/or urine will be collected from cancer subjects undergoing surgical resection. Blood and urine will be collected by point-of-care surgery nurses via venous and bladder catheter draws, respectively. Biobank staff will attend the surgical procedures to facilitate the timely transfer of resected tissues to surgical pathology. This process will serve to maximize specimen integrity and accommodate the documentation of preanalytical variables for quality control. Following pathological diagnosis and after all clinical needs are met, any leftover tissue(s) will be banked. In addition to malignant tissues, resections that are post-operatively diagnosed as benign or pre-cancerous, as well as marginal or local normal tissues, will also be banked. All solid tissue specimens collected by the WBB will be obtained as a result of the subject's routine clinical care and will not require any additional or altered procedures. Following biospecimen collection, corresponding subject data will be aggregated and the WBB will de-identify and code all data/biospecimens by stripping them of the 18 identifiers listed in the HIPAA Privacy Rule.

The WBB will also curate data/biospecimens from peripheral cancer studies at URMC to support institutional research, promote the consolidation and systemization of human tissue banking, and augment the volume and diversity of WBB inventory. Upon request, the WBB will provide subject enrollment, tissue procurement/processing, and/or sample storage services for investigators with active study protocols. Furthermore, URMC has partnered with the Indivumed global biorepository network through which the company is permitted to bank human cancer tissues by way of the University of Rochester Cancer Library (URCL, RSRB61977). This agreement entitles URMC investigators to access 50% of all tissues collected by the URCL for their independent research activities. The WBB will serve as the broker for these biospecimens by providing storage, endorsement, and distribution in a controlled and compliant manner.

Wilmot Biobank data/biospecimen collections will be made conditionally accessible to all URMC faculty for cancer research. The WBB website will prompt prospective users to contact Dr. Mills indicating their general research interest. If study requirements align with WBB inventory, the investigator will be granted access to the WBB Bio-Lab Informatics System (BLIS) user interface containing a de-identified and coded listing of our tissue inventory annotated with reportable case information. The subject/disease/treatment data collected will serve to improve the quality of human tissue research by reporting variables in a thorough, accurate, and standardized manner. Accordingly, Biospecimen Reporting for Improved Study Quality (BRISQ) guidelines will be adhered to, and a list of the variables, as well as the BRISQ elements they satisfy, are provided in **Attachment 1**[3]. If a researcher successfully identifies data/biospecimens of interest, they will be required to submit a formal request that includes a detailed description of research aims, experimental

approach, scientific merit, and anticipated data utilization for publications/grants. The submission will be reviewed by the WBB Biospecimen Utilization Committee (BUC), comprised of members representing Wilmot Cancer Institute (WCI) leadership, programmatic leadership, protocol review and monitoring (PRM), and community outreach/engagement (COE). The BUC will approve/deny requests upon evaluation of research feasibility, design, merit, and alignment with WCI directives, while also taking into account the value/ubiquity of any biospecimens requested. Investigator requests can be submitted before formal RSRB review, allowing for WBB approval to be referenced in subsequent RSRB protocol submissions. Recipient investigators must provide a Click IRB study number to the WBB, and *ancillary data and/or biospecimens will ONLY be released pending study approval.*

The WBB will support URMC investigator-led preclinical research and no data/specimens will be shared with, or transferred to, other institutions. The types of future-use research supported may include (but are not limited to) genomics, transcriptomics, proteomics, and cellular biology, however, prospective usage at the investigator level cannot be specifically identified. All secondary research will be performed on de-identified/coded biospecimens and recipient investigators will enter into an agreement with the WBB stating that under no circumstances will the identity of subjects be released to them. Prospective subjects will be informed of all potential future-use research applications at the time of consent.

Recipient investigators will receive any ancillary clinical data that is requested over a secure cloud-based transfer (i.e., UR Box), and tissues via pick-up at the WBB biospecimen storage room (6-6536). Any scientific findings generated through research using WBB data/specimens will not be returned to the donor subject. Furthermore, subjects will not be re-contacted regarding information related to past participation or future use of donated materials. Subjects may withdraw participation at any time by contacting the WBB Director. Following a withdrawal request, any subject information aggregated on the WBB database and/or biospecimens that were collected under the respective consent will be securely destroyed, and the withdrawal will be documented in WBB archival records.

4. Study Population

Given the nature of this resource, subject enrollment and data/specimen collection will be unlimited. All pregnant, mentally impaired, incarcerated, and/or non-English speaking patients will be excluded from enrollment. The current consent form for this study is only available in English, however, if otherwise eligible non-English speaking patients are identified for enrollment, a translated version of the consent form will be developed accordingly, and a translator will be provided. Patients age 18 and older undergoing a cancer screening or treatment (surgical or non-surgical) at URMC will be eligible for inclusion in WBB data/specimen collection. The WBB regularly communicates with the URCL regarding subject enrollment and tissue collection. An agreement has been reached if there is mutual interest in banking tissue(s) from a mutually-enrolled subject, stating that 50% of the available tissue will be allocated to each party.

Accrual rates will vary according to caseload, investigator demand, and WBB storage capacity, however annual inventory review and culling policies will support sustained enrollment and collection. We anticipate enrolling approximately 300 to 400 subjects annually at a steady state. Demographic distributions will be heavily influenced by the needs of institutional investigators, identified through the review of actively funded projects and institutional surveys at URMC. Prospective enrollment will also be guided by input from the WBB BAC which includes representatives from WCI leadership and the COE. This oversight will ensure that WBB collections align with the WCI strategic plan, intraprogrammatic research initiatives, catchment area needs, and community values.

5. Subject Identification and Recruitment

Subjects will be identified by the WBB Director through the weekly monitoring of the SMH OR Snapboard on Epic. Patients scheduled to undergo surgical resections will be identified, and their prospective appointments will be tracked to identify an appropriate time to initiate contact for recruitment. Dr. Mills is a Research Assistant Professor of Surgery, and a Wilmot Cancer Institute faculty member. Accordingly, he has routine access to the patient information that will be used to identify potential subjects on Epic and will be the only person monitoring these schedules. Dr. Mills will coordinate the recruitment of potential subjects, and WBB staff will initiate contact with the patients during an appointment before their procedure. The study protocol and inherent risks will be reviewed with the patient by a trained WBB staff member. To advertise and promote participation in tissue donation, the WBB will perform outreach in collaboration with the COE to identify and engage specific populations in our catchment area that are disproportionately impacted by cancer and/or underrepresented in our enrollment cohort.

6. Informed Consent

All subjects will be enrolled via written informed consent. If a patient expresses interest in participation following a discussion of the study protocol and review of inherent risks during recruitment, they will be offered enrollment. If they agree to participate, the consent form will be signed by the subject and WBB personnel.

7. Risks and Benefits

7.1. **Risks:** Enrollment in this study will not impact patient care in any way and there are no health risks associated with participation. There is a potential for breach of confidentiality as MRNs will be used to identify and aggregate case information. To minimize this inherent risk, subject information will be stripped of the 18 identifiers listed in the HIPAA Privacy Rule and coded immediately following data collection. The code key and digitized consent document will be made accessible to only the WBB Director and securely stored on the URMC Research Electronic Data Capture (REDCap) and Biological Specimen Inventory (BSI) web-based management systems, respectively.

Although recipient investigators will be apportioned de-identified and coded

data/biospecimens, if studies involve genomic research, it cannot be guaranteed that the identity of subjects will never become known because genetic information is unique to every subject. Furthermore, NIH-Funded research requires all data generated to be shared through an open-access database, creating the potential for further unspecified future-use research. Should re-identification occur, subjects' personal information, health status, and disease risks could become known to others, and they will not be protected from discrimination by companies that sell life insurance, disability insurance, or long-term care insurance under the Genetic Information Nondiscrimination Act (GINA). The risks associated with re-identification through genomic research and data sharing, specifically those posed to individuals with rare diseases or from populations with a higher risk of re-identification, will be reported in the consent document and expounded upon during the informed consent process. For protection against this risk, recipient investigators will enter into an agreement with the WBB stating that under no circumstances will the identity of subjects be released to them, and they will not attempt to re-identify any of the subjects using generated genomics data. Furthermore, users will be required to employ the URMC Genomics Research Center (GRC) for gene sequencing and utilize the URMC Center for Integrated Research Computing (CIRC) Blue Hive (BH) cluster for data transmission, analysis, and storage.

7.2. **Benefits:** Participation in this research offers no benefit to subjects.

8. Data Storage and Confidentiality

Subject MRN will be used to capture minimum reportable case information (BRISQ variables) following enrollment (**Attachment 1**). For each enrolled subject, a unique coded case record will be created in REDCap. The REDCap system is a secure, HIPAA-compliant, web-based application used for the electronic capture and management of research and clinical study data. Subject and disease information will be aggregated from Epic, de-identified, and stored in the coded REDCap case record with the corresponding MRN. Biospecimen quality control metrics, annotated by a blinded URMC pathologist upon histological examination, will also be entered and stored in the case record. Only the WBB Director will be authorized access to this source data record in REDCap.

Biospecimen information and processing details will be recorded and stored in the BSI system for quality assurance. The BSI system follows the International Society for Biological and Environmental Repositories (ISBER) and NCI Best Practices Guidelines for biospecimen tracking systems. It is a secure (role-based permissions structure), HIPAA-compliant, and server-based application used for tracking subject- and specimen-related data over time via detailed history reports. In addition to procedural variables, digitized versions of the dissection, processing, and signed consent (WBB Director access only) forms will be stored on the BSI system. The comprehensive, web-based data management system BLIS stores, integrates, analyzes, and securely shares biomedical research data. The system was built using the open-source LabKey Server which provides several modules for managing

workflows and flexible architecture for customization. A BLIS module will serve as a data portal to integrate the clinical, specimen, and laboratory variables assigned to case records. The recommended reportable case/specimen information (**Attachment 1**) will be imported from source data stored in REDCap/BSI and presented via an interactive user interface.

Beyond the storage and confidentiality of WBB data, the biobank will also require recipient investigators performing genomic research to adhere to a series of guidelines regarding the transmission and storage of sequencing data on WBB specimens. All raw sequencing data generated for these studies will be securely shared between the GRC and recipient investigator via the CIRC BH cluster. The CIRC supports secure computing for HIPAA-regulated data and permits URMC researchers to acquire, house, and analyze restricted-use data for scientific research. Following primary data generation through sequencing, both secondary (gene alignment and assembly) and tertiary (biological mining and interpretation) analyses will be performed on BH. All forms of data will be stored on the BH cluster and only the GRC and recipient investigator will have access to this private partition. Per the NIH GDS policy, aligned sequence data will be publicly shared on the open-access Sequence Read Archive (SRA) database promptly following analysis. A File Transfer Protocol (FTP) will be used to upload BAM files, and no limits will be placed on secondary research use. Data will be stored internally, on BH, for at least five years post-publication, and indefinitely on SRA.

9. REFERENCES

1. *NCI Best Practices for Biospecimen Resources*. http://biospecimens.cancer.gov/practices/.
2. Campbell LD, Astrin JJ, DeSouza Y, Giri, J, Patel AA, Rawley-Payne M, Rush A and Sieffert N. The 2018 Revision of the ISBER Best Practices: Summary of Changes and the Editorial Team's Development Process. Biopreservation and Biobanking 16(1): 3-6. https://doi.org/10.1089/bio.2018.0001.
3. Moore HM, Kelly A, McShane LM and Vaught, J. (2013). Biospecimen Reporting for improved study quality (BRISQ). Transfusion 53(7): e1. doi:10.1111/trf.12281.