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Pathology Core Facility Operations NU –NCI 00X3

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1.0 Introduction

The Pathology Core Facility of the Robert H. Lurie Comprehensive Cancer Center provides tissue analysis and tissue procurement services to the Northwestern University Medical School research community. Historically the operations was operated within in the NMH pathology department prior to July 2000 where tissue and blood procurement study under NU TB8524 and NU SB8524 was conducted. Other procurement across campus utilizing NMH consent (which does not comply with NBAC recommendation were also been used. It became necessary for Northwestern University to Centralize all procurement initiatives in order to improve compliance, specimen collection, and standardization requiring complex. This initiatives prompted the restructuring of the operations and increase access to non-cancer center members, and particularly not to compromise patient care and specimen analysis, as a result, the Pathology Core was established. For purposes of continous patient care and CAP retention policy, consented patient tissue block were allowed to reside in the hospital (NMH/VA) anatomic pathology storage.

Tissue Analysis services includes routine and complex laboratory pathology research. In addition to these basic services, the Pathology Core Facility will be adaptable and incorporate new tissue analysis-related technologies as they are developed and as they are needed by the medical school research community. Three examples of which are tissue microarrays, in situ hybridization and Laser Capture Microdissection. Tissue procurement services include acquisition of biological materials that are archived (paraffin-embedded tissue, for example) or prospective procurement of fresh tissue or fluid. An important role of the Pathology Core Facility is to ensure that proper procedures are followed in the acquisition of human biological materials and that patients are protected

2.0 **Objectives**

A. Act as the centralized repository, specimens procurement, processing, preservation, distribution, as well as providing pathology services to the research community. These include Clinical Trials, ECOG PCORL, NOCEDP, SPORE etc.

The Pathology Core Facility of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University Feinberg School of Medicine has two main components: (1) Pathology Research, and (2) Specimen Procurement.

The Pathology Research component provides all of the specimen processing and pathology services typically performed in a clinical laboratory but it is specifically dedicated to the needs of the Northwestern University Research community in general and the Comprehensive Cancer Center Programs and members in particular. The Pathology Core Facility is unique in that it has the capability and flexibility to address specific research protocol needs. Specifically, we are able to address tissue-processing needs of human or animal tissues that deviate from the standard protocols. In addition, we are able to apply standard or modified (antigen retrieval, for example) immunohistochemistry methods using novel antibodies generated by Northwestern University researchers. The director of the facility, Dr. Jian-Jun Wei, is uniquely qualified as a board certified pathologist and as a practicing general surgical pathologist, to provide the critical input regarding analytical interpretation and protocol modification.

While the main goal of the laboratory research component of the Pathology Core Facility is to address the Cancer Center Investigators needs, the Pathology Core Facility also addresses novel pathology-related technological needs at the forefront of basic and Translational research. Laser capture microdissection, for example is a powerful method for isolating tissue of interest from surrounding tissue, which can then be used for target cell RNA or DNA or even protein analysis. Tissue microarrays are another example of a powerful, relatively new technology useful in maximizing tissue available for histochemical and imunohistochemical analysis. Finally, the Pathology Core Facility will be an excellent resource to introduce new technology related to assay development, validation and specimen analysis as it becomes available.

B. The Specimen procurement component of the Pathology Core Facility will have two main functions: (1) Human tissue and fluid procurement, processing, storage and distribution, and (2) Quality assurance and protection of Human subjects. During the past several decades, investigators have focused on the study of tumor biology using animal models and cell lines. To a large degree, these investigators have exhausted the amount of information that can be ascertained from these models and in recent years, with new technologies, their focus has changed to the study of human Specimen. As this focus has changed, so have the requests for both normal and abnormal human specimens of various type and stages. The current practice at many institutions is to collect biological fluids as routine standard of care but for research purposes, or call the pathologist on an ad hoc basis and process tissue that remains after prognostic and diagnostic patient-care issues have been addressed; tissue that would otherwise be discarded. Many of these institutions have no standardized protocols for specimen procurement, processing, preservation, and tissue retrieval with the potential

consequences of compromised patient care and poor quality assurance. The Specimen procurement component of the Robert H. Lurie Comprehensive Cancer Center Pathology Core Facility of Northwestern University Fienberg School of Medicine addresses this growing need for human specimen, i.e. Cells, protein, DNA, RNA, organelles.

C. The benefits of the Pathology Core Facility (both components) to the Cancer Center research community are the following:
(1) The Pathology Core Facility facilitates the multipurpose needs of the NUMS research community in general and Cancer Center members in particular with a multifunctional facility.
(2) The Pathology Core Facility promotes research including translational research within the Northwestern University community and provides increased opportunities for collaboration.
(3) The Pathology Core Facility satisfies many of the requirements of clinical trials.
(4) The Pathology Core Facility serves as a centralized resource for acquisition of human biological materials and associated data.
(5) Finally, oversight by a pathologist satisfies state and other accrediting agency's (JCAHO, for example) requirements that a physician examine all human tissue. Most importantly, this oversight virtually guarantees that patient care is not compromised in the collection process and that measures designed to protect research subjects (recommendations from the National Bioethics Advisory Commission, for example) are implemented. The Pathology Core Facility operates according to the established guidelines approved by the Institutional Review Board (IRB) and regulatory agencies.

This Facility is on it's way to setting the "gold standard" for collection and preparation of cancer specimen of highest quality that will satisfy today's hungry researchers in their quest to conquer cancer as well as other diseases at any stage in this rapidly changing regulatory and technology environment.

D. Current Activities

The Pathology Core Facility currently coordinates several specialized specimen procurement efforts at Northwestern University. The efforts require a pro-active involvement of Pathcore Coordinators from protocol design through Informed Consent and specimen collection, processing, preservation and analysis. They include:

1. Therapeutic Clinical Trials Studies, including but not limited to investigator initiated, NIH sponsored, NCI Cooperative Groups, NCI directed initiatives. Most of these projects require time-point specific specimen procurement, processing, preservation, analysis, quality access and distribution. These specimen include, but not limited to pharmacokinetics, pharmacodynamics, pharmacogenomics, Peripheral Blood Mononuclear Cells, Bone Marrow Mononuclear Cells, Plasma Cells, Serum, Urine, Lavage, Buccal Swap, nails, fresh tissue, parafiin blocks, biopsies, etc.

2. NCI Spore Initiatives In lymphoma, Prostate and Breast where pre-operative , surgical, and post operative samples are collected, processed, quality access and preserved. Some intra-operative blood, and fluid are also collected where possible.

3. Early Detection Network Program in Ovarian where sample are collected from normal, high risk and cancer patients.

4. Eastern Cooperative Oncology Group Pathology Coordinating Office and Reference Laboratory where central pathology review for eligibility, central testing for study entry, procurement, characterization, processing and distribution of quality specimens to ECOG, and IRB approved investigators.

5. Some examples of Robert H. Lurie Comprehensive Cancer Center Disease Specific Multi-Disciplinary Repositories as shown in table below. Where possible, and if available during routine care, or if previously collected under a Protocol Specific Research.

Check all that apply	Code	Paraffin Block	Fresh Tissue Or biopsy	Purple Top or PBMC	Smears	Red Top	Lavage And/or Cells	Bone marrow	Others	Program
☐	AGC	X	X	X		X	X	X	X	AeroDigestive (Head & Neck, Lung
☐	BRN	X	X	X		X	X		X	Brain Tumor
☐	BSP	X	X	X		X	X		X	Breast SPORE – See Betty Weiss
☐	CTC	X	X	X	X	X		X		Cutaneous T- Cell Lymphoma
☐	LYMLEU	X	X	X	X	X	X cell suspension	X	X	Lymphoma Bank
☐	MYL		X	X	X	X		X	X	Myeloma
☐	ORC	X	X	X		X			X	Oral Cancer
☐	OVC	X	X	X	X	X	X		X	Ovarian CEDP/Gyne Program

☐	PAN	X	X	X		X	X	X	X	Pancreatic Tissue
☐	PSP	X	X	X		X	X		X	Prostate SPORE
☐	SAR	X	X	X		X	X		X	Sarcoma/ Soft Tissue
☐	OTH	X	X	X	X	X	X	X	X	Other: Rare, archived

Resources available at Northwestern University – Chicago Campus (RHLCCC, PCF, NMH and VA)

The Robert H. Lurie Comprehensive Cancer Center of Northwestern University (RHLCCC)

The RHLCCC is a multi-disciplinary clinical and laboratory research center, integrating the expertise and resources of the Northwestern University Medical School and its five affiliated hospitals. The Cancer Center was under the leadership of Dr. Steven T. Rosen since 1989 and is now under the new leadership of Dr. Leon Platanias since 2015. In 1993, it was awarded a three year NCI Cancer Center Support Grant from the NCI, which was renewed in 2001. Comprehensive status was granted to the Cancer Center in August, 1997.

Pathology Core Facility of the RHLCCC (PCF)
The PCF is a shared resource of the RHLCCC and is directed by Dr. Jian-Jun Wei. It oversees research pathology and specimen procurement needs of NU Medical School (NUMS) and non-medical school investigators on the Chicago and Evanston (including ENH and NU) campuses. A list of research pathology-related services includes but is not limited to the following: 1) Standard tissue processing, fixation, embedding and sectioning, 2) Routine histochemistry, automated immunohistochemistry, and novel histochemistry and immunohistochemistry, 3) RNA / DNA / protein extraction, 4) Generation of tissue microarrays, 5) Fluorescent and chromogenic in situ hybridization (FISH and CISH), 6) Generation of cell monolayers on glass slides from fluid using a Cytyc ThinPrep 2000 instrument, 7) Selective Cell sorting, 8)Special Serum Elisa, 9) others. The PCF actively participates in specimen procurement, storage and database management for the NU SPOREs in breast cancer (9/1/2000 – 8/31/2005), prostate cancer (6/1/2001 – 4/30/2006), and head and neck cancer (in submission), and lymphoma, oral cancer, and general procurement. In addition, the PCF actively participate in implementation of all Cancer clinical trials at NU and affiliates (Evanston, Silver Cross, and Ingalls Hospitals) Finally, the PCF works closely with investigators to insure that all regulatory agency/rules, guidiance, recommendations, policies and law (HIPPA, FDA, CLIA, CAP, JCAHO, CDC, IATA, OHRP/OPRS/IRB/ETHIC Committee, ORS, OSHA, NBAC, and VA) and other requirements related to human subject specimen procurement or research are addressed.

3.0 Selection of Patients:

a, prospective procurement.

Pathology Core Staff will work closely with Study coordinators, Clinics, and Physicians in coordinating and identifying and tracking consented patients. There are three types of prospective procurement activities that take place, as described below.

1. PCF works with investigators who have IRB approved protocols. For these projects specific procedures will be followed as described in the protocol, i.e cooperative group studies such as ECOG or RTOG trials , pharmaceutical sponsored trials, and investigator initiated studies . For these projects, PCF is notified of research subjects in two ways. First, study coordinators provide a weekly report of all study subjects to PCF. This is given to PCF each Friday, and includes all subjects scheduled for the next week. Secondly, coordinators or a health care provider complete a PCF requisition form, and page or phone PCF as subjects are enrolled and PCF services are required. Subject information and necessary forms must be received at PCF prior to the activity. Consented subject's schedule of protocol required events are monitored and tracked on NOTIS (the Northwestern Oncology Trial Information System, which is the electronic information system used by the Clinical Research Office), and verified/confirmed by patient care staff. The PCF requisition form, along with consent, HIPAA authorization, and any other protocol specific instructions for processing, are faxed over to PCF. A full copy of the consent and authorization are also stored in PCF file stations at CRO and Physician offices.

2. PCF also provides procurement (Banking) for unspecified uses that are not covered in other IRB approved projects. The IRB approved consent form for this project (NU 00X3) is used by the treating physician, surgeon, and or designated patient care staff for this type of banking. These patients are identified by the contributing physician/surgeon. The same notification mechanism as described above are followed if PCF services are being requested.

3.

a. Finally PCF also works on projects with IRB Consent waiver. As detailed in each protocol. Copies of IRB approval letter, application and PCF requisition form must be received in PCF before any services begin.

b. Retrospective specimens. PCF is also involved with retrospective specimen procurement. In this case, PCF is not involved in the consent process, but collects IRB or ACUC approval to ensure compliance when processing services are requested.

In addition, PCF will retrieve archived materials in collaboration with other repositories i.e NMH, CHTN, PCO, NIH, etc… on behalf of investigators for the purposes of de-identification and/or other laboratory services. In this case, the specimen collection is described in the protocol and subjects have provided consent, however, the specimens are not collected as subjects are enrolled, but at a later date (months to a year later, for example). In these projects, while some investigators do procure and bring their project specific samples to PCF for services, many specimens on consented subjects reside at various hospital pathology departments, including NMH/VA and the transfer of the tissue on consented subjects is done later in the life of the project.

4.0 **Patient Registration; Not Applicable**

5.0 Treatment Plan

Not applicable

6.0 Response Assessment/Measurement of Effect:

Not Applicable

7.0 Study Parameters;

Collection of human biological materials to facilitate research.

Protocol specific parameters will be followed with consent level. Where NU00X3 consent is used, materials and fluid will be collected only during patient care scheduled procedures. No surgical and/or phlebotomy procedure will be requested outside of routine care. In some cases, additional blood, no more than 50ml may be collected during routine phlebotomy. Bone marrow aspirates from collection syringes may be collected after the necessary amount for routine diagnostic purposes has been used. For bone marrow specimens, additional bone marrow is not taken from the patient, therefore it is possible that there may not be enough aspirate to provide to PCF on consented subjects, in which case the bone marrow in not procured.

Tissue Procurement

The tissue procurement component of the Pathology Core Facility collects preserves, and distributes unfixed, fresh tissues and cells, formalin-fixed or paraffin embedded tissue, and slides. Other biological Specimens such as Whole Blood, Serum, Plasma, PBMC, Lavage, etc… are also procured, process, preserved and distributed for translational research A piece of punched skin may also be taken during patient routine dermatology care . These skin biopsies are also for use within the lymphoma program. The Pathology Core Facility has a Standard Operating Procedure for collection of all specimens. All requests for tissue withdrawal and/or collections are made in advance and reviewed by the Pathology Core Facility use committees or similar bodies were appropriate. IRB approval or exemption, specific to that protocol/project, is required. Specialized Repository services are provided under Breast Spore, Prostate Spore, ECOG PCORL, Myeloma Bank, Lymphoma-Leukemia Bank, AeroDigestive Program, Brain Tumor Bank, Sarcoma NOCEDP, etc… Specific or general PCF consent forms are to be used for prospective procurements on repositories except where IRB approved waiver of consents have been granted.

- Tissue specimens are retrieved as soon as possible (preferably immediately after removal in the surgical suite) by paging a Pathology Core Facility technologist. Specimens are transported in sterile, leak-proof, polypropyline containers containing sterile media. Containers for samples are placed in an insulated carrier filled with absorbant material for safe transport to the Pathology Core Facility. All specimens are accompanied by a copy of the surgical pathology requisition. If it is anticipated that delivery time will be greater than 15 minutes the specimen is transported on ice.

- When tissue specimens are received in the laboratory they are processed according to an established protocol, which may be altered as per individual request. For most studies, this includes snap-freezing of tissue (foil-wrapped tissue is rapidly frozen in liquid nitrogen - cooled isopentane) in OCT media. In some instances, a cryomed

(rate controlled freezing device) is used to cryopreserve viable tumor or other cells or a laminar flow hood is used for sterile processing of specimens and material is stored in -70° or -80° centigrade freezers or in liquid nitrogen tanks.

- All specimens arriving in the Pathology Core Facility are logged in as follows. A bar code label is attached to the tissue and a copy of this bar code is attached to a Sample Identification form. Bar code labelers and networked terminals are located at all major tissue acquisition sites. The Sample Identification form includes the patient information, diagnosis, tissue type, date of the procedure, Surgical Pathology number and quality control information. This information is stored as a computerized record and is capable of providing, on request, information concerning all categories of specimens. This form is updated as pathological information becomes available (a copy of the pathology report is attached) and as quality control or utilization information becomes available. For all samples, the freezer or liquid nitrogen location is entered on freezer maps

- Standard biohazard and infection control measures are followed when handling tissues. We adhere to the guidelines and precautions as recommended by the CDC for handling HIV-Infected specimens as described CDC-NIH publication "Biosafety and Microbiological and Biomedical Laboratories Guidelines." The laboratory personnel wear gloves, laboratory coats or uniforms, and all work performed in Biosafety cabinets. Working surfaces are decontaminated at the end of each working assignment and before starting a new one. The universal precautions for handling all specimens are the same as those for preventing transmission of all blood borne infections. Only sterile plastics are used (no glass), and all discarded materials are collected in biohazard color-coded heavy plastic bags placed in covered containers. The Pathology Core Facility personnel are required to abide by the University's research safety policies and procedures.

- Standard biohazard and infection control measures are followed when handling tissues. We adhere to the guidelines and precautions (BSL2) as recommended by the CDC for handling HIV-Infected specimens as described CDC-NIH publication "Biosafety and Microbiological and Biomedical Laboratories Guidelines." The laboratory personnel wear gloves, laboratory coats or uniforms, and all work performed in Biosafety cabinets. Working surfaces are decontaminated at the end of each working assignment and before starting a new one. The universal precautions for handling all specimens are the same as those for preventing transmission of all blood borne infections. Only sterile plastics are used (no glass), and all discarded materials are collected in biohazard color-coded heavy plastic bags placed in covered containers. The Pathology Core Facility personnel are required to abide by the University's research safety policies, covered entity policies and procedures, as well as Government Agencies Regulations.

Additional Processing procedures are available in laboratory manuals.

8.0 **Drug Formulations and Procurement:** Not Applicable

9.0 **Statistical Considerations**; Not Applicable.

10.0 Records to be Kept; Laboratory and pathology diagnostic and prognostic values . Demographics and treatment outcome associated to the samples will be collected and kept in secured cabinets, as well as password protected electronic servers. Age, Pathology Diagnosis, treatment type, Laboratory Values (i.e. Ca-125 and Ethnicity information will be collected .

11.0 **Pathology Requirements**: Biological specimens both normal and cancer and associated data

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