NWBioSpecimen Service Descriptions for Grant Applications

# Center Description

NWBioSpecimen is a collaborative resource connecting well-characterized biospecimens and accompanying annotation data to innovative research projects aimed at improving prevention, diagnosis, and treatment of human diseases. Our researchers are located at the University of Washington (UW), Fred Hutchinson Cancer Research Center (FHCRC), and Seattle Children’s Hospital and Research Institute (SCH and SCRI), and at other institutions throughout Washington State and beyond. NWBioSpecimen provides a common portal for researchers seeking human biospecimens for Institutional Review Board (IRB) authorized studies. Biospecimens include high-quality human tissue, blood, and other body fluid samples, which may be annotated with medical records data and specimen-level data including diagnostic information and other detailed analyses such as digital pathology measurements. NWBioSpecimen aims to provide reliable and cost-effective service in a self-sustaining way. Specimens and data typically are distributed [de-identified/coded](http://biospecimens.cancer.gov/bestpractices/got/#H), unless a research team has specific IRB approval to receive identified specimens and data, such as for clinical trials. All biospecimen use must conform to the [University of Washington Human Biospecimen Use policy](http://www.washington.edu/research/hsd/policy/).

NWBioSpecimen provides the following services:

* Prospective collection of biospecimens using protocol-specific methods
* Procurement of remnant portions of routine clinical samples
* Annotation with patient-level and specimen-level data

A brochure is available at the following URL:

[http://depts.washington.edu/nwbios/files/qr/nwbiospecimen-flyer.pdf](http://depts.washington.edu/nwbt/files/qr/nwbiotrust-biospecimen-flyer.pdf)

# Patient Consenting

Consent for use of biospecimens and medical record data is sought of UW Medicine and Seattle Cancer Care Alliance (SCCA) patients through [NW BioTrust](http://www.nwbiotrust.org). Consent is obtained with IRB permission and oversight, is completely voluntary, and can be withdrawn at any time. A patient’s consent status is not revealed to clinical care providers and does not affect clinical care in any way. No specimens or data will be made available for research from patients who choose to “opt out” of the NW BioTrust consenting process, unless there is a study-specific patient authorization in place to do so (such as for a clinical trial). Consents may be requested through an electronic "front desk" system in SCCA clinics and UW Medicine clinics and hospitals, or through paper forms administered by NW BioTrust consenting staff or other study coordinators. Consent form responses are tracked in an electronic consent management module in the NWBioSpecimen information technology system(1-4).

# Biospecimen Procurement and Annotation

NWBioSpecimen tissue procurement activities occur in Pathology laboratories (frozen section room, gross room, and other laboratories), Laboratory Medicine facilities (for remnant portions of blood and other biospecimens), and other sites such as Radiology procedure suites and Seattle Cancer Center Alliance clinics. The frozen section room is equipped with a biosafety hood, gross photography stand with digital camera, dissecting platforms, scales, cryostat microtomes, computers connected to clinical and research barcoded label printers, a microscope with a digital video camera, a refrigerator, and equipment to snap-freeze and temporarily store specimens on dry ice prior to transport to researchers or biorepositories. Paraffin embedded archival block handling occurs in an office space located near the frozen section room. Blood processing and temporary specimen holding occur in a 150 ft2 facility in UWMC room RR019 equipped with auditable computerized keypad access. All freezers have temperature monitors and 24/7 on-call notification in case of failures.

Using the NWBioSpecimen information technology system(1-4), biospecimens may either be anticipated prospectively prior to their arrival in procurement areas, or may be identified as remnant portions of routine clinical samples already present in the laboratory. Variables resulting from the biospecimen search criteria, such as the diagnosis or other features that resulted in a biospecimen being identified as part of the search, may be provided to the researcher as part of the annotation data. Patient-level and biospecimen-level information including collection details (collection date/time and, for tissues, anatomical site of origin, diagnosis, weight, size, storage location, clamp time, tissue removal time, etc.) are entered by NWBioSpecimen staff into a biospecimen management system ([Labmatrix, BioFortis, Inc., Columbia, MD](http://www.biofortis.com/products/labmatrix/)). Additional annotation data may be extracted for research from the electronic medical record and other systems using informatics services of [Institute of Translational Health Sciences](https://www.iths.org/)(5). Further, detailed histopathologic evaluations may be obtained, including quantified results of immunohistochemical staining and features from whole slide digital images, using services available in the [Pathology Digital Imaging Core Facility](http://www.pathology.washington.edu/research/centers/pdicf/)(6).

Two NWBioS administrative office rooms, each 180 ft2, are located in Magnuson Health Sciences Building rooms RR844 and RR846. RR844 is equipped with a private office for the Assistant Director. RR846 is equipped with a private office for the Digital Imaging Coordinator. Each room is further equipped with auditable computerized keypad access and additional computer workstations. All computers are connected to an automated nightly network-based data backup service.

# Histology Services

Most histology functions are purchased from consulting laboratories including the UW Medical Center (UWMC) and Harborview Medical Center (HMC) hospital pathology laboratories. The primary techniques offered include formalin fixation or tissue freezing, processing, embedding for routine histology and electron microscopy, and tissue sectioning. Sections may be stained with hematoxylin & eosin or a variety of special processes such as immunohistochemistry (IHC), in situ hybridization and immunofluorescence. Additional histology services offered by NWBioSpecimen include digital photomicrography and preparation of publication-quality scientific figures.

# Tissue Microarray Manufacturing Facility

NWBioSpecimen offers tissue microarray (TMA) construction services to researchers utilizing tissues procured through NW BioSpecimen or from other sources. In addition to using tissue cores to construct TMAs for histological analyses (8-13), we may also punch blocks for tissue cores with high tumor cellularity (or other regions of interest) for downstream molecular analyses such as DNA sequencing(17-18).

The TMA facility is part of a 600 ft2 laboratory located in the HMC Research & Training Building and equipped with a Beecher MTA-1 arrayer, block warmer, magnifiers, oven, freezer, and all necessary supplies. Tissue cores may be transferred to recipient blocks, or transferred to microcentrifuge tubes for DNA/RNA/protein extraction and analysis(17-18). Although many punch sizes are available, NWBioSpecimen TMAs typically represent specimens as quadruplicate 1.0 mm cores for ease of downstream processing and analysis.

For TMA projects, NWBioSpecimen should be consulted at the time of project inception. For example, if antibody staining will be performed by IHC(8-13), a project-specific antibody optimization TMA can be made to incorporate positive and negative control tissues, so that each antibody can be optimized to replicate published staining patterns. After optimization, antibody optimization TMA sections may then be included with each experimental run as normalization controls. NWBioSpecimen staff have extensive experience quantifying results from TMA IHC experiments using whole slide digital imaging methods(8-13) using services provided by the [Pathology Digital Imaging Core Facility](http://www.pathology.washington.edu/research/centers/pdicf/)(6).

A more extended research guide for NWBioSpecimen TMA construction services can be found at this URL: <http://depts.washington.edu/nwbios/files/content/NWBioSpecimen_-_TMA_Construction.pdf>

# Pathology Digital Imaging Core Facility

NWBioSpecimen offers digital pathology services including whole slide scanning, image hosting, quantitative image analysis of histologic features(8-16), and preparation of publication quality figures.

The Pathology Digital Imaging Facility has two locations. A 180 ft2 office located in room RR846 of the UW Health Sciences Building has computerized (auditable) keypad access, a private office for the Digital Imaging Coordinator, and three additional workstations equipped with new PCs. The facility is equipped with an Aperio ScanScope CS digital whole slide scanner networked to two dedicated Dell PowerEdge R510 servers equipped with Aperio eSlide Manager server applications and Aperio Brightfield Toolbox image analysis software. These servers each contain 15TB of direct-attached storage, and are hosted in the University of Washington enterprise class data center with automated nightly backups to two secure geodiverse locations. One of the workstations is equipped with a Wacom Cintiq 24HD pen tablet annotation screen. An auxiliary 601 ft2 image analysis facility located in room 421 of the Research and Training Building on the UW Harborview Medical Center campus has 3 workstations with new PC computers and a Wacom Cintiq 22HD pen tablet annotation screen.

For digital pathology projects, NWBioSpecimen should be consulted at the time of project inception.

A more extended research guide for NWBioSpecimen TMA construction services can be found at this URL: <http://depts.washington.edu/nwbios/files/content/NWBioSpecimen_-_Slide_Scanning__Image_Analysis_-_Pathology_Digital_Imaging_for_Research.pdf>

# Fees-for-services

All NWBioSpecimen service fees are reviewed and formally approved through the [UW Management Accounting & Analysis office](http://f2.washington.edu/fm/maa/recharge)(7).

# Footnotes

1. Ponko, S, M Skilling, C Lau, L Crawford, M Provence, A Simms, P Fearn, KC O’Mara, K Lum, C Nathe, P Tarczy-Hornoch, N Anderson, R Schmidt, J Slattery, P Porter.  [NWBioTrust: A Cross-Institutional Informatics Infrastructure for Requesting and Managing Annotated Human Biospecimens](http://online.liebertpub.com/doi/pdfplus/10.1089/bio.2014.1228.abstracts).  Abstract 49 in Biopreservation and Biobanking June 2014: A-1-A-63. <http://online.liebertpub.com/doi/pdfplus/10.1089/bio.2014.1228.abstracts>
2. Poster (PDF) of NWBioTrust: A Cross-Institutional Informatics Infrastructure for Requesting and Managing Annotated Human Biospecimens, 2014 ISBER Annual Meeting & Exhibits presentation:<http://depts.washington.edu/nwbios/files/qr/2014-isber-nwbt-poster.pdf>
3. Henriksen JC, S Ponko, C Magnusson, M Skilling, S Bowell, D Chang, AE Rizzardi, P Tarczy-Hornoch, SC Schmechel. [Integration of a commercial biospecimen management software system and an Anatomic Pathology Laboratory Information System as components in the informatics workflow of a comprehensive biobank](http://online.liebertpub.com/doi/abs/10.1089/bio.2015.29016.pm). The 2015 ISBER Annual Meeting & Exhibits. Mullins Piper and Kozlakidis Zisis. Biopreservation and Biobanking. August 2015, 13(4): 304-305. doi:10.1089/bio.2015.29016.pm. <http://online.liebertpub.com/doi/abs/10.1089/bio.2015.29016.pm>
4. Poster (PDF) Integration of a commercial biospecimen management software system and an Anatomic Pathology Laboratory Information System as components in the informatics workflow of a comprehensive biobank, 2015 ISBER Annual Meeting & Exhibits: <http://depts.washington.edu/nwbios/files/qr/2015-ISBER-Poster-UW-NWBT-BSM.pdf>
5. ITHS Research Services - Biomedical Informatics: <https://www.iths.org/investigators/services/bmi/#/node/1103>
6. *Pathology Digital Imaging Core Facility:*
<http://www.pathology.washington.edu/research/centers/pdicf/>
7. *UW Management Accounting & Analysis - Recharge and Cost Center Information:*
[ttp://f2.washington.edu/fm/maa/recharge](http://f2.washington.edu/fm/maa/recharge)
8. *Imunohistochemical staining quantification of TMAs (Area quantification)*
[Trp53 haploinsufficiency modifies EGFR-driven peripheral nerve sheath tumorigenesis](http://www.ncbi.nlm.nih.gov/pubmed/24832557). Rahrmann EP, Moriarity BS, Otto GM, Watson AL, Choi K, Collins MH, Wallace M, Webber BR, Forster CL, Rizzardi AE, Schmechel SC, Ratner N, Largaespada DA. Am J Pathol. 2014 Jul;184(7):2082-98. doi: 10.1016/j.ajpath.2014.04.006. Epub 2014 May 13. PMID: 24832557.
9. *Imunohistochemical staining quantification of TMAs (Area quantification)*
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10. *Imunohistochemical staining quantification of TMAs (Area quantification)*
[Elevated hyaluronan and hyaluronan-mediated motility receptor are associated with biochemical failure in patients with intermediate-grade prostate tumors](http://www.ncbi.nlm.nih.gov/pubmed/24668563). Rizzardi AE, Vogel RI, Koopmeiners JS, Forster CL, Marston LO, Rosener NK, Akentieva N, Price MA, Metzger GJ, Warlick CA, Henriksen JC, Turley EA, McCarthy JB, Schmechel SC.  Cancer.  2014 Jun 15;120(12):1800-9.  doi: 10.1002/cncr.28646.  Epub 2014 Mar 25. PMID: 24668563.
11. *Cytoplasmic immunohistochemical staining quantification of TMAs (Cell quantification)*
[Canonical Wnt/β-catenin signaling drives human schwann cell transformation, progression, and tumor maintenance](http://www.ncbi.nlm.nih.gov/pubmed/23535903). Watson AL, Rahrmann EP, Moriarity BS, Choi K, Conboy CB, Greeley AD, Halfond AL, Anderson LK, Wahl BR, Keng VW, Rizzardi AE, Forster CL, Collins MH, Sarver AL, Wallace MR, Schmechel SC, Ratner N, Largaespada DA.  Cancer Discov.  2013 Jun;3(6):674-89.  doi: 10.1158/2159-8290.CD-13-0081.  Epub 2013 Mar 27.  PMID: 23535903.
12. *Imunohistochemical staining quantification of TMAs (Area quantification)*
[Expression of FGFR3 and FGFR4 and clinical risk factors associated with progression-free survival in synovial sarcoma](http://www.ncbi.nlm.nih.gov/pubmed/23664540). Charbonneau B, Vogel RI, Manivel JC, Rizzardi A, Schmechel SC, Ognjanovic S, Subramanian S, Largaespada D, Weigel B.  Hum Pathol.  2013 Sep;44(9):1918-26.  doi: 10.1016/j.humpath.2013.03.001.  Epub 2013 May 10.  PMID: 23664540.
13. *Tissue classification of TMAs (Automated tumor selection)*
[Quantitative comparison of immunohistochemical staining measured by digital image analysis versus pathologist visual scoring](http://www.ncbi.nlm.nih.gov/pubmed/22515559). Rizzardi AE, Johnson AT, Vogel RI, Pambuccian SE, Henriksen J, Skubitz AP, Metzger GJ, Schmechel SC.  Diagn Pathol.  2012 Jun 20;7:42.  doi: 10.1186/1746-1596-7-42.  PMID: 22515559.
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[Expression of FGFR3 and FGFR4 and clinical risk factors associated with progression-free survival in synovial sarcoma](http://www.ncbi.nlm.nih.gov/pubmed/23664540). Charbonneau B, Vogel RI, Manivel JC, Rizzardi A, Schmechel SC, Ognjanovic S, Subramanian S, Largaespada D, Weigel B.  Hum Pathol.  2013 Sep;44(9):1918-26.  doi: 10.1016/j.humpath.2013.03.001.  Epub 2013 May 10.  PMID: 23664540.
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