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NWBioSpecimen / University of Washington Department of Pathology

Tissue Microarray Construction

Introduction to Services and Pricing

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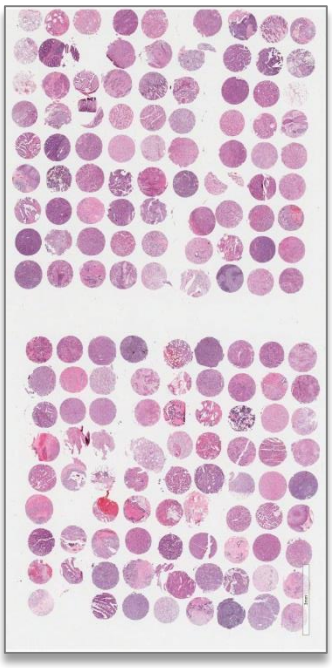
Introduction



NWBioSpecimen, a core facility housed within the University of Washington Department of Pathology, provides biospecimen procurement, annotation data associated with study participants and their biospecimens, and distribution of materials for research and education. *NWBioSpecimen brochure: https://goo.gl/4gwa64*.

Tissue Microarray (TMA) construction is a service offered by NWBioSpecimen. This service provides a simple way for researchers to inquire about TMA construction, request work, and receive a finished TMA product. In addition to TMA construction, we also have the ability to punch blocks for tissue cores with high tumor cellularity (or other regions of interest) for downstream molecular analyses such as DNA sequencing.

Facilities and Equipment: The Tissue Microarray Facility is located in Room 421 of the Harborview Research & Training Building. TMAs are constructed using a Beecher MTA-1 tissue microarrayer, multiple tissue core punch sets of varying sizes, incubators, freezers, and vacuum sealers for long term storage of TMA blocks/unstained sections with desiccant.

All NWBioSpecimen services are associated with fees to recover the costs (personnel, equipment, supplies, etc.) of providing services. Fees are reviewed and formally approved through the UW Management Accounting & Analysis office.

Step 1: Inquiry

Researchers interested in TMA construction must first register their study with NWBioSpecimen by emailing NWBioS@uw.edu to obtain current Study Registration forms and instructions. Once these forms have been completed, the project will mature through the following steps:

- First inquiry and study registration
- Understanding around the project and drafting of a Statement of Work (SOW) and Budget estimate. If biospecimens are coming from UW, a feasibility query will be performed to determine the number of eligible biospecimens in our archives for use.
- Formal contract acceptance (external projects) or go-ahead (for internal projects)

The cost of constructing TMAs varies. If TMAs are made from blocks provided by the researcher, the costs will largely constitute consulting time from the Scientific Coordinator for TMA design and construction. If TMAs are made from blocks pulled from UW Medicine clinical archival materials, costs will additionally include Pathologist time for case review and tissue authorization. Final costs are influenced by the number of cases, replicates, and complexity of tissue being analyzed (e.g., cores of tumor only will be less complicated than obtaining multiple cores for tissue elements of tumor, normal, and infiltrative inflammation).

In general, a 5x5 array containing 25 spots will be expected to cost approximately $1250-1500. However, many aspects of the project must be taken into consideration when developing a Budget estimate. NWBioSpecimen will work with you to develop a SOW and Budget Estimate for grant applications and proposed research.

Step 2: TMA Construction

After the SOW and Budget have been accepted and all regulatory documentation has been reviewed, NWBioSpecimen will move forward with TMA construction:

- Case slides and formalin-fixed paraffin-embedded (FFPE) blocks may be pulled from the archives and reviewed by a pathologist for authorizing the use of tissue from each individual case. This ensures that appropriate diagnostic material is retained for each case in the CLIA archives in the event of future patient need.
- The Scientific Coordinator will work with the study team to design the layout of cases for the TMAs in a completely randomized fashion to reduce the effect that staining artifacts and regional tissue spot loss has on downstream analysis.
- Tissue cores will be extracted from donor FFPE blocks and inserted into the recipient TMA block(s) according to the design layout. TMAs will be neatly organized and leveled so that each cut section maximizes use of biospecimens.

Step 3: Finished TMA Product

Researchers can request cuts/stains of the completed TMA from NWBioSpecimen for their downstream research projects. Alternatively, researchers may obtain TMAs for sectioning in other histology laboratories. For longer term storage, TMA blocks are stored in a vacuum sealed environment with desiccant at 4°C. TMA sections are stored in a vacuum sealed environment with desiccant at -20°C. Although there are not extensive studies describing ideal storage conditions, there is some evidence that storing the slides in this way decreases antigen degradation[9-12].

Additionally, NWBioSpecimen offers slide scanning and digital image analysis through the Pathology Digital Imaging Core Facility (*Brochure: https://goo.gl/mLybCv*). This facility provides brightfield whole-slide histologic imaging suitable to prepare publication-quality figures and quantification of selected features from digitized images.

Example publications using TMAs constructed by the NWBioS group:

1. ***Imunohistochemical staining quantification of TMAs (Area quantification)***
   Trp53 haploinsufficiency modifies EGFR-driven peripheral nerve sheath tumorigenesis. 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.
2. ***Imunohistochemical staining quantification of TMAs (Area quantification)***
   Evaluation of protein biomarkers of prostate cancer aggressiveness. Rizzardi AE, Rosener NK, Koopmeiners JS, Isaksson Vogel R, Metzger GJ, Forster CL, Marston LO, Tiffany JR, McCarthy JB, Turley EA, Warlick CA,

Henriksen JC, Schmechel SC. BMC Cancer. 2014 Apr 5;14:244. doi: 10.1186/1471-2407-14-244. PMID: 24708576.

3. ***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. 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.

4. ***Cytoplasmic immunohistochemical staining quantification of TMAs (Cell quantification)***
   Canonical Wnt/β-catenin signaling drives human schwann cell transformation, progression, and tumor maintenance. 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.
5. ***Imunohistochemical staining quantification of TMAs (Area quantification)***
   Expression of FGFR3 and FGFR4 and clinical risk factors associated with progression-free survival in synovial sarcoma. 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.

6. ***Tissue classification of TMAs (Automated tumor selection)***
   Quantitative comparison of immunohistochemical staining measured by digital image analysis versus pathologist visual scoring. 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.

Example publications using TMA cores provided by the NWBioS group for complementary DNA (cDNA) and germline DNA sequencing:

7. ***cDNA sequencing***
   Expression of FGFR3 and FGFR4 and clinical risk factors associated with progression-free survival in synovial sarcoma. 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.

8. ***cDNA sequencing***
   AR intragenic deletions linked to androgen receptor splice variant expression and activity in models of prostate cancer progression. Li Y, Hwang TH, Oseth LA, Hauge A, Vessella RL, Schmechel SC, Hirsch B, Beckman KB, Silverstein KA, Dehm SM. Oncogene. 2012 Nov 8;31(45):4759-67. doi: 10.1038/onc.2011.637. Epub 2012 Jan 23. PMID 22266865.

Other Referenced Publications

9. Paraffin section storage and immunohistochemistry. Effects of time, temperature, fixation, and retrieval protocol with emphasis on p53 protein and MIB1 antigen. Wester K, Wahlund E, Sundström C, Ranefall P, Bengtsson E, Russell PJ, Ow KT, Malmström PU, Busch C. Appl Immunohistochem Mol Morphol. 2000 Mar;8(1):61-70. PMID 10937051.

10. Loss of tumor marker-immunostaining intensity on stored paraffin slides of breast cancer. Jacobs TW, Prioleau JE, Stillman IE, Schnitt SJ. J Natl Cancer Inst. 1996 Aug 7;88(15):1054-9. PMID 8683636.

11. Assessment of problems in diagnostic and research immunohistochemistry associated with epitope instability in stored paraffin sections. van den Broek LJ, van de Vijver MJ. Appl Immunohistochem Mol Morphol. 2000 Dec;8(4):316-21. PMID 11127924.

12. Evaluation of methods for preserving PTEN antigenicity in stored paraffin sections. Gelb AB, Freeman VA, Astrow SH. Appl Immunohistochem Mol Morphol. 2011 Dec;19(6):569-73. doi: 10.1097/PAI.0b013e318217a3d3. PMID 21552118.