OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

BIOGRAPHICAL SKETCH

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NAME: **Menke, Joshua R.**

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Assistant Professor of Clinical Pathology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
College of William and Mary, Williamsburg, VA	B.A.	06/2007	History
University of Florida, Gainesville, FL	M.D.	06/2011	Medicine
Mayo Clinic, Rochester, MN	Residency	06/2012	Anatomic and Clinical Pathology
University of California, San Francisco, CA	Residency	06/2015	Anatomic and Clinical Pathology
Johns Hopkins Hospital, Baltimore, MD	Instructor	06/2016	Surgical Pathology
University of California, San Francisco, CA	Fellowship	06/2017	Cytopathology
Stanford University, Stanford, CA	Fellowship	06/2018	Hematopathology

A. Personal Statement

As a pathologist trained in both cytopathology (study of small-volume specimens) and hematopathology (study of myeloid and lymphoid neoplasms), my principle goal is to apply advanced proteomic and genomic analytic techniques to small-volume cytology specimens, especially those obtained for diagnosing hematolymphoid malignancies. During the course of my post-graduate training, I have been fortunate to work in multiple advanced clinical diagnostic laboratories at different academic medical centers pursuing diagnostic test development and exploring new molecular pathogenic mechanisms. During my pathology residency at University of California San Francisco (UCSF), I helped develop a *CALR* mutation PCR assay by capillary electrophoresis in the UCSF Molecular Diagnostics laboratory. This work characterized the spectrum of *CALR* mutations found in a large series of myeloproliferative neoplasms, including three novel *CALR* mutations, and culminated with clinical validation of the *CALR* assay at UCSF. Recently, I published next generation sequencing (NGS) data from a case of mantle cell lymphoma with t(11;12) that localized the breakpoint on chromosome 12 to a non-coding region that eliminates miRNA interaction elements and suggests that cyclin D1 can be up-regulated through loss of inhibition (Menke et al, Hum Pathol 2017). Most recently and relevant to the current proposal, I am funded by the UCSF Clinical Cancer Genomics Laboratory (CCGL) to optimize liquid based specimens, such as fine needle aspiration biopsy and body fluid supernatants, for established UCSF NGS platforms. This work has involved extensive analysis of various pre-analytic variables unique to cell-free tumor DNA, including comparing cell-free nucleic acid extraction kits originally designed for use on plasma. Early unpublished results show supernatants from malignant body effusion samples show marked enrichment for cell-free DNA with median DNA yields of 679 ng from only 1 ml of sample. Despite being a rich source of genetic material, cytology samples are drastically underutilized in the molecular diagnostic sphere (Ljung and Menke, Cancer Cytopathology 2017). I am excited to contribute my research experience in cell-free molecular diagnostics and assay development and my clinical experience as a combined cytopatholgoist and hematopathologist to this proposal and apply the advanced cell-free DNA analytic techniques to hematolymphoid malignancies.

B. Positions and Honors

Positions and Employment

2018-present Assistant Professor of Clinical Pathology, Departments of Pathology and Laboratory Medicine, University of California, San Francisco

Other Experience and Professional Memberships

2011-present College of American Pathologists, Member
2012-present Digital Pathology Association, Member
2012-present United States and Canadian Academy of Pathology, Member
2013-present American Society for Clinical Pathology, Member and former UCSF Resident Representative
2016-present American Society of Cytopathology, Member
2018-present South Bay Pathology Society, Member
2019-present Society for Hematopathology, Member

Honors

2008 Kaira Award for Endocrine Physiology, University of Florida College of Medicine
2010 Alpha Omega Alpha Medical Honor Society, University of Florida College of Medicine
2011 Dr. Sigurd J. Normann Excellence in Pathology Award, University of Florida College of Medicine
2012 Academic Achievement Award, Bronze Level, Mayo Graduate Medical Education
2012 O.T. Bailey-Helena Riggs Award for Best Presentation at the Diagnostic Slide Session, American Association of Neuropathologists
2014 Paul E. Strandjord Young Investigator Award, Academy of Clinical Laboratory Physicians and Scientists
2014 Laurence J. Marton Award for Excellence in Research, University of California San Francisco

C. Contribution to Science

1. One of my most significant contributions to science is the discovery of somatostatin receptor 2a (SSTR2a) as a biomarker of meningiomas. SSTR2a is the most sensitive and specific immunohistochemical marker of meningioma when compared to other markers such as epithelial membrane antigen (EMA) and progesterone receptor (PR); UCSF neuropathology uses this immunostain extensively to date on consult and in house cases as a result of these findings. For this paper, I was involved with concept design; data acquisition, analysis and interpretation; and drafting of the manuscript. Specifically, I retrospectively searched the UCSF pathology archives over a 10 year period to identify cases of meningioma for inclusion. I reviewed slides and selected blocks from each case for tissue microarray (TMA) construction and made a TMA master key for easy identification of each case. After sections from the TMA were stained with a monoclonal antibody against SSTR2a and scored by an outside pathologist, I also independently scored the TMA slides for SSTR2a immunostaining for all cases. I drafted the manuscript, designed the figures, and aided with statistical analysis.
    a. Menke JR, Raleigh DR, Gown AM, Thomas S, Perry A, Tihan T. Somatostatin receptor 2a is a more sensitive diagnostic marker of meningioma than epithelial membrane antigen. Acta Neuropathol. 2015 Sep; 130(3):441-3. PMID: 26195322

2. My second major contribution is describing unusual translocations in a series of mantle cell lymphoma, including one case with a t(11;12) that had a novel mechanism of CCND1 upregulation. Instead of the canonical t(11;14) IGH-CCND1 fusion that upregulates CCND1 in the majority of mantle cell lymphoma, next generation sequencing confirmed the breakpoint on chromosome 12 was agency, and instead mapped to a microRNA binding site. In this case, loss of microRNA inhibition was hypothesized to lead to CCND1 overexpression and lymphomagenesis. For this paper, I was involved with concept design; data acquisition, analysis and interpretation; and drafting of the manuscript. Specifically, I obtained images of the H&E stained sections and immunostains and cytogenetic karyotype results. I was also involved with interpretation of next generation sequencing data. I drafted the manuscript and designed the figures.
    a. Menke JR, Vasmatzis G, Murphy S, Yang L, Menke DM, Tun HW, King RL, Smoley SA, Ketterling RP, Sukov WR. Mantle cell lymphoma with a novel t(11;12)(q13;p11.2): a proposed alternative mechanism of CCND1 up-regulation. Hum Pathol. 2017 06; 64:207-212. PMID: 28132860

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1-wi189UquckG/bibliography/42399821/public/?sort=date&direction=ascending

D. Research Support

On-going Research Support

UCSF Clinical Cancer Genomics Lab (CCGL) Research Award Menke (PI)06/01/19-
Next Generation Sequencing of Body Fluid Supernatant Samples
Liquid-based samples are rapidly emerging as an important substrate for molecular testing. For instance, body fluid samples that are easily obtained from various anatomic sites, such as cerebrospinal fluid, urine, peritoneal fluid, pancreatic cysts, saliva, among others, have been shown in small studies to be enriched for tumor cell-free DNA (cfDNA). These tumor cfDNA fragments can be optimized for the full range of next-generation sequencing (NGS), from whole-genome sequencing to a limited gene panel. Similarly, fine needle aspiration (FNA) supernatants are also enriched for tumor cfDNA with higher yield, better nucleic acids quality, and higher tumor DNA fraction compared to formalin-fixed tissues. Various cfDNA extraction kits are available for use on plasma samples for detecting plasma cfDNA, but are not well studied in cytology samples.
We hypothesize that we can retrieve sufficient concentrations of nucleic acids for NGS from supernatants from body fluids performed for various new cancer diagnoses. Furthermore, we hypothesize that important prognostic, diagnostic, and therapeutic data can be derived from these specimens. Repurposing supernatants for required genetic testing may obviate the need for additional surgical interventions, and cell block FFPE can be saved for immunohistochemistry and other protein-based testing.
Aims: 1) Obtain sufficient DNA from body fluids supernatants for UCSF500 gene sequencing panel 2) Compare tumor mutational landscape obtained from supernatant sample with primary tumor excision specimen when available
Role: Principal Investigator

Completed Research Support

UCSF Pathology Department Resident Research Award Tihan (PI) 05/01/15-05/01/16
Meningioma Biomarkers Studied by Tissue Microarray
Along with several UCSF neuropathologists, I was granted this award to construct a tissue microarray (TMA) from formalin fixed paraffin-embedded tissue blocks from 176 meningiomas resected at UCSF between over a 10 year period. Immunostains for epithelial membrane antigen (EMA), progesterone (PR), and somatostatin receptor 2a (SSTR2a), were performed on the TMA blocks. Other mesenchymal tumors, including schwannomas, cellular schwannomas, malignant peripheral sheath tumors, and hemangiopericytomas, were also stained with SSTR2a. All 176 meningiomas demonstrated staining with SSTR2a, while 168 cases stained with EMA in both punches and 136 cases stained with PR in both punches. SSTR2a also reliably distinguished meningiomas from other mesenchymal tumors.
The meningioma TMA has also been used for several other investigators to identify new meningioma biomarkers since its construction.
Role: Research Associate