BIOGRAPHICAL SKETCH

NAME: Vezina, Chad M

eRA COMMONS USER NAME (agency login): CMVEZINA

POSITION TITLE: Associate Professor (with tenure)

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
St. Olaf College	B.A.	05/1998	Chemistry, Biology
University at Buffalo	Ph.D.	08/2003	Pharmacology and Toxicology

A. Personal Statement

Qualifications as Project 2 Co-Director: I have been conducting urologic research for over 16 years and have co-directed project 2 for four years. I am uniquely qualified to co-direct the current project 2 proposal, as it involves spatial mapping and quantification of cell types in mouse and human. I having served for nine years as a molecular anatomical mapping expert for mouse and human prostate as part of the GenitoUrinary Development Molecular Anatomy Project (GUDMAP). I collaborated with the Project 2 co-PI, Dr. Strand, to generate a new cellular-resolution map of the young adult human prostate, published in (Henry et al Cell Reports in 2019). Project 2 also requires use of mouse genetic models. I developed deep understanding of these approaches through the GUDMAP project I currently direct, which maps fifteen *cre* recombinase mouse strains to various prostatic stromal cell populations. Project 2 demands a sensitive and quantitative method for measuring collagens in mouse and human prostate. My group developed and published a new method for this purpose (Wegner et al J Histochem Cytochem 2017). Critical to Project 2's success is the ability to accurately phenotype mouse urinary physiology, a subject in which I am intimately familiar, having developed software (Void Whizzard) and optimized cystometric and spontaneous voiding assays for this purpose.

Qualifications in Community Outreach and Mentoring as for the Administrative Core: I will commit effort to the administrative core, where I will expand extramural collaborations and coordinate mentoring efforts. I am an active participant in urological and toxicological research fields, with roles as president of the Midwest Regional chapter of the Society of Toxicology and planning committee member for meetings of the Society of Toxicology, American Urological Society, and Society of Basic Urologic research. I view my role in developing the next generation of scientists as the most important and rewarding aspect of my career. I developed an online course for K award applicants in conjunction with the American Urological Association (I am a Member at Large candidate). I serve as a standing NIH study section member for career development (K) awards. I have been a faculty instructor for the Cold Spring Harbor Mouse Development, Stem Cells & Cancer Course and the Jackson Laboratories Workshop on Techniques in Modeling Human Cancer in Mice. I am an external advisor for NIH K12 and R25 career development programs. I am a member of the trainee affairs committee of the Society of Basic Urologic Research. I am director of the UW-Madison Molecular and Environmental Toxicology Graduate Program. I direct the UW-Madison Summer Program in Undergraduate Urology Research (SPUUR).

Qualifications as effective Obrien Center Collaborator: I have productive working relationships with all Obrien Center leaders. I co-authored three manuscripts with my Project 2 co-director (Dr. Stand) and my graduate student is now a post-doc in his lab. Dr. Bjorling (biomedical core) and I are co-investigators on an NIH R01 project, will be on another that recently received a fundable score, and we have co-authored nine manuscripts. Dr. Ricke (Center and Project 1 director) and I are collaborators on one R01 grant and have co-authored twelve manuscripts. Dr. Macoska (project 3 director) and I have visited each other's institutions at least four times in the last 12 months and have co-authored two manuscripts.

B. Positions and Honors

Positions and Employment

1998 - 2003	Research Assistant, University at Buffalo
2003 - 2009	Post-doctoral Fellow, University of Wisconsin Madison
2015 -	Associate Professor (with tenure), University of Wisconsin-Madison, Comparative Biosciences
2015 -	Affiliate Associate Professor, University of Wisconsin-Madison, Pharmaceutical Sciences
2015 -	Adjunct Associate Professor, University of Wisconsin-Madison, Urology
2015-	Director, Summer Program in Undergraduate Urology Research (SPUUR)
2017- 2018	Associate Director, Molecular and Environmental Toxicology Center, University of Wisconsin-Madison
2019-	Director, Molecular and Environmental Toxicology Center, University of Wisconsin-Madison

Other Experience and Professional Memberships

1999 -	Member, Society of Toxicology
2009 -	Member, GenitoUrinary Development Molecular Anatomy Project (GUDMAP)
2011 -	Member, Society for Basic Urologic Research
2012 -	Grant Reviewer, Medical Research Council (MRC) Molecular & Cellular Medicine Board, Swindon UK
2013 -	Editorial Board Member, American Journal of Clinical and Experimental Urology
2014 -	Grant Reviewer, NIH/NIDDK Special Emphasis Review Panel ZDK1 GRB-S (M1)
2014 -	Grant Reviewer (ad hoc), NIH/NIDDK Review Panel UGPP
2014 -	Grant Reviewer, NIH/NIDDK Special Emphasis Review Panel ZRG1 DKUS-P (80) S
2014 -	Editorial Board Member, American Journal of Physiology – Renal Physiology
2014 -	Grant Reviewer, UW-Madison Institute for Clinical and Translational Research (NIH CTSA)
2015 -	Grant Reviewer (ad hoc), Veterans Administration SURG1 Review Panel
2015 -	Grant Reviewer, NIH/NIDDK Special Emphasis Review Panel ZDK1 GRB-S (O4)
2016 -	Member, American Physiological Society
2016 -	Standing Member, NIH/NIDDK DDK-D Study Section
2016	Program Committee, American Urological Association (AUA) Summer Research Conference "Targeting Epigenetics and Genome Regulation to Improve Urologic Health," Lithicum, MD, 2016
2017	Invited Subject Matter Expert for creation of an online training module for NIH K-series career development awards for the American Urological Association (AUA)

Honors

2002	Society of Toxicology Colgate Palmolive Award for In Vitro Toxicology, Society of Toxicology (SOT)
2008	Manuscript “Dioxin causes ventral prostate agenesis by disrupting dorsoventral patterning in developing mouse prostate” selected as finalist Best Reproductive/Developmental Toxicology Paper in Toxicological Sciences, Society of Toxicology
2012	Young Investigator (of the year) Award, Young Investigator Award, Society for Basic Urologic Research (SBUR)
2016	Zoetis Award for Veterinary Research Excellence (given annually to top research in the UW-Madison School of Veterinary Medicine)

C. Contribution to Science

1. My group led efforts for assay optimization and distributed free software for evaluating mouse voiding function with the non-invasive void spot assay.
    a. Hill WG, Zeidel ML, Bjorling DE, **Vezina CM**. 2018. The Void Spot Assay: Recommendations on the Use of a Simple Micturition Assay for Mice. Am J Physiol Renal Physiol 2018 Nov 1;315(5):F1422-F1429. PubMed PMID: 30156116; PubMed Central PMCID: PMC6293303.
    b. Wegner KA, Abler LL, Oakes SR, Mehta GS, Ritter KE, Hill WG, Zwaans BM, Lamb LE, Wang Z, Bjorling DE, Ricke WA, Macoska J, Marker PC, Southard-Smith EM, Eliceiri KW, **Vezina CM**. Void

spot assay procedural optimization and software for rapid and objective quantification of rodent voiding function, including overlapping urine spots. Am J Physiol Renal Physiol. 2018 Oct 1;315(4):F1067-F1080. PubMed PMID: 29972322; PubMed Central PMCID: PMC6230749.

c. Keil KP, Abler LL, Altmann HM, Bushman W, Marker PC, Li L, Ricke WA, Bjorling DE, **Vezina CM**. Influence of animal husbandry practices on void spot assay outcomes in C57BL/6J male mice. Neurourol Urodyn. 2016 Feb;35(2):192-8. PubMed PMID: PMC4428995.

d. Bjorling DE, Wang Z, **Vezina CM**, Ricke WA, Keil KP, Yu W, Guo L, Zeidel ML, Hill WG. Evaluation of voiding assays in mice: impact of genetic strains and sex. Am J Physiol Renal Physiol. 2015 Jun 15;308(12):F1369-78. PubMed PMID: 25904700; PubMed Central PMCID: PMC4469884.

2. An incomplete map of the prostate made it impossible to determine the critical cell-cell signaling events involved in its development. My laboratory used mRNA expression as a means to improve the map's resolution. We developed a high-throughput method for visualizing and characterizing prostate cell- and developmental stage-specific expression patterns for over 100 unique mRNAs. We defined new prostate cell populations based on mRNA expression signatures and built a single-cell resolution atlas of mouse prostate and adjacent tissues. We recently assembled a human prostate map using similar principles:

   a. Henry GH, Malewska A, Joseph DB, Malladi VS, Lee J, Torrealba J, Mauck RJ, Gahan JC, Raj GV, Roehrborn CG, Hon GC, MacConmara MP, Reese JC, Hutchinson RC, **Vezina CM**, Strand DW. A Cellular Anatomy of the Normal Adult Human Prostate and Prostatic Urethra. Cell Rep. 2018 Dec 18;25(12):3530-3542.e5. PubMed PMID: 30566875; PMCID: In Process.

   b. Georgas KM, Armstrong J, Keast JR, Larkins CE, McHugh KM, Southard-Smith EM, Cohn MJ, Batourina E, Dan H, Schneider K, Buehler DP, Wiese CB, Brennan J, Davies JA, Harding SD, Baldock RA, Little MH, **Vezina CM**, Mendelsohn C. An illustrated anatomical ontology of the developing mouse lower urogenital tract. Development. 2015 May 15;142(10):1893-908. PubMed PMID: 25968320; PubMed Central PMCID: PMC4440924.

   c. Keil KP, Mehta V, Abler LL, Joshi PS, Schmitz CT, **Vezina CM**. Visualization and quantification of mouse prostate development by in situ hybridization. Differentiation. 2012 Oct;84(3):232-9. PubMed PMID: 22898663; PubMed Central PMCID: PMC3443266.

   d. Abler LL, Keil KP, Mehta V, Joshi PS, Schmitz CT, **Vezina CM**. A high-resolution molecular atlas of the fetal mouse lower urogenital tract. Dev Dyn. 2011 Oct;240(10):2364-77. PubMed PMID: 21905163; PubMed Central PMCID: PMC3583531.

   e. Abler LL, Mehta V, Keil KP, Joshi PS, Flucus CL, Hardin HA, Schmitz CT, **Vezina CM**. A high throughput in situ hybridization J Vis Exp. method to characterize mRNA expression patterns in the fetal mouse lower urogenital tract. J Vis Exp. 2011 Aug 19;PubMed PMID: 21876526; PubMed Central PMCID: PMC3177421.

3. My group identified beta-catenin signaling as a mediator of androgen action. We found that androgens activate beta-catenin in the developing prostate, beta-catenin dependent signals are among the first to mark prostate ducts, and the androgens directly regulate the beta-catenin responsive gene Wnt Inhibitory factor 1. Further, we demonstrated that beta-catenin functions by the activation-inhibition model to pattern prostate development. In other words, small population of cells activate beta-catenin while producing diffusible that inhibit duct formation nearby, yielding periodically spaced ducts, and informing the beta-catenin role in hyperplasia. We recently showed that beta-catenin controls ectodysplasin receptor expression, collagen density and collagen fiber orientation. We found that beta-catenin is upregulated in human BPH specimens, indicating a potential reawakening of this prostate developmental signaling pathway.

   a. Wegner KA, Mehta V, Johansson JA, Mueller BR, Keil KP, Abler LL, Marker PC, Taketo MM, Headon DJ, **Vezina CM**. Edar is a downstream target of beta-catenin and drives collagen accumulation in the mouse prostate. Biol Open. 2019 In Press. PubMed PMID: 30745437. (open access journal).

   b. Wegner KA, Keikhosravi A, Eliceiri KW, **Vezina CM**. Fluorescence of Picrosirius Red Multiplexed With Immunohistochemistry for the Quantitative Assessment of Collagen in Tissue Sections. J Histochem Cytochem. 2017 Aug;65(8):479-490. PubMed PMID: 28692327; PubMed Central PMCID: PMC5533271.

c. Bauman TM, **Vezina CM**, Huang W, Marker PC, Peterson RE, Ricke WA. Beta-catenin is elevated in human benign prostatic hyperplasia specimens compared to histologically normal prostate tissue. Am J Clin Exp Urol. 2014;2(4):313-22. PubMed PMID: 25606577; PubMed Central PMCID: PMC4297327.
d. Mehta V, Schmitz CT, Keil KP, Joshi PS, Abler LL, Lin TM, Taketo MM, Sun X, **Vezina CM**. Beta-catenin (CTNNB1) induces Bmp expression in urogenital sinus epithelium and participates in prostatic bud initiation and patterning. Dev Biol. 2013 Apr 15;376(2):125-35. PubMed PMID: 23396188; PubMed Central PMCID: PMC3602957.
e. Keil KP, Mehta V, Branam AM, Abler LL, Buresh-Stiemke RA, Joshi PS, Schmitz CT, Marker PC, **Vezina CM**. Wnt inhibitory factor 1 (Wif1) is regulated by androgens and enhances androgen-dependent prostate development. Endocrinol. 2012 Dec;153(12):6091-103. PubMed PMID: 23087175; PubMed Central PMCID: PMC3512059.

4. My group was the first to establish key regulatory mechanisms of DNA methylation in prostate proliferative growth. We mapped expression of DNA methylation modifying genes during mouse prostatic development and found they change in pattern as development proceeds. We found that the function of DNA methylation also changes as prostate development proceeds. In early development, DNA methylation of the androgen receptor protects against precocious development by restricting male hormone action. Later in development, DNA methylation of e-cadherin represses cell adhesion to permit ductal elongation into surrounding tissue. We also demonstrated that folic acid, a dietary methyl donor, improves urinary function in a mouse model of bladder outlet obstruction.

a. Joseph DB, Chandrashekar AS, Abler LL, Chu LF, Thomson JA, Mendelsohn C, **Vezina CM**. In vivo replacement of damaged bladder urothelium by Wolffian duct epithelial cells. Proc Natl Acad Sci U S A. 2018 Aug 14;115(33):8394-8399. PMID: 30061411; PubMed Central PMCID: 6099915.
b. Keil KP, Abler LL, Altmann HM, Wang Z, Wang P, Ricke WA, Bjorling DE, **Vezina CM**. Impact of a folic acid-enriched diet on urinary tract function in mice treated with testosterone and estradiol. Am J Physiol Renal Physiol. 2015 Jun 15;308(12):F1431-43. PubMed PMID: 25855514; PubMed Central PMCID: PMC4469891.
c. Keil KP, Abler LL, Laporta J, Altmann HM, Yang B, Jarrard DF, Hernandez LL, **Vezina CM**. Androgen receptor DNA methylation regulates the timing and androgen sensitivity of mouse prostate ductal development. Dev Biol. 2014 Dec 15;396(2):237-45. PubMed PMID: 25446526; PubMed Central PMCID: PMC4261055.
d. Keil KP, Abler LL, Mehta V, Altmann HM, Laporta J, Plisch EH, Suresh M, Hernandez LL, **Vezina CM**. DNA methylation of E-cadherin is a priming mechanism for prostate development. Dev Biol. 2014 Mar 15;387(2):142-53. PubMed PMID: 24503032; PubMed Central PMCID: PMC3976955.

Complete List of Published Work in My Bibliography (**74 Total Publications**):
http://1.usa.gov/1TntVvX

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

R01DK099328-01A1 07/15/14-06/30/19
NIDDK
Role of DNA methylation in prostate glandular development and urinary function: The goal is to determine the requirement of DNA methyltransferase in prostate development and urinary function
Role: Principal Investigator

R01ES001332-01A1 (PIs: Vezina/Peterson) 06/01/78-07/31/22
NIEHS
Reproductive and Developmental Toxicity of Dioxin: This proposal is to elucidate the mechanistic connection between TCDD exposure and urinary function; the proposed studies launch original lines of research into a disease process never before linked to developmental origins or AHR signaling.
Role: Principal Investigator

U01DK110807 07/01/16-06/30/21
NIDDK
Molecular and fate maps of prostatic stroma Roles of beta-catenin in urinary dysfunction: The goal is to create cell lineage, RNA, and protein maps across mouse and human prostatic stroma.
Role: Principal Investigator

U54DK104310 (PI: Ricke) 09/24/14-07/31/19
NIDDK
George M. O'Brien Urology Cooperative Research Centers Program: Mediators of fibrosis in the development of lower urinary tract dysfunction. The goal of this is to determine the role of hormones and other mediators of fibrosis in the development of BPH/LUTS.
Role: Principal Investigator of project “Roles of beta-catenin in urinary dysfunction”

R01CA204320 (PI: Shull) 03/01/17-02/28/22
NCI
Characterization of Emca4, the Rat Ortholog of the 8q24 Breast Cancer Risk Locus: The goal is to examine the role of Emca4 in breast cancer risk.
Role: Co-Investigator

T32 ES007015 (PI: Bradfield) 07/01/18-06/30/23
NIEHS
Molecular & Environmental Toxicology Pre- and Postdoctoral Training Grant: The goal is to provide mentored training for pre- and post-doctoral toxicology trainees at UW-Madison.
Role: Co-Investigator (Deputy Director)

R01HD094759-01 (PI: Hernandez) 07/20/18-04/30/23
NICHD
Influence of SSRI Use During Pregnancy and Lactation on Maternal Bone Health: The goal is to determine whether fluoxetine use during pregnancy sensitizes to osteoporotic bone diseases later in life.
Role: Co-Investigator

F31ES028594-01A1 (PI: Wegner) 04/01/18-03/31/20
TCDD reprograms prostate stroma and causes fibrosis to induce urinary dysfunction: The goal is to determine whether in utero and lactational exposure to TCDD causes prostatic fibrosis and voiding dysfunction.
Role: Primary Mentor

Completed Research Support
None