

**BIOGRAPHICAL SKETCH**

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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	BA	05/1998	Chemistry, Biology
University at Buffalo	PHD	08/2003	Pharmacology and Toxicology

**A. Personal Statement**

I am an Associate Professor of Comparative Biosciences at the University of Wisconsin-Madison School of Veterinary Medicine and a member of the University of Wisconsin-Madison George M. O'Brien Center for Benign Urology Research. My current research examines how the urinary tract develops and the mechanisms responsible for prostate-related urinary dysfunction in men. I am actively involved in building new research model systems and tools for microscopic image analysis and urodynamic testing in rodent models. I have dedicated substantial effort to resolving the landscape of the prostate through molecular mapping studies as part of the NIH-sponsored GenitoUrinary Development Molecular Anatomy Project (GUDMAP). I am also embedded in the urologic and toxicologic 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 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 created and lead the UW-Madison Summer Program in Undergraduate Urology Research. I have served as primary research mentor to 3 post-doctoral trainees, 6 PhD trainees, 3 veterinary trainees, 21 undergraduates and 3 high school students. Trainees in my laboratory have been productive and successful, evidenced by a rich publication record and numerous prestigious awards earned during and after tenure in my lab (Rhoades scholarship Finalist, Barry Goldwater Scholarship, NSF graduate research fellowship, NIEHS T32, F31 and K99 fellowships) and by placement in outstanding academic and industry positions. I have also served on 36 PhD/MS dissertation committees, 5 NIH post-doctoral fellow committees, and 6 junior faculty committees.

**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. An incomplete map of the developing 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.
  - a. 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](#).
  - b. 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](#).

- c. 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](#).
  - d. Abler LL, Mehta V, Keil KP, Joshi PS, Flucus CL, Hardin HA, Schmitz CT, Vezina CM. A high throughput in situ hybridization 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](#).
2. My group identified beta-catenin signaling as being a mediator of androgen action. We found that androgens activate the beta-catenin pathway in the developing prostate, beta-catenin dependent signals are among the first to mark nascent prostatic ducts, and the beta-catenin responsive gene Wnt Inhibitory factor 1 is directly regulated by androgens. Further, we demonstrated that beta-catenin functions by the activation-inhibition model to pattern prostate development. In other words, beta-catenin is activated in a small population of cells to activate prostatic duct formation, while producing diffusible that inhibit duct formation nearby, yielding periodically spaced ducts. These results shed new light on how positive and negative paracrine signals are orchestrated by prostatic epithelium. We also determined that beta-catenin is upregulated in human BPH specimens, indicating a potential reawakening of this prostate developmental signaling pathway.
- a. 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](#).
  - b. 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](#).
  - c. 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. *Endocrinology.* 2012 Dec;153(12):6091-103. PubMed PMID: [23087175](#); PubMed Central PMCID: [PMC3512059](#).
  - d. Mehta V, Abler LL, Keil KP, Schmitz CT, Joshi PS, Vezina CM. Atlas of Wnt and R-spondin gene expression in the developing male mouse lower urogenital tract. *Dev Dyn.* 2011 Nov;240(11):2548-60. PubMed PMID: [21936019](#); PubMed Central PMCID: [PMC3177998](#).
3. 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](#).
  - 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](#).
4. My group has lead 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. In Press.
- 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](#).
- 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](#).

Complete List of Published Work in My Bibliography (74 Total Publications):

<http://1.usa.gov/1TntVvX>

## D. Research Support

### Ongoing Research Support

R01 DK099328-01A1

Vezina, Chad M (PI)

07/15/14-06/30/19

Role of DNA methylation in prostate glandular development and urinary function

Role: PI

R01ES001332-01A1, National Institute of Environmental Health Sciences (NIEHS)

Vezina, Chad M (PI) and Peterson, Richard E, Co-PI)

08/01/2017-07/31/2022

Reproductive and Developmental Toxicity of Dioxin

Role: PI

U01DK110807, National Institute of Diabetes and Digestive and Kidney Diseases

Vezina, Chad (PI)

7/1/16-6/30/21

Molecular and fate maps of prostatic stroma Roles of beta-catenin in urinary dysfunction

The goal is to elucidate beta-catenin roles in lower urinary tract fibrosis and urinary dysfunction.

The goal is to create cell lineage, RNA, and protein maps across mouse and human prostatic stroma.

Role: PI

U54DK104310, National Institute of Diabetes and Digestive and Kidney Diseases

Ricke, William (PI)

09/24/14-07/31/19

Mediators of fibrosis in the development of lower urinary tract dysfunction

Role: PI of project "Roles of beta-catenin in urinary dysfunction"

R01CA204320, National Cancer Institute

Shull, James (PI)

1/1/2017-12/31/2018

Characterization of Emca4, the Rat Ortholog of the 8q24 Breast Cancer Risk Locus

Role: Co-Investigator

F31ES028594-01A1 National Institute of Environmental Health Sciences (NIEHS)

Kyle Wegner (PI)

4/1/2018-3/30/2019

TCDD reprograms prostate stroma and causes fibrosis to induce urinary dysfunction

Role: Primary Mentor

T32 ES007015 National Institute of Environmental Health Sciences (NIEHS)

Christopher Bradfield (PI)

7/01/2018-6/30/2023

Molecular & Environmental Toxicology Pre- and Postdoctoral Training Grant

Role: Co-Investigator (Deputy Director)

R01 HD094759-01 National Institute of Child Health and Human Development

Laura Hernandez (PI)

07/20/2018 – 04/30/2023

Influence of SSRI Use During Pregnancy and Lactation on Maternal Bone Health

Role: Co-Investigator

### **Completed Research Support**

R01ES001332, National Institute of Environmental Health Sciences (NIEHS)

Peterson, Richard E. (PI)

09/01/10-08/31/15

Reproductive and Developmental Toxicity of Dioxin

The goal is to identify molecular mechanisms responsible for impaired mouse prostate development and increased prostate disease risk following in utero and lactational TCDD exposure.

Role: Co-Investigator

P20DK097826, National Institute of Diabetes and Digestive and Kidney Diseases

Bushman, Wade (PI)

09/29/12-08/31/15

Urinary Biomarkers of Lower Urinary Tract Symptoms (LUTS) in Men

Role: Co-Investigator