BIOGRAPHICAL SKETCH

NAME: Bjorling, Dale

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

POSITION TITLE: Professor and Associate Dean for Research and Graduate Training

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
University of Illinois, Champaign, IL	B.S.	05/1976	Veterinary Medicine
University of Illinois, Champaign, IL	D.V.M.	05/1978	Veterinary Medicine
University of Georgia, Athens, GA	M.S.	05/1982	Physiology
University of Oklahoma, Norman, OK	Other training	05/1974	Zoology
University of California, Davis, CA	Other training	06/1979	Internship
University of Georgia, Athens, GA	Resident	06/1982	Small Animal Surgery

A. PERSONAL STATEMENT

Qualifications as Biomedical Core Director

My laboratory has a long-standing interest in investigation of mechanisms underlying bladder pain and inflammation. I am currently co-Director of the University of Wisconsin George M. O'Brien Center in Benign Urologic Research and Director of the Biomedical Core of the Center. I developed and direct the Rodent Urinary Tract Function Testing (RUFT) Laboratory, a facility that has supported research performed as part of all three projects in the initial funding cycle of the Center. These activities have resulted in multiple publications co-authored by the Principal Investigators of these projects, Drs. Ricke, Vezina, and Macoska. We have also published a description of performance of the void spot assay and are in the process of creating a Wiki page to provide investigators with information on performance of uroflowmetry. This webpage will also provide investigators with access to software we have developed for collection of videorecording of individual voids by mice. We have also collaborated with a number of investigators on studies entailing assessment of lower urinary tract function in mice. Collaborating institutions include Harvard University, Johns Hopkins University, Oakland University William Beaumont School of Medicine, University of Texas-Southwestern, Vanderbilt University, and Washington University, St. Louis. These collaborations have resulted in a publication with Dr. Michelle Southard Smith at Vanderbilt, and other manuscripts are in preparation. Dr. Southard Smith had an NIH R01 application (R01 DK120025) funded subsequent to publication of this paper, and the RUFT lab provided data for the application and will perform testing as part of the work supported by this award. The RUFT laboratory served as a consultant for an NIH application by Dr. Arthur Burnett of Johns Hopkins University that was not funded. Other NIH awards for which the RUFT provided data and support include R01 ES001332 (Richard Peterson, PI), F31 ES028594 (Kyle Wegner, PI), K99 ES029537 (Kim Keil, PI), K01 DK114334 (Bernadette Zwaans, PI), and a TL1 award from the University of Wisconsin Clinical and Translational Science Award (CTSA) to support graduate training of Hannah Ruetten. A recent NIH R01 application for which I am lead PI and Dr. Jianghui Hou, Washington University, St. Louis, is co-PI received a priority score of 25 that placed it in the 11th percentile. This application evolved from work performed in the RUFT in collaboration with Dr. Hou.

B. POSITIONS AND HONORS

Positions and Employment

1982-85	Assistant Professor, University of Georgia, Department of Small Animal Medicine, Athens, GA
1983-84	Assistant Professor , University of Georgia, Department of Physiology and Pharmacology, Athens, GA
1985-88	Assistant Professor, University of Wisconsin, Department of Surgical Sciences, Madison, WI

1988-94	Associate Professor, University of Wisconsin, Department of Surgical Sciences, Madison, WI
1988-11	Department Chair, University of Wisconsin, Department of Surgical Sciences, Madison, WI
1994	Professor, University of Wisconsin, Department of Surgical Sciences, Madison, WI
2008	Professor, University of Wisconsin, Department of Urology, Madison, WI
2011	Associate Dean for Research , University of Wisconsin, School of Veterinary Medicine, Madison, WI

Other Experience and Professional Memberships

2008-	Member, NIH Comparative Medicine SEP ZRR1 CM-B
2008	Member, NIH NCRR ZRR1 CM-3 SEP
2009	Member, VA Merit Review Neurodegenerative SEP
2010	Member, NIH UKGD Study Section Ad Hoc
2011	Member, USDA NIFA NCAC002 Animal Health Advisory Committee
2011-12	Member, NIH NIDDK SEP ZDK1 GRB-6 (01)
2014	Member, NIH CSR ZRG1 IMST-S (80) SEP
2014	Member, NIH NIDDK ZRG1 DKUS-G (90) SEP
2015	Member, NIH NIDDK ZRG1 DKUS-N (90) SEP
2016	Member, NIH NIDDK ZDK1 GRB-2 (M3) GUDMAP RFA
2017	Member, NIH ZRG1 IMST-U (80) Mentored Training in Comparative and Veterinary Medicine (T32 & K01)
2017	Member, Department of Defense PRMPR Program Application Review
2017	Member, USDA NCAC-02 Program Review
2018	Member, NIH GRB-M (O2) Bladder Function P01
2018	Member, NIH ZDK1 GRB-M (O1) Bladder Physiology P01
2018	Member, NIH ZRG1 IMST-D (80) Training in Comparative and Veterinary Medicine (T32 & T35)
2018	Member, NIH ZDK1-GRB-3 (J2) NIDDK Undergraduate Summer Research Applications (R25)
2018	ZDK1 GRB-6 (O1) Program Project Review (P01)

Honors

1976	BS with Honors, University of Illinois
1978	DVM with Honors, University of Illinois
1985	Diplomate (by examination), American College of Veterinary Surgeons
2006	International Award for Scientific Achievement, World Small Animal Veterinary Association

C. Contributions to Science

1. It has been conclusively demonstrated that cannabinoids (including endocannabinoids) have the capacity to decrease pain and inflammation in peripheral tissues. Recent research demonstrates that this is also true for visceral organs, including the bladder. Opioids are currently the most common drug option for treatment of chronic, intense bladder pain. Unfortunately, opioids have an undesirable side-effect profile, making manipulation of endocannabinoid concentrations an attractive alternative. We have observed that endocannabinoids can mitigate bladder pain and inflammation in experimental models. However, the mechanisms by which cannabinoids exert these effects, as well as the anatomical location (e.g., bladder urothelium, peripheral innervation, DRG, spinal cord, brain) remain unclear. Our research indicates that determining the location and mechanism by which cannabinoids (and endocannabinoids) will facilitate modulation of pain and inflammation of the lower urinary tract.

    a. Merriam FV, Wang ZY, Guerios SD, **Bjorling DE**. Cannabinoid receptor 2 is increased in acutely and chronically inflamed bladder of rats. Neurosci Lett 2008 445:130-134. PubMed Central PMCID: PMC2592089.

b. Merriam FV, Wang ZY, Hillard CJ, Stuhr KL, **Bjorling DE**. Inhibition of fatty acid amide hydrolase suppresses referred hyperalgesia induced by bladder inflammation. 2011 Brit J Urol Internat 108:1145-1149. PubMed Central PMCID: PMC3505723.
c. Wang Z-Y, Wang P, **Bjorling DE**. Activation of cannabinoid receptor 2 inhibits experimental cystitis. Am J Physiol Regul Integr Comp Physiol 2013;3054:R846-853. PubMed Central PMCID: PMC3652164.
d. Wang ZY, Wang P, **Bjorling DE**. Treatment with a cannabinoid receptor 2 agonist decreases severity of established cystitis. J Urol 2014;191:1153-1158. PubMed Central PMCID: PMC4163202.
e. Wang ZY, McDowell T, Wang P, Alvarez R, Gomez T, **Bjorling DE**. Activation of CB1 inhibits NGF-induced sensitization of TRPV1 in adult mouse afferent neurons. Neuroscience 2014;277:679-89. PubMed Central PMCID: PMC4626020.
f. Wang ZY, Wang P, Hillard CJ, **Bjorling DE**. Attenuation of cystitis and pain sensation in mice lacking fatty acid amide hydrolase. J Mol Neurosci 2015;55:968-976. PubMed Central PMCID: PMC4355044.
g. Wang ZY, Wang P, **Bjorling DE**. Activation of cannabinoid receptor 1 inhibits increased bladder activity induced by nerve growth factor. Neurosci Lett 2015 4;589:19-24. PubMed Central PMCID: PMC4339033.
h. Jones MR, Wang ZY, **Bjorling DE**. Intrathecal cannabinoid-1 receptor agonist prevents referred hyperalgesia in acute acrolein-induced cystitis in rats. Am J Clin Exp Urol 2015;3:28-35. PubMed Central PMCID: PMC4446380.
i. **Bjorling DE**, Wang ZY. Potential of endocannabinoids to control bladder pain. Front Syst Neurosci 2018;12:17. doi: 10.3389/fnsys.2018.00017. PubMed Central PMCID: PMC5962905.

2. Our laboratory and others have demonstrated a critical role for nerve growth factor (NGF) in pain associated with bladder inflammation.

a. Guerios SD, Wang ZY, **Bjorling DE**. Nerve growth factor mediates peripheral mechanical hypersensitivity that accompanies experimental cystitis in mice. Neurosci Lett 2006;392:193-197.
b. Guerios SD, Wang ZY, Boldon K, Bushman W, **Bjorling DE**. Blockade of NGF and trk receptors inhibits increased peripheral mechanical sensitivity accompanying cystitis in rats. Am J Physiol Regul Integr Comp Physiol 2008;295:R111-R122. PubMed Central PMCID: PMC2494812.
c. McDowell TS, Wang ZY, Singh R, **Bjorling D**. CB1 cannabinoid receptor agonist prevents NGF-induced sensitization of TRPV1 in sensory neurons. Neurosci Lett 2013;551:34-28. PubMed Central PMCID: PMC3752375.

3. Assessment of lower urinary tract function remains problematic in rodent models of lower urinary tract disease. We have developed a laboratory that incorporates multiple sophisticated methods of evaluation of lower urinary tract function in models of lower urinary tract disease, and we have investigated a number of factors that can affect voiding. Improvement of capabilities in this area are crucial to carefully link phenotypes, genotypes, and various methods of intervention with outcomes that can be applied to spontaneous lower urinary tract disease in humans.

a. **Bjorling DE**, Wang Z, Vezina CM, et al. Evaluation of voiding assays in mice: impact of genetic strains and sex. Am J Physiol Renal Physiol 2015;308:F1369-F1378. PubMed Central PMCID: PMC4469884.
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;308:F1431-F1443. PubMed Central PMCID: PMC4469891.
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;35:192-198. PubMed Central PMCID: PMC4469891.
d. Ritter KE, Wang Z, Vezina CM, **Bjorling DE**, Southard-Smith EM. Serotonin receptor 5-HT3A affects development of bladder innervation and urinary bladder function. Front Neurosci 2017; December 12; doi: 10.3389/fnins.2017.00690. PubMed Cental PMCID: PMC5732969.
e. 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;315:F1067-F1080. doi: 10.1152/ajprenal.00245.2018. PubMed Cental PMCID: PMC6230749.

f. Hill WG, Zeidel ML, **Bjorling DE**, Vezina CM. The void spot assay: Recommendations on the use of a simple micturition assay for mice. Am J Physiol Renal Physiol 2018; Aug 29. doi: 10.1152/ajprenal.00350.2018. Epub ahead of print. PubMed Cental PMCID: PMCID: PMC6293303.

g. Macoska JA, Wang Z-Y, Virta J, Zacharias N, **Bjorling DE**. Therapeutic inhibition of the CXCL12/CXCR4 axis prevents peri-urethral collagen accumulation and lower urinary tract dysfunction in vivo. Prostate 2019; DOI: 10.1002/pros.23781, in press.

4. Another collaborative strategy pursued by our laboratory and other investigators at the University of Wisconsin has entailed investigating the presence of biomarkers in urine obtained from men with benign prostatic hyperplasia or from mouse models of this disorder. The goal of these investigations is to identify markers in urine that can be used to assess the onset and progression of lower urinary tract disease resulting from disorders of the prostate.

a. Hao L, Greer T, Page D, Shi Y, Vezina CM, Macoska JA, Marker PC, **Bjorling DE**, Bushman W, Ricke WA, Li L. In-depth characterization and validation of human urine metabolomes reveal novel metabolic signatures of lower urinary tract symptoms. Sci Rep 2016; Aug 9;6:30869. doi: 10.1028/srep30869. PubMed Central PMCID: PMC4977550.

b. Greer T, Hao L, Nechyporenko A, Lee S, Vezina CM, Ricke WA, Marker PC, **Bjorling DE**, Bushman W, Li L. Custom 4-plex DiLeu Isobaric labels enable relative quantification of urinary proteins in men with lower urinary tract symptoms (LUTS). PLoS One. 2015 Aug 12;10(8):e0135415. doi: 10.1371/journal.pone.0135415. PubMed Central PMCID: PMC4534462.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/dale.bjorling.1/bibliography/44047982/public/?sort=date&direction=ascending

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

Ongoing Research Support

U54DK104310 09/24/14-07/31/19
NIH/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.
George M. O'Brien Center for Benign Urology Research
Role: Biomedical Core Principal Investigator

R01DK099328 (PI: Vezina) 07/01/14-06/30/19
NIH/NIDDK
Role of DNA Methylation in Prostate Glandular Development and Urinary Function: The goal of this research is to test the hypothesis that normal prostate development and subsequent function of the lower urinary tract are dependent upon appropriate DNA methylation during development and aging.
Role: Co-Investigator

K12DK100022-06 (PIs: Bjorling/Bushman) 08/01/13-09/13/23
NIH/NIDDK
Wisconsin Multidisciplinary K12 Urologic Research Career Development Program
I am co-director of this program that provides advanced training in benign urological research for PhDs, MDs, and DVMs. No overlap.
Role: Principal Investigator (contact)

T35OD011078-09 (PI: Bjorling) 06/18/11-03/31/21
NIH
Short-Term Research Training of Veterinary Students in Wisconsin

This award provides support for short-term (12 week) research training of veterinary students typically during the summer. No overlap.
Role: PI

MSN204306 (PI: Bushman) 11/25/16-11/24/19
Veterans Administration Merit Award
Role of Inflammation and Fibrosis in Benign Prostatic Hyperplasia and Lower Urinary Tract Symptoms
This research will investigate the relationship between prostatic inflammation and development of fibrosis using a mouse model of bacterial prostatitis and histological evaluation of human tissues. No overlap.
Role: Co-Investigator

Completed Research Support

P20DK12003 (PI: Bushman) 01/12/12-08/31/15
NIH/NIDDK
Urinary Biomarkers of Lower Urinary Tract Symptoms
The goal of this research is to develop the infrastructure to detect proteomic and metabolomics changes that correlate with symptoms of lower urinary tract disease. These techniques and data will be used to submit a program/project application
Role: Co-Investigator

R01 DK088806-04 (PI: Bjorling) 09/01/10-06/30/16
NIH/NIDDK
Endogenous Cannabinoids and NGF Signaling in Pain Associated with Cystitis
The goal of this research is to investigate regulation of afferent sensitivity by the endocannabinoid system in the presence of cystitis. No overlap.
Role: PI