BIOGRAPHICAL SKETCH

NAME: Ricke, William

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

POSITION TITLE: Professor, Director of Research

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
Walter Reed Army Medical Center, Washington DC	Vet. Tech certificate	05/1990	Veterinary Sciences
Iowa State University, Ames, IA	B.S.	08/1993	Animal Science
North Dakota State University, Fargo, ND	M.S.	08/1996	Endocrinology
University of Missouri, Columbia, MO	Ph.D.	05/2000	Endocrinology
University of California, San Francisco, CA	Fellow	06/2005	Urology/Anatomy

A. Personal Statement

Qualifications as O'Brien Center Director, and Administrative Core and Project 1 Leader: I have led a NIH funded research program for the past 15 years focused on elucidating the molecular, cellular, and physiological mechanisms involved in the development of prostate diseases. Research in my laboratory focuses on: 1) Defining cellular processes (fibrosis, smooth muscle contractility, hyperplasia) involved in the development of BPH/LUTS, 2) Elucidating the molecular mechanisms of hormone action in the development of prostate disease, and 3) Translating laboratory findings into clinically relevant therapeutics, predictive/prognostic biomarkers, and treatment strategies. Our meaningful research has been published in impactful basic and clinical journals.

Qualifications as effective Inter-Centers' Leader: I have a nationally recognized track record of leadership and academic governance. I have served in a number of leadership categories successfully including: **1)** PI of the U54/UW O'Brien Center-Developed the U54 Interactions Core, **2)** UW Carbone Cancer Center-Senior Leadership (Program Leader, Tumor Microenvironment-Interaction with O'Brien Center), **3)** Maintaining a NIH funded research lab for over 15 years, **4)** Department of Urology leadership including overseeing all of the research in our department as I serve as the Director of Research for the Department of Urology at the University of Wisconsin (UW), and serve on the Dept's Executive Committee. **5)** I also serve or have served as a Director of other campus facilities, cores (e.g. Animal Technology Core-UCSF Prostate SPORE) and for a number of different didactic courses for which I interact with many faculty, staff, and trainees. **6)** I have served in National/International leadership roles with the Society of Basic Urologic Research (SBUR, executive committee) as well as a number of other leadership positions are listed below including as an expert for the French Agency for Food, Environmental and Occupational Health & Safety (**ANSES**), where I helped influence policy towards estrogenic compounds found in the food chain. **7)** My University leadership includes my role as a UW Faculty Senator as well as participation in the UW-SMPH Promotions Committee and SMPH space and planning committee. Importantly, working in these leadership positions (and others) requires transcendence through a range of different personalities, management styles, and research emphases (e.g. clinical and basic sciences), which I have navigated successfully.

Qualifications in Community Outreach and Mentoring for the Administrative Core: Education and outreach is the cornerstone for developing our next generation of scientists. To promote this, I have over 70 trainees (junior faculty, K-scholars, residents, fellows, postdoctoral students, and professional students (graduate, medical, MSTP, and PharmD) of whom I have successfully trained since becoming a faculty member. Importantly, these talented trainees consist of underrepresented minorities, first generation college students, as well as other capable women and men. I have solicited NIH (U54 supplements) and UW funds exceeding $1 million explicitly for education and outreach. Furthermore, I was closely involved in the writing and acquisition of multiple training awards including T32 programs, K12 programs, F-awards (F30, 31, 32) and other fellowships on campus. In addition, I participated in R13 in support of both SBUR and AUA meetings. Local teaching and training is a priority, however I have served in National leadership training roles with the Society of Basic Urologic Research (SBUR, Trainee Affairs committee) and the American Urological

Association's Research, Education, Conferences and Communication Committee. Moreover, I am committed to the training of our next generation and have served on more the 20 official mentoring committees on campus and world-wide. Suffice to say, I have a passion for education and training and promote this in the current proposal. Collectively, these scientific, administrative and educational experiences make me an ideal person to lead the proposed O'Brien Center.

1. Cunha GR, Vezina CM, Isaacson D, **Ricke WA**, Timms BG, Cao M, Franco O, Baskin LS. Development of the human prostate. Differentiation 2018; 103:24-45.
2. Strand DW, Costa DN, Francis F, **Ricke WA**, Roehrborn CG. Targeting phenotypic heterogeneity in benign prostatic hyperplasia. Differentiation 2017; 96:49-61.
3. Liu TT, Grubisha MJ, Frahm KA, Wendell SG, Liu J, **Ricke WA**, Auchus RJ, DeFranco DB. Opposing Effects of Cyclooxygenase-2 (COX-2) on Estrogen Receptor beta (ERbeta) Response to 5alpha-Reductase Inhibition in Prostate Epithelial Cells. J Biol Chem 2016; 291:14747-14760.
4. 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; 10:e0135415.

B. Positions and Honors

Positions and Employment

1989-1995 U.S. Army and Reserves, **Veterinary Technician** 91T
1990-1991 U.S. Army, Operation Desert Storm/Shield, **Veterinary and Microbiology Lab Technician**
2003-2005 University of California, San Francisco, CA, **Co-Director** of Animal Technology Core, UCSF Prostate SPORE
2005-2010 University of Rochester, Rochester, NY, **Assistant Professor (Tenure track)**
2010-2013 University of Wisconsin, Madison, WI, **Assistant Professor (Tenure track)**
2013-2017 University of Wisconsin, Madison, WI: **Associate Professor (Tenure),** Department of Urology
2017-present University of Wisconsin, Madison, WI: **Professor (Tenure),** Department of Urology

Other Experience, Accolades and Professional Memberships

1993-present Membership: AACR, ENDO, SBUR, AUA, SOT, BOR
2008-2010 Executive Committee, **Board Member**, Society of Basic Urologic Research
2010-present University of Wisconsin, Madison, WI, **Director of Research**
2010-2013 Finance Committee, Society of Basic Urologic Research
2011 Guest **Editor**, *Differentiation*, special edition on benign prostatic hyperplasia
2011-present University of Wisconsin Carbone Cancer Center **Member**
2011 **Organizing committee**, Society of Basic Urologic Research
2011-present **Abstraction Selection Committee**, Society of Basic Urologic Research
2012 **Organizing Committee**, Society of Basic Urologic Research
2012-present **Awards Committee**, Society of Basic Urologic Research
2012-present University of Wisconsin Cancer Biology **Trainer**
2012-present University of Wisconsin Molecular Environmental Toxicology Center: **Trainer, Member**
2012-2015 University of Wisconsin, **Faculty Senator**
2012-present University of Wisconsin, **Urology Executive Council**
2012-present Rodent Urinary Function Testing Facility: **CoDirector**
2014-present NIDDK, Urology U54 Steering Committee
2012-present University of Wisconsin Molecular Environmental Toxicology Center: **Trainer, Member**
2014-present University of Wisconsin, George M. O'Brien Center-**Director**
2014-present University of Wisconsin Molecular Environmental Toxicology Center: **Steering Committee**
2014-present University of Wisconsin, George M. O'Brien Center-**Steering Committee**
2014-present University of Wisconsin, George M. O'Brien Center-**Senior Executive Committee**
2015-present UW Medical Foundation Professor of Urologic Research, **Endowed Professorship**
2017-present **CoLeader**, Tumor Microenvironment, Senior Leadership-UW-Carbone Cancer Center
2017-Present Member, Research, Education, Conferences, Communications (RECC) Committee, AUA

Honors/Distinctions

- Iowa State Math and Science Award (1988, 1989)
- **Army Achievement Medal**, Operation Desert Shield/Desert Storm (1991)
- **Army Commendation Medal**, Operation Desert Shield/Desert Storm (1991)

- North Dakota State University, Research Enhancement Award (1994-95)
- International Reproduction Meeting Travel Award (1998)
- Society for the Study of Reproduction National Meeting, Larry Ewing Memorial Award (1995, 1997, 1999, 2000)
- Society for Basic Urologic Research Scholar Award (2001, 2002, 2003, 2004)
- First place award presentation, UCSF-Joint Breast, Brain and Prostate Cancer SPORE Meeting (2004)
- American Association for Cancer Research, Frontiers in chemoprevention-Travel Fellowship (2004)
- First runner up award presentation, UCSF-Prostate Cancer Retreat (2005)
- **Young Investigator Award**, Society for Basic Urological Research (2009)
- Best Abstracts, American Urological Association, Orlando, FL (2014)
- Speaker: Fibrosis and Prostate Disease In: *Targeting Fibrosis in Kidney, Bone Marrow, and Urological Diseases;* pp 9-11, Bethesda, MD. (2014)
- Plenary talk, American Urological Association, San Diego, CA (2016)

C. Contribution to Science

1. Experimental BPH/LUTS: Assessment of lower urinary tract function remains problematic in rodent models of lower urinary tract disease. We have developed a laboratory that incorporates multiple integrated technologies/methods of evaluation of lower urinary tract function in models of lower urinary tract disease. 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 lower urinary tract disease in humans. Our contributions have led to a new animal core (the only one of its kind) at the University of Wisconsin that will assist other laboratories around the world to measure urinary function in rodents. Our findings have also led to a better understanding of how urinary changes are altered differently among animal strains and how this may be important in humans.
    a. 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.
    b. Nicholson TM, Nguyen JL, Leverson GE, Taylor JA, Vom Saal FS, Wood RW, **Ricke WA**. The endocrine disruptor Bisphenol-A is implicated in urinary voiding dysfunction in male mice. Am J Physiol Renal Physiol 2018.
    c. Nicholson TM, Ricke EA, Marker PC, Miano JM, Mayer RD, Timms BG, vom Saal FS, Wood RW, **Ricke WA**. Testosterone and 17beta-estradiol induce glandular prostatic growth, bladder outlet obstruction, and voiding dysfunction in male mice. Endocrinology 2012; 153:5556-5565.
    d. **Ricke WA**, Lee CW, Clapper TR, Schneider AJ, Moore RW, Keil KP, Abler LL, Wynder JL, Lopez Alvarado A, Beaubrun I, Vo J, Bauman TM, Ricke EA, Peterson RE, Vezina CM. In Utero and Lactational TCDD Exposure Increases Susceptibility to Lower Urinary Tract Dysfunction in Adulthood. Toxicol Sci 2016; 150:429-440.

2. Biomarker and pathway analysis: Our laboratory and others have identified biomarkers in disease progression. We have utilized and contributed to the identification of new and novel biomarkers of disease using technologies that provide a large number of candidate biomarkers which can be screened against publically available databases to validate biomarkers in patient populations. Use of these technologies and approaches has given new pathways to target therapeutically in the treatment and/or prevention of disease. Our research has also provided new methods and data to study cancer progression that are available to biomedical community as a whole.
    a. Thomas S, Hao L, **Ricke WA**, Li L. Biomarker discovery in mass spectrometry-based urinary proteomics. Proteomics Clin Appl 2016; 10:358-370.
    b. 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; 6:30869.
    c. Liu TT, Ewald JA, Ricke EA, Bell R, Collins C, **Ricke WA**. Modeling Human Prostate Cancer Progression in vitro. Carcinogenesis 2018.

d. Ewald JA, Downs TM, Cetnar JP, **Ricke WA**. Expression microarray meta-analysis identifies genes associated with Ras/MAPK and related pathways in progression of muscle-invasive bladder transition cell carcinoma. PLoS One 2013; 8:e55414.

3. Stromal-Epithelial interactions and hormone action: We and others have identified that in normal and pathological conditions, there is a dialogue between epithelial and stromal components of all organs including the prostate. Although epithelium is commonly how an organ/cancer is defined (e.g. prostate is defined by the production of seminal plasma which is produced by the epithelial cells; or prostate cancer which is a cancer of the epithelium), the surrounding stroma also plays a role. In fact, we have demonstrated that prostate cancer is dependent upon the stroma for progression to malignancy. Additionally we have demonstrated that sex steroids mediate there effects primarily through the stroma during the development of disease. Collectively, we have identified the pertinent spatial and temporal sex hormone receptors critical for disease progression in the prostate. Our research has changed the way the biomedical community thinks about the development of BPH and prostate cancer as well as how we may treat or prevent it in the future.
    a. Theberge AB, Yu J, Young EW, **Ricke WA**, Bushman W, Beebe DJ. Microfluidic multiculture assay to analyze biomolecular signaling in angiogenesis. Anal Chem 2015; 87:3239-3246.
    b. Ricke EA, Williams K, Lee YF, Couto S, Wang Y, Hayward SW, Cunha GR, **Ricke WA**. Androgen hormone action in prostatic carcinogenesis: stromal androgen receptors mediate prostate cancer progression, malignant transformation and metastasis. Carcinogenesis 2012; 33:1391-1398.
    c. Niu Y, Altuwaijri S, Lai KP, Wu CT, **Ricke WA**, Messing EM, Yao J, Yeh S, Chang C. Androgen receptor is a tumor suppressor and proliferator in prostate cancer. Proc Natl Acad Sci U S A 2008; 105:12182-12187.
    d. *Wu CT, *Altuwaijri S, ***Ricke WA**, Huang SP, Yeh S, Zhang C, Niu Y, Tsai MY, Chang C. Increased prostate cell proliferation and loss of cell differentiation in mice lacking prostate epithelial androgen receptor. Proc Natl Acad Sci U S A 2007; 104:12679-12684.

4. Clinical/translational BPH/LUTS: Benign prostatic hyperplasia remains a burden to healthcare because it is an overwhelmingly prevalent disease in aged men and is a significantly costly disease. A major problem for the study of BPH/LUTS is that clinical aspects of this disease need to be determined before moving into an experimental setting. As such our research has added to the identification of important endocrine and cell biological factors and processes within patients, which we have started translating into animal models. We have identified spatial and temporal changes in hormone receptors, growth factors, and fibrosis in diseased prostates from patients. Furthermore, we have identified that these factors change in patients that are resistant to medical therapies. These contributions have helped lead to a new Center of Research Excellence in the study of fibrosis in prostatic disease.
    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; 2:313-322.
    b. Bauman TM, Sehgal PD, Johnson KA, Pier T, Bruskewitz RC, **Ricke WA**, Huang W. Finasteride treatment alters tissue specific androgen receptor expression in prostate tissues. Prostate 2014; 74:923-932.
    c. Bauman TM, Nicholson TM, Abler LL, Eliceiri KW, Huang W, Vezina CM, **Ricke WA**. Characterization of fibrillar collagens and extracellular matrix of glandular benign prostatic hyperplasia nodules. PLoS One 2014; 9:e109102.
    d. Nicholson TM, Sehgal PD, Drew SA, Huang W, **Ricke WA**. Sex steroid receptor expression and localization in benign prostatic hyperplasia varies with tissue compartment. Differentiation 2013; 85:140-149.

5. Prevention research: Use of drugs/compounds to prevent disease are a desired therapy by patients and physicians alike because they can be used on healthier patients, the patient has a longer time to respond to therapy/preventative, and multiple preventatives can be used if the first therapy is ineffective. Through our basic science laboratory we have elucidated molecular mechanisms/pathways and subsequently targeted them to prevent BPH/LUTD and prostate cancer in mice. This research has led to clinical trials assessing the efficacy of therapies as well as the development of future strategies and development of drugs to target these pathways (e.g. estrogen receptors and aryl-hydrocarbon receptor). Our progress has changed the way the biomedical community thinks about treatment of BPH and prostate cancer.

a. Moses MA, Henry EC, **Ricke WA**, Gasiewicz TA. The heat shock protein 90 inhibitor, (-)-epigallocatechin gallate, has anticancer activity in a novel human prostate cancer progression model. Cancer Prev Res (Phila) 2015; 8:249-257.
b. Ball LJ, Levy N, Zhao X, Griffin C, Tagliaferri M, Cohen I, **Ricke WA**, Speed TP, Firestone GL, Leitman DC. Cell type- and estrogen receptor-subtype specific regulation of selective estrogen receptor modulator regulatory elements. Mol Cell Endocrinol 2009; 299:204-211.
c. **Ricke WA**, McPherson SJ, Bianco JJ, Cunha GR, Wang Y, Risbridger GP. Prostatic hormonal carcinogenesis is mediated by in situ estrogen production and estrogen receptor alpha signaling. FASEB J 2008; 22:1512-1520.
d. Nicholson TM, Moses MA, Uchtmann KS, Keil KP, Bjorling DE, Vezina CM, Wood RW, **Ricke WA**. Estrogen receptor-alpha is a key mediator and therapeutic target for bladder complications of benign prostatic hyperplasia. J Urol 2015; 193:722-729.

A More Comprehensive List of Published Work in MyBibliography: https://www.ncbi.nlm.nih.gov/myncbi/william.ricke.1/bibliography/public/

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

Ongoing Research Support

U54UDK104310 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.
Role: Principal Investigator

3U54DK104310-05S1 09/15/18-07/31/19
NIH/NIDDK
George M. O'Brien Urology Cooperative Research Centers Program: Mediators of fibrosis in the development of lower urinary tract dysfunction; These supplemental funds are used to develop and maintain the NIDDK O'Brien Centers' web site, which is meant to facilitate interactions between O'Brien and P20 Centers and K12 KURe training programs, biomedical community, NIH/officials, and advocates of benign urology; the site will serve as a resource for all. Additionally, to develop a summer training program in benign urology
Role: Principal Investigator

R01ES001332 (PIs: Peterson/Vezina) 06/01/78-07/31/22
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: Co-Investigator

W81XWH-16-1-0246, DoD fellowship: Sarah Neuman 06/30/16-12/31/19
Effects of Phthalates on Androgen Receptor Regulation Associated with Castration-Resistant Prostate Cancer Development. Goal: understand the role of EDCs in castration resistance in the prostate.
Role: Principal Investigator

Completed Research Support

3U54DK104310-04S1 09/01/17-07/31/18
George M. O'Brien Urology Cooperative Research Centers Program: Mediators of fibrosis in the development of lower urinary tract dysfunction. Development of the O'Brien Centers' Interaction Core; This core promotes interactions between NIDDK funded researchers and organizations, especially O'Brien and P20 Centers and K12 KURe training programs, biomedical community, NIH/officials, and advocates of urology.
Role: Principal Investigator

3U54DK104310-03S1, S2 09/01/15-07/31/17
George M. O'Brien Urology Cooperative Research Centers Program: Mediators of fibrosis in the development of lower urinary tract dysfunction. Development of the O'Brien Centers' Interaction Core; This core promotes interactions between NIDDK funded researchers and organizations, especially O'Brien and P20 Centers and K12 KURe training programs, biomedical community, NIH/officials, and advocates of urology.
Role: Principal Investigator