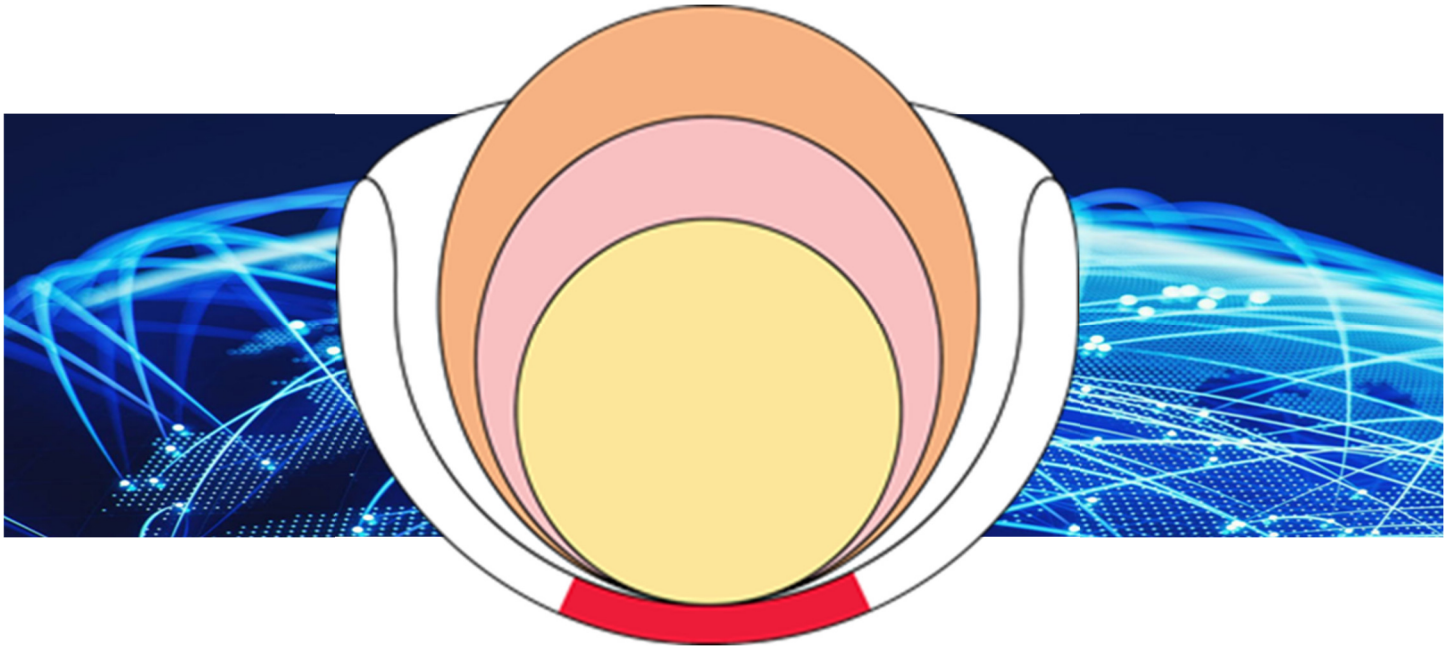
THE SOCIETY FOR PELVIC RESEARCH

FIFTH ANNUAL MEETING



MEETING PROGRAM

December 11-13, 2020
Virtual Meeting

#PelvRes20

Sponsored in part by:

1R13 AG071166-01 from the
National Institute on Aging (NIA)

In Partnership with:

The **International Continence Society**

AUA Urology Research Conferences Advisory Board (URCAB)

Special Thanks to:

Ms. Meredith Morran, the Zoom Support Specialist in charge of running the actual meeting**.** She may be contacted for providing Zoom Support Services at <mermorran@gmail.com>

The 2020 SPR Abstract Review Committee

Matthew O. Fraser, PhD
Vivian Cristofaro, PhD
Michael E. DiSanto, PhD
Francis "Monty" Hughes, Jr., PhD
Michael R. Ruggieri, Sr, PhD
Sylvia O. Suadicani, PhD
Maryrose P. Sullivan, PhD

The 2020 SPR Online Meeting Preparation / Execution Volunteers

Trainee Affairs Committee Workshop
- Michael R. Odom, PhD Candidate
- Zhonghua "Aileen" Ouyang, PhD Candidate

NIH P20 Satellite Symposium
- Kelvin P. Davies, PhD
- Sylvia O. Saudicani, PhD

Main Meeting
- Matthew O. Fraser, PhD
- Michael R. Ruggieri, Sr, PhD
- Johanna L. Hannan, PhD
- The SPR BOD

The 2020 SPR Trainee Awards Committee

Mary F. Barbe, PhD
Francis "Monty" Hughes, Jr., PhD
All those faculty that participated in judging

All those who attended and participated in the Fifth Annual Meeting

Our Mission Statement

To promote the highest standards of basic and translational science research directed toward understanding benign pelvic visceral and musculoskeletal function and dysfunction through education, interaction, and advocacy.

Our Vision Statement

The Society for Pelvic Research will be the premier professional organization for career basic and translational scientists and engineers interested in benign urogenital, distal gut and pelvic floor research.

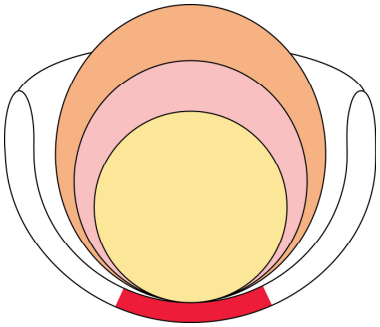
It will promote multidisciplinary interaction, intellectual cross-fertilization, networking for collaboration and career development through the regular dissemination of information via online resources, annual meetings and workshops, and published guidelines and standards for basic and translational science research.

Our History

The beginnings of the SPR trace back to the 2006 at a scientific meeting reception. Over refreshments, Matt Fraser and Mike DiSanto discussed starting a society that would serve the needs of the career basic/translational researchers in the field of Pelvic Medicine. It took until December of 2013 to take that initial thought and do something about it. An email went out to the original group and discussions and plans began. Additional Board Members were selected and invited to join in order to gain their expertise and a multidisciplinary balance.

After 5 years of Annual Meetings under two Presidents, we continue to forge new alliances with other scientific societies, have included a satellite symposium, and have been awarded an NIH R13.

Long Live the Society for Pelvic Research!



Our Board of Directors

President and **Annual Meeting Chair**
Michael R. Ruggieri, Sr, PhD
Professor, Department of Anatomy and Cell Biology, Temple University School of Medicine

Treasurer
Maryrose P. Sullivan, PhD
Assistant Professor, Department of Surgery, Harvard Medical School and VA Boston Healthcare System

Secretary
Carol A. Podlasek, PhD
Associate Professor, Department of Urology, University of Illinois at Chicago

Business Operations Committee Chair
Michael E. DiSanto, PhD
Professor and Chair, Department of Biomedical Sciences, Cooper Medical School of Rowan University

Membership Committee Chair
Vivian Cristofaro, PhD
Instructor, Department of Surgery, Harvard Medical School and VA Boston Healthcare System

Social Media Committee Chair
Johanna L. Hannan, PhD
Assistant Professor, Department of Physiology, The Brody School of Medicine, East Carolina University

Charitable Donation Committee Chair
Sylvia O. Suadicani, Ph.D.
Associate Professor, Departments of Urology and Neuroscience, Albert Einstein College of Medicine

Trainee Awards Committee Chair
Mary F. Barbe, PhD
Professor, Department of Anatomy and Cell Biology, Temple University School of Medicine

Trainee Affairs Committee Chair
Michael R. Odom, PhD
Post-Doctoral Research Fellow, Department of Surgery, Duke University

Members at Large
Kelvin P. Davies, PhD
Professor, Departments of Urology and Physiology & Biophysics, Albert Einstein College of Medicine

Francis M. Hughes, Jr., PhD
Assistant Professor, Department of Surgery, Duke University

Georgi V. Petlov, PhD
Professor and Chair, Department of Pharmaceutical Sciences, University of Tennessee Health Science Center, College of Pharmacy

Past President
Matthew O. Fraser, PhD (2015-2019)
Associate Professor, Department of Surgery, Duke University and Durham VA Medical Centers

Program Summary

Friday, December 11, 2020

11:00 AM **Trainee Affairs Committee Workshop**
Moderators - Michael Odom, PhD and Aileen Ouyang, PhD Candidate
Special Guest Workshop Leader - **Tierney Bates, EdD**
Q & A

12:00 PM **Break**

1:00 PM **SPR 2020 Satellite Symposium - Application of Nanotechnology in the Field of Benign**

Moderators - Kelvin Davies, PhD and Sylvia Suadicani, PhD
Introduction - Kelvin Davies, PhD
Keynote Address - Daniel Heller, PhD
Oral Presentations
Invited Speaker - Serkan Karakus, MD
Q & A

3:15 PM **Break**

SPR 2020 Main Meeting - Day 1, Session 1

4:00 PM **Welcome, Day 1, Opening Remarks, Mission of SPR - Michael Ruggieri, Sr, PhD**

4:05 PM **Session 1: NIH Funding Opportunities**
Moderators - Armand Allkanjari, MD and Michael Ruggieri, Sr, PhD
Special Guest Lecture - Candace Kerr, PhD
Q & A

4:55 PM **Adjourn Day 1**

Saturday, December 12, 2020

SPR 2020 Main Meeting - Day 2, Sessions 2-4

12:00 PM **Welcome, Day 2 - Maryrose Sullivan, PhD**

12:05 PM **Session 2: Novel Therapeutics and Diagnostics**
Moderators - Olivia Giovannetti, PhD Candidate and Matthew Fraser, PhD
Keynote Address - Irwin Goldstein, MD
Q & A
Oral Presentations - Abstracts S2A1-S2A5
Q & A

1:55 PM **Break**

Saturday, December 12, 2020

2:10 PM **Session 3: Models and Methods**
Moderators - Nagat Frara, PhD and Georgi Petkov, PhD
Oral Presentations - Abstracts S3A6-S3A10
Q & A

3:10 PM **Session 4: Physiology & Pharmacology I**
Moderators - Michael Odom, PhD and Maryrose Sullivan, PhD
State of the Art Lecture - Jason Kutch, PhD
Q & A
Oral Presentations - Abstracts S4A11-S5A15
Q & A

5:00 PM **Adjourn Day 2**

Sunday, December 13, 2020

SPR 2020 Main Meeting - Day 3 - Sessions 5-7

12:00 PM **Welcome, Day 3 - Matthew Fraser, PhD**

12:05 PM **Session 5: Neuroscience**
Moderators - Dania Giaddui, BS and Vivian Cristofaro, PhD
Keynote Address - Barry Komisaruk, PhD
Q & A
Oral Presentations - Abstracts S5A16-S5A20
Q & A

1:55 PM **Break**

2:10 PM **Session 6: Physiology & Pharmacology II**
Moderators - Ekta Tiwari, PhD and Sylvia Suadicani , PhD
Oral Presentations - Abstracts S6A20-S6A25
Q & A

3:10 PM **Session 7: Physiology & Pharmacology III**
Moderators - Aileen Ouyang, PhD Candidate and Kelvin Davies, PhD
State of the Art and ICS Lecture - Phillip Smith, MD
Q & A
Oral Presentations - Abstracts S7A26-S7A30
Q & A

5:00 PM **Trainee Awards Presentations**
Moderators - Mary Barbe, PhD and F. Monty Hughes, Jr., PhD

5:05 PM **Closing Remarks - Michael Ruggieri, Sr, PhD**

5:10 PM **MEETING ADJOURNS**

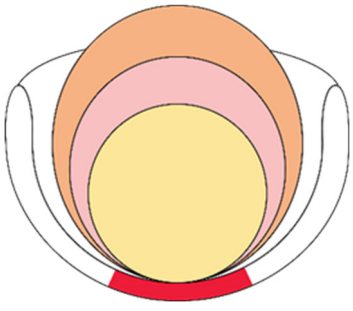
The Top Ranked Abstracts by the Abstract Review Committee *

S3A6*°	**Afrida Rahman-Enyart PhD**	*Acyloxyacyl hydrolase mediates gut microbiome in a mouse model of interstitial cystitis*
S5A16*	**Arezoo Geramipour PhD Candidate**	*Loss of urethral sensitivity leads to functional deficits in rat model: implications for age-related underactive bladder*
S2A4*	**Ritesh Kumar MS**	*Soft silicone-based neural interface to modulate bladder function*
S7A26*	**Violeta N. Mutafova-Yambolieva PhD**	*Transurothelial Transport of ATP Metabolites*
S2A1*	**Mary F. Barbe PhD**	*Nerve transfer for restoration of lower motor neuron-lesioned bladder function: Correlation between histological changes and nerve evoked contractions*

Best Trainee Presentation Awards °

Judges—Rosalyn Adam PhD, Jonathan Beckel PhD, Barry Komisaruk PhD, Jason Kutch PhD, Dennis Leo PhD, Robert Moreland PhD, Violetta Mutafova-Yambolieva PhD, Phillip Smith MD

First Place (tie)	**S5A18°**	**Afrida Rahman-Enyart PhD**	*Acyloxyacyl hydrolase regulates pelvic pain and memory by microglia activation*
	S6A22°	**Danielle S. Porecca MD-PhD Candidate**	*Long-term decentralization of the canine bladder changes the location and pharmacology of intramural nerve nicotinic receptors mediating acetylcholine release*
Second Place	**S3A6*°**	**Afrida Rahman-Enyart PhD**	*Acyloxyacyl hydrolase mediates gut microbiome in a mouse model of interstitial cystitis*
Third Place	**S5A17°**	**Cara C. Hardy**	*Alzheimer's Disease-associated Pathology in a Transgenic Mouse Model Results in Altered Voiding Function*



Program in Detail

Friday, December 11, 2020

SPR 2020 Trainee Affairs Committee Workshop

Moderators - Michael Odom, PhD and Aileen Ouyang, PhD

11:00 AM	**Tierney Bates, EdD**	***Workshop* - *Career Planning and Professional Networking in a World of Social Distance***
12:00 PM		***BREAK***

SPR 2020 Satellite Symposium

Application of Nanotechnology in the Field of Benign Urologic Disease

NIH P20 Center, Albert Einstein College of Medicine, NY

Moderators - Kelvin Davies, PhD and Sylvia Suadicani, PhD

1:00 PM	**Kelvin Davies, PhD**	***Introduction***
1:10 PM	**Daniel Heller, PhD**	***Keynote Address* - *Nanomedicines for the Treatment of Renal Disease***
1:40 PM	**Joel Friedman MD, PhD and Parimala Nacaharaju, PhD**	*The "Einstein Nanoparticle": Background and History, Synthesis, Physico-chemical Characteristics and Adaptations to Benign Urologic Disease Research*
2:00 PM	**Kelvin Davies, PhD and Moses Tar, MD**	*Application of Nanotechnology to Sexual Medicine*
2:20 PM	**Sylvia Suadicani, PhD**	*Nanotechnology applied to development of delivery systems for bladder targeted therapeutics*
2:40 PM	**Serkan Karakus, MD**	***Invited Speaker* - *NO-releasing nanoparticles ameliorate detrusor overactivity in transgenic sickle cell mice via restored NO/ROCK signaling***
3:00 PM		*Q & A*
3:15 PM		***BREAK***

SPR 2020 Main Meeting - Day 1

4:00 PM	**Michael R. Ruggieri, Sr, PhD**	**Welcome, Day 1, Opening Remarks, Mission of SPR**

Session 1: Funding Opportunities

Moderators - Armand Allkanjari, MD, Urology Resident (PGY3) and Michael Ruggieri, Sr, PhD

4:05 PM	**Candace Kerr, PhD**	***Special Guest Lecture* - *Basic/Translational Science Funding Opportunities at NIA***
4:45 PM		*Q & A*
4:55 PM		***Adjourn Day 1***

Saturday, December 12, 2020

SPR 2020 Main Meeting - Day 2

12:00 PM		**Maryrose Sullivan, PhD**	**Welcome, Day 2**

Session 2: Novel Therapeutics and Diagnostics

Moderators - Olivia Giovannetti, PhD Candidate and Matthew O. Fraser, PhD

12:05 PM		**Irwin Goldstein, MD**	***Keynote Address - Translating Basic Science Research into Clinical Management of Men and Women with Genito-Pelvic Dysesthesia (GPD)***
12:45 PM			*Q & A*
12:55 PM	**S2A1***	**Mary F. Barbe**	*Nerve transfer for restoration of lower motor neuron-lesioned bladder function: Correlation between histological changes and nerve evoked contractions*
1:05 PM	S2A2	**Alan J. Wolfe**	*The Female Bladder and Urethra Harbor Distinct Microbial Communities*
1:15 PM	S2A3	**Ekta Tiwari**	*Nerve transfer for restoration of lower motor neuron-lesioned bladder, urethral and anal sphincter function: Exploring sensory and motor reinnervation*
1:25 PM	**S2A4***	**Ritesh Kumar**	*Soft silicone-based neural interface to modulate bladder function*
1:35 PM	S2A5	**Nagat Frara**	*Nerve transfer for restoration of lower motor neuron-lesioned bladder function: Attenuation of ex-vivo, nerve-evoked, purinergic, bladder smooth muscle contractions.*
1:45 PM			*Q & A*
1:55 PM			***BREAK***

Session 3: Models and Methods

Moderators - Nagat Frara, PhD, Postdoctoral Fellow and Georgi Petkov, PhD

2:10 PM	**S3A6*°**	**Afrida Rahman-Enyart**	*Acyloxyacyl hydrolase mediates gut microbiome in a mouse model of interstitial cystitis*
2:20 PM	S3A7	**Lindsey K. Burleson**	*Chronic high fat diet increases vaginal sphincter laxity but does not affect pelvic floor muscle function in mice*
2:30 PM	S3A8	**Olivia Giovannetti**	*Investigation of sensory and autonomic innervation using immunohistochemistry following cadaveric simulation of mid-urethral sling surgery*
2:40 PM	S3A9	**Timothy J. Searl**	*Microarray analysis of human corpora cavernosa tissue from erectile dysfunction patients with diabetes and Peyronie's*
2:50 PM	S3A10	**Diane Tomalty**	*Immunohistochemical Characterization of Glandular Tissue in the Female Periurethral Space Targeted by Mid-Urethral Sling Procedures*
3:00 PM			*Q & A*

Session 4: Physiology & Pharmacology I

Moderators - Michael Odom, PhD, Postdoctoral Fellow and Maryrose Sullivan, PhD

3:10 PM		**Jason Kutch, PhD**	***State of the Art Lecture* - *Motor Cortical Treatment Targets for Chronic Pelvic Pain: Big Data, Small Data, and Clinical Trials***
3:50 PM			*Q & A*
4:00 PM	S4A11	**Armand Allkanjari**	*Diabetic bladder dysfunction progresses from early overactivity to an underactive bladder state in Akita diabetic mice*
4:10 PM	S4A12	**Sarah Y. Martin**	*Peptide amphiphile nanofiber hydrogel delivery of Sonic hedgehog protein to the penis and cavernous nerve, suppresses intrinsic and extrinsic apoptotic signaling mechanisms, which are an underlying cause of erectile dysfunction*
4:20 PM	S4A13	**Nagat Frara**	*Enhanced neurogenic activity and nerve density in smooth muscle strips taken from closer to the serosal side of the human and dog bladder*
4:30 PM	S4A14	**Dania Giaddui**	*Lateralization of Bladder Function in Normal Female Canines*
4:40 PM	S4A15	**Shelby N. Harper**	*Annexin A1 inhibits NLRP3 and prevents inflammation during bladder outlet obstruction*
4:50 PM			*Q & A*
5:00 PM			***Adjourn Day 2***

Sunday, December 13, 2020

SPR 2020 Main Meeting - Day 3

12:00 PM		**Matthew O. Fraser, PhD**	***Welcome, Day 3***

Session 5: Neuroscience

Moderators - Dania Giaddui, BS and Vivian Cristofaro, PhD

12:05 PM		**Barry Komisaruk, PhD**	***Keynote Address* - *Genital dysesthesias in relation to pelvic sensory nerves and their projections***
12:45 PM			*Q & A*
12:55 PM	**S5A16***	**Arezoo Geramipour**	*Loss of urethral sensitivity leads to functional deficits in rat model: implications for age-related underactive bladder*
1:05 PM	**S5A17º**	**Cara C. Hardy**	*Alzheimer's Disease-associated Pathology in a Transgenic Mouse Model Results in Altered Voiding Function*
1:15 PM	**S5A18º**	**Afrida Rahman-Enyart**	*Acyloxyacyl hydrolase regulates pelvic pain and memory by microglia activation*
1:25 PM	S5A19	**Ramalakshmi Ramasamy**	*Urinary Pathophysiology of a Demyelination Model of Multiple Sclerosis*
1:35 PM	S5A20	**Alex C. Turner**	*Prostatic Radiation Increases Bladder Cholinergic Nerve Density Leading to Enhanced Nerve-Mediated Contractions*
1:45 PM			*Q & A*

1:55 PM			***BREAK***

Session 6: Physiology & Pharmacology II

Moderators - Ekta Tiwari, PhD, Postdoctoral Fellow and Sylvia Suadicani, PhD

2:10 PM	S6A21	**Francis M. Hughes, Jr.**	*The endogenous anti-inflammatory protein Annexin-A1 normalizes inflammation and urodynamic parameters during bladder outlet obstruction and after deobstruction surgery*
2:20 PM	**S6A22°**	**Danielle S. Porreca**	*Long-term decentralization of the canine bladder changes the location and pharmacology of intramural nerve nicotinic receptors mediating acetylcholine release*
2:30 PM	S6A23	**Sarah Y. Martin**	*Sonic hedgehog signaling in corpora cavernosal cells from prostatectomy, diabetic, hypertension and Peyronie's patients with erectile dysfunction*
2:40 PM	S6A24	**Michael R. Odom**	*NLRP3-Dependent Mechanisms Downregulate Genes Controlling Urothelial Barrier Function in Diabetic Mice*
2:50 PM	S6A25	**Shaojing Ye**	*The role of MIF downstream signaling in PAR4-induced bladder pain*
3:00 PM			*Q & A*

Session 7: Physiology & Pharmacology III

Moderators - Aileen Ouyang, PhD Candidate and Kelvin Davies, PhD

3:10 PM		**Phillip P. Smith, MD**	***State of the Art and ICS Lecture* - *The Aging Bladder Phenotype: In the Lab***
3:50 PM			*Q & A*
4:00 PM	**S7A26***	**Violeta N. Mutafova-Yambolieva**	*Transurothelial Transport of ATP Metabolites*
4:10 PM	S7A27	**Alan S. Braverman**	*M_2 and M_3 muscarinic receptors contribute to the maximal contraction differently in rat and mouse bladders.*
4:20 PM	S7A28	**Vivian Cristofaro**	*Agonist-induced contractions promote F-actin polymerization in bladder smooth muscle tissue*
4:30 PM	S7A29	**M. Dennis Leo**	*Novel insights into human detrusor smooth muscle function: cell-signaling pathways regulating $K_{Ca}1.1\alpha$ subunit subcellular localization and trafficking*
4:40 PM	S7A30	**Jillene M. Brooks**	*Non-voiding Contractions are not Dyssynergic Voiding Contractions: A Study in Suprasacral Spinal Cord Injured Rats*
4:50 PM			*Q & A*
5:00 PM		**Mary Barbe, PhD and Monty Hughes, Jr., PhD**	***Trainee Awards Presentations***
5:05 PM		**Michael Ruggieri, Sr, PhD**	***Closing Remarks***
5:10 PM			***MEETING ADJOURNS***

AUA 2021 SEPT 10–13 Las Vegas

Annual Meeting Research Symposia

Basic Sciences Symposium: "Microbes and Inflammation in Urology"
Program Chair: Timothy L. Ratliff, PhD
Sunday, September 12

Challenges for Urologic Research: "Tracking Outcomes for Gender-Affirming Surgery in Transgender/Non-Binary Patients"
Program Chair: Lee Zhao, MD
Saturday, September 11

Urologic Oncology Research Symposium: "Personalizing Cancer Management: Are we improving with Genomics?"
Program Chairs: Daniel Lin, MD and James Brooks, MD
Friday, September 10

Research Forum: "Early-Career Investigators Showcase"
Sunday, September 12

SPR 2020 Special Guest Speakers

Dr. Tierney Bates, EdD

University Career Services
University of North Carolina, Chapel Hill , NC

Dr. Tierney Bates EdD is the Assistant Vice Chancellor for Special Projects and Interim Executive Director of University Career Services at the University of North Carolina, Chapel Hill. Dr. Bates holds a Doctor of Education in educational leadership from Spalding University, an MBA from Bryan College, a master's degree in Higher Education Administration, and a bachelor's degree in Mass Media Communication with a minor in African American History from the University of Akron. Dr. Bates has established a distinguished higher education career as a leader, speaker, fundraiser, networker, and career coach. Prior to his appointment at the University of North Carolina, he served as Vice President for Enrollment Management and Student Affairs at Virginia Union University and Assistant Vice Chancellor for Student Affairs at North Carolina Central University. He has also held appointments at the University of Louisville, the University of Tennessee, and Bowling Green State University.

Dr. Bates has a wide breadth of experience in career services, advising, multicultural and diversity initiatives, and student engagement and leadership. He is a highly sought-after speaker and advocate in the areas of diversity, equity, and inclusion, fundraising, and career coaching. He is the founder of the University of Tennessee Black Issue Conference, recipient of Knoxville Business Journal Top 40 under 40 award, and board members of six major community and company boards. Dr. Bates is a Cleveland, Ohio native who loves movies and sports and is a former lacrosse player.

———

Dr. Candace Kerr, PhD

Division of Aging Biology, National Institute on Aging
Bethesda, MD

Dr. Candace Kerr, PhD is the program officer for the Stem Cell Program in the Aging Physiology Branch of the Division of Aging Biology at the National Institute on Aging. NIA's Stem Cell Program has supported major findings on the genetics regulating stem cell lifespan and genomic stability, the relationships between stem cell survival and aged health, and the discovery of molecules that facilitate stem cell depletion and cellular senescence.

Before joining the NIA in 2017, Dr. Kerr was on the faculty of the University of Maryland School of Medicine researching human adult and cancer stem cells, and earlier on the faculty at Johns Hopkins University School of Medicine where her laboratory studied human pluripotent stem cells and the translation of these cells to treat reproductive and neurological conditions. She received her M.S. in molecular genetics at the University of Maine and her Ph.D. in quantitative genetics and biochemistry from Pennsylvania State University. As a postdoctoral fellow at Johns Hopkins University School of Public Health, she also studied the glycobiological interactions in receptor binding and endocrine functions in mice fertility and reproduction. She is the author of 35 peer-reviewed research papers and 14 review articles, textbook chapters, and commentaries. She has also shared her expertise as editor for several journals related to the stem cell biology field.

Dr. Kerr covers the basic and translational areas in aging of the Stem Cell Biology Program, Cardiovascular Biology Program, Endocrinology Program, and the Digestive, Pulmonary and Reproductive Programs.

P20 Keynote Speaker

Dr. Daniel Heller, PhD

Memorial Sloan-Kettering Cancer Center, Weill Cornell Medicine of Cornell University
NY, NY

Dr. Daniel A. Heller PhD is Head of the Cancer Nanomedicine Laboratory, Bristol-Myers Squibb/James D. Robinson III Junior Faculty Chair, and an Associate Member in the Molecular Pharmacology Program at Memorial Sloan-Kettering Cancer Center, and an Associate Professor in the Department of Pharmacology at Weill Cornell Medicine of Cornell University. His work focuses on the development of nanoscale technologies for the treatment, diagnosis, and research of cancer.

Dr. Heller obtained his PhD in chemistry from the University of Illinois at Urbana-Champaign in 2010, working in the laboratory of Michael Strano. He completed a Damon Runyon Cancer Research Foundation Postdoctoral Fellowship in the laboratory of Robert Langer at the David H. Koch Institute for Integrative Cancer Research at MIT in 2012. He is a 2012 recipient of the National Institutes of Health Director's New Innovator Award, a 2015 Kavli Fellow, a 2017 recipient of the Pershing Square Sohn Prize for Young Investigators in Cancer Research, a 2018 American Cancer Society Research Scholar, a 2018 NSF CAREER Awardee, and a 2018 recipient of the CRS Nanomedicine and Nanoscale Drug Delivery Focus Group Junior Faculty Award.

P20 Special Guest Speaker

Dr. Serkan Karakus, MD

Johns Hopkins University School of Medicine
Baltimore, MD

Dr. Serkan Karakus MD is a clinical fellow in sexual medicine at the James Buchanan Brady Urological Institute, Johns Hopkins University School of Medicine. Dr. Karakus received his medical degree from Trakya University Faculty of Medicine, Turkey, and completed his residency in urology at Istanbul University Faculty of Medicine, Turkey. Upon completion of his urology residency, he started his research fellowship under the mentorship of Dr. Arthur Burnett at the Basic Science Laboratory in Neuro-urology of the Brady Urological Institute in 2014. Since then, his research has focused on nitric oxide pathway following cavernous nerve injury, abnormalities of erectile and voiding function, more specifically priapism and bladder dysfunction in sickle cell disease and androgen effects and regulatory actions related to erection physiology.

His recent work focused on mechanisms of cavernous nerve regeneration and neuroprotection to develop possible new therapies to promote cavernous nerve functional recovery, thus erection recovery after cavernous nerve injury. He received a Sexual Medicine Society of North America (SMSNA) Research Grant Award in 2017 and subsequently American Urological Association (AUA) Research Scholar Award in 2018 for his project entitled, "Implantable Neurostimulator Improves Recovery of Erection and Micturition via cAMP-PKA-dependent Mechanisms in a Rat Model of Cavernous Nerve Injury." He continues his research studies along with his clinical training in sexual medicine at Brady Urological Institute, Johns Hopkins University.

SPR 2020 State of the Art Speakers

Dr. Jason Kutch, PhD

Herman Ostrow School of Dentistry of USC, University of Southern California
Los Angeles, CA

Dr. Jason Kutch PhD Jason J. Kutch received the B.S.E degree in Mechanical Engineering from Princeton University and then the Ph.D. degree in Applied and Interdisciplinary Mathematics from the University of Michigan. After a postdoctoral fellowship with Dr. Francisco Valero-Cuevas at the University of Southern California he accepted a faculty position in the Division of Biokinesiology and Physical Therapy, Herman Ostrow School of Dentistry of USC, University of Southern California where he is now Associate Professor with Tenure and director of the Applied Mathematical Physiology Laboratory (AMPL). He is a principal investigator of the University of Southern California discovery site of the Multi-Disciplinary Approach to the Study of Chronic Pelvic Pain collaborative research network.

His research is at the intersection of chronic pain and movement control. His career has been devoted to understanding brain and spinal cord networks controlling muscle fibers with neuroimaging, electrophysiology, and mathematical models as well as optimizing rehabilitation for restoring normal control of muscle in individuals with chronic pain. The AMPL is particularly interested in how the nervous system controls pelvic floor muscles, as well as how brain dysfunction contributes to chronic pelvic pain. Current research in AMPL is focused on developing non-invasive brain stimulation approaches for augmenting chronic pain treatment.

———

Dr. Phillip Smith, MD

Division of Urology, Department of Surgery, UConn Health
Farmington, CT

Dr. Phillip Smith, MD is an Ohio native and graduated with a B.A. in chemistry from Kenyon College in 1980 and his M.D. from the University of Cincinnati in 1984. He subsequently completed a residency in obstetrics and gynecology at the University of Cincinnati. He obtained his board certification in OB/GYN in 1990, and recertified in 2000 and 2010. Following several years of private practice, he returned to academia to pursue his interests in pelvic floor dysfunction, serving three years of fellowship training in voiding dysfunction and female urology in the Scott Department of Urology at Baylor College of Medicine. He has been in practice as a member of the Division of Urology, Department of Surgery, UConn Health since completion of his fellowship training. In 2013, Dr. Smith was in the first group of physicians achieving ACGME subspecialty board certification in female pelvic medicine and reconstructive surgery (FPMRS).

SPR 2020Keynote Speakers

Dr. Irwin Goldstein, MD

San Diego Sexual Medicine, Alvarado Hospital and University of California at San Diego
San Diego, CA

Dr. Irwin Goldstein, MD is the director of San Diego Sexual Medicine, where he maintains his clinical practice, Director of Sexual Medicine at Alvarado Hospital and Clinical Professor of Surgery at University of California at San Diego. Dr. Goldstein has had a long career providing medical help to those with sexual problems, having been involved with sexual dysfunction research since the late 1970's.

Dr. Goldstein holds a bachelor's degree in engineering from Brown University, with an honors thesis in biomedical engineering. In 1975, he graduated from McGill University Faculty of Medicine in his hometown of Montreal, Quebec, Canada. He was on the faculty of Boston University School of Medicine for 25 years where he was Professor of Urology and Gynecology and founding Director of the former Institute for Sexual Medicine at BUSM.

———

Dr. Barry Komisaruk , PhD

Department of Psychology, Rutgers University
Newark, NJ

Dr. Barry Komisaruk, PhD received a B.S. in biology at The City University of New York and Ph.D. in psychobiology from Rutgers University. He was a National Institute of Mental Health postdoctoral fellow in neuroendocrinology at the Brain Research Institute, University of California at Los Angeles. Joining the Rutgers-Newark faculty in 1966, Komisaruk was a professor in the Institute of Animal Behavior and Department of Zoology. He is now Distinguished Professor in the Psychology Department, director of the Minority Biomedical Research Support Program, and former associate dean of the Graduate School. With a penchant for finding new research avenues to explore, Komisaruk received a Board of Trustees of Rutgers University Excellence in Research award and the Hugo G. Beigel Research Award of the Society for the Scientific Study of Sexuality.

His major research interests include: functional neuroimaging of genital sensory response; neurophysiology, neuropharmacology and neuroendocrinology of reproductive behavior; and neural control of autonomic genital function. He is senior author of The Science of Orgasm, a comprehensive look at the biology and neuroscience of orgasm, published by The Johns Hopkins University Press, as well as The Orgasm Answer Guide, a general readership book from the same publisher. He has published more than 155 academic journal articles and chapters.

S2A1

Title: Nerve transfer for restoration of lower motor neuron-lesioned bladder function: Correlation between histological changes and nerve evoked contractions

Authors: Mary F. Barbe[1], Courtney L. Testa[1], Geneva E. Cruz[1], Nagat A. Frara[1], Ekta Tiwari[2], Lucas J. Hobson[1], Brian S. McIntyre[3], Danielle S. Porreca[2], Dania Giaddui[2], Alan S. Braverman[2], Emily P. Day[1], Mamta Amin[2], Justin M. Brown[4], Michael Mazzei[5], Michel A. Pontari[6], Ida J. Wagner[5], Michael R. Ruggieri, Sr.*[1,2]

Affiliations: Department of Anatomy and Cell Biology, Lewis Katz School of Medicine, Temple University, PA, USA [1], Department of Electrical and Computer Engineering, College of Engineering, Temple University, PA, USA[2], Drexel University College of Medicine, Philadelphia, PA, USA[3], Department of Neurosurgery, Massachusetts General Hospital, Boston, MA, USA[4], Department of Surgery, Lewis Katz School of Medicine, Philadelphia, PA, USA[5], Department of Urology, Lewis Katz School of Medicine, Temple University Hospital, Philadelphia, PA, USA[6].

Introduction/Objectives: Our objective was to examine for the first time, the effects of long-term decentralization of 9-13 months and then reinnervation (followed by an 8-12 month post-reinnervation recovery period), versus the effects of 11-21 months of decentralization, on the histology of the urinary bladder, compared to sham/unoperated control animals.

Methods: Twelve dogs underwent decentralization by bilateral transection of coccygeal and sacral (S) spinal roots, dorsal roots of lumbar (L)7, and hypogastric nerves. One was euthanized at 11 and three at 18-21 months post-decentralization. Eight were reinnervated 9-13 months post-decentralization with obturator-to-pelvic nerve and sciatic-to-pudendal nerve transfer, then euthanized 8-12 months later. Controls included 11 sham-operated and 3 unoperated animals. Before euthanasia, pelvic or transferred nerves and L1-S3 spinal roots were stimulated and maximum detrusor pressure (MDP) recorded. Bladder specimens were collected for histological and *ex vivo* smooth muscle contractility studies.

Results: Decentralized and reinnervated animals showed loss of urothelium integrity, fewer intramural ganglia, and more inflammation and collagen, than controls, although percent muscle was maintained. In reinnervated animals, pgp9.5+ axon density was higher, compared to decentralized animals. *Ex vivo* smooth muscle contractions in response to KCl correlated positively with submucosal inflammation, detrusor muscle thickness and pgp9.5+ axon density. *In vivo*, decentralized and reinnervated animals showed lower MDP than controls after stimulation of transferred or pelvic nerves and L7-S3 roots. Reinnervated animals showed higher MDP after stimulation of L1-L6 roots, compared to L7-S3 roots. MDP correlated negatively with detrusor collagen and inflammation, and positively with pgp9.5+ axon density and intramural ganglia numbers.

Conclusions: Despite the loss of intramural ganglia and ganglionic neurons, some bladder smooth muscle function was maintained in reinnervated animals in which the obturator nerve, a lumbar originating somatic nerve, was transferred to the pelvic nerve's anterior vesicle branch. We hypothesize that this was due to the change in innervation, indicated by an increase in pgp9.5+ axonal density in the ObNT Reinn animals and increased MDP in these same animals after stimulation of L1-L6 spinal roots. Although percent muscle and some bladder smooth muscle function was maintained in reinnervated animals, perhaps due to the innervation change, enhanced collagen deposition and inflammation were associated with decreased contractile function.

Funding Source(s): NINDS R01NS070267.

S2A2

Title: The Female Bladder and Urethra Harbor Distinct Microbial Communities

Authors: Alan J. Wolfe[a], Baylie Hochstedler[a], Yufan B. Chen[b], Thythy T. Pham[b], Marian Acevedo Alvarez, Elizabeth R. Mueller[b]

Affiliations: [a]Department of Microbiology and Immunology, Loyola University Chicago; [b]Departments of Obstetrics/Gynecology and Urology, Loyola University Medical Center

Introduction/Objectives: It is now confirmed that the typical adult female bladder is not sterile. Multiple groups have used modern sensitive methods to reproducibly detect microbes in urine obtained by suprapubic aspiration or transurethral catheterization. These microbial communities (microbiota) are similar but not identical to those found in the vagina. The relationship between the urethral microbiota and those of adjacent pelvic floor niches is an outstanding research gap. Thus, we examined the urethral microbiota, determined if it differs from the bladder urinary and vulvo-vaginal microbiota, and assessed if its composition differs based on patient demographic factors and presence of lower urinary tract symptoms.

Methods: Patients presenting to our urogynecology clinic were enrolled. Demographic information and responses to the Pelvic Floor Distress Inventory questionnaire were collected. All participants provided midstream voided urine, periurethral swab, transurethral swab and catheterized urine samples, which were analyzed by Expanded Quantitative Urine Culture and MALDI-TOF mass spectrometry. Bray-Curtis dissimilarity analysis assessed diversity between sample types for each participant. Kruskal-Wallis, chi-square, McNemar, Wilcoxon signed rank and Fisher's exact tests tested for significance.

Results: 49 patients participated. Bladder microbiota was dissimilar to urethral, periurethral and voided urine microbiota ($p < 0.0001$). Urethral and periurethral microbiota were similar ($p > 0.05$), but urethral microbiota was dissimilar to voided urine microbiota ($p = 0.001$), while the peri-urethral microbiota was not ($p > 0.05$). Women less than 55 years old were more likely to be sexually active, premenopausal and Hispanic compared to women 55 years old or older. *Lactobacillus* and *Gardnerella* were cultured from urethral samples more frequently and more abundantly from the younger cohort than from the older cohort. There was no significant association between symptoms and frequency or abundance of urethral bacteria species.

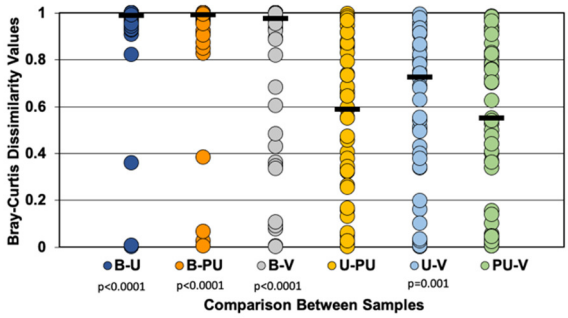


Figure 1. Microbiota Diversity Comparison Between Sample Sources Within Each Individual. Bray-Curtis Dissimilarity Index values comparing each sample within participants. Each circle represents the score for that sample comparison for one participant. Average score for each sample comparison is denoted by a black dash.

Conclusions: The microbiota of the adult female bladder and urethra differ. Age, menopausal status and sexual activity may affect the microbiota along the female lower urinary tract. More research is needed to determine the function and clinical significance of the urethral microbiota.

Funding Source: R01 DK104718 (awarded to AJW).

S2A3

Title: Nerve transfer for restoration of lower motor neuron-lesioned bladder, urethral and anal sphincter function: Exploring sensory and motor reinnervation.

Authors: Ekta Tiwari,[1*] Alan S. Braverman,[1] Lucas Hobson,[1] Nagat A. Frara,[1] Geneva Cruz,[1] Danielle S. Porreca,[1] Courtney L. Testa,[1] Dania Giaddui, [1] Justin M. Brown,[2] Michael Mazzei,[3] Michel A. Pontari,[4] Ida J. Wagner,[3] Mary F. Barbe,[1] and Michael R. Ruggieri Sr.,[1,5]

Affiliations: [1]Department of Anatomy and Cell Biology, Lewis Katz School of Medicine, [3]Department of Medicine, [4]Department of Urology, and [5]The Shriners Hospital of Philadelphia Temple University, 3501 North Broad Street, Philadelphia, PA 19140, [2]Department of Neurosurgery, Neurosurgery Paralysis Center, Massachusetts General Hospital, 55 Fruit Street, Boston, MA 02114.

Introduction/Objectives: Previously, an interim pilot study suggested that new neuronal pathways created by somatic nerve transfer can restore bladder sensation and motor function in long-term decentralized lower motor neuron-lesioned canines. In this study, we continued exploring the effectiveness of reinnervation in nerve-transferred canines by examining micturition behaviors, functional electrical stimulation, and retrograde labeling from the bladder in dorsal root ganglia.

Methods: Twelve female canines underwent bilateral transection of coccygeal and sacral (S) spinal roots, dorsal roots of lumbar (L)7 and hypogastric nerves. One was euthanized at 11 and three at 18-21 months post-decentralization. The remaining 8 went under nerve transfer procedure at 9-13 months post-decentralization, and then euthanasia after an 8-12 months post reinnervation recovery period. Controls included 5 sham-operated and 3 unoperated animals. Squat-and-void postures were tracked pre and post decentralization, post reinnervation, and during awake bladder filling procedures. Three weeks prior to euthanasia, a retrograde dye (Fluorogold) was injected into the bladder. At euthanasia, transferred nerves were electrically stimulated to evaluate motor function. Dorsal root ganglia were assessed for retrogradely labelled neurons.

Results: Eight of twelve canines showed none or few squat and void postures during the long-term decentralization period. In four, postures were observed with high frequency (>10) during the initial months; and reduced when bladder bacteriuria was cleared with antibiotic treatment. Seven of the eight canines that went under nerve transfer began showing postures by 6 months post reinnervation. One of eight also showed voluntarily voiding twice following nonanesthetized bladder filling. Four of seven showed elevated detrusor pressure after stimulation of obturator-to-pelvic transferred nerves. Four of eight showed elevated urethral and all eight showed elevated anal sphincter pressure after stimulation of sciatic-to-pudendal transferred nerves. Detrusor pressure was higher in reinnervated animals after stimulation of L2-L6 roots, compared to L7-S3. Reinnervation was further confirmed by increased fluorogold labelled cells in L2-L6 segmental levels, compared to sham, source of obturator nerve in canines.

Conclusions: New neuronal pathways created by nerve transfer can restore bladder sensation and motor function in lower motor neuron-lesioned canines after long term decentralization.

Funding Source(s): NIH 1R01NS070267

S2A4

Title: Soft silicone-based neural interface to modulate bladder function

Authors: Ritesh Kumar[1], Chaitanya H. Gopinath[2], Tyler Simpson[2], David M Weir[2], Maria K Jantz[1], Alexander Thiessen[3], Danny McDonnall[3], Robert A Gaunt[2]

Affiliations: [1]Department of Bioengineering, University of Pittsburgh, [2]Department of Physical Medicine and Rehabilitation, University of Pittsburgh, [3]Ripple LLC, Salt lake city

Introduction/Objectives: Bladder wall stimulation has been attempted for many decades to restore bladder function in people with spinal cord injury and other voiding dysfunctions. However, these efforts were limited by co-activation of the urethra, legs and other pelvic organs at stimulus intensities that evoked bladder contractions. Neural interfaces for the detrusor muscle itself face several challenges due to its structure and the volume changes it undergoes in normal function. We designed a stretchable soft silicone net that is placed around the bladder body to anchor a soft electrode array that interfaces directly with the base of bladder. This design overcomes the previous technological limitations of direct bladder wall stimulation. We hypothesized that soft silicone electrode nets can overcome the mechanical and electrical limitations of direct bladder wall stimulation and can be used as a neural interface to generate bladder contractions in conditions where the bladder is underactive or atonic.

Methods: We tested this neural interface in intact cats under isoflurane anesthesia (n=11, 9 males, 2 females) and characterized the functional and electromechanical properties of this polymer electrode. Bladder pressure was recorded using a transurethral catheter as a functional outcome. Fine wire electromyography electrodes were placed in adjacent muscles to measure current spread. Soft silicone electrodes were placed on the dorsal, ventral, and both lateral aspects of the bladder for stimulation at different amplitude and frequency parameters.

Results: We first tested these electrodes at constant bladder volume and found that electrodes positioned near the bladder neck around the ureterovesical junction elicited the largest bladder contractions, up to ~45 cmH_2O, while other locations such as the bladder dome generated significantly smaller contractions ($p<0.05$). Bipolar stimulation limited activation of the urethral sphincter and hind limbs through current spread compared to monopolar stimulation as shown by a significant reduction in EMG activity with similar increases in bladder pressure($p<0.05$). Finally, we found that the passive mechanical effects of the soft silicone net around the bladder had a minimal impact on bladder pressure and high positional stability.

Conclusions: Overall, the data in acute experiments show that soft silicone electrode nets can be used as a neural interface to generate bladder contractions in cats. We optimized the electrode locations on bladder to create a fully functional mesh, which confines and accommodates to the changes in bladder volume and is postionally stable. Bladder dysfunction has been an alarming cause of fatality after spinal cord injury and other neurological disorders. Direct bladder wall stimulation was first worked upon in 1951 and the functional efficacy was found in preclinical and clinical studies. This research was demotivated in 21st century due to technological challenges. From our pre-clinical acute experiment data, we believe it overcomes the technological limitations in an attempt for this interface to be potential LUT neuromodulation alternative as neural interfacing of a visceral organ directly has many surgical and pathological advances.

Funding Source(s): NIH SPARC OT2OD025297

S2A5

Title: Nerve transfer for restoration of lower motor neuron-lesioned bladder function: Attenuation of ex-vivo, nerve-evoked, purinergic, bladder smooth muscle contractions.

Authors: Nagat Frara[1*], Dania Giaddui[1], Alan S. Braverman[1], Daohai Yu[2], Danielle S. Porreca[1], Ekta Tiwari[1], Lucas J. Hobson[1], Courtney L. Testa[1], Michael Mazzei[3], Ida J. Wagner[4], Justin M. Brown[5], Michel A. Pontari[6], Mary F. Barbe[1], Michael R. Ruggieri, Sr.[1,7]

Affiliations: [1]Department of Anatomy and Cell Biology and [2]Department of Clinical Sciences, Lewis Katz School of Medicine, Temple University, Philadelphia, PA, USA
[3]Department of Medicine, Temple University Hospital, Philadelphia, PA, USA
[4]Department of Surgery and [6]Department of Urology, Lewis Katz School of Medicine, Temple University Hospital, Philadelphia, PA, USA,
[5]Department of Neurosurgery, Massachusetts General Hospital, Boston, MA, USA
[7]Shriners Hospitals for Children, Philadelphia, PA, USA

Introduction/Objectives: This study determined the effect of pelvic organ decentralization and reinnervation one year later on the contribution of muscarinic and purinergic receptors to *ex-vivo*, nerve-evoked, bladder smooth muscle contractions.

Methods: Twelve canines underwent decentralization by bilateral transection of all coccygeal and sacral (S) spinal roots, dorsal roots of lumbar (L)7 and hypogastric nerves. One was euthanized at 11 months and three at 18-21 months post-decentralization. Eight were reinnervated 12 months post-decentralization with obturator-to-pelvic nerve and sciatic-to-pudendal nerve transfer, then euthanized ten months later. Controls included six sham-operated and three unoperated animals. Bladder tissues were assessed for contractile responses to potassium chloride (KCl) and electric field stimulation (EFS) before and after purinergic receptor desensitization with alpha, beta-methylene adenosine triphosphate (α,β-mATP), muscarinic receptor antagonism with atropine, or sodium channel blockade with tetrodotoxin.

Results: Atropine inhibited EFS-induced contractions more in decentralized and reinnervated animals than normal controls. The maximal contractile response to α,β-mATP did not differ between the three groups. In strips from decentralized and reinnervated animals, the neurogenic sensitivity to EFS was enhanced at lower frequencies and the myogenic response to KCl was increased compared to normal control animals.

Conclusions: The observation of increased blockade of nerve-evoked contractions by muscarinic antagonist with no change in responsiveness to purinergic agonist suggests either decreased ATP release or increased ectoATPase activity in detrusor muscle as a consequence of the long-term decentralization. The reduction in the frequency required to produce maximum contraction following decentralization may be due to enhanced nerve sensitivity to EFS or a change in the effectiveness of the neurotransmission.

Funding Source(s): NINDS R01NS070267.

S3A6

Title: Acyloxyacyl hydrolase mediates gut microbiome in a mouse model of interstitial cystitis

Authors: Afrida Rahman-Enyart[1], Wenbin Yang[1], Ryan E. Yaggie[1], John M. Rosen[1], Charles Rudick[3], Colleen Bushell[4], Michael Welge[4], Bryan A. White[4,5], Anthony J. Shaeffer[1], and David J. Klumpp[1,2]

Affiliations: Departments of Urology[1] and Microbiology-Immunology[2], Feinberg School of Medicine, Northwestern University, Chicago IL; Department of Clinical Pharmacology and Toxicology[3], Indiana University School of Medicine, Gary IN; Carl R. Woese Institute for Genomic Biology[4] and Applied Research Institute[5], University of Illinois, Urbana-Champaign, IL

Introduction/Objectives: Interstitial cystitis/bladder pain syndrome (IC/BPS) is a debilitating condition characterized by mild to severe chronic pelvic pain and urinary urgency. Patients with IC/BPS are more susceptible to several comorbidities, such as anxiety/depression and gut dysbiosis. We have previously identified the locus encoding acyloxyacyl hydrolase (*Aoah*) as a modulator of pelvic pain severity. AOAH-deficient mice spontaneously exhibit increased evoked behaviors consistent with pelvic pain and an increased response to induced pelvic pain models, and also exhibit an anxiety/depressive-like phenotype. Since IC/BPS patients show fecal dysbiosis, we sought to characterize the gut microbiome of AOAH-deficient mice and define roles in modulating symptoms of IC/BPS.

Methods: Wild-type (WT) C57BL/6 and AOAH-deficient mice were utilized. To determine cecum and cecal content mass, samples were weighed and reported as the fraction of total body mass. A microarray followed by transcriptome analyses were used to identify differences in altered gene expression in the cecum. Gut microbiome composition was analyzed using 16S rRNA sequencing of fecal and cecal stool. Gas chromatography-mass spectrometry was implemented to identify altered fecal metabolites. Transepithelial electrical resistance was measured in an Üssing chamber to identify intestinal permeability. To identify if the microbiome mediates pelvic pain severity, mice were co-housed or received fecal microbiota transfer (FMT) from donor mice prior to measuring responses to von Frey filaments applied to the pelvic region or quantifying visceromotor responses (VMR) to bladder distension. To measure anxiety, FMT experiments were conducted prior to measuring defensive burying behaviors.

Results: We observed that both female and male AOAH-deficient mice exhibited enlarged ceca and increased gut permeability compared to WT mice. However, only male AOAH-deficient mice exhibited increased mass of cecal contents, suggesting sex differences. Transcriptome analyses revealed altered cytoskeletal remodeling pathways, as well as genes associated with immune function/inflammation. We also identified that the gut flora and fecal metabolites were altered in female AOAH-deficient mice, and several bacterial strains and metabolites were absent or only present in AOAH-deficient mice compared to WT. Co-housing of AOAH-deficient and WT mice converged the microbiota and partially alleviated pelvic allodynia in AOAH-deficient mice. AOAH-deficient mice gavaged with stool slurry from WT mice showed alleviation of pelvic pain measured by VMR at levels similar to WT. Consistent with these results, gavage with WT stool slurry relieved anxiety-like behaviors in AOAH-deficient mice.

Conclusions: We show that AOAH mediates normal gut microbiota, and the dysbiosis accompanying AOAH deficiency is linked to pelvic pain severity and anxious behavior. The gut microbiome may be a potential therapeutic target for treating symptoms of IC/BPS.

Funding Source(s): NIDDK awards U01 DK082342 and R01 DK066112-06S1

S3A7

Title: Chronic high fat diet increases vaginal sphincter laxity but does not affect pelvic floor muscle function in mice

Authors: Lindsey K. Burleson[1]*, Michael R. Odom[2], Adam A. Amarose[1], Espen E. Spengenburg[1], Johanna L. Hannan[1]

Affiliations: [1]Department of Physiology, Brody School of Medicine, East Carolina University, Greenville, NC, USA; [2]Department of Urology, Duke University, Durham, NC, USA

Introduction/Objectives: Pelvic organ prolapse (POP) is a prevalent disorder that is caused by weakness in the pelvic floor muscles, causing the pelvic organs to protrude into or through the vaginal vault. POP is a direct cause of female sexual dysfunction (FSD) by producing pain during intercourse or a reluctance to engage in sexual activity. The largest risk factors for POP include parity, obesity, and advanced age. Obesity, a modifiable risk factor, is believed to increase intra-abdominal pressure and weaken the pelvic floor muscles and fascia. The isolated impact of obesity on vaginal smooth muscle versus pelvic floor skeletal muscle has not been studied in animal models of POP. We will examine the structure and function of the vagina and pelvic floor in female mice fed a chronic high fat diet (HFD).

Methods: Adult female C57/Blk6N mice (10 weeks, n=32) were fed a control (10% kcal fat) or HFD (45% kcal fat) for 24 weeks. Ex vivo external vaginal sphincter contraction to increasing concentrations of adrenergic agonist norepinephrine and relaxation to nitric oxide donor DEA NONOate and electric field stimulation (EFS) was measured. Iliococcygeus (IC) muscles of the pelvic floor were isolated and set to optimal length and tetanic contractions were performed at increasing frequencies to asses absolute and specific force. Fatigue was measured following repetitive stimulations over 5 minutes. IC muscle fiber types were characterized with anti-myosin antibodies and cross-sectional area (CSA) of each fiber type was measured. Statistical analysis was completed using Prism 6, groups were compared using two-way analysis of variance

Results: Vaginal sphincter adrenergic-mediated contraction was a significantly decreased in HFD-fed mice ($p<0.05$). The vaginal sphincter smooth muscle relaxation in response to a nitric oxide donor was greater in the HFD mice ($p<0.05$). Neurogenic-mediated EFS vaginal relaxations were also enhanced in the HFD mice ($p<0.05$). Surprisingly, chronic HFD did not impact iliococcygeus muscle specific force, absolute force, or muscle fatigue. Furthermore, HFD did not affect the CSA or population of type I, IIa, IIX, or IIb iliococcygeus muscle fibers.

Conclusions: HFD-induced obesity in mice leads to pelvic floor weakness by enhancing relaxation and decreasing tone of vaginal smooth muscle. Interestingly, the function or composition of pelvic skeletal muscle was unaffected. As the vagina provides significant support to pelvic organs, obesity-induced decreased vaginal sphincter tone and structure may lead to POP and FSD.

Funding Source(s): Alpha Omega Alpha Honor Society, International Society for the Study of Women's Sexual Health

S3A8

Title: Investigation of sensory and autonomic innervation using immunohistochemistry following cadaveric simulation of mid-urethral sling surgery

Authors: Olivia Giovannetti[1*], Diane Tomalty[1], Dionne Gaudet[1], Diandra Clohosey[1], Autumn Forster[1], Madeline Monaghan[1], Barry Komisaruk[2], Sue Goldstein[3], Johanna Hannan[4], Irwin Goldstein[3], Michael Adams[1]

Affiliations: [1]Queen's University, Kingston, ON, Canada. [2]Rutgers University, New Brunswick, NJ, USA. [3]San Diego Sexual Medicine, San Diego, CA, USA. [4]East Carolina University, Greenville, NC, USA.

Introduction/Objectives: Sexual dysfunction (SD) in women has been reported following the mid-urethral sling (MUS) procedure for treatment of stress urinary incontinence. The mechanism is hypothesized to be MUS surgery-induced injury of (genital) sensory and/or autonomic innervation of the female periurethral tissue (FPT), where the MUS is surgically implanted. The study aims to determine: (i) whether there are multiple types of innervation (sensory and autonomic) in FPT, and (ii) the potential for structural damage to the innervation of the FPT based on the location of an implanted MUS relative to the IHC-defined nerve bundles.

Methods: FPT from four fresh cadavers was excised. Prior to dissection, one cadaver underwent simulation of a fascial MUS placement by a urogynecologist. All samples were paraffin embedded, sectioned, and stained with hematoxylin. Serial sectioning and IHC were performed to identify nerves. General nerve stain protein gene product 9.5 (PGP9.5) was used as well as markers determining the presence of autonomic (tyrosine hydroxylase (TH)) and peripheral sensory innervation (sodium channel $Na_v1.8$, S100ß and calcitonin gene-related peptide (CGRP)).

Results: Positive PGP9.5 immunoreactivity revealed substantial innervation throughout the FPT. Immunoreactivity for both sensory ($Na_v1.8$, and S100ß) and autonomic (TH) nerves were found within the region. A subset of S100ß-positive nerves also showed immunoreactivity for CGRP. The IHC findings combined with the surgical simulation revealed the potential for damage to both autonomic and sensory nerves as a result of the procedure.

Conclusions: This study provides preliminary evidence of potential injury to sensory and autonomic innervation as a consequence of MUS implantation. Future studies are needed to ascertain whether surgery-induced changes to the FPT innervation could result in SD in women.

Funding Source(s): None.

S3A9

Title: Microarray analysis of human corpora cavernosa tissue from erectile dysfunction patients with diabetes and Peyronie's.

Authors: Timothy J. Searl, Ph.D.[1*], Samuel Ohlander, M.D.[1], Daniel A. Harrington, Ph.D.[2], Samuel I. Stupp, Ph.D.[3], Kevin T. McVary, M.D.[4], Carol A. Podlasek, Ph.D.[1]

Affiliations: [1]University of Illinois at Chicago; [2]UT Health; [3]Northwestern University, [4]Loyola University Stritch School of Medicine.

Introduction/Objectives: Erectile dysfunction (ED) is a debilitating medical condition that affects men and their partners. Current treatments are minimally effective in diabetic patients due to peripheral neuropathy of the cavernous nerve, which causes apoptosis of penile smooth muscle, remodeling of the corpora cavernosal architecture, and ED. In order to identify factors that play a role in the development of diabetes induced ED, and to devise novel ED therapies that are effective in diabetic patients, we performed pathway analysis on changes in RNA identified by microarray in corpora cavernosal tissue from diabetic and Peyronie's patients.

Methods: Human corpora cavernosal tissue was obtained from diabetic and Peyronie's (control) patients (n=7) that were undergoing prosthesis implant to treat ED. RNA was extracted using TRIzol, DNase treated, and purified by column chromatography using the Qiagen Mini Kit. Microarray analysis was performed using the Human Gene 2.0 ST Array (Thermo Fisher). Two technical replicates were performed and an adj. P. Val (FDR) < 0.15 was used to select for significant changes in gene expression. Over Representation Analysis (ORA) of differentially expressed genes was compared using several open access web-based analytical methods, including ShinyGO (http://bioinformatics.sdstate.edu/go/) and Metascape (www.metascape.org), for Gene Ontology (GO), Kyoto Encyclopedia of Genes and Genomes (KEGG), Reactome, DisGeNET and Wikipathway enrichment.

Results: 182 differentially expressed protein encoding genes were identified from the microarray analysis. Similar enrichments were observed between different analytical tools, when the same enrichment libraries were utilized. ORA identified downregulation in gene expression related to blood vessel formation/ development and changes in gene expression for apoptotic pathways (GO biological process). DNA transcription processes (GO Molecular Function), and the activating protein-1 (AP-1) complex involved in transcription regulation (GO Cellular Component) were down regulated. ORA of KEGG and Wikipathway libraries showed differential gene expression for MAP kinase, PI3K-Akt, and NGF signaling pathways. Reactome showed enrichment associated with a downregulation of inflammatory response pathways.

Conclusions: Microarray analysis of corpora cavernosal tissue from diabetic patients found significant differential gene expression compared to Peyronie's patients. ORA analysis identified altered molecular pathways and cellular processes corresponding to a loss of genes associated with blood vessel development and remodeling and also a loss of genes associated with inflammatory response and tissue repair. These changes suggest that the corpora cavernosal tissue in ED patients lacks critical vascular maintenance repair and regeneration mechanisms as well as suffering from a loss of normal immunological and transcriptional response pathways; these are key factors when considering ED therapy development in diabetic patients.

Funding Source(s): NIH/NIDDK DK101536

S3A10

Title: Immunohistochemical Characterization of Glandular Tissue in the Female Periurethral Space Targeted by Mid-Urethral Sling Procedures

Authors: Diane Tomalty[1]*, Oliva Giovannetti[1], Johanna Hannan[2], Barry Komisaruk[3], Sue Goldstein[4], Irwin Goldstein[4], Michael Adams[1]

Affiliations: [1]Queen's University, Kingston, ON, Canada, [2]East Carolina University, Greenville, NC, USA, [3]Rutgers University, Newark, NJ, USA, [4]San Diego Sexual Medicine, San Diego, CA, USA.

Introduction/Objectives: Sexual dysfunction (SD) has been reported in some women following mid-urethral sling (MUS) surgery. Evidence suggests the female periurethral tissue (FPT), where the MUS is implanted contains glandular tissue. Our hypothesis is that these glandular structures, commonly referred to as the female prostate, are involved in the female sexual response (FSR). As such, they should contain both autonomic and sensory innervation, reflecting their role as a secretory tissue, as well as a tissue that may respond to arousal stimuli. The primary objective of this study was to describe the glandular tissue in the region of MUS implantation using of known markers of prostatic tissue, and markers of general and autonomic innervation. The relationship of a simulated MUS implantation to the glandular tissue in the surgical field of the MUS procedure was also examined.

Methods: FPT was dissected from fresh female cadavers. Prior to dissection, one cadaver underwent simulation of a fascial MUS placement by a urogynecologist. Serial sectioning and immunohistochemistry (IHC) were performed to determine the expression of prostate-specific markers prostate specific antigen (PSA), androgen receptor (AR), and Hoxb13. Tissues were also stained with protein gene product 9.5 (PGP9.5), a marker of general innervation; and choline acetyl transferase (ChAT), a marker of autonomic innervation.

Results: Positive immunoreactivity of the glandular tissue for PGP9.5, and ChAT was identified. Serial sections of the same glandular structures also stained positively for prostate markers PSA, AR, and Hoxb13. Glandular structures were identified in close proximity (within approximately 6.5 mm) to the implanted fascial sling.

Conclusions: These results provide emerging evidence that disruption of this glandular tissue and its associated neurovascular structures in the surgical field of MUS implantation could be responsible for the SD reported following MUS surgery in a subgroup of women.

Funding Source(s): None

S4A11

Title: Diabetic bladder dysfunction progresses from early overactivity to an underactive bladder state in Akita diabetic mice

Authors: Armand Allkanjari, MD[1,*]; Francis M. Hughes PhD[1]; Shelby Harper[1]; Todd J Purves M.D. PhD[1,2]

Affiliations: [1]Division of Urology, Department of Surgery, Duke University Medical Center, Durham, NC. [2]Department of Pediatrics, Duke University Medical Center, Durham, NC.

Introduction/Objectives: Diabetic Bladder Dysfunction (DBD) is a common complication of diabetes, yet no specific treatment is available. Patients with DBD may present with urinary frequency and urgency typical of overactive bladder (OAB), or detrusor underactivity and bladder decompensation typical of underactive bladder (UAB), or even some combination thereof. Contemporary scientific theories suggest there is actually a progression from OAB to UAB. Our laboratory has successfully used the Akita diabetic mouse (heterozygote for the Akita mutation at the Ins2 gene) to show that OAB is present in these mice by 15 weeks of age. The purpose of this study is to explore the potential progression of DBD from an overactive state to underactivity in this diabetic mouse model.

Methods: Awake, restrained cystometry was performed on wild type and Akita diabetic female mice from three age groups: 15, 30 and 45 weeks of age. Suprapubic tubes were implanted in the bladder, secured with a purse string suture, tunneled subcutaneously and externalized at the mid-scapular region. One week later, the animals were placed in a restrainer inside a cystometry station and positioned above an analytical balance. The catheter was connected to a syringe pump via an in-line pressure transducer and sterile saline infused at 15 µL/min for 60-120 minutes. Scale and pressure readings were continuously recorded.

Results: Blood glucose was significantly increased in all diabetic mice. At 15 weeks diabetic mice show a decrease of 58% in void volume ($P < 0.001$) and increase in urinary frequency of 90% ($P < 0.01$). Post-void residual (PVR) volume was significantly increased in the diabetic mice ($P < 0.01$); no PVR was ever detected in any of the nine nondiabetic mice examined. At 30 weeks in diabetics there is a drastic shift to increased void volume by 77% ($P < 0.001$) and 55% decrease in urinary frequency ($P < 0.01$). PVR volume remains higher in diabetics. Preliminary data show that decreased frequency, increased volume and elevated PVR persist at 45 weeks.

Conclusions: This study demonstrates that DBD in diabetic mice progresses from an early OAB-like presentation to an UAB state. These findings reinforce the progressive nature of DBD and provide strong support for the Akita model in future explorations of the molecular mechanisms underlying DBD progression.

Funding Source(s): Research support was provided by the National Institute of Diabetes and Digestive and Kidney Diseases (R01DK117890 to JTP) and intramural funds from Duke University.

S4A12

Title: Peptide amphiphile nanofiber hydrogel delivery of Sonic hedgehog protein to the penis and cavernous nerve, suppresses intrinsic and extrinsic apoptotic signaling mechanisms, which are an underlying cause of erectile dysfunction.

Authors: Sarah Y. Martin, B.S.[1*], Daniel A. Harrington, Ph.D.[2], Samuel Ohlander, M.D.[1], Samuel I. Stupp, Ph.D.[3], Kevin T. McVary, M.D.[4], Carol A. Podlasek, Ph.D.[1]

Affiliations: [1]University of Illinois at Chicago; [2]UT Health; [3]Northwestern University, [4]Loyola University Stritch School of Medicine.

Introduction/Objectives: Erectile dysfunction (ED) is a common and debilitating condition with high impact on quality of life. An underlying cause of ED is apoptosis of penile smooth muscle, which occurs with cavernous nerve injury, in prostatectomy, diabetic and aging patients. We are developing peptide amphiphile (PA) nanofiber hydrogels as an *in vivo* delivery vehicle for Sonic hedgehog (SHH) protein to the penis and pelvic ganglia (PG)/cavernous nerve (CN) to prevent the apoptotic response. In this study we examine two important aspects required for clinical application of the biomaterials, if SHH PA suppresses intrinsic (caspase 9) and extrinsic (caspase 8) apoptotic mechanisms, and if suppressing one apoptotic mechanism forces apoptosis to occur via a different mechanism.

Methods: TUNEL assay for apoptosis, immunohistochemical analysis, and western analysis for caspase 3-cleaved, caspase 9-cleaved and caspase 8-cleaved (active forms) were performed on corpora cavernosal tissue from adult Sprague Dawley rats (n=55) that underwent: 1.) SHH inhibition in the penis for 2 days, 2.) SHH inhibition in the PG/CN for 2 days, 3.) SHH PA treatment of the penis for 1-9 days, and 4.) caspase 9 inhibition in the penis for 2 days.

Results: Inhibition of the SHH pathway occurs in the penis and PG/CN after CN injury. SHH inhibition in the penis and PG/CN induces apoptosis through the intrinsic caspase 9 dependent pathway. SHH PA treatment of the penis after CN injury, suppresses primarily the caspase 9 apoptotic pathway, but also caspase 8 dependent mechanisms. Caspase 9 inhibition shows that inhibiting intrinsic apoptotic signaling does not shift apoptosis to an extrinsic mechanism, but rather truly suppresses the apoptotic response.

Conclusions: Understanding how apoptosis takes places after CN injury and in response to SHH inhibition is critical for translation of SHH PA to ED patients. These studies show that SHH PA treatment is effective in inhibiting both intrinsic and extrinsic apoptotic mechanisms that occur in ED patients, and suppresses the apoptotic response, rather than shifting it to another apoptotic mechanism, and therefore should be effective for therapy development in ED patients and our animal models.

Funding Source(s): NIH/NIDDK DK101536

S4A13

Title: Enhanced neurogenic activity and nerve density in smooth muscle strips taken from closer to the serosal side of the human and dog bladder

Authors: Nagat Frara[1*], Dania Giaddui[1], Mary F. Barbe[1], Alan S. Braverman[1], Lucas J. Hobson[1], Geneva E. Cruz[1], Mamta Amin[1] and Michael R. Ruggieri, Sr.[1,2]

Affiliations: [1]Department of Anatomy and Cell Biology, Lewis Katz School of Medicine, Temple University, Philadelphia, PA, USA
[2]Shriners Hospitals for Children, Philadelphia, PA, USA

Introduction/Objectives: In normal dog and human bladders, we aimed to investigate regional variations in muscle strip responses to different neurogenic and myogenic stimulations; with the assumption that the smooth muscle of the bladder has similar contractile properties throughout the bladder wall thickness.

Methods: Bladders were harvested from seven normal male dogs and another three were obtained from human organ transplant donors; one male and two females. Smooth muscle strips were dissected from the dorsal and the ventral aspects of the body of the bladder at least 1 cm above the ureteral orifices. Mucosa was removed and muscle strips were dissected from tissue adjacent to the mucosa and separate strips adjacent to the serosa. Strips were suspended in Tyrode's solution aired with 95% O_2 and 5% CO_2 at 37^{o}C and stretched to 2 grams. Maximal responses to electric field stimulation (EFS) and 120 mM potassium chloride (KCl) were determined. After washing and re-equilibration, responses to 30μM of the muscarinic receptor agonist bethanechol were determined. At the end of each experiment, muscle strips were collected, fixed and stained for the axonal marker protein gene product 9.5 (PGP9.5) to assess axonal density.

Results: In dog bladders, strips from adjacent to the serosa showed more expression of the axonal marker PGP9.5 and greater axon density, than the strips from close to the mucosa. While, EFS-induced contractions were significantly increased in the sub-serosal strips from dog bladders, compared to sub-mucosal strips, responses to EFS were not different between the sub-mucosal and sub-serosal strips from human bladders. In dog bladders, muscle contractions induced by either KCl or bethanechol were greater in strips adjacent to the mucosa than strips dissected immediately beneath the serosa. However, in human bladders, responses to KCl or bethanechol were similar in strips from either the mucosal or the serosal side.

Conclusions: Much of the previous literature on contractile responses of bladder muscle strips incorporates the implicit assumption that strips from the dorsal versus ventral aspects and across the thickness of the bladder respond similarly to pharmacological agents. We observed for the first time that in dog bladder, the contractile responses to neurogenic and myogenic stimulators were different in muscle strip taken from close to the lumen than in strips taken from closer to the outer surface. The increase in the density of nerves in the smooth muscle that is closer to the outer surface of the bladder suggesting higher numbers of intramural axons. This finding may have important implications in the understanding of the physiology and biophysics of bladder emptying.

Funding Source(s): NINDS R01NS070267.

S4A14

Title: Lateralization of Bladder Function in Normal Female Canines

Authors: Dania Giaddui[1], Mary F. Barbe[1], Ekta Tiwari[1], Danielle S. Porreca[1], Nagat Frara[1], Lucas J. Hobson[1], Sandra M. Gomez-Amaya[1], Alan S. Braverman[1], Justin M. Brown[4], Michael Pontari[3], Michael R. Ruggieri, Sr.[1,2]

Affiliation: [1]Department of Anatomy and Cell Biology, Lewis Katz School of Medicine, Temple University, Philadelphia, PA, USA
[2]Shriners Hospitals for Children, Philadelphia, PA, USA
[3]Department of Urology, Lewis Katz School of Medicine, Temple University Hospital, Philadelphia, PA, USA
[4]Department of Neurosurgery, Massachusetts General Hospital, Boston, MA, USA

Introduction/Objective: Many organs in the body have either left or right dominance in their innervation. Since the bladder receives innervation from the right and left sides through the spinal cord and the pelvic plexus, this study aimed to examine if stimulations of either the spinal roots or pelvic nerve cause a greater bladder contraction on the left versus the right side.

Methods: Forty-four female canines were included in this study. Functional electrical stimulation (3-5 second trains at 20Hz, 0.02 msec, 0.5-10 mA) of bilateral lumbar (L)6 through sacral (S)3 spinal cord roots and the left and right pelvic plexuses were performed for all animals. Changes in detrusor pressure were continuously recorded during stimulations. Strength of nerve-evoked bladder contractions after spinal root and pelvic plexus stimulations were derived from differences between the resting baseline pressure and the peak pressure obtained during the stimulation. The dominant side for each spinal root and pelvic nerve in each animal was determined by calculating the percent difference (25%) between the left and right stimulation. Bladders are considered left or right sided if differences are greater or less than 25%, respectively. If differences are within 25%, bladders are considered bilaterally innervated.

Results: The functional bilateral spinal root stimulation in 2/3 of the 44 dogs examined indicated that the maximum detrusor pressure was shown to be associated with either the left or right side of the spinal cord that was stimulated. Bladders were left side dominant in seventeen dogs (38.6%), right side dominant in 12 dogs (27.2%) and bilateral in 15 dogs (34%). Functional electrical stimulation of pelvic nerve revealed that about 3/4 of the 19 dogs tested, changes in detrusor pressure was shown to be associated with the side that was stimulated. Bladders were left side dominant in 8 dogs (42.1%), right side dominant in 6 dogs (31.6%) and bilateral in the remaining 5 dogs (26.3%).

Conclusions: Overall, these data provide evidence for asymmetry of the bladder function in the normal female dogs. Although, the current observations were obtained from normal animals, the determined left and right dominance of the bladder function might provide the basis for understanding the consequences of lateralization of bladder innervation in patients with bladder dysfunctions.

Funding Source: NINDS R01NS070267.

S4A15

Title: Annexin A1 inhibits NLRP3 and prevents inflammation during bladder outlet obstruction

Authors: Shelby N. Harper[1]*, Francis M. Hughes, Jr.[1], Brent D. Nosé[1], Michael Zheng[1], Huixia Jin[1], J. Todd Purves[1]

Affiliations: [1]Division of Urology, Department of Surgery, Duke University Medical Center, Durham, NC

Introduction/Objectives: Inflammation is a delicate balance between activators and inhibitors. A pivotal activator of inflammation is the NLRP3 inflammasome, which our lab has shown to be a central mediator of bladder inflammation in response to bladder outlet obstruction (BOO). However, little is known about endogenous inhibitors of inflammation within the bladder. Studies in other tissues have found Annexin A1 (ANXA1) has profound anti-inflammatory properties mediated through its interaction with the formyl peptide receptors (FPRs). One study has noted the presence of ANXA1 within bladder urothelia, but it is currently unknown if ANXA1 may interact with NLRP3 and/or inhibit inflammation in this tissue. In this study, we explore ANXA1's relationship with NLRP3 in bladder urothelia *in vitro* and its ability to attenuate inflammation during BOO *in vivo*.

Methods: Female rats (~200 g) were used. *In vitro*, primary urothelium were plated (o/n, 96-well plate), then treated with Ac2-26 for 1 hour followed by 0.625 mM ATP for an additional hour before being assayed for caspase-1 activity. Controls were treated with 1.25 mM ATP for maximal caspase activation. *In vivo*, rats underwent BOO surgery via insertion of a transurethral catheter (1 mm o.d.), tying of silk suture around the urethra, and removing the catheter. Ac2-26 (an ANXA1 mimetic; 1 mg/kg/day, i.p.) or PBS was administered for 12 days. Immunohistochemistry, Evans blue (inflammation), and caspase-1 (inflammasome activity) assays were then performed.

Results: *In vitro*, Ac2-26 decreased ATP-stimulated caspase-1 activity in a dose dependent fashion (figure 1). *In vivo*, immunocytochemistry showed ANXA1, FPR1 and FPR2 were present in bladder urothelium, while Ac2-26 decreased BOO-induced inflammasome activation and inflammation (figure 2).

Conclusions: ANXA1 is a functional antagonist of NLRP3 and can suppress inflammation during BOO suggesting it may be a useful pharmacologic target for inflammatory conditions in the bladder.

Funding Source(s): NIDDK: R01DK103534

Figure 1:

The Annexin A1 mimetic Ac2-26 inhibits NLRP3 within urothelium *in vitro* in a dose-dependent fashion

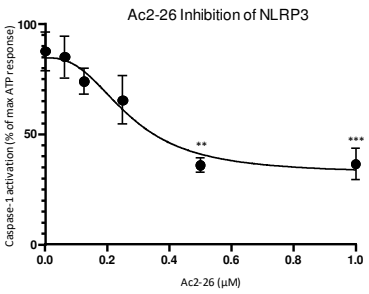
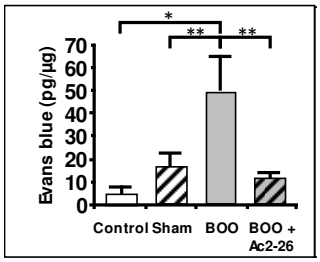


Figure 2:

The Annexin A1 mimetic Ac2-26 suppresses inflammation *in vivo* in bladder outlet obstruction (BOO)-induced inflammation



S5A16

Title: Loss of urethral sensitivity leads to functional deficits in rat model: implications for age-related underactive bladder

Authors: Arezoo Geramipour, Zachary C Danziger

Affiliations: Biomedical Engineering Department, Florida International University

Introduction/Objectives: Age-related underactive bladder (UAB) affects 10% of elderly people in the U.S., has high associated healthcare expenses, and leads to many lower urinary tract dysfunctions. Age-related UAB remains difficult to treat because its underlying causes are still unknown. Our previous work showed that voiding reflexes evoked by urethral sensation are weaker in older animals. That motivates us to hypothesize that the sensitivity of urethral afferents decreases with age, which could lead to a disruption of the voiding reflexes required to establish efficient voiding. To test this, we measure directly the urethral afferents activity to investigate if urethral signaling weakens with age and if this loss of sensitivity drives reduced reflex function.

Methods: To understand the effects of aging on neural signaling, we measured the difference in urethral afferent response to fluid flow between two groups of urethane-anesthetized female Sprague–Dawley rats (young (3-7mo), old (18-24mo)). We passed a catheter through the intravesical space into the urethra from the bladder dome to allow infusion of fluid through the urethra. The abdomen was sutured closed but we left the bladder incision open so that the bladder remained empty during the experiment. We connected a syringe pump to the catheter in series with a pressure transducer and used it to pass a solution of room temperature saline through the urethra at controlled flow rates. We exposed the pudendal nerve using a posterior approach and a bipolar nerve cuff electrode was placed on its sensory branch. At 2-minute intervals, the urethra was infused at a pseudorandomly selected flow rates and flow-evoked neural response and flow-evoked urethral pressure were measured in young and old animals.

Results: The results show that urethra afferent signaling in response to same urethral flow rates is weaker in older animals. That is, higher flow rates are required in older animals to recruit the urethra afferents. Therefore, the signaling reduction of urethra afferents to flow may weaken the functionality of augmenting reflex and contribute to incomplete bladder emptying in elderly population. Furthermore, the same flow rates evoked less pressure in the urethra in old animals, indicating that the urethra muscle compliance decreases with age. Since urethral pressure is the putative driver of urethral afferents, the reduced flow-evoked urethral pressure can decrease the activity of urethral afferents in response to urethral flow.

Conclusions: Reduced flow-evoked urethral pressure with age weakens the sensitivity of urethral afferents, which could disrupt the activation of augmenting reflex and lead to inefficient voiding.

S5A17

Title: Alzheimer's Disease-associated Pathology in a Transgenic Mouse Model Results in Altered Voiding Function

Authors: Cara C. Hardy[1,2,4], Dawn A. Rosenberg[1,3], Ramalakshmi Ramasamy[1,2,4], Xiangyou Hu[2], Phillip Smith[1,2,4,5]

Affiliations: 1. Center on Aging, UConn Health, Farmington, CT USA
2. Department of Neuroscience, University of Connecticut SOM, Farmington, CT USA
3. Department of Cell Biology, University of Connecticut SOM, Farmington, CT USA
4. CT Institute for the Brain and Cognitive Sciences (IBACS), University of Connecticut, Storrs, CT USA
5. Department of Surgery, University of Connecticut SOM, Farmington, CT USA

Introduction/Objectives: Alzheimer's disease (AD) is a devastating disorder primarily affecting older adults and is the most common neurodegenerative disease in the US. More than one in three AD patients experience AD-associated urinary dysfunction (ADUD), which directly contributes to their institutionalization. While ADUD has been clinically regarded as a result of poor cognitive control over urinary function, the physiology underlying loss of urinary control remains unknown. We hypothesize that beta-amyloidosis in the CNS results in pathologic changes in urinary structure and function.

Methods: Male and female Tg-APP/PS1DE9 mice were used before plaque deposition (4-6 months) and after plaque accumulation (8-10 months) and compared to their WT littermates. Pressure-flow cystometry was conducted under urethane anesthesia to assess urinary performance at the level of the autonomic nervous system in the absence of cortical control. Pharmacomyography was performed on bladder strips to determine tissue-level changes in the absence of CNS input.

Results: In Tg-APP/PS1DE9 mice, plaque accumulation resulted in diminished volume sensitivity and decreased voiding efficiency. Pharmacologic studies showed aberrant drug responses, altered cholinergic signaling, and decreased resilience of tissue longevity after plaque accumulation.

Conclusions: Based on our findings, we conclude that the AD-related pathology of Aβ accumulation results in a distinct urinary phenotype in our model, analogous to the ADUD observed in AD patients. Establishing and expanding models of ADUD to other mouse models of AD-associated pathology may improve the efficacy of treating ADUD and increase quality of life for patients and their caregivers.

Funding Source(s): R21 AG061609-01

S5A18

Title: Acyloxyacyl hydrolase regulates pelvic pain and memory by microglia activation

Authors: Afrida Rahman-Enyart[1], Wenbin Yang[1], Ryan E. Yaggie[1], Anthony J. Shaeffer[1], and David J. Klumpp[1,2]

Affiliations: Departments of Urology[1] and Microbiology-Immunology[2], Feinberg School of Medicine, Northwestern University, Chicago IL

Introduction/Objectives: Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic condition characterized by recurring pelvic pain and urinary dysfunction, where anxiety/depression are often comorbidities. A lack of biomarkers and unidentified etiology make IC/BPS challenging to diagnose. We have previously identified *Aoah*, the locus encoding acyloxyacyl hydrolase, as a modulator of pelvic pain severity, where AOAH-deficient mice have heightened responses to induced pelvic pain models and also exhibit an anxious/depressive phenotype. Previous studies have linked activated microglia, the resident immune cells of the central nervous system (CNS), to neuropathic pain. Microglial activation is also observed in memory deficits, which are common in anxiety/depression. Therefore, we examined the microglial phenotype in AOAH-deficient mice and the role of microglia in modulating pelvic pain, as well as spatial and recognition memory.

Methods: Brains from wild type (WT) C57BL/6, AOAH-deficient, and AOAH/toll-like receptor-4 (TLR-4)-deficient mice were sectioned and stained for the microglial marker P2RY12 followed by skeletal analyses using Image J. Cytokine abundance was measured in brain lysates using a proteome profiler array. Array results were corroborated by immunohistochemistry. Epithelial barrier function was assessed by measuring transepithelial electrical resistance (TEER) in an Üssing chamber. To address the functional roles of microglia in pelvic pain and cognition, microglia were eliminated from the CNS of AOAH-deficient and WT mice by oral gavage of PLX5622. Pelvic allodynia was measured by response to von Frey filaments applied to the pelvic region prior to and following microglial elimination. Spatial and recognition memory were measured by novelty object recognition task and object location task, respectively.

Results: Skeletal analyses revealed that AOAH-deficient mice have an activated microglia phenotype in multiple circuits mediating pain and mood, including the prefrontal cortex (PFC), paraventricular nucleus of the hypothalamus, and dentate gyrus. These data were consistent with increased cytokine release and increased IL-4 staining in the PFC of AOAH-deficient mice. Pharmacologic ablation of microglia resulted in decreased pelvic allodynia and improved recognition memory in AOAH-deficient mice. As AOAH-deficient mice exhibit gut dysbiosis, we hypothesized that microglial activation in AOAH-deficient mice is mediated by microglial TLR4 via microbial products leached from the gut. Consistent with this hypothesis, TEER revealed that AOAH-deficient mice exhibit increased gut permeability, suggesting possible leach of bacterial-derived TLR ligands across the intestinal barrier to the brain. In addition, mice deficient for both AOAH and TLR4 show rescued gut permeability, decreased pelvic allodynia, and low levels of IL-4 immunostaining similar to WT.

Conclusions: Our data confirm that microglia-mediated pelvic pain and recognition memory are dependent on AOAH, suggesting microglia-specific receptors or cytokines may be considered as future therapeutic targets for treating IC/BPS.

Funding Source(s): NIDDK awards U01 DK082342 and R01 DK066112-06S1

S5A19

Title: Urinary Pathophysiology of a Demyelination Model of Multiple Sclerosis

Authors: Ramalakshmi Ramasamy, M.Tech.[1,2,3*], Cara C. Hardy, BS[1,2,3], Dawn A. Rosenberg, BS[1,2], Stephen J. Crocker, PhD[1], Phillip P. Smith, PhD[1,2]

Affiliations:

[1]*Department of Neuroscience, UConn Health, Farmington, CT, USA*

[2]*Center on Aging, UConn Health, Farmington, CT, USA*

[3]*The Connecticut Institute for the Brain and Cognitive Sciences, Storrs, CT, USA*

Introduction/Objectives: Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease, characterized by several randomly distributed focal lesions in the central nervous system (CNS) caused by a myelin-destructive auto-immune response, resulting in delayed and interrupted neuronal pathways. MS is a debilitating disease that affects more than 2.3 million people worldwide with women three times more affected than men. Of note, over 80% of MS patients have urinary symptoms as one of their earliest symptoms, which includes hesitancy, urgency, frequency and incontinence, significantly affecting their quality of life. Inflammation and demyelination in the CNS are two important factors that affect functional output in MS patients. While most MS drugs to date reduce inflammation and decrease myelin damage, effective remyelinating drugs and their timely delivery are critical to restoring myelin before axon functionality is permanently lost. To effectively address this, understanding the precise impact of CNS demyelination on urinary performance is essential since the micturition circuit regulating bladder function involves several regions of the CNS vulnerable to MS-associated demyelination. In this study, we seek to elucidate the impact of CNS demyelination on urinary performance using the cuprizone model, a classic mouse model used to study the effects of CNS demyelination and spontaneous remyelination. We hypothesize that CNS demyelination in the cuprizone mouse model will result in aberrant changes in urinary function, and that after remyelination occurs this dysfunction will be alleviated.

Methods: C57Bl/6 mice were treated with dietary cuprizone (0.2% w/w) for four weeks to induce demyelination, after which one group was switched to normal diet for the next four weeks to recover from demyelination, while another group continued an additional four weeks of cuprizone treatment. Following this treatment paradigm, voiding spot assay and pressure/flow cystometry were performed to assess demyelination-induced differences in urinary performance.

Results: Mice with cuprizone-induced demyelination develop aberrant bladder function characterized by significantly increased micturition frequencies and reduced urine volume per micturition, compared to their control littermates as seen from voiding spot assay (VSA). Cystometric studies reveal changes in volume sensitivity and voiding efficiency. Recovery from cuprizone restores bladder function as seen from VSA.

Conclusions: Based on our findings, we conclude that CNS demyelination results in urinary pathophysiology. Therapeutics aimed at increasing the remyelination potential of the CNS neurons offer the possibility of alleviating urinary dysfunction associated with MS and improving the quality of life in aging MS patients.

Funding Source(s): The National Multiple Sclerosis Society

S5A20

Title: Prostatic Radiation Increases Bladder Cholinergic Nerve Density Leading to Enhanced Nerve-Mediated Contractions

Authors: Alex C. Turner[1]*, Shelby A. Powers[1], Elena S. Pak[1], Kathleen Ashcraft[2], Bridget Koontz[2], Johanna L. Hannan[1]

Affiliations: [1]Department of Physiology, Brody School of Medicine, East Carolina University, Greenville, NC; [2]Department of Radiation Oncology, Duke Cancer Institute, Durham, NC

Introduction/Objectives: In the US, prostate cancer affects 1 in 9 men. Though prostatic radiation therapy (RT) does not directly irradiate the bladder, the nerves supplying the bladder are located on the prostate's posterolateral surface and often receive a direct dose. Radiation-induced damage to these nerves can cause bladder dysfunctions. This study examines the impact of prostatic RT on bladder smooth muscle contractility and innervation.

Methods: Male Sprague-Dawley rats (8 weeks) received a single dose of prostatic radiation (0 or 22 Gy). The bladders and the major pelvic ganglia (MPG) were collected 2 and 10 weeks post-RT. The bladder was separated into strips for contractility experiments and the top portion was fixed for histology. Contractile responses to electrical field stimulation (EFS) and carbachol were measured. Bladder sections were stained with Masson's trichrome for smooth muscle content. Additional sections underwent immunofluorescent staining for neuron-specific class III beta-tubulin (non-specific neuronal marker), choline acetyltransferase (ChAT; cholinergic nerve marker), a-smooth muscle actin, and 4',6-diamidino-2-phenylindole (DAPI). Gene expression was assessed in MPGs by qPCR for ubiquitin carboxy-terminal hydrolase L1 (Uchl1;) and ChAT.

Results: Bladder smooth muscle content was significantly increased at 2 weeks post-RT and was not different from controls at 10 weeks post-RT. Both EFS-mediated and carbachol stimulated bladder contractions were significantly decreased at 2 weeks post-RT. Following 10 weeks of RT, nerve-mediated contractions were markedly increased while carbachol contractions were unchanged. No change was found in the number of non-specific neurons within the bladder smooth muscle layer 2 or 10 weeks post-RT. However, 2 weeks post-RT showed a significant increase in the number of cholinergic neurons compared to controls. By 10 weeks post-RT, detrusor cholinergic neuron density was unchanged from controls. MPG gene expression of ChAT was increased at 2 weeks and decreased at 10 weeks post-RT. In contrast, there was no change in Uchl1 at 2 or 10 weeks post-RT.

Conclusions: At early time points post-RT, both carbachol and nerve-mediated contractions are decreased, and ChAT MPG gene expression is increased. EFS bladder contractions become elevated by 10 weeks post-RT. In parallel to the amplified bladder contraction, the number of cholinergic nerve endings was also increased at 10 weeks post-RT. Augmented innervation and bladder contractility post-RT may contribute to long-term bladder dysfunction following prostatic RT in cancer survivors.

S6A21

Title: The endogenous anti-inflammatory protein Annexin-A1 normalizes inflammation and urodynamic parameters during bladder outlet obstruction and after deobstruction surgery

Authors: Francis M. Hughes, Jr., Shelby N. Harper, Brent D. Nosé, Huixia Jin, J. Todd Purves

Affiliations: Div. Urology, Dept. Surgery, Duke University Medical Center, Durham, NC

Introduction/Objectives: Inflammation plays a central role in many benign urological disorders including bladder outlet obstruction (BOO). Contemporary discoveries have shown that inflammation results from a balance of proinflammatory mechanisms, such as inflammasomes, and anti-inflammatory mechanisms, such as the pro-resolving protein Annexin-A1. Recently, we have shown that the NLRP3 inflammasome plays a central role in promoting inflammation during BOO. In the present study we explore the ability of the anti-inflammaotry Annexin-A1 to reduce that inflammation and voiding dysfunction and speed recovery after deobstruction.

Methods: Rats underwent BOO via proximal urethral ligation around a 1 mm (o.d.) catheter. Suprapubic catheters were placed for urodynamics. An Annexin-A1 mimetic (Ac2-26) or vehicle was injected (i.p.) 1 hr prior to surgery and daily for 12 days. In some rats the ligature was removed after 12 days and Ac2-26 or vehicle administered prior to deobstruction and daily for 2 days. Inflammation was assessed by Evans blue and bladder function by urodynamics.

Results: Bladder inflammation was increased by BOO but remained at control levels when given Ac2-26. After deobstruction, inflammation decreased and there was enhanced resolution with Ac treatment. As expected, urodynamics showed high voiding pressures and low flow rates with BOO. These were not relieved by AC2-26 although they were restored by deobstruction with no apparent effect of AC2-26. Void volume was reduced with BOO while frequency increased, consistent with an overactive phenotype. PVR values also increased which reflected a decrease in voiding efficiency.. Void volume and frequency were normalized by treatment with AC2-26 but, PVRs and voiding efficiency were not changed. Following deobstruction void volumes increased, frequency decreased, PVR decreased and efficiency increased, nearing or approaching control values. Ac2-26 treatment further normalized these values.

Conclusions: Annexin-A1 prevents inflammation and bladder overactivity during BOO although it did not affect voiding efficiency. In addition, it sped recovery of normal bladder function following deobstruction. Thus, Annexin-A1 represents an important therapeutic target for both preventing negative effects of BOO and speeding recovery following deobstructive surgery.

Funding Source(s): NIDDK: R01DK103534, R01DK103534, Duke intramural funds

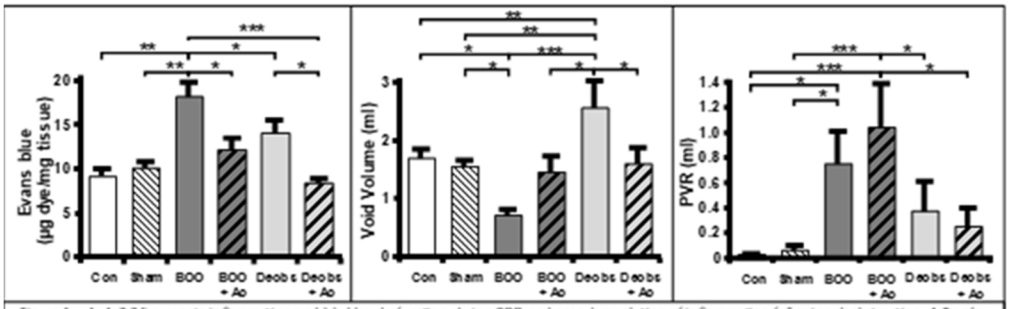


Figure 1 – A. Ac2 26 prevents inflammation and bladder dysfunction during BOO and speeds resolution of inflammation following deobstruction. A Evan's blue extravasation assay. N=7,7,27,9,14 and 21, respectively. B. Void volume during urodynamics. N=15,13,8,7,9 and 7, respectively C. PVR assessed after urodynamics. N=15,13,8,7,9 and 7, respectively. *p<0.05, **p<0.01, ***p<0.001 by Anova followed by Student Newman Keuls.

S6A22

Title: Long-term decentralization of the canine bladder changes the location and pharmacology of intramural nerve nicotinic receptors mediating acetylcholine release

Authors: Nagat Frara[1], Dania Giaddui[1], Danielle S. Porreca[1*], Alan S. Braverman[1], Ekta Tiwari[1], Lucas J. Hobson[1], Courtney L. Testa[1], Michael Mazzei[2], Ida J. Wagner[3], Justin M. Brown[4], Michel A. Pontari[5], Mary F. Barbe[1], Michael R. Ruggieri, Sr.[1,6]

Affiliations: [1]Department of Anatomy and Cell Biology, Lewis Katz School of Medicine, Temple University, Philadelphia, PA, USA
[2]Department of Medicine, Temple University Hospital, Philadelphia, PA, USA
[3]Department of Surgery and [5]Department of Urology, Lewis Katz School of Medicine, Temple University Hospital, Philadelphia, PA, USA,
[4]Department of Neurosurgery, Massachusetts General Hospital, Boston, MA, USA
[6]Shriners Hospitals for Children, Philadelphia, PA, USA

Introduction/objectives: We previously found that bladder smooth muscle contractility is preserved after decentralization indicative of functional muscarinic receptors. Also, we reported the expression of the functional neuromuscular nicotinic receptors in reinnervated bladders as a result of nerve transfer surgeries. Here, utilizing *ex vivo* studies, we evaluate alterations in the expression of nicotinic receptors after long-term decentralization and delayed reinnervation.

Methods: Mucosa-denuded bladder muscle strips were obtained from 11-21 month decentralized (N-4), reinnervated 12 months after decentralization (N=8) and sham operated (N=6) female canines. Strips were suspended in muscle baths and the maximal contractile responses to 120 mM potassium chloride (KCl) were measured. Then, strips were incubated with different antagonists for 20 minutes. Next, contractions to nicotinic agonist epibatidine (10μM) were determined. Responses are expressed as percentages of KCl-induced contraction.

Results: Epibatidine caused atropine sensitive contractions in all groups. The sodium channel blocker tetrodotoxin (TTX, 1μM) inhibited epibatidine-induced contractions in strips from decentralized, but not reinnervated or control bladders. Competitive neuromuscular nicotinic receptor antagonists atracurium (5μM) or tubocurarine (0.1 μM) inhibited the epibatidine induced contractions in strips from reinnervated and control, but not decentralized bladders. The neuronal (α3β4) selective antagonist SR16584 (3-10 μM) inhibited epibatidine contractions in all groups.

Conclusions: Atropine blockade of epibatidine contractions indicates that these nicotinic receptors induce release of acetylcholine that acts on muscarinic receptors to induce bladder muscle contraction. Because TTX does not block epibatidine contractions in reinnervated and control bladders, this suggests that nicotinic receptors are likely located on nerve terminals and their antagonist pharmacology suggests that these consist of both α3β4 neuronal and (α1)2β1δε neuromuscular subtypes. TTX blockade of contractions in the decentralized group suggests that long term decentralization causes nicotinic receptors to relocate from the nerve terminals to along the axons of the presynaptic neurons distant from the neuromuscular junction and their antagonist pharmacology is consistent with neuronal (α3β4) nicotinic receptor subtypes.

Funding Source(s): NINDS R01NS070267.

S6A23

Title: Sonic hedgehog signaling in corpora cavernosal cells from prostatectomy, diabetic, hypertension and Peyronie's patients with erectile dysfunction.

Authors: Sarah Y. Martin, B.S.[1*], Timothy J. Searl, Ph.D.[1], Samuel Ohlander, M.D.[1], Daniel A. Harrington, Ph.D.[2], Samuel I. Stupp, Ph.D.[3], Kevin T. McVary, M.D.[4], Carol A. Podlasek, Ph.D.[1]

Affiliations: [1]University of Illinois at Chicago; [2]UT Health; [3]Northwestern University, [4]Loyola University Stritch School of Medicine.

Introduction/Objectives: Erectile dysfunction (ED) treatments are minimally effective in prostatectomy and diabetic patients due to injury to the cavernous nerve. With denervation the critical smooth muscle undergoes apoptosis and the penis becomes fibrotic, thus altering the corpora cavernosal architecture. In order to devise novel ED therapies, prevention of corpora cavernosal remodeling is critical. In this study we examine the response of human corpora cavernosal cells from several ED patient populations, to determine if ED deriving from mechanisms other than prostatectomy, are responsive to SHH treatment, and we examine signaling molecules critical for smooth muscle growth and regeneration.

Methods: Human corpora cavernosal tissue was obtained from prostatectomy, diabetic, hypertension, and Peyronie's (control) patients (n=36) that were under going prosthesis implant to treat ED. Primary cultures (n=11) were established, and corpora cavernosal cells from passage 3-4 were treated with SHH protein, MSA (control), PBS (control), BMP4, and Gremlin. Growth was quantified by counting the number of cells using a hemocytometer at 3-4 days. The concentration of SHH protein for maximal growth was examined, in addition to a lipid modified more active SHH peptide.

Results: SHH treatment increased smooth muscle growth in human corpora cavernosal cells from prostatectomy, diabetic, hypertension and Peyronie's patients in a similar manner (33-51%). There was no difference in growth using 25ug and 10ug SHH peptide. A more active (150X) SHH peptide further enhanced growth, with more pronounced enhancement in corpora cavernosal cells from hypertension patients. BMP4 increased and Gremlin decreased growth in corpora cavernosal cells from hypertension patients, but not in cells from diabetics, or post prostatectomy.

Conclusions: Corpora cavernosa cells from prostatectomy, diabetic, and hypertension patients increased in response to SHH treatment in a similar manner, suggesting that SHH treatment would be beneficial to enhance smooth muscle regeneration in patients with ED of multiple origins. There is a threshold concentration of SHH protein above which smooth muscle growth is enhanced. Tissue from patients with hypertension responds more strongly to lipid modified SHH, and upregulate BMP4 and down regulate Gremlin, suggesting stimulation of fibrotic signaling, that was not present in cells of other ED origin. Understanding how human corpora cavernosal tissue responds to SHH treatment is critical for clinical translation to ED patients.

Funding Source(s): NIH/NIDDK DK101536

S6A24

Title: NLRP3-Dependent Mechanisms Downregulate Genes Controlling Urothelial Barrier Function in Diabetic Mice

Authors: Michael R Odom[1]; Francis M Hughes Jr[1]; Huixia Jin[1]; J. Todd Purves[1,2]

Affiliation: [1]Department of Surgery, Division of Urology, Duke University Medical Center, Durham, NC. [2]Department of Pediatrics, Duke University Medical Center, Durham, NC.

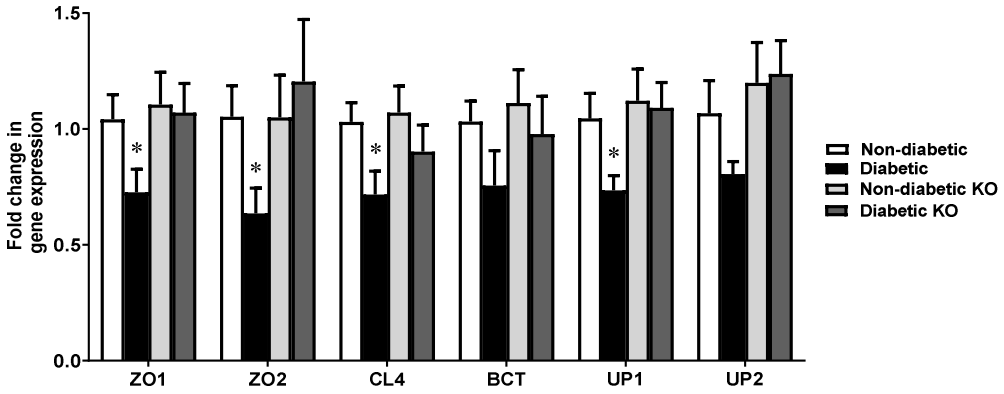
Introduction: Diabetic bladder dysfunction (DBD) is a progressive deterioration of urinary function commonly occurring in patients with diabetes. In addition to high glucose levels, diabetes is associated with metabolic derangement and the production of numerous potentially harmful metabolites which accumulate in the circulation as well as the urine. Bladder urothelia normally maintain an impenetrable barrier to protect underlying smooth muscle but this barrier is known to breakdown during diabetes. We have previously shown in the Akita diabetic mouse model that the NLRP3 inflammasome, a multimeric structure which activates inflammatory cascades, is responsible for diabetic bladder inflammation and dysfunction. In this study we hypothesize NLRP3 activation decreases urothelial barrier function, thus exposing the underlying tissue to high levels of harmful diabetic metabolites. This increases inflammation and bladder dysfunction. Additionally, the loss of barrier function may be a major factor in the increased susceptibility to urinary tract infections. As an initial investigation into this hypothesis, we examined changes in expression of barrier genes in diabetic mice with either intact NLRP3 or genetically deleted NLRP3.

Methods: Four groups of 15 week old female mice were used: non-diabetic control (non-diabetic, n=9), type 1 diabetic Akita mice (diabetic, n=7), non-diabetic control mice with NLRP3 knocked out (non-diabetic KO, n=12), and diabetic NLRP3 knock-out mice (diabetic KO, n=12). Previously we have shown DBD symptoms in the Akita mice at this time point. Urothelia was harvested from each mouse and used for qPCR studies. The following gene expression markers of barrier function were assessed: zona occludin 1 (ZO1), zona occludin 2 (ZO2), Claudin 4 (CL4), beta catenin (BCT), uroplakin 1b (UP1), and uroplakin 2 (UP2).

Results: Urothelia from diabetic mice exhibit significant decreases in expression of ZO1, ZO2, CL4 and UP1. No significant changes in BCT or UP2 gene expression are noted. Importantly, these changes in barrier gene expression did not occur in the diabetic KO mice.

Conclusions: Diabetes reduces expression of genes regulating urothelial barrier function in a NLRP3-dependent manner. This finding provides insight into how DBD develops, and may identify a much needed therapeutic target for patients living with DBD.

Funding: NIH-K12DK100024; PI: Amundsen



S6A25

Title: The role of MIF downstream signaling in PAR4-induced bladder pain.

Authors: Shaojing Ye[1,2*], Fei Ma[1,2], Dlovan F. D Mahmood[1,2], Katherine L Meyer-Siegler[3], Pedro L Vera[1,2]

Affiliations: 1. Lexington VA Health Care System, Lexington, KY; 2. University of Kentucky, College of Medicine, Lexington, KY; 3. St Petersburg Community College, St Petersburg, FL.

Introduction/Objectives: MIF plays a critical role in bladder pain. Activation of intravesical PAR4 receptors leads to non-inflammatory bladder pain through release of urothelial MIF and urothelial HMGB1. Studies have shown that MIF deficiency and/or MIF antagonism at the bladder protect against bladder hyperalgesia (BHA) in mice however the mechanism is still elusive. Accumulated evidence also supports that downstream of MIF signaling is ERK phosphorylation, nitro-oxidative (RNOS) stress and HMGB1 release. We hypothesized that blocking these downstream effects of MIF signaling at the level of the bladder would prevent/reduce bladder pain and potentially open up novel potential therapeutic strategies to treat not inflamed bladder pain.

Methods: We induced bladder pain in female (C57BL6) mice using intravesical PAR4 (100 uM; 1hr) under isoflurane anesthesia as reported previously. Bladder pain (lower abdominal von Frey (VF) 50% threshold) was measured before (baseline) and 24 hr post PAR4-AP or scrambled PAR4 peptide infusion. Intravesical pre-treatment (10 min prior to PAR4) with PBS, FR180204 (FR; selective ERK1/2 inhibitor); methocellulose (methcell; solvent for FR180204); N-acetylcysteine amide (NACA; ROS scavenger) or ethyl pyruvate (EP; to prevent urothelial HMGB1 release) were tested. Post-24 hr treatment, voided volume and frequency on awake mice were also assessed. Additionally, we used anesthetized (urethane) cystometry to determine the effects of PAR4 on micturition parameters. At end of experiment, bladders were collected for histology. All analyses were performed using R.

Results: PAR4 induced BHA was partially blocked by intravesical pre-treatment with and NACA, but not FR180204 (Figure 1). No effects were noted on awake micturition volume or frequency. Finally, no changes were observed in several parameters measured during single cystometry (peak pressure, micturition threshold, voided volume) or intercontraction interval during continuous cystometry between the scrambled peptide-treated and PAR4-treated groups.

Conclusions: PAR4 induced BHA had no change in awake micturition or anesthetized cystometry parameters. Intravesical antagonism of RNOS stress or blockade of HMGB1 release were effectively reducing bladder pain. Blockage of downstream MIF signaling might be a novel way to treat non-infectious bladder pain. Future studies should focus on how RNOS stress leads to non-inflammatory bladder pain.

Funding Source(s): DK121695

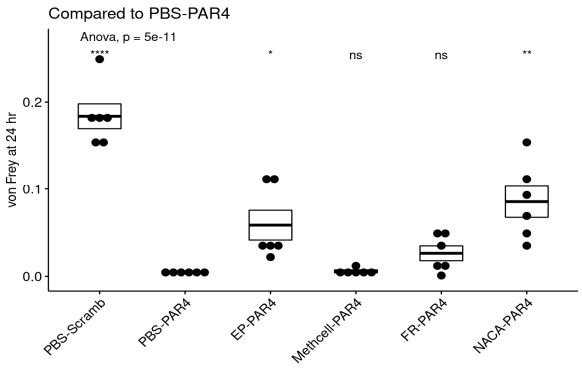


Figure 1. Lower mechanical sensitvity due to PAR 4 and different pretreatments. *** = $p < 0.001$, ** = $p < 0.01$, * = $p < 0.05$

S7A26

Title: Transurothelial Transport of ATP Metabolites

Authors: Violeta N. Mutafova-Yambolieva

Affiliations: Department of Physiology and Cell Biology, University of Nevada Reno School of Medicine, Reno, NV 89557, USA

Introduction/Objectives: Extracellular purinergic signaling is paramount to bladder physiology and pathophysiology. The excitatory purines ATP and ADP and the inhibitory purines AMP, NAD and adenosine contribute to the "purine pool" deep in the bladder wall that regulates bladder excitability. We have recently found that these purines are available at different proportions in suburothelium and in lumen during bladder filling. However, the mechanisms that underlie the differential distribution of biologically active purines on both sides of the urothelium remain elusive. The present study was designed to test whether transurothelial transport of ATP or ATP metabolites contributes to the disproportionate availability of purines in suburothelium and lumen during bladder filling.

Methods: We used an *ex vivo* detrusor-free murine bladder model to obtain direct access to the suburothelium during bladder filling. Preparations were placed in 3-mL chambers containing oxygenated Krebs bicarbonate solution (KBS, pH 7.4, 37^{o}C) and filled with KBS at 15 mL/min until voiding pressure. 1,N^{6}-etheno-ATP (eATP, 2 mM) was applied either to the suburothelium surface or in the lumen of bladder preparations from C57BL/6J mice. Possible appearance of eATP, eADP, eAMP or eADO on the opposite side of eATP application was evaluated by HPLC-FLD in samples collected 1 hour after eATP application.

Results: Sixty minutes after intraluminal application of eATP, equal amounts of eAMP and eADO, but no eATP or eADP appeared in the suburothelium. Notably, eATP was completely degraded to eAMP and eADO in the bladder lumen at the end of the 60-minute period. Sixty minutes after suburothelial application of eATP, eATP was partially degraded to eADP, eAMP and eADO; however only eADO appeared in the lumen at the end of the 60-minute period. Therefore, bladder filling is associated with asymmetric metabolism of ATP on both sides of the urothelium and with asymmetric bilateral purine transport. Lack of eATP on the opposite side of eATP application might be due to i) rapid degradation of transported eATP, ii) rapid degradation of eATP at the site of its application followed by transport of its metabolites to the opposite side, and/or iii) uptake of eATP within the urothelium that is followed by its complete metabolism in the urothelium and appearance of its metabolites on the opposite side of eATP application.

Conclusions: Asymmetric transport of ATP metabolites from lumen to suburothelium and from suburothelium to lumen likely contributes to the asymmetric availability of excitatory and inhibitory purine mediators in suburothelium and lumen during bladder filling. Transurothelial transport of endogenous purines during bladder filling could be a novel therapeutic target in bladder excitability disorders.

Funding Source: NIH grant DK119482

S7A27

Title: M_2 and M_3 muscarinic receptors contribute to the maximal contraction differently in rat and mouse bladders.

Authors: Alan S. Braverman[1] and Michael R. Ruggieri, Sr.[1,2]

Affiliations: [1]Department of Anatomy and Cell Biology, Lewis Katz School of Medicine, Temple University, Philadelphia, PA, USA
[2]Shriners Hospitals for Children, Philadelphia, PA, USA

Introduction/objectives Although the M_2 muscarinic receptor has the greatest density, the M_3 subtype predominantly mediates contraction of the normal urinary bladder as well as most smooth muscles. The aims of this study were to first to determine the contribution of the M_2 and the M_3 receptor subtypes in mediating carbachol induced bladder contraction in wild type mice (WT) and mice lacking either the M_2 or the M_3 receptor subtype. In addition, M_2 and M_3 receptors were selectively inactivated in rat bladders to determine if the contribution of the M_2 and the M_3 receptor to muscarinic receptor stimulation is the same in rat and mouse bladders.

Methods: Full thickness muscle strips obtained from mouse and rat bladders were suspended in muscle baths and the maximal contractile response was determined using KCl then a concentration response curve to carbachol was performed by the cumulative addition of carbachol. To selectively inactivate M_3 receptors, muscle strips were incubated with 4-damp mustard in the presence of methoctramine. To inactivate M_2 receptors, strips were incubated with phenoxybenzamine in the presence of darifenacin. Subtype selective immunoprecipitation was used to calculate the density of M_2 and M_3 receptors following receptor inactivation.

Results: In the mouse bladder, the M_3 receptor alone can mediate about 80% of the muscarinic stimulated contractile response while the M_2 receptor alone can mediate about 5% of the maximal response. This is different than in the mouse stomach where the M_2 receptor alone can mediate about 25% of the response. In the rat bladder, when the majority of M_3 receptors are inactivated, M_2 receptors induce about 50% of the maximal response. When most M_2 receptors are inactivated, M_3 receptors also induce about 50% of maximal contraction.

Conclusions: Differences exist in the contribution of the M_2 and M_3 muscarinic receptors to mediate contraction between species and within a species for different smooth muscles. Whether human bladder smooth muscle is more similar to the rat or mouse bladder is unknown. Caution must be used when using results from one species as evidence for a similar function in a different species.

Funding Source(s): NIH R01DK043333

S7A28

Title: Agonist-induced contractions promote F-actin polymerization in bladder smooth muscle tissue

Authors: Vivian Cristofaro[*1,2], Josephine A. Carew[1,2], Maryrose P. Sullivan[1,2]

Affiliations: [1]VA Boston Healthcare System, [2]Harvard Medical School

Introduction/Objectives: In response to mechanical stimuli, bladder smooth muscle is able to rapidly adapt by remodeling of the cytoskeleton to restore wall stress. However, the role of actin cytoskeletal dynamics in force transduction and contraction in the bladder are not well understood. Actin polymerization is a reversible process in which filamentous actin (F-actin) is formed from monomeric globular actin (G-actin). In this study we investigated whether changes in BSM evoked responses were associated with dynamic changes in actin polymerization.

Methods: Mouse BSM tissue without mucosa were equilibrated in organ baths containing Kreb's solution at 37℃ under 0.5 grams of tension. Carbachol (CCh, 1μM) responses were recorded under baseline conditions as well as after incubation with either jasplakinolide (0.5μM), an agent that promotes actin-polymerization, or cytochalasin-D (2μM), a selective inhibitor of actin polymerization. Parallel BSM strips that remained unstimulated for the same time period were used as control. At the end of the experiment each strip of tissue was processed to detect changes in F/G-actin ratio among different treatments.

Results: Compared to unstimulated control, CCh-stimulated tissues displayed significantly higher levels of F/G-actin ratio. Moreover, the F/G-actin ratio further increased in CCh-stimulated tissue in the presence of jasplakinolide. In contrast, the administration of cytochalasin-D significantly decreased the amplitude of CCh responses compared to tissue stimulated in absence of cytochalasin -D and prevented the increase in F/G-actin ratio induced by CCh stimulation.

Conclusions: The increases in the amplitude of evoked contractions in CCh-stimulated BSM tissue that parallel the increase in F/G-actin ratio indicate that dynamic changes in F-actin polymerization contribute to force transduction in response to physiologic stimuli.

Funding Source(s): Department of Veteran Affairs, Research Service, Washington DC.

S7A29

Title: Novel insights into human detrusor smooth muscle function: cell-signaling pathways regulating $K_{Ca}1.1\alpha$ subunit subcellular localization and trafficking

Authors: M. Dennis Leo[1], Eric S. Rovner[1,2], Robert W. Wake[1,3], Somasundaram Raghavan[1], Wenkuan Xin[1], John Malysz[1], Georgi V. Petkov[1,3,4]

Affiliations: [1]Department of Pharmaceutical Sciences, College of Pharmacy, University of Tennessee Health Science Center, Memphis, TN; [2]Department of Urology, Medical University of South Carolina, Charleston, SC; [3]Department of Urology and [4]Department of Pharmacology, College of Medicine, University of Tennessee Health Science Center, Memphis, TN

Introduction/Objectives: $K_{Ca}1.1$ (also known as "BK") channels, composed of a pore-forming α- and regulatory β-subunits, are key regulators of detrusor smooth muscle (DSM) excitability and contractility. The molecular and cellular mechanisms that control the expression and trafficking of $K_{Ca}1.1\alpha$ proteins to the DSM plasma membrane (cell surface) are unknown. Here, we examined the $K_{Ca}1.1\alpha$ channel trafficking mechanisms and their regulation by muscarinic and protein kinase-A (PKA) signaling pathways in rat and human DSM.

Methods: We employed a novel technique called '***surface biotinylation***' in conjunction with immunocytochemistry to examine the overall cell membrane versus intracellular localization of $K_{Ca}1.1\alpha$ subunits. Human and rat DSM tissue strips were incubated with non-cell permeable biotin tagged reagents that specifically bind to cysteine and lysine protein residues. Biotinylated surface proteins were then separated using avidin beads, eluted and Western blotting performed to determine the overall cell surface (plasma membrane) to intracellular localization of the channel subunit proteins. Immunohistochemistry analyses for biotin-tagged proteins was also performed on biotinylated and PFA-fixed DSM strips.

Results: To validate the surface biotinylation technique in DSM, we used Western blot to examine the distribution profile of cytochrome C, a mitochondrial protein not appearing on the surface. Cytochrome C localization was entirely intracellular. Biotinylated DSM strips probed with AlexaFluor546-tagged streptavidin showed staining through all layers of DSM confirming the effectiveness of our protocol. Surface biotinylation revealed that in rat DSM, ~95% of total $K_{Ca}1.1\alpha$ was surface localized, with the remaining intracellular. Similarly, comparative experiments on human DSM showed that $K_{Ca}1.1\alpha$ surface expression was ~93% of the total protein. In rat and human DSM, bethanechol (1 μM), a muscarinic receptor-selective agonist, decreased surface $K_{Ca}1.1\alpha$ expression by ~70%, compared to untreated controls. PKI, a PKA inhibitor, decreased both total and surface expression of $K_{Ca}1.1\alpha$ by ~40% compared to untreated DSM controls.

Conclusions: By employing ***surface biotinylation***, a novel approach in urological research, we revealed that in rat and human DSM, $K_{Ca}1.1\alpha$ subunits are primarily surface localized. Muscarinic receptor and PKA signaling pathways differentially modulate the DSM $K_{Ca}1.1\alpha$ subcellular localization. These exciting new data reveal paradigm-shifting novel regulatory pathways of $K_{Ca}1.1\alpha$ ion channel subunit trafficking mechanisms that regulate human urinary bladder function.

Funding Sources: NIH P20 DK-123971, NIH R01 DK-106964, NIH R01 HL-149662, and VanVleet Endowment.

S7A30

Title: Non-voiding Contractions are not Dyssynergic Voiding Contractions: A Study in Suprasacral Spinal Cord Injured Rats

Authors: Jillene M. Brooks[1], Danielle J. Degoski[1], Matthew O. Fraser[1,2]*

Affiliations: [1]Institute for Medical Research, [2]Duke University and Durham VA Medical Centers

Introduction/Objectives: Neurogenic bladder with detrusor overactivity secondary to suprasacral spinal cord injury (sSCI) is often occasioned by high pressure non-voiding contractions (NVC) that may or may not precede a voiding contraction (VC). In humans with complete sSCI, a primitive spinal micturition reflex VC may be revealed, although because it is characterized by phasic striated sphincter activity and is not under conscious control, it is considered to be both detrusor-sphincter dyssynergia (Blaivas Type 2 DSD) and incontinence. In many mammalian species studied to date, phasic activity of the striated sphincter (SSA) may be utilized normally during the micturition reflex, and this phasic SSA appears to be generated within the lower lumbar spinal cord. Following spinal shock and return of bladder-to-bladder reflexes in the complete sSCI rat, phasic SSA may once again be employed for voiding. However, as in all species, there may also occur numerous high pressure NVC prior to any VC, if present. These NVC have been discussed/described/treated as blocked void attempts due to tonic SSA during an attempted VC (e.g. Blaivas Type 3 DSD in humans). In other words, the very word, dyssynergia, implies a blocked void attempt. Our laboratory has long been interested in the physiological differences between NVC and VC and here report that there are differences in rates of contraction and relaxation that support different origins of the two types, supporting the assertion that DSD, as described, is an inaccurate term.

Methods: We opportunistically revisited prior experiments in 4-week post-sSCI female SD rats (n=14) undergoing cystometric evaluation of drug effects on NVC. We examined the NVC and VC during the control periods in traces that demonstrated both high pressure prodromal NVC and spinal micturition center-mediated void events (as evidenced by phasic SSA). We converted intravesical pressure traces to their differential curves and measured maximum and minimum values during VC and the immediately preceding 1-3 NVC. A minimum of 2 cycles were sampled from each animal during the final stages of the treatment control period and/or after normal saline vehicle, parallel-dosing control administrations (ml/kg). NVC and VC means from each animal were used to represent that animal in the statistical analysis. Data were analyzed by 2-tailed Wilcoxon matched-pairs signed rank test for both maximal and minimal NVC vs VC values.

Results: Rates of rise were significantly faster in VC vs NVC (medians 3.5 vs 2.1 cmH2O/sec, resp., P=0.0001), as were rates of relaxation (-3.4 vs -2.0 cmH2O/sec, resp., P=0.0001). While differences in relaxation rate may, in part, be accounted for by post-void decreased intravesical volume, this does not explain the differences seen in rise rates.

Conclusions: These results provide support for the involvement of different physiological mechanisms governing the contractions of NVC and VC, that, together with pharmacological data, also support the notion that NVC are primarily of myogenic while VC are of neurogenic (i.e. parasympathetic) origins. In other words, NVC are not sphincter-blocked (dyssynergic) VC.

Funding Source(s): DoD SCIRP IIR–SC110031

5th Annual Meeting of the Society for Pelvic Research

December 11-13, 2020

Virtual Format

#PelvRes20

Start Time	End Time	Duration	Abst #		Presenter
Friday, December 11, 2020					
Trainee Workshop					
				Trainee Affairs Committee Workshop - Moderators: Michael Odom, PhD and Aileen Ouyang, PhD Candidate	
11:00 AM	12:00 PM	1:00		Career Planning and Professional Networking in a World of Social Distance	Tierney Bates, EdD
SPR 2020 Satellite Symposium - NIH P20 Center, Albert Einstein College of Medicine, NY					
				Application of Nanotechnology in the Field of Benign Urologic Disease	
1:00 PM	1:10 PM	0:10		Introduction	Kelvin Davies, PhD
1:10 PM	1:40 PM	0:30		Keynote Address - Nanomedicines for the Treatment of Renal Disease	Daniel Heller, PhD
1:40 PM	2:00 PM	0:20		The "Einstein Nanoparticle": Background and History, Synthesis, Physico-chemical Characteristics and Adaptations to Benign Urologic Disease Research	Joel Friedman MD, PhD and Parimala Nacaharaju, PhD
2:00 PM	2:20 PM	0:20		Application of Nanotechnology to Sexual Medicine	Kelvin Davies, PhD and Moses Tar, MD
2:20 PM	2:40 PM	0:20		Nanotechnology applied to development of delivery systems for bladder targeted therapeutics	Sylvia Suadicani, PhD
2:40 PM	3:00 PM	0:20		Invited Speaker - NO-releasing nanoparticles ameliorate detrusor overactivity in transgenic sickle cell mice via restored NO/ROCK signaling	Serkan Karakus, MD
3:00 PM	3:15 PM	0:15		Q & A	
Main Meeting					
4:00 PM	4:05 PM	0:05		Welcome, Day 1, Opening Remarks, Mission of SPR	Michael Ruggieri, Sr, PhD
				Session 1: Funding Opportunities - Moderators: Armand Allkanjari, MD, Urology Resident (PGY3) and Michael Ruggieri, Sr, PhD	
4:05 PM	4:45 PM	0:40		Special Guest Lecture - Basic/Translational Science Funding Opportunities at NIA	Candace Kerr, PhD
4:45 PM	4:55 PM	0:10		Q & A	
Saturday, December 12, 2020					
12:00 PM	12:05 PM	0:05		Welcome, Day 2	Maryrose Sullivan, PhD
				Session 2: Novel Therapeutics and Diagnostics - Moderators: Olivia Giovannetti, PhD Candidate and Matthew Fraser, PhD	
12:05 PM	12:45 PM	0:40		Keynote Address - Translating Basic Science Research into Clinical Management of Men and Women with Genito-Pelvic Dysesthesia (GPD)	Irwin Goldstein, MD
12:45 PM	12:55 PM	0:10		Q & A	
12:55 PM	1:05 PM	0:10	S2A1*	Nerve transfer for restoration of lower motor neuron-lesioned bladder function: Correlation between histological changes and nerve evoked contractions	Barbe, MF
1:05 PM	1:15 PM	0:10	S2A2	The Female Bladder and Urethra Harbor Distinct Microbial Communities	Wolfe, AJ
1:15 PM	1:25 PM	0:10	S2A3	Nerve transfer for restoration of lower motor neuron-lesioned bladder, urethral and anal sphincter function: Exploring sensory and motor reinnervation	Tiwari, E
1:25 PM	1:35 PM	0:10	S2A4*	Soft silicone-based neural interface to modulate bladder function	Kumar, R
1:35 PM	1:45 PM	0:10	S2A5	Nerve transfer for restoration of lower motor neuron-lesioned bladder function: Attenuation of ex-vivo, nerve-evoked, purinergic, bladder smooth muscle contractions.	Frara, N
1:45 PM	1:55 PM	0:10		Q & A	
1:55 PM	2:10 PM	0:15		BREAK	
				Session 3: Models and Methods - Moderators: Nagat Frara, PhD, Postdoctoral Fellow and Georgi Petkov, PhD	
2:10 PM	2:20 PM	0:10	S3A6*◊	Acyloxyacyl hydrolase mediates gut microbiome in a mouse model of interstitial cystitis	Rahman-Enyart, A
2:20 PM	2:30 PM	0:10	S3A7	Chronic high fat diet increases vaginal sphincter laxity but does not affect pelvic floor muscle function in mice	Burleson, LK
2:30 PM	2:40 PM	0:10	S3A8	Investigation of sensory and autonomic innervation using immunohistochemistry following cadaveric simulation of mid-urethral sling surgery	Giovannetti, O
2:40 PM	2:50 PM	0:10	S3A9	Microarray analysis of human corpora cavernosa tissue from erectile dysfunction patients with diabetes and Peyronie's	Searl, TJ
2:50 PM	3:00 PM	0:10	S3A10	Immunohistochemical Characterization of Glandular Tissue in the Female Periurethral Space Targeted by Mid-Urethral Sling Procedures	Tomalty, D
3:00 PM	3:10 PM	0:10		Q & A	
				Session 4: Physiology & Pharmacology I - Moderators: Michael Odom, PhD, Postdoctoral Fellow and Maryrose Sullivan, PhD	
3:10 PM	3:50 PM	0:40		State of the Art Lecture - Motor Cortical Treatment Targets for Chronic Pelvic Pain: Big Data, Small Data, and Clinical	Jason Kutch, PhD
3:50 PM	4:00 PM	0:10		Q & A	
4:00 PM	4:10 PM	0:10	S4A11	Diabetic bladder dysfunction progresses from early overactivity to an underactive bladder state in Akita diabetic mice	Allkanjari, A
4:10 PM	4:20 PM	0:10	S4A12	Peptide amphiphile nanofiber hydrogel delivery of Sonic hedgehog protein to the penis and cavernous nerve, suppresses intrinsic and extrinsic apoptotic signaling mechanisms, which are an underlying cause of erectile dysfunction	Martin, SY
4:20 PM	4:30 PM	0:10	S4A13	Enhanced neurogenic activity and nerve density in smooth muscle strips taken from closer to the serosal side of the human and dog bladder	Frara, N
4:30 PM	4:40 PM	0:10	S4A14	Lateralization of Bladder Function in Normal Female Canines	Giaddui, D
4:40 PM	4:50 PM	0:10	S4A15	Annexin A1 inhibits NLRP3 and prevents inflammation during bladder outlet obstruction	Harper, SN
4:50 PM	5:00 PM	0:10		Q & A	
Sunday, December 13, 2020					
12:00 PM	12:05 PM	0:05		Welcome, Day 3	Matthew Fraser, PhD
				Session 5: Neuroscience - Moderators: Dania Giaddui, BS and Vivian Cristofaro, PhD	
12:05 PM	12:45 PM	0:40		Keynote Address - Genital dysesthesias in relation to pelvic sensory nerves and their projections	Barry Komisaruk, PhD
12:45 PM	12:55 PM	0:10		Q & A	
12:55 PM	1:05 PM	0:10	S5A16*	Loss of urethral sensitivity leads to functional deficits in rat model: implications for age-related underactive bladder	Geramipour, A
1:05 PM	1:15 PM	0:10	S5A17	Alzheimer's Disease-associated Pathology in a Transgenic Mouse Model Results in Altered Voiding Function	Hardy, CC
1:15 PM	1:25 PM	0:10	S5A18	Acyloxyacyl hydrolase regulates pelvic pain and memory by microglia activation	Rahman-Enyart, A
1:25 PM	1:35 PM	0:10	S5A19	Urinary Pathophysiology of a Demyelination Model of Multiple Sclerosis	Ramasamy, R
1:35 PM	1:45 PM	0:10	S5A20	Prostatic Radiation Increases Bladder Cholinergic Nerve Density Leading to Enhanced Nerve-Mediated Contractions	Turner, AC
1:45 PM	1:55 PM	0:10		Q & A	
1:55 PM	2:10 PM	0:15		BREAK	
				Session 6: Physiology & Pharmacology II - Moderators: Ekta Tiwari, PhD, Postdoctoral Fellow and Sylvia Suadicani , PhD	
2:10 PM	2:20 PM	0:10	S6A21	The endogenous anti-inflammatory protein Annexin-A1 normalizes inflammation and urodynamic parameters during bladder outlet obstruction and after deobstruction surgery	Hughes, FM
2:20 PM	2:30 PM	0:10	S6A22	Long-term decentralization of the canine bladder changes the location and pharmacology of intramural nerve nicotinic receptors mediating acetylcholine release	Porreca, DS
2:30 PM	2:40 PM	0:10	S6A23	Sonic hedgehog signaling in corpora cavernosal cells from prostatectomy, diabetic, hypertension and Peyronie's patients with erectile dysfunction	Martin, SY
2:40 PM	2:50 PM	0:10	S6A24	NLRP3-Dependent Mechanisms Downregulate Genes Controlling Urothelial Barrier Function in Diabetic Mice	Odom, MR
2:50 PM	3:00 PM	0:10	S6A25	The role of MIF downstream signaling in PAR4-induced bladder pain	Ye, S
3:00 PM	3:10 PM	0:10		Q & A	
				Session 7: Physiology & Pharmacology III - Moderators: Aileen Ouyang, PhD Candidate and Kelvin Davies, PhD	
3:10 PM	3:50 PM	0:40		State of the Art and ICS Lecture - The Aging Bladder Phenotype: In the Lab	Phillip Smith, MD
3:50 PM	4:00 PM	0:10		Q & A	
4:00 PM	4:10 PM	0:10	S7A26*	Transurothelial Transport of ATP Metabolites	Mutafova-Yambolieva, VN
4:10 PM	4:20 PM	0:10	S7A27	M_2 and M_3 muscarinic receptors contribute to the maximal contraction differently in rat and mouse bladders.	Braverman, AS
4:20 PM	4:30 PM	0:10	S7A28	Agonist-induced contractions promote F-actin polymerization in bladder smooth muscle tissue	Cristofaro, V
4:30 PM	4:40 PM	0:10	S7A29	Novel insights into human detrusor smooth muscle function: cell-signaling pathways regulating $K_{Ca}1.1\alpha$ subunit subcellular localization and trafficking	Leo, MD
4:40 PM	4:50 PM	0:10	S7A30	Non-voiding Contractions are not Dyssynergic Voiding Contractions: A Study in Suprasacral Spinal Cord Injured Rats	Brooks, JM
4:50 PM	5:00 PM	0:10		Q & A	
5:00 PM	5:05 PM	0:05		Trainee Awards Presentations	Mary Barbe, PhD and Monty Hughes, PhD
5:05 PM	5:10 PM	0:05		Closing Remarks	Michael Ruggieri, Sr, PhD
	5:10 PM			MEETING ADJOURNS	

Disclaimer

Funding for this conference was made possible, in part, by 1R13 AG071166-01 from the National Institute on Aging (NIA).

The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention by trade names, commercial practices, or organizations imply endorsement by the U.S. Government.

———

Final Announcements

SPR 2021 to be held in Charlotte, NC

(if possible)

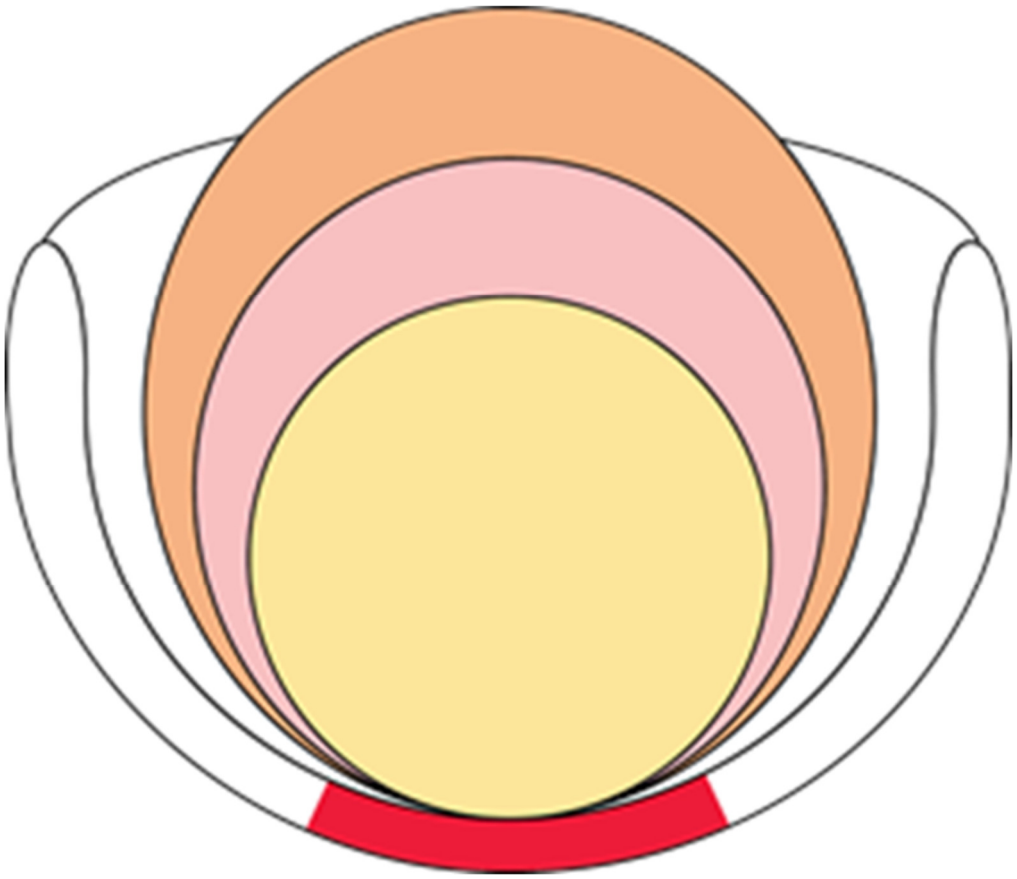
Open Post-Doctoral Research Positions

POSTDOCTORAL RESEARCH POSITION IN EXPERIMENTAL NEUROSCIENCE Through the SPARC program, an NIH-sponsored postdoctoral research position is available in in vivo experimental neuroscience. The project goal is to develop a new framework for understanding neural control of autonomic organ systems, with a special focus on the lower urinary tract. We use rodent models of the urinary tract to understand how multiple reflexes interact to regulate organ function using electrophysiology, neuromodulation, cystometry, and longitudinal metabolic studies. FIU is leading groups of mathematicians and computer scientists (at the Universities of Missouri, Northeastern, Wisconsin-Madison, and US Military Academy) to incorporate the results of these experiments into a new type of computational model, with a long-term goal of improving neuromodulation therapy for the lower urinary tract and other organ systems. The postdoc will lead this consortium effort with the PI (Zachary Danziger, zdanzige@fiu.edu). More at anil.fiu.edu.

Web link: https://anil.fiu.edu/wp-content/uploads/PD_SPARC_Ad_Danziger2020.pdf

POSTDOCTORAL FELLOWSHIP IN AGING/LOWER URINARY TRACT PHYSIOLOGY The Smith Lab is seeking a mature postdoctoral fellow with experience and interest in the impact of aging on lower urinary tract control physiology. We are principally interested in discovering the mechanisms by which a bladder/brainstem feedback loop may regulate bladder sensory afferent sensitivity to bladder volume, the mechanisms of age-determined compromise the fidelity of feedback control, and how impaired regulatory control contributes to the increasing incidence of bladder control disorders in older humans. Our principle focus is on an ion channel which may mediate autonomic/neuroendocrine and urothelial/paracrine influence over detrusor smooth muscle and possibly bladder DRG neurons. Our lab is part of the UConn Center on Aging complex, and collaboration with investigators from a variety of disciplines with a shared interest in aging is a central theme.

PI is Dr. Phillip P. Smith MD (ppsmith@uchc.edu).



#PelvRes20