BIOGRAPHICAL SKETCH

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NAME: Malykhina, Anna P

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

POSITION TITLE: Professor and Director of Basic and Translational Urology Research

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Belorussian State University, Minsk, Belarus	M.Sc	1993	Biology/Physiology
Institute of Radiobiology, National Academy of Sciences, Belarus	Ph.D	1998	Physiology / Electrophysiology
University of Oklahoma, OUHSC, Dept. of Physiology	Postdoc	2001-2004	Electrophysiology

A. Personal Statement

I have relevant research expertise and mentoring track record to serve as a training faculty on T32 application. I am a trained physiologist/electrophysiologist with over 25 years of experience in physiology and pathophysiology of urinary bladder dysfunction with particular emphasis on the mechanisms underlying chronic pelvic pain, pelvic organ cross-sensitization, pediatric dysfunctional voiding, detrusor over- and underactivity, interplay between urologic and nervous systems, and neurogenic voiding bladder. I have been continuously involved in mentoring undergraduate and graduate students, postdoctoral fellows and junior faculty since 2008. I served as Chair of the Selection Committee and Coordinator of Summer Research Scholarship Program funded by the Urology O`Brien Center at University of Pennsylvania (UPenn, NIH/NIDDK P50 DK052620), and Director of Educational Enrichment Program supported by NIH/NIDDK P20 DK097819 Center grant. I served as mentoring faculty in several Educational Programs including Penn Center for Undergraduate Research and Fellowships (SURF Program); Women's Reproductive Health Research (WRHR) Career Development program (NIH sponsored K12 grant); Undergraduate Student Scholars Program (NIH R25 grant) in the Center for Molecular Studies in Digestive and Liver Diseases at UPenn; and Surgical Research Program for Medical students in the Department of Surgery at the UCD. I have also been a member of the Recruitment and Admissions Committee for the Neuroscience Graduate Program at the UCD since 2016.

Within the last 5 years, I had mentored 8 undergraduate students, 5 graduate students, 9 postdoctoral fellows, and 2 junior faculty. I always encourage my trainees to participate in activities required to identify and transition into careers in the biomedical research workforce that are consistent with their skills, interests, and values. I am currently an Instructor leading one of the discussion groups for the course “Responsible conduct of research”, and provide a constructive feedback to my students regarding rigor and reproducibility of the research; development of unbiased experimental design, methodology, analysis, interpretation, and reporting of the results. I personally encourage my trainees to take informal courses to address unconscious bias in the workplace, diversity training, and cultural differences. I truly believe that diversity, equity and inclusion play key role in the overall success of our Graduate Program. Under my supervision, my mentees received 4 national and international awards, successfully competed for 7 research grants, and published 21 manuscripts in clinical, translational and basic science research. Below are examples of the papers published by my trainees:

a) Lei Q., **Malykhina A.P**. (2012) Colonic inflammation up-regulates voltage-gated sodium channels in bladder sensory neurons via activation of peripheral transient potential vanilloid 1 receptors. *Neurogastroenterology and Motility* Jun: 24(6):575-85, e257, PMID:22420642
b) Lei Q., Pan X.-Q., Villamor A.N., Asfaw T.S., Chang S., Zderic S.A., **Malykhina A.P**. (2013) Lack of transient receptor potential vanilloid 1 channel modulates the development of neurogenic bladder dysfunction induced by cross-sensitization in afferent pathways. *J Neuroinflammation,* Jan 11;10(1):3. PMID:23305398
c) Lei Q., Pan X.-Q., Chang S, Malkowicz S.B., Guzzo T.J., **Malykhina A.P** (2014) Response of the human detrusor to stretch is regulated by TREK-1, a two-pore domain (K2P) mechano-gated potassium channel. *J Physiology (London),* July 15, 592 (Pt 14):3013-30. PMID: 24801307
d) Lee S, Nedumaran B, Hypolite J, Caldwell B, Rudolph MC, **Malykhina AP.** (2019) Differential neurodegenerative phenotypes are associated with heterogeneous voiding dysfunction in a coronavirus-induced model of multiple sclerosis. *Sci Rep*. Jul 26;9(1):10869. PMID: 31350464

Active grant support:

R01 DK121506 Malykhina (PI) 08/01/2019-07/30/2023
NIH/NIDDK
Regulation of pelvic pain and micturition reflex by VEGF in urological chronic pelvic pain syndrome
Role: PI
This application evaluates the role of VEGF pathways in neurogenesis and neural plasticity of the neural pathways innervating the lower urinary tract.

R01 DK116648 Malykhina (PI) 09/08/2020-06/30/2023
NIH/NIDDK
Mechanisms of neurogenic bladder dysfunction in a viral murine model of multiple sclerosis
Role: PI
The project investigates the mechanisms of lower urinary tract symptoms (LUTS) in neurodegenerative disorders such as multiple sclerosis (MS). The application includes translational animal studies to evaluate the role of neurodegenerative changes in the nervous system in the occurrence of neurogenic LUTS.

R01 DK129260 Xie (PI, Malykhina-Co-investigator) 08/05/2021-05/30/2026
NIH/NIDDK
Activating Peripheral Glia to Relieve Visceral Pain in Animal Models of Urological Chronic Pelvic Pain Syndrome (UCPPS)
Role: Co-investigator
The overall objective of this application is to identify signaling pathways in sensory satellite glial cells (SGCs) that can be targeted to alleviate the symptoms of Urological Chronic Pelvic Pain Syndrome (UCPPS)

K23 DK125673 Cost (PI, Malykhina -Mentor) 07/08/2020-04/30/2024
NIH/NIDDK
Impact of Systemic Cytotoxic Chemotherapy on Bladder Function in Children
Role: Mentor
The project investigates the effects of cytotoxic chemotherapy on the function of the urinary bladder in children with cancer.

B. Positions, Scientific Appointments, and Honors

Positions

2001-2004 Postdoctoral Fellow, Department of Physiology, University of Oklahoma HSC, Oklahoma, OK
2004-2006 Research Associate, Department of Physiology, University of Oklahoma HSC, Oklahoma, OK
2006-2008 Assistant Professor of Research, Department of Physiology, University of Oklahoma HSC Oklahoma City, OK
2008-2014 Assistant Professor, Division of Urology, Department of Surgery, University of Pennsylvania

Perelman School of Medicine, Philadelphia, PA

2014-2020 Associate Professor, Division of Urology, Department of Surgery, University of Colorado Denver, Anschutz Medical Campus, Aurora, CO

2018- Director, Basic and Translational Urology Research Program, Division of Urology, Department of Surgery, University of Colorado Denver, Anschutz Medical Campus, Aurora, CO

2020- Professor, Division of Urology, Department of Surgery, University of Colorado Denver, Anschutz Medical Campus, Aurora, CO

Scientific Appointments

2009 Member, NIH Special Emphasis Study Section ZDK1 GRB -6 (O2), UROLOGY ARRA

2007- Member, American Gastroenterological Association (AGA)

2008- Member, International Pelvic Pain Society

2009- Member, American Urological Association (AUA)

2010- Member, American Physiological Society (APS)

2011- Member, Society for Basic Urologic Research (SBUR)

2010 Member, NIH Special Emphasis Study Section ZDK1-GRB-G (M1), KUH-Fellowship review

2010 Review Editor, Frontiers in Autonomic Neuroscience

2010 Co-Chair, Workshop “Neurogenic Bladder Dysfunction” at the BIT`s 1st Annual Symposium NeuroTalk, Singapore

2011 Member, NIH Special Emphasis Study Section ZDK1-GRB-G (M1), KUH-Fellowship review

2011 Think Tank 9 Lead, International Consultation on Incontinence–Research Society (ICI-RS), Bristol, UK

2011 Ad Hoc Member, NIH Somatosensory and Chemosensory Systems (SCS) Study Section

2011 Member and UPenn Representative, RUM Protocol Development Committee (ROSETTA trial), Pelvic Floor Disorders Network (U01)

2013 Invited Reviewer, Medical Research Council (MRC), United Kingdom

2014 Member, NIH Special Emphasis Study Section ZDK1 GRB-S (M3) – NIDDK P20 Developmental Centers Review Panel

2014 Member, NIH Special Emphasis Study Section ZDK1 ZDK1 GRB-G (M3 and M4), NIDDK MAPP Network Review Panel

2012 Member, NIH Special Emphasis Study Section ZDK1 GRB-G (O1), NIDDK KUH Fellowship Review

2015 Member, NIH Special Emphasis Study Section ZDK1 GRB-3 (O1), U54 O`Brien Centers Review Panel

2015- Editorial Board, Neurourology and Urodynamics

2015 Member, NIH Special Emphasis Study Section, ZRG1 DKUS G 90 (former UGPP study section), Urology and Urogynecology

2016 Member, NIH Special Emphasis Study Section ZDK1 GRB-3 (02) “George O`Brien Urology Cooperative Research Centers Program (U54)” Review Panel

2017- Participating Site Director, Pediatric Urology Research Fellowship Program, UCD

2017 Podium Session Moderator, PD70: Urodynamics/Lower Urinary Tract Dysfunction/Female Pelvic Medicine: Basic Research & Pathophysiology III, AUA meeting, Boston, MA

2017 Member, NIH Special Emphasis Panel/Scientific Review Group NGTT (53) 1, SPARC grants

2018 Member, NIH Special Emphasis Study Section, ZDK1 GRB-3 O1, Urology O’Brien Centers (U54) Review Meeting

2017-2019 Member, Research Advocacy Committee of the AUA Research Council

2018-2020 Chair, Membership Committee, Society for Basic Urologic Research (SBUR)

2018 Member, NIH Special Emphasis Study Section, ZDK1 GRB-3 O1, Urology O’Brien Centers (U54) Review Meeting

2019 Member, NIH Special Emphasis Study Section, ZDK1 GRB-G-M1/M2, NIDDK KUH Fellowship Review (3 meetings a year)

2019 Member, NIH Special Emphasis Study Section, ZDK1 GRB-M (M2), NIDDK Lower Urinary Tract Symptoms (LURN II) Network Limited Competition

2019 Member, NIH Special Emphasis Study Section, ZRG1 DKUS- B(90), Urologic and Urogynecologic Applications

2020 Member, Department of Defense CPMRP IIR-2 panel of the Chronic Pain Management Research Program
2020 Member, NIH Special Emphasis Study Section, ZGM1 RCB-3 (C1) Review of Centers of Biomedical Research Excellence (COBRE) Applications
2020 Co-Chair, NIH Special Emphasis Study Section, ZRG1 DKUS-R (90), Urologic and Urogynecologic Applications, October 29-30
2021 Member, NIH/NIDDK Special Emphasis Study Section, ZDK1 GRB-T (M3), Urology O'Brien Centers (U54) Review Meeting, March 18-19
2021 Member, NIH/NIDDK Special Emphasis Study Section, ZRG1 DKUS-L (54) R, R21 applications in Kidney Diseases Review Meeting, March 31

Honors

2000 Award Grant "Outstanding PhD Young Scientist" (under age of 30) from the President of Belarus
2002 Abbott Laboratories and American Physiological Society (GI Section), Postdoctoral Fellow Award
2008 American Gastroenterological Association, ASW08 Scholar
2008 Prize Winning Abstract NGM 2008, Lucerne, Switzerland
2008 Scholar, NGM 2008 Young Investigator Meeting, Lucerne, Switzerland
2012 Prize Winning Abstract, SBUR Fall Symposium, Miami, Florida
2013 "Best of Posters" Award, AUA annual meeting, San Diego, CA
2016 UCD Graduate School Nomination for BEST Faculty Award

C. Contributions to Science

1. The role of mechanosensitive ion channels in detrusor overactivity. This research direction emerged from my postdoctoral work on expression and function of several ion channels in the lower gastrointestinal tract, and their role in excitability and contractility of the visceral smooth muscle. We established for the first time that activation of peripheral TRPV1 receptors in the colon triggered an increase in voltage-gated Na+ channels (VGSC) in lumbosacral bladder dorsal root ganglion (DRG) neurons, and also clarified the role of TRPV1/VGSC "cross-talk" in the development of pelvic organ cross-sensitization. The recent studies from my laboratory determined that TREK-1 channel is the predominantly expressed member of stretch-activated K2P channels in the human detrusor, and its expression and function are diminished in patients with overactive LUTS. We also identified two TREK-1 mutations in the human urinary bladder associated with overactive LUTS, which are the first mutations reported in human bladder TREK-1 channels. Our animal studies from TREK-1 KO mice revealed an elevated basal muscle tone, enhanced spontaneous activity and increased contractile responses in the detrusor without significant changes in bladder morphology. We use human bladder specimens from patients with overactive LUTS, human DRG, TREK-1 KO animals, two animal models of overactive LUTS, as well as newly created in our laboratory genetically modified mice for these studies.

a) Lei Q., **Malykhina A.P.** (2012) Colonic inflammation up-regulates voltage-gated sodium channels in bladder sensory neurons via activation of peripheral transient potential vanilloid 1 receptors. *Neurogastroenterology and Motility* Jun: 24(6):575-85, e257, PMID:22420642
b) Lei Q., Pan X.-Q., Villamor A.N., Asfaw T.S., Chang S., Zderic S.A., **Malykhina A.P**. (2013) Lack of transient receptor potential vanilloid 1 channel modulates the development of neurogenic bladder dysfunction induced by cross-sensitization in afferent pathways. *J Neuroinfl,* Jan 11;10(1):3. PMID: 23305398
c) Lei Q., Pan X.-Q., Chang S, Malkowicz S.B., Guzzo T.J., **Malykhina A.P** (2014) Response of the human detrusor to stretch is regulated by TREK-1, a two-pore domain (K_{2P}) mechano-gated potassium channel. *J Physiology (London),* July 15, 592 (Pt 14):3013-30. PMID: 24801307
d) Pineda R.H., Nedumaran B., Hypolite J., Pan X.-Q., Wilson S., Meacham R.B., **Malykhina A.P**. (2017) Altered expression and modulation of the two-pore domain (K_{2P}) mechano-gated potassium channel TREK-1 in overactive human detrusor. *Am J Physiol Renal Physiol* 2017 Aug 1;313(2):F535-F546. PMID: 28539337.

2. **Neurogenic bladder dysfunction in neurological disorders.** Patients with neurological disorders such as multiple sclerosis (MS), Parkinson`s disease, Alzheimer's disease, and amyotrophic lateral sclerosis develop a wide range of lower urinary tract symptoms, including urinary urgency, urinary incontinence, nocturia, a sensation

of incomplete emptying, and a weak urinary stream. Additionally, patients with a neurogenic bladder have higher risk of developing multiple urologic complications, including hydronephrosis, vesicoureteral reflux, renal failure, urinary tract infections, calculus disease, bladder cancer, sexual dysfunction, and the destroyed bladder and urethra. The lack of understanding of pathophysiology and mechanisms underlying lower urinary tract dysfunctions in neurological disorders hampers the development of therapeutic strategies and treatment options for these patients. We established a new mouse model of neurogenic bladder dysfunction induced by coronavirus as a model of multiple sclerosis, and evaluated the mechanisms of underlying voiding dysfunction in both animal studies and patients with MS experiencing LUTS.

a) Braverman A.S., Lamarre N.S., **Malykhina A.P**., Barbe M.F, Ruggieri M.R. Sr (2014) Alterations in nerve-evoked bladder contractions in a coronavirus-induced mouse model of multiple sclerosis. *PLOS One,* Oct 13;9(10):e109314. PMID: 25310403.
b) McMillan M., Pan X.Q., Smith A.L., Newman D.K., Weiss S.R., Ruggieri M.R., **Malykhina A.P**. (2014) Coronavirus-induced demyelination of the neural pathways triggers neurogenic bladder overactivity in a mouse model of multiple sclerosis. *Am J Physiol Renal Physiol*, Sep 1;307(5):F612-22. PMID 25007876.
c) Weissbart S.J., Pechersky D., **Malykhina A**., Bavaria T., Parillo L., Arya L.A., Bilello M., Wein A.J., Smith A.L. (2016) The impact of pontine disease on lower urinary tract symptoms in patients with multiple sclerosis.
d) Lee S, Nedumaran B, Hypolite J, Caldwell B, Rudolph MC, **Malykhina AP.** Differential neurodegenerative phenotypes are associated with heterogeneous voiding dysfunction in a coronavirus-induced model of multiple sclerosis. *Sci Rep*. 2019 Jul 26;9(1):10869. PMID: 31350464

3. Mechanisms of pelvic-organ cross-sensitization and chronic pelvic pain. Chronic pelvic pain (CPP) is a common symptom of many urologic and gastrointestinal disorders including interstitial cystitis/bladder pain syndrome (IC/BPS) and irritable bowel syndrome (IBS). Our group was at the forefront of the research efforts aimed at understanding the mechanisms underlying co-morbid CPP disorders and provided initial evidence that cross-sensitization via neural pathways triggers the development of neurogenic inflammation in the pelvis and chronic pelvic pain of unknown etiology. We determined that transient colonic inflammation causes neurogenic bladder dysfunction evaluated by cystometry, triggers hyperexcitability of bladder sensory and spinal neurons, increases pro-inflammatory neuropeptides in the bladder, and alters detrusor contractility. We currently test the hypothesis that neurogenic bladder dysfunction develops due to aberrant signal transduction in sensory neurons (peripheral cross-sensitization), interference of pain pathways with the micturition reflex in the brainstem (central cross-sensitization), and neuronal epigenetic changes underlying the transition from acute to chronic pelvic pain.

a) Lei Q., Pan X.-Q., Villamor A.N., Asfaw T.S., Chang S., Zderic S.A., **Malykhina A.P**. (2013) Lack of transient receptor potential vanilloid 1 channel modulates the development of neurogenic bladder dysfunction induced by cross-sensitization in afferent pathways. *J Neuroinflammation,* Jan 11;10(1):3. PMID: 23305398.
b) Lei Q., **Malykhina A.P**. (2012) Colonic inflammation up-regulates voltage-gated sodium channels in bladder sensory neurons via activation of peripheral transient potential vanilloid 1 receptors. *Neurogastroenterology and Motility* Jun: 24(6):575-85, e257, PMID:22420642
c) Asfaw T.S., Hypolite J., Northington G.M., Arya L.A., Wein A.J., **Malykhina A.P**. (2011) Acute colonic inflammation triggers detrusor instability via activation of TRPV1 receptors in a rat model of pelvic organ cross-sensitization. *Am J Physiol Regul Integr Comp Physiol*. 300: R1392–1400. PMID:21474425
d) Pan X.-Q., Gonzalez J.A., Chang S., Chacko S, Wein A., **Malykhina A.P**. (2010) Experimental colitis triggers the release of substance P and calcitonin gene-related peptide in the urinary bladder via TRPV1 signaling pathways. *Exp Neurology.* 225(2):262-73. PMID:20501335

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/anna.malykhina.1/bibliography/41046368/public/?sort=date&direction=ascending