BIOGRAPHICAL SKETCH

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NAME: Hsi-Yang Wu

eRA COMMONS USER NAME:

POSITION TITLE: Associate Professor of Urology

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
Harvard College. Cambridge, MA	A.B.	05/1989	Chemistry
University of Pennsylvania. Philadelphia, PA	M.D.	05/1993	Medicine
University of California, San Francisco. San Francisco, CA	Residency	06/1999	Urology
Children's Hospital of Philadelphia. Philadelphia, PA	Fellowship	06/2002	Pediatric Urology

A. Personal Statement

My interest in studying bladder physiology started during residency, when I studied the clinical effects of early intervention for neurogenic bladder and the in-vitro limitations of tissue engineering for bladder reconstruction. During fellowship, I studied the maturation of bladder contractility in the neonatal mouse with Sam Chacko, PhD, utilizing the K12 grant at the University of Pennsylvania. As an assistant professor at the University of Pittsburgh, William "Chet" de Groat, PhD was the mentor for my K08 grant, studying the neural regulation of maturation of bladder function in neonatal rats. Since coming to Stanford, I have focused on the regulation of the external urethral sphincter and the interplay of the serotonergic and adrenergic systems in the development of urinary continence. I have extensive experience with rodent cystometry, and am well qualified to train the members of the lab in the performance and interpretation of urethane - anesthesized mouse cystometry.

B. Positions and Honors

2002 – 2008 Assistant Professor of Urology, University of Pittsburgh
2008 – present Associate Professor of Urology, Stanford University Medical Center
2009 – present Pediatric Urology Fellowship Director, Lucile Packard Children's Hospital

Medical Licensure:
1993 California
1999 Pennsylvania

Certification:
2004 American Board of Urology
2008 Subspecialty certification in Pediatric Urology

Honors
1989 Magna Cum Laude with Highest Honors
2003, 2007 Children's Hospital of Pittsburgh Patient Satisfaction Top 25 Physicians
2006 Children's Hospital of Pittsburgh Patient Satisfaction Top 10 Physicians
2009 American Academy of Pediatrics, Section on Urology, Basic Science Prize Contest, Second Place

Editorial Board: Assistant Editor, Journal of Pediatric Urology
Ad-hoc peer review: Journal of Urology, Urology, Journal of Pediatric Urology

Stanford Internal Grant Review: Child Health Research Institute Grants and Postdoctoral Support Panel Chair

C. Contribution to Science

1. Maturation of bladder physiology during neonatal life

The development of urinary continence during childhood was previously thought to be delayed due to the need for central nervous system maturation. Chet de Groat's pioneering work on the postnatal transfer of bladder reflexes from a sacral circuit to the mature circuit involving bladder afferents, the pontine micturition center, and the cerebral cortex led me to study the maturation of bladder smooth muscle and the effects of cholinergic, serotonergic, and adrenergic compounds on the bladder and external urethral sphincter during the acquisition of urinary continence. The major findings and translational implications were: 1. The onset of the mature voiding reflex is not delayed by neonatal bladder distension, but the disappearance of the immature reflex is prolonged (**a**). Pediatric urinary incontinence may represent an overlay of immature reflexes which have not been downregulated, on top of the mature voiding reflex. 2. Neonatal bladder smooth muscle develops progressive inhibition of spontaneous contractions due to increased activity of large conductance K_{Ca} channels (**b**). The pediatric bladder becomes a better storage organ over time via maturation of smooth muscle and neurotransmitter function. Reconstructive surgical procedures on the bladder will have a higher success rate after this maturation occurs. 3. Neonatal bladder reduction causes the early onset of voiding at the expense of later increased voiding pressures and larger bladders in female rats, which can be reversed by serotonergic and beta adrenergic agonists (**c,d**). Early medical intervention for poor bladder emptying can prevent long term alterations in bladder function, while later treatment with serotonergic and beta-adrenergic agonists remain effective at improving external urethral sphincter and bladder function.

a. **Wu HY** and de Groat WC: Maternal separation uncouples reflex from spontaneous voiding in rat pups. J Urol, 175(3): 1148-1151, 2006.

b. Ng YK, de Groat WC, **Wu HY**: Smooth muscle and neural mechanisms contributing to the down-regulation of neonatal rat spontaneous bladder contractions during postnatal development. Am J Physiol, Regul Integr Comp Physiol, 292: R2100-2112, 2007.

c. Chien C, Chang HY, **Wu HY**. Sex differences in neonatal and young adult rat lower urinary tract function caused by bladder reduction. J Ped Urol, 11:197.e1-197.e7, 2015.

d. Chien C, **Wu HY**. Young rats exhibit an age and sex dependent bladder response to alpha-antagonists but not beta-agonists. J Ped Urol, 12:92.e1-e8, 2016.

2. Treatment of neurogenic bladder

The prophylactic use of clean intermittent catheterization and anticholinergic medications in the treatment of children with neurogenic bladder due to myelomeningocele was controversial, as one group of clinicians felt it should be universal, while another group felt that it should be instituted after evidence of deterioration. The 1997 paper (**a**) was the first to show a decreased rate of bladder augmentation in the patients managed with prophylactic medical management compared to controls. This has subsequently been confirmed in other publications and prophylactic treatment is considered standard of care. The 1999 paper (**c**) showed that acellular bladder matrix grafts in rats required the adjoining smooth muscle to infiltrate the graft, pointing out that the physiology of the regenerated bladder would mimic the host bladder. This was later confirmed in human studies, conducted by other investigators using larger tissue engineered grafts.

a. **Wu HY**, Baskin LS, Kogan BA: Neurogenic bladder dysfunction due to myelomeningocele: neonatal versus childhood treatment. J Urol, 157(6):2295-7, 1997.

b. **Wu HY**, Kogan BA, Baskin LS, Edwards MSB: Long-term benefits of early neurosurgery for lipomyelomeningocele. J Urol, 160(2):511-4, 1998.

c. **Wu HY**, Baskin LS, Liu W, Li YW, Hayward SW, Cunha GR: Understanding bladder regeneration: Smooth muscle ontogeny. J Urol, 162 (3):1101-1105, 1999.

3. Fertility potential of the undescended testis

The two proposed etiologies for the undescended testis are mechanical abnormalities of the gubernaculum and hypogonadotrophic hypogonadism. Using the testis database at Children's Hospital of Philadelphia, we showed that the histology of the contralateral testis in patients with

vanishing testis was normal (**a**), whereas testes that ascend later in life have the same histology as testes which have always been undescended (**b**). Since the histology of the undescended testis can be predictive of future fertility (**c**), a select group of patients with unilateral undescended testes may benefit from early hormonal treatment to improve their fertility potential.

a. Huff DS, Wu HY, Snyder HM, Hadziselimovic F, Blyth B, Duckett JW: Evidence in favor of the mechanical (intrauterine torsion) theory over the endocrinopathy (cryptorchidism) theory in the pathogenesis of testicular agenesis. J Urol, 146(2):630-1, 1991.

b. Fenig DM, Snyder HM, **Wu HY**, Canning DA, Huff DS: The histopathology of iatrogenic cryptorchid testes: An insight into etiology. J Urol, 165(4):1258-1261, 2001.

c. Rusnack SL, **Wu HY**, Huff DS, Snyder HM, Carr MC, Bellah RD, Zderic SA, Canning DA: Testis histopathology in cryptorchid boys correlates with future fertility potential. J Urol, 169(2): 659-662, 2003.

4. Endoscopic management of pediatric kidney stones

The use of ureteroscopy for pediatric kidney stones increased rapidly during the early 2000's. The unknown success rates for stone clearance, risk of injury to the ureter, and the number of anesthetics required for multiple procedures were concerns that initially limited its use compared to the well-established technique of shock wave lithotripsy. We showed that ureteroscopy was safe and effective for pediatric stone disease, especially for stones < 15 mm in the lower pole (**a,b**), and parents should be advised that prior stent placement would be required in 40% of children undergoing ureteroscopy (**c**). Ureteroscopy is now first line treatment for pediatric stone disease.

a. Smaldone MC, Cannon GM, **Wu HY**, Bassett JC, Polsky EG, Bellinger MF, Docimo SG, Schneck FX: Is ureteroscopy first line treatment for pediatric stone disease? J Urol, 178(5): 2128-2131, 2007.

b. Cannon GM, Smaldone MC, **Wu HY**, Bassett JC, Bellinger MF, Docimo SG, Schneck FX: The ureteroscopic management of lower pole stones in a pediatric population. J Endourol, 21(10): 1179-1182, 2007.

c. Corcoran AT, Smaldone MC, Mally D, Ost MC, Bellinger MF, Schneck FX, Docimo SG, **Wu HY**: When is prior ureteral stent placement necessary to access the upper urinary tract in prepubertal children? J Urol, 180(4): 1861-1864, 2008.

D. Research Support

2012-2015 Arline and Pete Harman Endowed Faculty Scholar, PI. Neural prosthetic control of the lower urinary tract. The goals were to optimize electrical stimulation parameters of pelvic and pudendal nerves, and to map locations from the spinal cord to the peripheral ganglia to achieve specific control over bladder emptying and external urethral sphincter relaxation.