

NIRAV R. SHAH

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SUMMARY

- Pharmacologist with award-winning communication skills and publications in high-impact journals, including Nature Communications and Molecular Cell
- Applied concepts from translational pharmacology, pharmacometrics, and molecular biology to pre-clinical and early clinical drug discovery and development
- Experience designing and implementing *in vitro* and *in vivo* pharmacokinetic/pharmacodynamic (PK/PD) studies to support translational and clinical drug development
- Investigated cellular mechanisms pertinent to oncology, immunology, and infectious disease
- Collaborated with cross-functional teams from Eurofins, the FDA, and Entasis Therapeutics on preclinical PK/PD analyses

EDUCATION

PhD Pharmacology	The Ohio State University	2012 - 2018
MS Pharmacology	The Ohio State University	2012 - 2014
MS Biotechnology	University of Central Florida	2010 - 2012
BS Pharmacy	Bombay College of Pharmacy	2006 - 2010

STRENGTHS & EXPERTISE

Molecular / Cellular Biology	PK/PD Modeling & Simulation	<u>Therapeutic Areas:</u>
Fluorescence & Confocal Microscopy	Phoenix WinNonlin, S-ADAPT	Oncology
Mammalian & Primary Cell Culture	Berkeley Madonna, NONMEM, R	Immunology
CRISPR, RT-PCR, ELISA	GraphPad, SigmaPlot, XLSTAT	Infectious Diseases
Flow Cytometry & FACS	Scientific & Medical Writing	Cardiovascular Diseases
Cloning, Transfection, Western Blot	Project & Time Management	
Pre-Clinical Animal Models	Data Interpretation & Analysis	
Scientific & Clinical Data Presentation	Mentoring	

PROFESSIONAL EXPERIENCE

Postdoctoral Associate (Advisor: Jürgen Bulitta, PhD) **Nov 2018-Present**
Center for Pharmacometrics and Systems Pharmacology, University of Florida, Orlando, FL

Ongoing Projects

1. Next-generation combination dosing strategies to combat drug-resistant bacterial superbugs

- Lead a multidisciplinary group of faculty and postdocs to create the first morphological profiles of *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Mycobacterium abscessus* in response to >45 clinical and non-clinical β -lactam antibiotics using confocal microscopy and flow cytometry
- Identified receptor occupancy patterns for >45 compounds using receptor-binding assays and principal component analysis (in XLSTAT, SIMCA)
- Performed advanced analyses of preclinical data to determine the safety and efficacy of synergistic antibiotic combinations against multidrug resistant bacteria (in SADAPT, Berkeley Madonna)
- Leveraged bacterial growth-inhibition data obtained from static time-kill curves in gram-negative bacteria to develop translational quantitative and systems pharmacology (QSP) models that optimize β -lactam mono or combination antibiotic therapies

2. Population pharmacokinetics of cephalosporins in cystic fibrosis patients and healthy volunteers

- Developed population model to compare the pharmacokinetics of cephalosporin antibiotics between cystic fibrosis patients and healthy volunteers (using the S-ADAPT and Berkeley Madonna software). Performed Monte Carlo simulations to predict the probability of target attainment for different dosage regimens.

3. Preclinical mouse model of *Acinetobacter baumannii* infection for antibacterial development (FDA project)

- Developed population pharmacokinetic models for the four individual components of polymyxin B in infected mice.
- Developed optimal designs to estimate PK parameters based on plasma and lung (ELF) concentrations precisely.
- Designed efficacious and safe dosing strategies to humanize the drug concentration profiles in infected mice.

4. Safety and efficacy evaluation of antibiotics against murine *K. pneumoniae* and *P. aeruginosa* thigh-infection models (Eurofins project, NIH funded)

- Leveraged published literature to identify and simulate expected plasma concentration time profiles, $fAUC/MIC$, fC_{max}/MIC and $fT_{>MIC}$ values for levofloxacin, colistin and ceftazidime to design mouse infection model studies.
- Developed population PK/PD models for mouse datasets with destructive sampling in the S-ADAPT software.
- Performed simulations in Berkeley Madonna to design dose range and dose fractionation studies.

Ph.D. Research Assistant (Advisor: Nam Lee, PhD)

Sept 2012-Aug 2018

The Ohio State University, Columbus, OH

Thesis: Novel signaling mechanisms for transforming growth factor- β activated kinase-1 (TAK1) in microtubule and endoplasmic reticulum dynamics

- Employed extensive molecular/cellular biology techniques to elucidate cellular signaling mechanisms in oncology and angiogenesis using preclinical models; results published in high-impact journals, including Nature Communications and Molecular Cell (impact factor 12-14)
- Characterized pancreatic cancer cell lines, animal models, and patient samples to identify key diagnostic biomarkers using advanced imaging analyses and flow cytometry
- Used CRISPR-Cas9 to create knockouts/knock-ins of serine-threonine kinase (AKT) to understand its effect on pancreatic cancer cell survival and proliferation
- Isolated retinas from β -spectrin-deficient mice to study angiogenesis
- Lead multidisciplinary groups of faculty, graduates, and undergraduates in monthly discussions of novel cancer drug targets and existing treatment options
- Communicated scientific information to specialist and non-specialist audiences, winning multiple awards for oral (2) and poster (3) presentations
- Taught senior undergraduates animal handling techniques, including routes of drug administration, drug response measurement, dissection, and analysis of vital tissues/organs
- Mentored graduate students in advanced laboratory skills and experimental design, including via tutorial seminars on confocal/fluorescence microscopy

M.S. Research Assistant (Advisor: Deborah Altomare, PhD)

Sep 2010-Aug 2012

University of Central Florida, Orlando, FL

Thesis: A Novel Link between Akt1 and Twist in Ovarian Tumor Cell Motility and Invasiveness

- Investigated cell-signaling pathways in ovarian cancer by profiling ovarian cancer cell lines and patient samples
- Employed microarray analysis to dissect signal transduction pertaining to epithelial-mesenchymal transition (EMT) in aggressive metastasized ovarian cancer cell lines
- Taught senior undergraduates principles in biotechnology and genetics

PUBLICATIONS

1. **Shah NR**, Bulitta JB, Kinzig M, Landersdorfer CB, Jiao Y, Sutaria DS, Tao X, Höhl R, Holzgrabe U, Kees F, Stephan U, Sörgel F. Novel Population Pharmacokinetic Approach to Explain the Differences between Cystic Fibrosis Patients and Healthy Volunteers via Protein Binding. **Pharmaceutics**; 2019. [PMID: 31216743](#)
2. **Shah N**, Kumar S, Zaman N, Pan CC, Bloodworth JC, Lei W, Streicher JM, Hempel N, Mythreye K, Lee NY. TAK1 activation of alpha-TAT1 and microtubule hyperacetylation control AKT signaling and cell growth. **Nature Communications**; 2018. [PMID: 29703898](#)
3. Pan CC, **Shah N**, Kumar S, Wheeler SE, Cinti J, Hoyt DG, Beattie CE, An M, Mythreye K, Rakotondraibe LH, Lee NY. Angiostatic actions of capsicodendrin through selective inhibition of VEGFR2-mediated AKT signaling and dysregulated autophagy. **Oncotarget**; 2017. [PMID: 27177332](#)
4. **Shah N**, Lee NY. Regulation of gene expression and mitochondrial dynamics by SMAD. **Molecular Cellular Oncology**; 2016. [PMID: 27857972](#)
5. Kumar S, Pan CC, **Shah N**, Wheeler SE, Hoyt KR, Hempel N, Mythreye K, Lee NY. Activation of Mitofusin2 by Smad2-RIN1 Complex during Mitochondrial Fusion. **Molecular Cell**; 2016. [PMID: 27184078](#)
6. Pan CC, Kumar S, **Shah N**, Bloodworth JC, Hawinkels LJ, Mythreye K, Hoyt DG, Lee NY. Endoglin Regulation of Smad2 Function Mediates Beclin1 Expression and Endothelial Autophagy. **The Journal of Biological Chemistry**; 2015. [PMID: 25931117](#)
7. Pan CC, Kumar S, **Shah N**, Hoyt DG, Hawinkels LJ, Mythreye K, Lee NY. Src-mediated post-translational regulation of endoglin stability and function is critical for angiogenesis. **The Journal of Biological Chemistry**; 2014. [PMID: 25070888](#)

WORKSHOPS / COURSES / MEMBERSHIPS

- Introduction to Pharmacokinetics and Biopharmaceutics with **Phoenix WinNonlin** (UF,FL, 2020)
- **PK-Sim and MoBi** workshop on PBPK and PBPK-based QSP (UF, FL, 2019)
- Modeling and simulation with **Monolix Suite** (UF,FL, 2019)
- Introductory workshop in Population PK data analysis with **NONMEM7[®]** (UF, FL, 2019)
- Hands on experience with Model-informed drug development using **Simcyp** (UF, FL, 2018)
- Population PK/PD modeling using **S-ADAPT** (University of Buffalo, NY, 2018)
- Audited courses at the Center for Pharmacometrics and Systems Pharmacology: Pharmacokinetics & Biopharmaceutics, Translational Clinical Pharmacology, and Model-Informed Drug Development
- Affiliations with the International Society of Pharmacometrics/American Conference on Pharmacometrics (**ISoP/ACoP**) and the American Society for Clinical Pharmacology and Therapeutics (**ASCPT**)

SELECTED SCIENTIFIC PRESENTATIONS (Complete list available on request)

1. **Shah NR**, Pan CC, Kumar S, Lee NY. Novel crosstalk between Insulin and TGF-beta signaling in vascular endothelial cells. Experimental Biology, **ASBMB 2017**, Chicago, IL.
2. **Shah NR**, Sutaria DS, Moya B, Oyer J, Jiao Y, Tao X, Copik A, Boyce JD, Bonomo RA, Louie A, Drusano GL, Bulitta JB. Morphological Profiling of *Acinetobacter baumannii* in Response to 13 β -lactams and β -lactamase Inhibitors with Different Penicillin-Binding Protein (PBP) Occupancy Patterns. **ASM Microbe 2019**, San Francisco, CA, June 20-24, 2019.
3. Sutaria DS, **Shah NR**, Ropy A, Moya B, Jiao Y, Tao X, Zhou J, Lang Y, Shin E, Louie A, Drusano GL, Bulitta JB. Comprehensive Penicillin-Binding Protein (PBP) Occupancy Patterns of 29 Drugs in *Klebsiella pneumoniae*. **ASM/ESCMID 2019**; Boston, MA, September 3-6, 2019.

4. Tao X, **Shah NR**, Lang Y, Zhou J, Sutaria DS, Ropy A, Moya B, Jiao Y, Shin E, Louie A, Drusano GL, Schweizer HP, Bonomo RA, Lee RE, Bulitta JB. Characterizing Outer Membrane (OM) Permeability and Morphological Changes for Beta-lactam Antibiotics against *Acinetobacter baumannii* (Ab). **ASM/ESCMID 2019**, Boston, MA; September 3-6, 2019.
5. **Shah NR**, Bulitta JB, Kinzig M, Landersdorfer CB, Jiao Y, Sutaria DS, Tao X, Höhl R, Holzgrabe U, Kees F, Stephan U, Sörgel F. Novel population pharmacokinetic approach to explain the differences between cystic fibrosis patients and healthy volunteers via protein binding. American Conference on Pharmacometrics (**ACoP10**); Orlando, FL; October 20-23, 2019.

HONORS AND AWARDS

NJ Uretsky Award for graduate excellence (\$2500 for research supplies and travel)	out of 30 applicants, OSU	2016-2017
Dr. Papat Patil Graduate Student Fellowship (\$15000 for stipend and research supplies)	out of 8 applicants, OSU	2015-2016
Best Poster, College of Pharmacy	out of 45 participants, OSU	May 2015
Best Poster, Hayes Graduate Forum	1 of 10 out of 500 participants, OSU	Feb 2013
Best Oral Presentation, College of Medicine	out of 30 participants, UCF	May 2012
Best Poster, Graduate School-wide	1 of 10 out of 300 participants, UCF	Apr 2012
Best Oral Presentation	out of 60 participants, BCP	Sept 2009

LEADERSHIP EXPERIENCE

- Organized networking events and a seminar series inviting industry and academic thought leaders (while a graduate student representative for the pharmacology department)
- Served as a founding member of the networking group Diversity in Medical Affairs (DiMA)
- Trained postdoctoral fellows in imaging techniques and helped mentor graduate and undergraduate students

Postdoctoral fellows

Sanjay Kumar, PhD
 Nagaraj Nagre, PhD
 Euna Kwak, PhD
 Alaa Ropey Sayed, PhD

Graduate Students

Naveed Zaman, MS
 Sarah Wheeler, PharmD
 Eunjeong Shin
 Carolin Werkman

Undergraduate Students

Lauren Williams
 Alex Tran
 Mary Kate Stevens
 Keisha Cadet
 Rossie Jimenez

REFERENCES

<p>Jürgen Bulitta, PhD Professor, Pharmacotherapy & Translational Research College of Pharmacy, University of Florida jbulitta@cop.ufl.edu 407-988-4752 (cell) / 407-313-7010 (office)</p> <p>Nam Lee, PhD Associate Professor Pharmacology, Chemistry & Biochemistry College of Pharmacy, University of Arizona namlee@email.arizona.edu 919-599-7059 (cell) / 520-626-6400 (office)</p>	<p>Alicja Copik, PhD Associate Professor College of Medicine, University of Central Florida alicja.copik@ucf.edu 510-495-5927 (cell) / 407-266-7132 (office)</p> <p>Kari Hoyt, PhD Professor Pharmaceutics and Pharmacology College of Pharmacy, The Ohio State University hoyt.31@osu.edu 614-292-6636 (office)</p>
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