BIOGRAPHICAL SKETCH

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NAME: Zhou, Zhongren

eRA COMMONS USERNAME (agency login): zhongrenzhou

POSITION TITLE: Professor, Director of Anatomic Pathology and Vice Chair of Translational Research

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
School of Medicine, Hebei United University, Tangshan, Hebei, China	MD	07/1986	Medicine
Capital University of Medical Science, Beijing, China	MS	08/1989	Human Anatomy
Shanghai Medical College, Fudan University, Shanghai	PHD	07/1993	Neurobiology
Biomedical Engineering Center, Harvard-MIT Division of Health Sciences and Technology, Cambridge, MA	Postdoctoral Fellow	07/1998	Neurobiology
Boston University School of Medicine, Boston, MA	Resident	06/2006	Pathology
Baylor College of Medicine, Houston, TX	Fellow	06/2007	Cytology
MD Anderson Cancer Center, Houston, TX	Fellow	06/2008	Oncologic Surgical Pathology

A. Personal Statement

I am a physician-scientist with expertise in both the diagnosis of gastrointestinal and liver disease and translational research for esophageal diseases. I routinely diagnose gastroesophageal reflux disease (GERD), Barrett's esophagus (BE), esophageal dysplasia, and adenocarcinoma (EAC) on human esophageal biopsies as a clinical gastrointestinal pathologist. My research focuses in two major areas. First, I have been studying the biomarkers of esophageal diseases using tissue microarrays and banked frozen human tissue specimens for gene amplification, overexpression, methylation and mutation in EAC and precancerous lesions. I was also involved in The Cancer Genome Atlas Project (TCGA) at the National Cancer Institute to study the genetic mutations in esophageal and gastric carcinoma. Based on our molecular study, we develop a new cytopathology screening test for Barrett's esophagus. We combine EsophaCap cytology diagnosis with immunohistochemistry and next generation sequencing to detect Barrett's esophagus and high-risk patients. The study has been supported by Genome Canada and NIH R01 grants since 2013. Multiple papers were published in pathologic or other journals including Nature and Nature Genetics. We have been investigating the mechanisms of GERD and Barrett's esophagus formation and developing new potential prevention or treatment approaches for GERD. Our laboratory first developed an *in vitro* cell culture system that mimics the esophageal squamous epithelium using an immortalized primary esophageal keratinocyte cell line. Using this system, we have shown that bile salts at low pH stalled the stratification of esophageal epithelium grown in transwell culture and caused dilated intercellular space (DIS) with reducing the functional tight junctions and decreasing transepithelial resistance, mimicking the initial steps of GERD causing DIS in humans. The papers were published in *J Gastrointest Surg.* Now we collaborated with David Dean, who first applied electroporation of gene to the lung, the vasculature, and multiple organs and developed effective gene delivery approaches for several pulmonary diseases at the University of Rochester. We have studied the mechanism of the prevention or treatment of GERD with genomic transfer of the 1 subunit of the Na^+,K^+-ATPase to upregulate tight and adherens junction proteins and increased barrier function in GERD organoids and living animals. The study has been supported by NIH R01 since 2020.

I have been also involved in tissue banking for many years. I was the first Director of tissue bank at Wilmot Cancer Center of University of Rochester. As the Director of Banking Protocols and Pathology for the Biospecimen Repository and Histopathology Shared Resource at Rutgers Cancer Institute of New Jersey, our goal is to support transdisciplinary and translational research and cancer clinical trials through cost effective, quality-controlled tissue collection (biospecimen procurement) and processing.

Ongoing and recently completed projects that I would like to highlight include:

1R01DK120680
David Dean and David Zhou (MPI)
4/1/20 – 3/31/24
NIH/NIDDK
Gene therapy for GERD-associated esophageal epithelial barrier dysfunction
Role: PI at Rutgers University

2R01DK116548
(PI: Bishr Omary); Role on Grant: Co-investigator
NIDDK
Mechanism of Proteotoxicity and Experimental Therapeutic Approaches in Porphyria
Funding Period: 2022-2027

1R01CA272578
NIH
(PI: Jian Cao); Role on Grant: Co-investigator
Funding Period: 2022-2027
Hepatitis B virus integrations in KMT2B drive hepatocellular carcinoma

R01 CA208599-01A1
Godfrey (PI); Role: site PI at Rutgers University
12/1/16 – 11/30/22
NIH/NCI
Development of diagnostic and prognostic tests for esophageal adenocarcinoma

B. Positions and Honors

Positions and Employment

2019—present	Professor, Rutgers University, NJ
2019---present	Director of Gastrointestinal and Liver Pathology
2018---2019	Associate Professor and Director of Cytopathology, Washington University, St Louis, MO
2015---2017	Director of Bio-tissue banking, University of Rochester Medical Center, Rochester, NY
2013—2017	Associate Professor, University of Rochester Medical Center, Rochester, NY
2008—2013	Assistant Professor, University of Rochester Medical Center, Rochester, NY
1998—2002	Research Instructor, Brigham & Women's Hospital, Harvard Medical School, Boston, MA
1994—1998	Research Fellow, Harvard-MIT Division of Health Sciences and Technology, Cambridge, MA

Honors

2017	Best Abstract in Annual Pathology Research Day at URMC 2017
2016	URMC "**Strong Star"** for excellent patient care
2016	Health Care Management Award for LEAN project, URMC
2016	Gold Award for Cytology turnaround time LEAN project at Greater Rochester Quality Council
2014	URMC Team Based Care Award for outstanding teamwork
2011	CAPA Award for the best research abstract.
1992	Guang-Hua Award for outstanding graduate student; Shanghai Medical University.
1992	Annual Science Festival Award for outstanding research work, Shanghai Medical University.

C. Contribution to Science

1. My early research training and research were in neurobiology. During my research training at Shanghai Medical College and early research career at Health Science and Technology, MIT and Harvard University, my study focused on two areas. One was the mechanisms of pain with central and local pain control; the

other was the mechanisms of synaptic plasticity in the central nervous system. We first reported the mechanism of endothelin-1 algogenic actions on tetrodotoxin-resistant sodium channels. We also first reported the expression of c-fos gene in central nervous system following acupuncture and electrostimulation of the rat tail. For synaptic plasticity in brainstem, we were the first to report the phasic and long-term depression in brainstem. In addition, we developed a new field recording method for the brainstem

a. **Zhou Z**, Davar G, Strichartz G. Endothlin-1 selectively enhances the activation gating of tetrodotoxin-resistant sodium currents in rat sensory neurons: A mechanism for the algogenic actions of ET-1. J. Neuroscience. 2002; 22(15):6325-6330. PMID: 12151509.
b. **Zhou Z**, Poon CS. Field potential analysis of synaptic transmission in spiking neurons in a sparse and irregular neuronal structure in vitro. J. Neurosci Methods. 2000; 94(2):193-203. PMID: 10661839.
c. Poon CS, **Zhou Z**, Champagnat J. NMDA receptor activity in utero averts respiratory depression and anomalous long-term depression in newborn mice. J. Neurosci. 2000; 20 (9):RC73. PMID: 10777815.
d. **Zhou Z**, Champagnat J, Poon CS. Phasic and long-term depression in brainstem NTS neurons: differing roles of AMPA receptor desensitization. J. Neurosci. 1997; 17(14):5349-5356. PMID: 9204919.

2. Biomarkers of esophageal adenocarcinoma and precancerous lesions. We first reported the diagnostic criteria of HER2 expression and genetic amplification in esophageal adenocarcinoma. In addition, we first reported multiple gene expression profiles in esophageal adenocarcinoma and precancerous lesions.

a. Hu Y, Bandla S, Godfrey TE, Tan D, Luketich JD, Pennathur A, Qiu X, Hicks DG, Peters JH, **Zhou Z.** HER-2 Amplification, overexpression and score criteria in esophageal adenocarcinoma. Modern Pathology. 2011; 24(7):899-907. PMCID: PMC3138485.
b. Choy B, Bandla S, Xia Y, Tan D,Pennathur A, Luketich JD, Godfrey TE, Peters JH, Sun J, **Zhou Z.** Clinicopathological characteristics of high expression of Bmi-1 in esophageal adenocarcinoma and squamous cell carcinoma. *BMC Gastroenterology.* 2012; **12**:146. PMCID: PMC3544684.
c. Huber AR, Tan D, Sun J, Dean DA, Wu T, **Zhou Z**. High expression of carbonic anhydrase IX is significantly associated with glandular lesions in gastroesophageal junction and with tumorigenesis markers BMI1, MCM4 and MCM7. BMC Gastroenterology. 2015; 15:80. PMCID: PMC4495619
d. Lin S, Liu K, Zhang Y, Jiang M, Lu R, Folts CJ, Gao X, Noble MD, Zhao T, **Zhou Z**, Lan X, Que J. Pharmacological targeting of p38 MAP-Kinase 6 (MAP2K6) inhibits the growth of esophageal adenocarcinoma. Cell Signal. 2018 Nov;51:222-232. doi: 10.1016/j.cellsig.2018.08.008. Epub 2018 Aug 11. PMID: 30102978.

3. Early screening test for Barrett's Esophagus (BE), dysplasia and esophageal adenocarcinoma (EAC) with EsophaCap cytology and circulating DNA. We develop a new screening test combined EsophaCap cytology samples, immunohistochemistry and next generation sequencing to screen Barrett's esophagus, dysplasia and esophageal adenocarcinoma and to detect high risk BE patients to develop to EAC. We also detect circulating DNA for EAC diagnosis. The study was supported by Genome Canada and R01 grants.

a. **Zhongren Zhou**, Irina Kalatskaya, Donna Russell, Norman Marcon, Maria Cirocco, Paul Krzyzanowski, Cathy Streutker, Hua Liang, Virginia Litle, Tony Godfrey, Lincoln Stein Combined EsophaCap Cytology and MUC2 Immunohistochemistry for Screening of Intestinal Metaplasia, Dysplasia and Carcinoma Clinical and Experimental Gastroenterology 15 May 2019 Volume 2019:12 Pages 219—229;PMCID: PMC6527096
b. Matthew Egyud; Mohamedtaki Tejani; Arjun Pennathur, James Luketich, Praveen Sridhar, Emiko Yamada, Anders Ståhlberg, Stefan Filges, Paul Krzyzanowski, Jennifer Jackson, Irina Kalatskaya, Wei Jiao, Gradon Nielsen, **Zhongren Zhou**, Virginia Litle, Lincoln Stein, Tony Godfrey Detection of circulating tumor DNA in Plasma: a potential biomarker for esophageal adenocarcinoma. The Annals of Thoracic Surgery 2019;108(2):343-349. PMCID:PMC6676214

4. Genetic change in esophageal adenocarcinoma and precancerous lesions. I joined the TCGA Gastrointestinal committee for the genomic study of gastrointestinal solid tumor in esophageal and gastric

adenocarcinoma. We were the first to use next generation sequencing to compare the genomic differences between Barrett's esophagus and columnar metaplasia. The TCGA team also first used whole genome sequencing and exomic genome sequencing to compare the genomic differences between esophageal adenocarcinoma and esophageal squamous cell carcinoma as well as gastric adenocarcinoma.

a. Cancer Genome Atlas Research Network. Integrated genomic characterization of oesophageal carcinoma. Nature 2017. 541(7636):169-175. PMID:28052061
b. Bandla S, Peters JH, Ruff D, Chen SM, Li CY, Song K, Thoms K, Litle VR, Watson T, Chapurin N, Lada M, Pennathur A, Luketich JD, Peterson D, Dulak A, Lin L, Bass A, Beer DG, Godfrey TE, **Zhou Z.** Comparison of cancer-associated genetic abnormalities in columnar-lined esophagus tissues with and without Goblet Cells. Ann. Surg. 2014; 260(1):72-80. PMCID: PMC4047149.
c. Kim J, Fox C, Peng S, Pusung M, Pectasides E, Matthee E, Hong YS, Do IG, Jang J, Thorner AR, Hummelen P, Rustgi AK, Wong KK, **Zhou Z,** Tang P, Kim KM, Lee J, Bass AJ. Pre-existing oncogenic events impact Trastuzumab sensitivity in ERBB2-amplified gastroesophageal adenocarcinoma. J. Clin. Invest. 2014; 124(12):5145–5158. PMCID: PMC4348950.
d. Dulak AM, Stojanov P, Peng S, Lawrence MS, Fox C, Stewart C, Bandla S, Imamura1 Y, Schumacher SE, Shefler E, McKenna A, Carter SL, Cibulskis K, Sivachenko A, Saksena G, Voet D, Ramos AH, Auclair D, Thompson K, Sougnez C, Onofrio RC, Guiducci C, Beroukhim R, **Zhou Z,** Lin L, Lin J, Reddy R, Chang A, Landrenau R, Pennathur A, Ogino S, Luketich JD, Golub TR, Gabriel SB, Lander ES, Beer DG, Godfrey TE, Getz G, Bass AJ. Exome and whole-genome sequencing of esophageal adenocarcinoma identifies recurrent driver events and mutational complexity. Nature Genetics, 2013; 45(5):478-486. PMCID: 3678719.

5. I have been very interested in the mechanisms of progression of GERD to EAC. Our collaborated team first found a group cells generate Barrett's esophagus and reported multiple genomic change with GERD. We have studied the dilation of intercellular junctions induced by bile acid and the molecular signatures of EAC, squamous cell carcinoma, Barrett's esophagus, and GERD. These studies are leading to possible prevention and treatment strategies, some of which are described in this application.

a. Ming J, H Li, Y Zhang, Y Yang, R Lu, K Liu, S Lin, X Lan, H Wang, H Wu, J Zhu, **Zhou Z**, J Xu, D Lee, L Zhang, Y Lee, J Yuan, JA Abrams, TG Wang, AR Sepulveda, Q Wu, H Chen, X Sun, J She, X Chen, and J Que Transitional basal cells at the squamous-columnar junction generate Barrett's oesophagus. Nature 2017 Oct 12. doi: 10.1038/nature24269 PMID: 29019984
b. Pang C., A Lalonde, TE Godfrey, J Que, J Sun, T Wu, and **Zhou Z** Bile salt receptor TGR5 is highly expressed in esophageal adenocarcinoma and precancerous lesions with significantly worse overall survival and gender differences Clinical and Experimental Gastroenterology 7 February 2017: 29-37 PMID: 28223834
c. Ghatak S, Reveiller M, Toia L, Ivanov AI, **Zhou Z**, Redmond EM, Godfrey TE, Peters JH. Bile Salts at Low pH Cause Dilation of Intercellular Spaces in In Vitro Stratified Primary Esophageal Cells, Possibly by Modulating Wnt Signaling J Gastrointest Surg. 2016. 20(3):500-9. PMID: 26715559
d. Reveiller M, Ghatak S, Toia L, Kalatskaya I, Stein L, D'Souza M, **Zhou Z**, Bandla S, Gooding WE, Godfrey TE, Peters JH. Bile Exposure Inhibits Expression of Squamous Differentiation Genes in Human Esophageal Epithelial Cells. Ann. Surg. 2012; 255(6):1113-20. PMID: 22498892.

Complete List of Published Work in My Bibliography:
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