BIOGRAPHICAL SKETCH

NAME Husain, Sohail Z	POSITION TITLE Professor
eRA COMMONS USER NAME SHUSAIN	

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

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
Binghamton University, Binghamton, NY	B. S.	May 1994	Biological Sciences
Tufts University School of Medicine, Boston, MA	M. D.	May 1998	Medicine
New York University School of Medicine, NY, NY		June 2001	Pediatrics
Yale University School of Medicine, New Haven, CT		June 2004	Pediatric Gastroenterology

A. Personal Statement.

I am a Pediatric Gastroenterology Physician-Scientist whose overarching goal is to come up with targeted therapies for exocrine pancreatic disorders, particularly pancreatitis. I serve as Professor of Pediatrics and Chief of the Division of Pediatric Gastroenterology, Hepatology, and Nutrition at Stanford University. Prior to coming to Stanford, I was at the University of Pittsburgh for 8 years, and before that, I was at Yale for 10 years. My research efforts are focused on probing the mechanisms underlying pancreatitis. In this context, I identified a pathological role for pancreatic acinar cell Ca^{2+} release from the intracellular Ca^{2+} channel the ryanodine receptor (RyR). Thereafter, I was able to implicate a novel role for a downstream Ca^{2+}-activated phosphatase calcineurin (Cn) in initiating and propagating the inflammatory signals that lead to pancreatitis. Recently, I have deciphered a novel role for the epigenetic regulators the histone deacetylases (HDAC) in mediating pancreatic recovery and regeneration of the pancreas. I also have a keen interest in uncovering the basis for various forms of drug-induced pancreatitis. I have published experience in clinical-translational work through active participation within a collaborative group of Pediatric Pancreatologists (called INSPPIRE). I have been active in publications, patents, grants, and in training clinician-scientists. I filed three patents that disclose a novel Cn formulation for pancreatitis. I currently serve as the single PI on one R01 grant from NIDDK that focuses on mechanisms underlying the role of Cn in pancreatitis and single PI on a Department of Defense grant to optimize a novel formulation to prevent post-ERCP pancreatitis. I also serve as PI on an industry grant award to perform a discovery metabolomic and lipidomic screen in children who succumbed to pancreatitis due to the cancer drug asparaginase. **Overall, combined with a solid expertise in the molecular pathogenesis of pancreatitis and a translational understanding of the clinical entity, I believe that I am ideally suited to achieve the goals of identifying effective therapies for pancreatitis.**

B. Positions and Honors

Positions and Employment

1998-2001	Resident, Pediatrics, New York University Medical Center, New York, NY
2001–2002	Clinical fellow, Pediatric Gastroenterology, Hepatology & Nutrition, Yale University School of Medicine, New Haven, CT
2002–2004	Postdoctoral research fellow, Laboratory of Fred S. Gorelick, Digestive Diseases, Yale University School of Medicine, New Haven, CT
2004-2006	Associate Research Scientist, Pediatrics, Yale University School of Medicine, New Haven, CT
2005-2011	Assistant Fellowship Director for Pediatric Gastroenterology at Yale
2006-2011	Assistant Professor, Pediatrics, Yale University School of Medicine, New Haven, CT
2009-2010	Chair, Study Section for the Children's Digestive Health and Nutrition Foundation
2010-2013	Chair, Research Committee, North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN)
2010-present	Editorial Board, *Pancreapedia*
2011-2018	Associate Professor, Pediatrics, University of Pittsburgh, Pittsburgh, PA

2014-2019 Member Faculty, McGowan Institute for Regenerative Medicine (MIRM) at the University of Pittsburgh, Pittsburgh, PA
2017-2019 Director, Exocrine Pancreas Center, Children's Hospital of Pittsburgh of UPMC
2017-present Chair, Pancreas Committee, NASPGHAN
2018-2019 Professor (with tenure), Pediatrics, University of Pittsburgh, Pittsburgh, PA
2019-present Professor, Medical Center Line (MCL), Pediatrics, Stanford University, Palo Alto, CA
2019-present Chief of the Division of Pediatric Gastroenterology, Hepatology, and Nutrition, Stanford University, Palo Alto, CA

Other Experience and Professional Memberships

American Pancreatic Association (2002-present); NASPGHAN (2002-present); American Gastroenterological Association (2002-present); American Board of Pediatrics, Board eligible in General Pediatrics (2002-present); and Board certified in Pediatric Gastroenterology, Hepatology, and Nutrition (2005-present); Study section member, Research Advisory Committee, Children's Hospital of Pittsburgh of UPMC (2012-2019); Advisory Board, NASPGHAN Foundation, 2010-2013

Honors

1990 Edgar Davis Memorial Scholarship in Medicine
1993 Golden Key National Honor Society
1994 Graduated Magna Cum Laude from Binghamton University
2004 American Gastroenterological Association AstraZeneca Faculty Transition Basic Science Award
2006 Humanitarian Achievement Award, from Humanity First USA (for role in Asian Tsunami and Katrina disaster relief)
2006 Children Digestive Health/Nutrition Foundation (CDHNF) Young Investigator Award
2009-2010 Chair, Study Section for Children's Digestive Health and Nutrition Foundation grants
2009 Yale Pediatric Department Mae Gailani Award for Junior Faculty Research and Mentorship
2010 Recognition Award as Medical Trip Leader to Haiti for Earthquake Relief, Humanity First USA
2012-2018 Best Doctors, Pittsburgh Magazine and Best Doctors in America
2014-2018 Standing section member, NIH Clinical, Integrative and Molecular Gastroenterology Study Section (CIMG)

C. Contributions to Science

1. Discovering a prominent role for the Ca^{2+} target the Ca^{2+}-activated phosphatase calcineurin (Cn) in pancreatitis. Our studies on pathologic Ca^{2+} signals progressed to determining potent Ca^{2+} targets leading to pancreatic injury and pancreatitis. We discovered that the Ca^{2+}-dependent serine, threonine phosphatase calcineurin (Cn) is a novel target of this pathological Ca^{2+} signal. We used genetic and pharmacologic strategies to examine the role of Cn in clinically relevant experimental models of pancreatitis *in vivo* and specifically within the pancreatic acinar cell. We believe that this emerging and highly translationally relevant work will provide a basis for understanding the role of Cn in various forms of pancreatitis and will lay the framework for novel clinical trials that target pancreatitis using Cn inhibitors.

a. **Husain SZ,** Grant WM, Gorelick FS, Nathanson MH, Shah AU. Caerulein-induced intracellular pancreatic zymogen activation is dependent on calcineurin. ***Am J Physiol Gastrointest Liver Physiol*** 2007;292(6):G1594-9. PMCID: PMC1242288*. (This was the first paper to demonstrate that Cn is a key target in acinar cell pancreatitis responses.)*
b. Jin S, Orabi AI, Le T, Javed TA, Sah S, Eisses JF, Bottino R, Molkentin JD, **Husain SZ.** Exposure to Radiocontrast Agents Induces Pancreatic Inflammation by Activation of Nuclear Factor-kB, Ca^{2+} Signaling, and Calcineurin. ***Gastroenterology***. 2015 May 13. pii: S0016-5085(15)00676-9. PMID: 25980752. *(This is the first paper to implicate aberrant Ca^{2+} signals and subsequent activation of Cn in mediating post-ERCP pancreatitis and its early inflammatory signals. The work also puts in application for the first time novel adeno-associated viruses (AAV) delivery of luminescent reporters selectively into the pancreas.)*
c. Orabi AI∗, Wen L∗, Javed TA, Le T, Guo P, Sanker S, Ricks D, Boggs K, Eisses JF, Castro C, Xiao X, Prasadan K, Esni F, Gittes GK, **Husain SZ**. Targeted Inhibition of Pancreatic Acinar Cell Calcineurin Is a Novel Strategy to Prevent Post-ERCP Pancreatitis. ***Cell Mol Gastroenterol Hepatol***. 2017 Jan;3(1):119-128. PMID: 28090570. http://www.cmghjournal.org/article/S2352-345X(16)30101-1/fulltext
d. Wen L, Javed TA, Yimlamai D, Mukherjee A, Xiao X, **Husain SZ**. Transient High Pressure in Pancreatic Ducts Promotes Inflammation and Alters Tight Junctions via Calcineurin Signaling in Mice. **Gastroenterology**. 2018 Jun 18. pii: S0016-5085(18)34658-4. PMID: 29928898.

2. Identifying a pathological role for pancreatic acinar cell Ca^{2+} release from the intracellular Ca^{2+} channel the ryanodine receptor (RyR). My early work demonstrated that abnormal acinar cell Ca^{2+} signals play a crucial role in initiating acute pancreatitis. We showed for the first time that abnormally elevated Ca^{2+} signals in the basal region are associated with pathologic intra-acinar protease activation, an early and critical event in the development of pancreatitis. This Ca^{2+} signal is mediated by an endoplasmic reticulum (ER) Ca^{2+} channel, the ryanodine receptor (RyR). We went on to examine mechanisms that regulate this pathologic RyR Ca^{2+} release in the acinar cell and showed that increasing cAMP in acinar cells caused RyR opening, likely through RyR phosphorylation. We also found that the RyR was an important trigger for alcohol, a leading cause of pancreatitis. We further demonstrated that human acinar cells express functional RyRs which mediate acinar pathology.

a. **Husain SZ**, Prasad P, Grant WM, Kolodecik TR, Nathanson MH, Gorelick FS. The ryanodine receptor mediates early zymogen activation in pancreatitis. ***Proc Natl Acad Sci U S A***. 2005 Oct 4;102(40):14386-91. PMCID: PMC1242288. *(This was the first paper to implicate a role for the intracellular Ca^{2+} channel the ryanodine receptor in acinar cell pathology and pancreatitis.)*
b. **Husain SZ**, Orabi AI, Muili KA, Luo Y, Sarwar S, Mahmood SM, Wang D, Choo-Wing R, Singh VP, Parness J, Ananthanaravanan M, Bhandari V, Perides G. Ryanodine receptors contribute to bile acid-induced pathological Ca^{2+} signaling and pancreatitis in mice. ***Am J Physiol Gastrointest Liver Physiol***. 2012 Apr 19. PMID: 22517774. PMCID: PMC3774209. *(The importance of this paper is that it implicates ryanodine receptor-Ca^{2+} in the pathogenesis of the most common cause of pancreatitis, gallstone-induced, or biliary pancreatitis.)*
c. Orabi AI, Muili KA, Javed TA, Jin S, Jayaraman T, Lund FE, **Husain SZ.** Cluster of differentiation 38 (CD38) mediates bile-acid induced acinar cell injury and pancreatitis through cyclic ADP ribose and intracellular Ca^{2+} release. ***J Biol Chem***. 2013 Aug 12. PMID: 23940051. PMCID: PMC3779711. *(The importance of this work is that it implicates the synthesis of an upstream putative ligand of the RyR, namely cADP ribose, to acinar cell Ca^{2+} and cell injury due to bile acid exposure.)*
d. Lewarchik CM, Orabi AI, Jin S, Wang D, Muili KA, Shah AU, Eisses JF, Malik A, Jayaraman T, **Husain SZ**. The ryanodine receptor is expressed in human pancreatic acinar cells and contributes to acinar cell injury. ***Am J Physiol Gastrointest Liver Physiol***. 2014 Jul 10. PMID: 25012845. PMCID: PMC4154117. *(This is the first demonstration that a large Ca^{2+} channel the ryanodine receptor, which has been characterized in murine models, is expressed in the human pancreas and that it exerts an important role in Ca^{2+} signaling during pancreatic acinar cell injury.)*

3. Characterizing a major epigenetic switch during pancreatic regeneration, through histone deacetylases (HDACs). In the hot pursuit of pancreatitis therapies, we hypothesized that a novel, alternate strategy to treating pancreatitis would be to examine the recovery mechanisms of the pancreas in response to injury. Based on 3 key observations: (1) that valproic acid (VPA), a drug which is definitely associated with pancreatitis, is an inhibitor of an important class of epigenetic proteins the histone deacetylases (HDACs); (2) that HDACs mediate pancreas development; and (3) that elements of pancreas development are recapitulated during pancreatic recovery—we further hypothesized that HDACs are crucial for activating the programs necessary for pancreatic recovery.

a. Eisses JF, Criscimanna A, Dionise ZR, Orabi AI, Javed TA, Sarwar S, Jin S, Zhou L, Singh S, Poddar M, Davis AW, Tosun AB, Ozolek JA, Lowe ME, Monga SP, Rohde GK, Esni F, **Husain SZ**. Valproic Acid Limits Pancreatic Recovery after Pancreatitis by Inhibiting Histone Deacetylases and Preventing Acinar Redifferentiation Programs. **Am J Pathol**. 2015 Dec;185 (12):3304-15. PMID: 26476347
b. Eisses JF, Davis A, Tosun AB, Dionise ZR, Cheng C, Ozolek JA, Rohde GK and **Husain SZ**. A Computer-Based Automated Algorithm for Assessing Acinar Cell Loss after Experimental Pancreatitis. ***PLoS One***. 2014 Oct 24;9(10):e110220. PMID: 25343460. PMCID: PMC4208778. *(This is the first paper to use a machine learning algorithm to quantify pancreatic acinar cell dropout during pancreatitis and its recovery during pancreatic regeneration. The tool will be broadly indispensable in providing an objective measure in the field of pancreatic injury and regeneration.)*
c. Huang Y, Liu C, Eisses JF, **Husain SZ**, Rohde GK. A supervised learning framework for pancreatic islet segmentation with multi-scale color-texture features and rolling guidance filters. ***Cytometry A***. 2016. Aug 25. PMID: 27560544.
d. Boggs K, Wang T, Orabi AI, Mukherjee A, Eisses JF, Sun T, Wen L, Javed TA, Esni F, Chen W, **Husain SZ**. Pancreatic gene expression during recovery after pancreatitis reveals unique transcriptome profiles. **Sci Rep**. 2018 Jan 23;8(1):1406. PMID: 29362419

4. Developing novel gene delivery tools for assessing early inflammatory events in pancreatitis *in vivo,* as well as establishing reproducible *ex vivo* and *in vivo* models of pancreatitis. We have recently developed several methods to detect early inflammatory signals in a highly sensitive, live, dynamic fashion through gene delivery of adeno-associated viruses (AAVs) selectively into the pancreatic duct. We have also established several methods to induce pancreatitis *ex vivo* and *in vivo*. We believe these techniques offer a valuable tool to study real-time activation of factors such as NF-κB in experimental models *in vivo*.

a. Orabi AI, Muili KA, Wang D, Jin S, Perides G, **Husain SZ.** Preparation of pancreatic acinar cells for the purpose of Ca^{2+} imaging, cell injury measurements, and adenoviral infection. ***J Vis Exp***. 2013 Jul 5;(77):e50391. PMID: 23851390. PMCID: PMC3731432.
b. Xiao X, Guo P, Prasadan K, Shiota C, Peirish L, Fischbach S, Song Z, Gaffar I, Wiersch J, **Husain SZ**, Gittes G, Gohary Y. Pancreatic cell tracing, lineage-tagging, and targeted genetic manipulations in multiple cell types using pancreatic ductal infusion of adeno-associated viral vectors and/or cell-tagging dyes. ***Nature Protocols***. 2014 Dec;9(12):2719-24. PMID: 25356582. PMC Journal–In Process. *(This paper provides detailed methods for a novel pancreatic gene delivery using intraductal infusion of adeno-associated viruses.)*
c. Orabi AI, Sah S, Javed TA, Lemon KL, Good ML, Guo P, Xiao X, Prasadan K, Gittes GK, Jin S, **Husain SZ**. Dynamic imaging of pancreatic NF-κB activation in live mice using AAV infusion and bioluminescence. ***J Biol Chem***. 2015 Mar 23. PMID: 25802340. PMCID: PMC4416837.
d. Hernandez G, Luo T, Javed TA, Wen L, Kalwat MA, Vale K, Ammouri F, **Husain SZ**, Kliewer SA, Mangelsdorf DJ. Pancreatitis is an FGF21-deficient state that is corrected by replacement therapy. **Sci Transl Med.** 2020 Jan 8;12(525). PMID: 31915301. PMCID: PMC7034981.

5. Progressing the clinical-translational aim of improving the understanding and management of patients with pancreatic disorders. In 2010, a group of us Pediatric Pancreatologists formed a consortium called INSPPIRE (International Study Group of Pediatric Pancreatitis: In Search for a Cure) with the purpose of studying the natural history of pancreatitis in children, establishing a registry (with biorepository), and optimizing current management strategies. Some of the papers below are from INSPPIRE, and others are from my emerging interest in bridging the gap between basic science and clinical application.

a. Bai HX, Lowe ME, **Husain SZ**. What have we learned about acute pancreatitis in children? ***J Pediatr Gastroenterol Nutr.*** 2011 Mar;52(3):262-70. PMCID: 3626416.
b. Morinville VD*, **Husain SZ*** **(*Shared first author)**, Bai H, Barth B, Alhosh R, Durie PR, Freedman SD, Himes R, Lowe ME, Pohl J, Werlin S, Wilschanski M, Uc A; on behalf of the INSPPIRE Group. Definitions of Pediatric Pancreatitis And Survey Of Current Clinical Practices: Report From Insppire (International Study Group Of Pediatric Pancreatitis: In Search For A Cure). ***J Pediatr Gastroenterol Nutr.*** 2012 Sep;55(3):261-5. PMCID: PMC3626452*. (This was the first publication of INSPPIRE.)*
c. **Husain SZ**, Srinath AI. What's unique about acute pancreatitis in children: risk factors, diagnosis and management. **Nature reviews. Gastroenterology & hepatology**. 2017; 14(6):366-372. PMID: 28293024.
d. Uc A, **Husain SZ**. Pancreatitis in Children. **Gastroenterology**. 2019 May;156(7):1969-1978. PMID: 30716320. PMCID: PMC6730664.

Complete List of Published Work in MyBibliography: http://www. ncbi. nlm. nih. gov/sites/myncbi/sohail. husain. 1/bibliography/40406768/public/?sort=date&direction=ascending.

D. Research Support.

Ongoing

R01 DK093491 **Husain (PI)** **7/01/16 – 6/30/21**
NIH/NIDDK, Calcineurin in Post-ERCP Pancreatitis
The major goal of this project is to examine the central role of the Ca^{2+}-activated phosphatase calcineurin in post-ERCP pancreatitis.

DoD PRMRP Technology/Therapeutic Development Award Log Number PR181014
Husain (PI) **9/24/19 – 9/24/22**
Department of Defense (DoD), Optimizing a novel intraductal delivery of calcineurin inhibitors as a radiocontrast infusion formulation to prevent post-ERCP pancreatitis

The major goal the current proposal is to perform investigational new drug (IND)-enabling preclinical safety and efficacy studies of two novel calcineurin inhibitor-radiocontrast formulations that have established proof-of-concept data in preventing post-ERCP pancreatitis.

Shire Oncology Husain (PI) 1/01/18 – 1/01/21
Preventing asparaginase-associated pancreatitis using the novel dimension of metabolomics
The major goal of this project is to dicepher the metabolic dyscrasias that predispose some patients to the development of pancreatitis with the cancer drug asparaginase. This will be achieved by performing targeted and non-targetted metabolomic and lipidomic studies in patients and matched controls.

Completed

R01 DK103002 Husain (PI) 7/1/14 - 6/30/19
NIH/NIDDK, HDACs in pancreatic recovery after injury
The major goal of this project is to examine the role of histone deacetylases as major epigenetic regulators of pancreatic recovery after injury. Role: PI

R01 DK093491 Husain (PI) 7/01/11 – 6/30/16
NIH/NIDDK, Calcineurin in Pancreatitis
The major goal of this project is to examine the role of the Ca^{2+}-activated phosphatase calcineurin in clinically relevant models of pancreatitis. Role: PI

R01 DK083327 Husain (PI) 5/30/09 - 5/30/15
NIH/NIDDK, Ryanodine Receptor in Pancreatitis
The major goal of this project is to examine the role that phosphorylation of the ryanodine receptor Ca^{2+} channel plays in mediating premature intracellular zymogen activation and pancreatitis. Role: PI

R03DK078707 Husain (PI) 6/1/08 - 5/31/10
NIH/NIDDK, Calcineurin and Pancreatic Zymogen Activation
The major goal of this project is to examine the role of the Ca^{2+}-activated phosphatase calcineurin as a mediator of premature intracellular zymogen activation, an early mediator of acute pancreatitis. Role: PI

K08 DK06811601 Husain (PI) 9/1/04 - 9/1/10

NIH/NIDDK, Ryanodine Receptor and Pancreatic Zymogen Activation
The major goal of this project is to examine the role of the Ca^{2+} release channel the ryanodine receptor in mediating premature intracellular zymogen activation, an early mediator of acute pancreatitis. Role: PI

Young Investigator Development Award Husain (PI) 7/1/07 – 6/30/09
Children's Digestive Health and Nutrition Foundation (CDHNF)
Ryanodine Receptor and Pancreatic Zymogen Activation
The major goal of this project is to examine the role of the ryanodine receptor ligand CD38, or cADP ribose, in mediating the aberrant Ca^{2+} signal observed with stimuli that cause pancreatic zymogen activation and pancreatitis. Role: PI

AGA Aztra Zeneca Transition Award Husain (PI) 7/1/04 – 6/30/06
American Gastroenterological Association (AGA),
Ryanodine Receptor and Pancreatic Zymogen Activation
Using pharmacologic tools, the major goal of this project is to examine the role of the Ca^{2+} release channel the ryanodine receptor in mediating pancreatitis. Role: PI

K12 HD001401 Hostetter (PI) 7/1/04 - 6/30/06
NIH/NICHD, Ryanodine Receptor and Pancreatic Zymogen Activation
The major goal of this project is to examine the role of the Ca^{2+} release channel the ryanodine receptor in mediating premature zymogen activation, an early mediator of acute pancreatitis. Role: Junior Investigator

T32 DK07017 Binder (PI) 7/1/02 - 6/30/04

NIH/NIDDK, Digestive Diseases Research Training Grant. Role: Research Fellow