BIOGRAPHICAL SKETCH

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NAME: Hu, Guochang

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

POSITION TITLE: Associate Professor of Anesthesiology and Pharmacology

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
Xuzhou Medical College	M.D.	07/1988	Medicine
China Medical University	Ph.D.	07/2004	Inflammation and vascular biology

A. Personal Statement

The long-term goal of our research is to define how vascular endothelial barrier function in sepsis can be modulated to maximize protection and minimize tissue damage, thereby identifying potential therapeutic targets for prevention and treatment of sepsis. Over the past 15 years, my research has focused on vascular endothelial permeability, acute lung injury, innate immunity and inflammation. I have established a record of successful and productive research in the areas highly relevant to lung inflammatory injury. We have recently demonstrated that Yes-associated protein controls endothelial activation and vascular inflammation in sepsis (*Circ Res*, 2018). We have provided solid evidence to support the important role of transcellular endothelial permeability in the inflammatory response (*Circ Res*, 2009, 2008). We also showed that vascular endothelial (VE) cadherin recycling is essential for reannealing of endothelial junctional gap following septic injury (*Arterioscler Thromb Vasc Biol*, 2016).

1. Lv Y, Kim K, Sheng Y, Cho J, Qian Z, Zhao YY, Hu G, Pan D, Malik AB, **Hu G***. YAP Controls Endothelial Activation and Vascular Inflammation through TRAF6. *Circ Res*. 2018;123:43-56.
2. Yan Z, Wang ZG, Segev N, Hu S, Minshall RD, Dull RO, Zhang M, Malik AB, **Hu G***. Rab11a Mediates Vascular Endothelial-Cadherin Recycling and Controls Endothelial Barrier Function. *Arterioscler Thromb Vasc Biol*. 2016;36:339-349. PMCID: PMC4732894
3. Yang Z, Sun D, Yan Z, Reynolds AB, Christman JW, Minshall RD, Malik AB**, Hu G*.** Differential role for p120-catenin in regulation of TLR4 signaling in macrophages. *J Immunol*. 2014; 192: 5647-5650. PMCID: PMC4119481.
4. Wang YL, Sun Y, Malik AB, Hu S, Albert B. Reynolds AB, Minshall RD, and **Hu G***. Innate Immune Function of the Adherens Junction Protein p120-Catenin in Endothelial Response to Endotoxin. *J Immunol*, 2011;186: 3180–3187.

B. Positions and Honors

Positions and Employment

1988-1993 Assistant professor, Department of Clinical Anesthesia, Xuzhou Medical College, China.
1994-1997 Associate Professor and Chairman, Department of Anesthesiology, Xuzhou Medical College, China.
1998-1999 Research Fellow, Intensive Therapy Unit, Royal North Shore Hospital, The University of Sydney, Sydney, Australia.
2000-2002 Visiting Scholar, Department of Anesthesiology, Advocate Illinois Masonic Medical Center and University of Illinois at Chicago, IL
2002-2003 Instructor, Department of Anesthesiology, Advocate Illinois Masonic Medical Center and University of Illinois at Chicago, IL
2003-2005 Research Assistant Professor, Department of Anesthesiology, Advocate Illinois Masonic Medical Center and University of Illinois at Chicago, IL
2005-2010 Research Assistant Professor, Department of Pharmacology, University of Illinois College of Medicine, IL
2010-2016 Assistant Professor (tenure track), Departments of Anesthesiology and Pharmacology, University of Illinois College of Medicine, IL
2016- Associate Professor (tenured), Departments of Anesthesiology and Pharmacology, University of Illinois College of Medicine, IL

Other Experience and Professional Memberships

1997 Chairman (Spinal Anesthesia and Nerve Blocks), the 7th National Congress of Anesthesiology, Chinese Medical Association, Shenyang, China.
2010-2016 Committee member, American Heart Association, Peer Review, Vascular Wall Biology 2
2010- National Natural Science Foundation, China, Peer Review, Lung biology
2012 Mail Reviewer, Physicians' Services Incorporated Foundation, Canada
2013 Mail Reviewer, NIAA e-grants, The National Institute of Academic Anaesthesia, UK
2012- Membership Committee Member, American Physiological Society
2005- Ad hoc reviewer (44 journals): American Journal of Physiology, American Journal of Respiratory Cell and Molecular Biology, Anesthesiology, Autophagy, BBA Molecular Basis of Disease, Critical Care Medicine, European Respiratory Journal, The FASEB Journal, Journal of Immunology, Molecular Cell Biology, PLOS Pathogens, Science Signaling, Scientific Report, etc.
2013-2014 Abstract Review Subcommittee on Critical Care, American Society of Anesthesiologists
2017-2018 Ad hoc Committee member, NIH – Surgery, Anesthesiology, and Trauma Study Section, February and September 2017, February 2018.
2018 Organizing committee and Session Chair, 10th World Immunology, Madrid, Spain
2018 Mail Reviewer, Physicians' Services Incorporated Foundation, Canada.
2016-2018 Guest Editor – Frontiers in Immunology
2018-2021 Editorial Board, Refresher Course Publication, American Society of Anesthesiologists.
2018-2022 Committee member, NIH – Surgery, Anesthesiology, and Trauma Study Section.
2018- Associate Editor – Frontiers in Immunology

Honors

1991 First Prize for Achievement in Science and Technology, The Health Ministry of Jiangsu Province, China
1992 Outstanding Young Scientist, Xuzhou Academy of Science & Xuzhou Association of Science, China
1992 Outstanding Young College Teacher, the Education Committee of Jiangsu Province, China
1995 Outstanding Young College Teacher, Xuzhou Medical College, China
1997 Outstanding Young College Teacher, the Education Committee of Jiangsu Province, China
1997 Outstanding Academic Member, The Education Committee of Jiangsu Province, China
1998 Outstanding Young Committee Member, the Chinese Association of Medicine, China
2002 Best General Poster Award, Advocate Health Care, Chicago, IL
2003 Best General Poster Award, Advocate Health Care, Chicago, IL
2003 Best Patient Safety Research Poster, Advocate Health Care, Chicago, IL

2003 Best of Meeting, Top Ten, 77th International Anesthesia Research Society (IARS) Clinical and Scientific Congress
2004 Best General Poster Award, Advocate Health Care, Chicago, IL
2006 Scientist Development Award, American Heart Association
2006 Young Investigator Award, American Heart Association, 2006
2007 Best Poster, Resuscitation Science, 2006 Resuscitation Science Symposium, AHA, Chicago

C. Contributions to Science

I. Vascular endothelial barrier function. Vascular hyperpermeability and protein-rich edema resulted from disruption of the endothelial barrier is a key hallmark of inflammation. The normally restrictive paracellular pathway, which can become "leaky" during inflammation when gaps are induced between endothelial cells at the level of adherens junctional complexes, and the transcellular pathway, which transports plasma proteins the size of albumin via transcytosis in vesicle carriers originating from cell surface caveolae. Caveolin-1 phosphorylation-dependent signaling plays a crucial role in oxidative stress-induced pulmonary vascular hyperpermeability via transcellular and paracellular pathways. Thus, caveolin-1 phosphorylation may be an important therapeutic target for limiting oxidant-mediated vascular hyperpermeability, protein-rich edema formation, and acute lung injury. We also found that Rab11a/Rab11 family-interacting protein 2-mediated vascular endothelial (VE)-cadherin recycling is required for formation of adherens junctions and restoration of VE barrier integrity and hence a potential target for clinical intervention in inflammatory disease. Finally, our recent study demonstrated that YAP modulated the activation of endothelial cells and suppressed vascular inflammation through preventing TRAF6-mediated NF-κB activation and was hence essential for limiting the severity of sepsis-induced inflammation and organ failure.

1. Lv Y, Kim K, Sheng Y, Cho J, Qian Z, Zhao YY, Hu G, Pan D, Malik AB, **Hu G***. YAP Controls Endothelial Activation and Vascular Inflammation through TRAF6. *Circ Res.* 2018;123:43-56. PMCID: PMC6014930.
2. Yan Z, Wang ZG, Segev N, Hu S, Minshall RD, Dull RO, Zhang M, Malik AB, **Hu G*.** Rab11a Mediates Vascular Endothelial-Cadherin Recycling and Controls Endothelial Barrier Function. *Arterioscler Thromb Vasc Biol*. 2016;36:339-349. PMCID: PMC4732894.
3. Sun Y, **Hu G***, Zhang X, Minshall RD. Phosphorylation of caveolin-1 regulates oxidant- induced pulmonary vascular permeability via paracellular and transcellular pathways. *Circ Res.* 2009;105:676-685. **(*Correspondent**). PMCID: PMC2776728.
4. **Hu G**, Vogel SM, Schwartz DE, Malik AB, Minshall RD. Intercellular adhesion molecule-1-dependent neutrophil adhesion to endothelial cells induces caveolae-mediated pulmonary vascular hyperpermeability. *Circ Res*. 2008;102:e120-131. PMCID: PMC2664169.

II. Alveolar macrophages in lung inflammation and resolution. Alveolar macrophages reside in the airspaces juxtaposed with epithelial cells and function as critical regulators of pulmonary host defenses against bacterial, viral, and fungal infection. Our data showed that Rab1a activity was elevated in alveolar macrophages from septic patients and positively associated with severity of sepsis and respiratory dysfunction. Rab1a-mediated NLRP3 inflammasome activation in alveolar macrophages induced lung inflammatory injury during sepsis while inhibition of Rab11a activity in alveolar macrophages promoted phagocytosis of apoptotic neutrophils and facilitated the resolution of sepsis-induced lung injury. In addition, enhancement of Toll-like receptor 4 internalization by p120-catenin in alveolar macrophages attenuated lung inflammation following lipopolysaccharide (LPS) challenge. Finally, mechanical ventilation also activated NALP3 inflammasome in alveolar macrophages which mediated lung inflammation and injury.

1. Zhang Y, Wang L, Lv Y, Jiang C, Wu G, Dull RO, Minshall RD, Malik AB, **Hu G***. The GTPase Rab1 is required for NLRP3 inflammasome activation and inflammatory lung injury. *J Immunol*. 2019;202:194-206.
2. Jiang C, Liu Z, Hu R, Bo L, Minshall RD, Malik AB, **Hu G***. Inactivation of Rab11a GTPase in macrophages facilitates phagocytosis of apoptotic neutrophils. *J Immunol*. 2017. PMCID: PMC5296368.
3. Yang Z, Sun D, Yan Z, Reynolds AB, Christman JW, Minshall RD, Malik AB, **Hu G***. Differential role for p120-catenin in regulation of TLR4 signaling in macrophages. *J Immunol*. 2014; 192: 5647-5650. PMCID: PMC4119481.
4. Wu J, Yan Z, Malik AB, Schwartz DE, Yu J, **Hu G***. Mechanical stretch activates NALP3 inflammasome in alveolar macrophages. *J Immunol*, 2013;190:3590-3599. PMCID: PMC3608749.

III. p120-Catenin and Toll-like receptor 4 signaling. The main focus of my research has been on understanding mechanisms underlying lung inflammatory injury and resolution. My colleagues and I for the first time showed that p120 isthe immunomodulatory function of an adherens junction protein p120-catenin in sepsis-induced lung injury. p120 expression in macrophages and endothelial cells negatively regulates Toll-like receptor 4 signaling and inflammatory response. We also found that activation of inflammasome in alveolar macrophages mediated neutrophilic lung inflammation. These studies highlight that appropriate modulation of excessive inflammatory response through inhibition of Toll-like receptor 4 signaling pathways and inflammasome may have considerable potential as therapeutics for inflammatory disorders

1. Yang Z, Sun D, Yan Z, Reynolds AB, Christman JW, Minshall RD, Malik AB**, Hu G*.** Differential role for p120-catenin in regulation of TLR4 signaling in macrophages. *J Immunol*. 2014; 192: 5647-5650. PMCID: PMC4119481.
2. Wang YL, Malik AB, Sun Y, Hu S, Reynolds AB, Minshall RD, **Hu G*.** Innate immune function of the adherens junction protein p120-catenin in endothelial response to endotoxin. *J Immunol*. 2011;186:3180-3187. PMCID: PMC4277845.
3. Wang Y, Minshall RD, Schwartz DE, **Hu G***. Cyclic stretch induces alveolar epithelial barrier dysfunction via calpain-mediated degradation of p120-catenin. *Am J Physiol Lung Cell Mol Physiol*. 2011;301:L197-L206. PMCID: PMC3154624.
4. Jiao H, Zhang Y, Yan Z, Wang ZG, Liu G, Minshall RD, Malik AB, **Hu G***. Caveolin-1 Tyr14 Phosphorylation Induces Interaction with TLR4 in Endothelial Cells and Mediates MyD88-Dependent Signaling and Sepsis-Induced Lung Inflammation. *J Immunol*. 2013;191:6191-6199. PMCID: PMC3874812

IV. Ventilator-induced lung injury. Mechanical ventilation is necessary to support patients with acute lung injury or its most severe form, acute respiratory distress syndrome (ARDS); however, it has also been shown to exacerbate lung injury, the so-called ventilator-induced lung injury (VILI). Our studies have shown that activation of autophagy, NLRP3 inflammasome and calpain mediated mechanical stretch-induced lung inflammation. These findings provide a new insight into the molecular mechanisms and the pathophysiology of VILI.

1. Zhang Y, Liu G, Dull RO, Schwartz DE, **Hu G***. Autophagy in pulmonary macrophages mediates lung inflammatory injury via NLRP3 inflammasome activation during mechanical ventilation. *Am J Physiol Lung Cell Mol Physiol*. 2014;307:L173-185. PMCID: PMC4101793.
2. Wu J, Yan Z, Malik AB, Schwartz DE, Yu J, **Hu G*.** Mechanical stretch activates NALP3 inflammasome in alveolar macrophages. *J Immunol*, 2013;190:3590-3599. PMCID: PMC3608749.
3. Liu D, Yan Z, Minshall RD, Schwartz DE, Chen Y, **Hu G***. Activation of calpains mediates early lung neutrophilic inflammation in ventilator-induced lung injury. *Am J Physiol Lung Cell Mol Physiol*. 2012;302:L370-379. PMCID: PMC3289265.
4. Wang Y, Minshall RD, Schwartz DE, **Hu G***. Cyclic stretch induces alveolar epithelial barrier dysfunction via calpain-mediated degradation of p120-catenin. *Am J Physiol Lung Cell Mol Physiol*. 2011;301:L197-L206. PMCID: PMC3154624.

V. Anti-inflammatory effects of volatile anesthetics. In addition to the contributions described above, with a team of collaborators, I directly investigated the effectiveness of volatile anesthetics isoflurane and sevoflurane on the neutrophil-endothelium interactions in the heart. Isoflurane and sevoflurane protects the heart via K_{ATP} channel-dependent and adenosine receptor-mediated pathways.

1. **Hu G**, Schwartz DE, Shahajan AN, Visintine DJ, Salem MR, Crystal GJ, Albrecht RF, Vogel SM, Minshall RD. Isoflurane, but not sevoflurane, increases transendothelial albumin permeability in the isolated rat lung: role for enhanced phosphorylation of caveolin-1. *Anesthesiology* 2006;104:777-785. PMID: 16571974.
2. **Hu G**, Salem, MR, and Crystal GJ. Role of adenosine receptors in volatile anesthetic preconditioning against neutrophil-induced contractile dysfunction in isolated rat hearts. *Anesthesiology* 2005;103:287-295. PMID: 16052111.
3. **Hu G**, Salem, MR, and Crystal GJ. Isoflurane and sevoflurane precondition against neutrophils-induced contractile dysfunction in isolated rat hearts. *Anesthesiology* 2004;100:489-497. PMID: 15108960.

4. **Hu G**, Vasiliauskas T, Salem, MR, Rhone DP, and Crystal GJ. Neutrophils pretreated with volatile anesthetics lose ability to cause cardiac dysfunction. *Anesthesiology* 2003;98:712-718. PMID: 12606916.

Complete List of Published Work in My Bibliography:

https://www.ncbi.nlm.nih.gov/pubmed/?term=guochang+hu

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

2R01 HL104092 Hu (PI) 01/01/16-06/30/21
Role of p120-catenin in Sepsis-induced Lung Injury
The overarching theme of this project is to determine the role of p120-catenin in efferocytosis and resolution of lung injury.

Pending Research Support

2R01 HL104092 Hu (PI) 09/01/19-08/31/24
Targeting the host immune response during sepsis
The proposed studies of this project are to examine the role of macrophage p120-catenin in bacterial clearance during sepsis

Completed Research Support

1R01HL104092 Hu (PI) 08/01/10-05/31/15
Role of p120-catenin in Sepsis-induced Lung Injury
The project focuses on the role of endothelial p120-catenin in the regulation of Toll-like receptor signaling and subsequently lung inflammation and injury during sepsis.
Role: PI

AHA-SDG 0730331N Hu (PI) 01/01/07-12/31/10
Role of oxidant signaling in activation of transcellular albumin hyperpermeability
The project determined how reactive oxygen species generated by neutrophils and endothelial cells regulated transcellular albumin permeability induced by activated neutrophils.
Role: PI

R01 HL071626 Minshall (PI) 04/01/02-11/30/12
Src Regulation of Endothelial Barrier Function
Determined 1) the role of ICAM-1 dependent activation of Src and NO signaling in the mechanism of inflammatory endothelial hyperpermeability, and 2) whether phosphorylated Cav-1 functions as a negative-feedback regulatory mechanism to inhibit eNOS and Src signaling and terminate lung inflammation.
Role: Co-investigator