BIOGRAPHICAL SKETCH

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NAME: Bo Liu

eRA COMMONS USER NAME (credential, e.g., agency login): bol2001

POSITION TITLE: Associate Professor

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
Beijing University, Beijing, China	B.S.	July/1984	Biology
Beijing University, Beijing, China	M.S.	July/1986	Physiology
SUNY Downstate, New York, NY	Ph.D.	Dec/1993	Biochemistry

A. Personal Statement

I am a vascular biologist with a broad background in molecular biology, cell biology, biochemistry, and inflammation. The ultimate goal of my research is to develop clinically applicable diagnostic and therapeutic strategies for vascular diseases. Specifically, we study cell death including intracellular regulatory mechanisms as well as signaling mechanisms through which a dying cell communicate with circulating inflammatory cells and progenitors. We also actively investigate how extracellular matrix proteins influence vascular aging and inflammation.

Closely related to research is my passion for teaching and mentoring. Using individualized approaches, I guide students and mentees through a leaning process that focuses on problem solving and discoveries. I devote energy to make my lab a place that fosters creativity, collaboration and integrity.

B. Positions and Honors

Positions and Employment

1/94-9/96 Postdoctoral fellow, laboratory of Dr. James H. Schwartz, Center for Neurobiology and Behavior, Columbia University
10/96 -5/99 Postdoctoral fellow, laboratory of D. Eseng Lai, Dept. of Cell Biology, Memorial Sloan-Kettering Cancer Center
5/99-2/06 Assistant Professor, Department of Surgery, Weill Cornell Medical College
2/06-9/08 Associate Professor, Department of Surgery, Weill Cornell Medical College
10/08- Associate Professor, Department of Surgery, School of Medicine and Public Health, University Wisconsin, Madison

Other Experience and Professional Memberships

2000- American Heart Association
2003- North American Vascular Biology Organization
2004- American Society for Biochemistry and Molecular Biology
2009- Association for Academic Surgery
2009- American Society of Physiology
2013- Co-chair, grant review panel-Vascular Wall II, American Heart Association

Honors

1988 Brooks Award, Health Science Center at Brooklyn
1988-1991 Competitive Graduate School Fellowships
1996-1998 NIH National Research Service Award (postdoctoral fellowship)

C. Contribution to Science

1. The role of cell death in vascular inflammation and progression of abdominal aortic aneurysm.

My early work on abdominal aortic aneurysm focused on apoptosis of smooth muscle cells. The conventional view is that apoptosis contributes to aneurysm pathogenesis by reducing smooth muscle cells which is a major source of extracellular matrix proteins. Data generated by my lab indicate a new role for apoptosis, i.e. amplification of the pro-inflammatory signal. We showed that apoptotic smooth muscle cells secret chemokines such as monocyte chemoattractant protein-1 (MCP-1) which are critical for vascular inflammation. We identified protein kinase C-delta (PKCδ) as an important modulator of the apoptosis-inflammation crosstalk. Our more recent work addresses a novel necrotic process called necroptosis. We showed for the first time that gene deletion of a key necropoptotic regulator called receptor interacting protein kinase3 (RIP3) protects mice from developing aneurysm. Our studies also revealed a novel interaction between PKCδ and RIP3, which implies a fundamental connection between cell apoptosis and necrosis as well as inflammation. We have developed two new mouse models of abdominal aortic aneurysm. I served as the PI of the above mentioned studies.

- Yamanouchi D, Kato K, Morgan S, Lengfeld J, Zhang F, and **Liu B**. Effects of caspase inhibitor on angiotensin II-induced abdominal aortic aneurysm in apolipoprotein E-deficient mice. Arterioscler Thromb Vasc Biol 2010 30:702-707
- Morgan S, Yamanouchi D, Harberg C, Wang Q, Keller, M, Burlingham W, Seedial S, Lengfeld J, and **Liu B**. Protein Kinase C-delta regulates inflammation in mouse abdominal aortic aneurysm through monocyte chemoattractant Protein-1. Arterioscler Thromb Vasc Biol. 2012 32:2493 (PMC3442600)
- Liu Z, Wang Q, Ren J, Assa CR, Morgan S, Giles J, Han Q, and **Liu B** A murine abdominal aortic aneurysm model by orthotopic allograft transplantation of elastase-treated abdominal aorta. J Vas Surg 2014 S0741-5214(14)01000-3 (PMC24974783)
- Wang Q, Liu Z, Ren J, Assa C, Morgan S, and **Liu B**. Receptor-interacting protein kinase-c contributes to abdominal aortic aneurysm via smooth muscle cell necrosis and inflammation. Circ Res 2015 116:600-11 (PMC4329096)

2. Regulation of vascular inflammation by extracellular proteins

Another research interest of mine is to understand how risk factors including aging affect pathophysiology of aneurysm. In collaboration with Dr. Naomi Chesler of Biological Medical Engineering, we are testing the hypothesis that age-associated changes in extracellular matrix proteins affect aneurysm progression by skewing infiltrating macrophages toward pro-inflammatory phenotypes. We have recently obtained an R21 to explore this novel concept. In collaboration with Dr. Nader Sheibani (Eye Institute) and Dr. Deane Mosher (Department of Medicine), we investigate how matricellular proteins such as thrombospondin-1 affect inflammatory invasion during aneurysm development. I am the co-PI or PI of these studies.

- Liu Z, Morgan S, Ren J, Wang Q, Annis DS, Mosher DF, Zheng J, Sorenson CM, Sheibani N, and Liu B. Thrombospondin-1 (TSP1) Contributes to the Development of Vascular Inflammation by Regulating Monocytic Cell Mobility in Mouse Models of Abdominal Aortic Aneurysm. Circ Res 2015 117:128-41 (PMC4490953)

3. Vascular progenitor cells in occlusive vascular disease

A long standing interest of mine is intimal hyperplasia or the development of a hyperplasic lesion in the subintimal space of blood vessels. The source of neointimal cells is an unsolved problem in vascular biology. To this end, our lab explores the paracrine effects of vascular smooth muscle cells on adventitial fibroblasts. Recently, we discovered rather unexpectedly that induction of smooth muscle apoptosis in denuded carotid

arteries caused acceleration in endothelial regeneration. Our preliminary results support the hypothesis that apoptotic smooth muscle cells recruit progenitor cells from bone marrow. Using various genetic and molecular approaches, we showed that the pro-apoptotic regulation PKCδ plays a critical role in the expression of pro-angiogenic chemokines. A new collaboration with Dr. William Murphy, the co-Director of Stem Cell and Regenerative Medicine Center has been established to investigate homing of circulating progenitors. I am the PI of these studies.

- Yamanouchi D, Kato K, Ryer RJ, Zhang F, and **Liu B**. Protein kinase C-delta mediates arterial injury responses through regulation of vascular smooth muscle cell apoptosis. Cardiovascular Res 2010 85:434-43
- Si Y, Ren J, Wang P, Rateri D, Daugherty A, Shi X, Kent KC, and **Liu B**. Protein kinase C-delta mediates adventitial cell migration through regulation of monocyte chemoattractant protein-1 expression in a rat angioplasty model. Arterioscler Thromb Vasc Biol. 2012 32:943-54 (PMC3311123)
- Shi X, Guo LW, Seedial SM, Si Y, Wang B, Takayama T, Suwanabol PA, Ghosh S, DiRenzo D, **Liu B**, Kent KC. TGF-β/Smad3 inhibits vascular smooth muscle cell apoptosis through an autocrine signaling mechanism involving VEGF-A. Cell Death Dis. 2014 5:e1317 (PMC4123076)
- Ren J, Wang Q, Morgan S, Si Y, Ravichander A, Dou C, Kent KC, and **Liu B** Protein Kinase C-delta regulates pro-inflammatory chemokine expression through cytosolic interaction with the NFκB subunit p65 in vascular smooth muscle cells. J Biol Chem 2014 289:9013 (PMC3979373)

4. Development of nanoparticle-based gene/drug delivery

A major limiting factor of gene therapy is the lack of safe and efficient gene transferring reagents. Even in animal studies, delivering genes or sRNAs often involves the use of viral vectors. Viral vectors are often expensive to construct and post potential health risks to researchers. Through a collaborative effort first with the Biomedical Engineering Program of Cornell University and later with Engineering School of University of Wisconsin (David Lynn), we test synthetic materials as non-viral carriers for gene therapies in animal models of vascular disease. I am the co-investigator of these studies.

- Yamanouchi D, Jun Wu, Lazar AN, Kent KC, Chu CC, and **Liu B.** Biodegradable arginine-based poly(ester-amide)s as non-viral gene delivery reagents. Biomaterials 2008 29:3269-3277
- Saurer EM, Yamanouchi D, **Liu B**, Lynn DM. Delivery of plasmid DNA to vascular tissue in vivo using catheter balloons coated with polyelectrolyte multilayers. Biomaterials. 2011 32:618-8 (PMC2991550) (LB and LDM are co-senior authors)
- Bechler S, Si Y, Yu Y, Ren J, **Liu B**, and Lynn DM. Reduction of intimal hyperplasia in injured rat arteries promoted by catheter balloons coated with polyelectrolyte multilayers that contain plasmid DNA encoding PKCdelta. Biomaterials 2013 34:226 (PMC3483441) (LB and LDM are co-senior authors)

An expanded list of publications can be found at:

http://www.ncbi.nlm.nih.gov/sites/myncbi/bo.liu.2/bibliograpahy/42730945/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

R01HL122562-01 (Liu, PI) 07/15/14-04/30/19
NIH/NHLBI
Vascular smooth muscle cell apoptosis in intimal hyperplasia.
The long-term objective of the proposed studies is to delineate how apoptosis of arterial smooth muscle cells affect the regeneration of endothelium and arterial remodeling.
Role: PI

R01HL088447 Liu (PI) 12/15/10-11/30/14
NIH/NHLBI (in no cost extension)
Molecular mechanisms of abdominal aortic aneurysms.

The goal of this R01 is to determine how the signaling protein PKCdelta contributes to pathogenesis of aneurysms and to test the potential of PKCdelta inhibition as a therapeutic strategy.
Role: PI

R21HL121493 (Chesler and Liu, PIs)
NIH/NHLBI 9/1/14-8/31/16
Impact of the micromechanical environment on inflammation in AAA progression.
The results obtained from this study will provide a new concept in understanding aging-associated AAA formation and lay a foundation for future mechanistic studies and drug development.
Role: Co-PI

3R01-HL 68673-01 Kent (PI) 9/1/14- 8/31/19
NIH/NHLBI
TGF-beta in intimal hyperplasia after vascular bypass.
The goal of this project is to understand the role of TGF-beta signaling proteins SMAD in vascular smooth muscle proliferation and matrix production and to develop specific gene manipulation to prevent or reverse restenosis.
Role: Co-investigator

T32 HL110853 Kent (PD) 7/1/12-6/30/17
NIH/NHLBI
Vascular Surgery Research Training Program
The purpose of this program is to provide collaborative training to postdoctoral fellows (MDs and/or PhDs) in multiple disciplines of basic, translational and clinical vascular research.
Role: Co-Program Director

14PRE18560035 Wang (PI) 1/1/14-12/31/15
American Heart Association
RIP-mediated necroptosis as a therapeutic target for abdominal aortic aneurysm.
This is a pre-doctoral fellowship to support Qiwei Wang's thesis work.
Role: Mentor

15PRE 25670074 Ren (PI) 7/1/15-6/30/16
University of Wisconsin, Madison
PKCdelta-mediated vascular injury response as a therapeutic target for preventing intimal hyperplasia.
This research award is to support Jun Ren for his thesis work in Liu's lab.
Role: Mentor

Recently Completed

R01-HL 081424 Liu (PI) 8/1/05- 12/31/12
NIH/NHLBI
PKC-delta in intimal hyperplasia after vascular bypass.
The goal of this project is to understand the role of protein kinase C-delta signaling in vascular smooth muscle function (proliferation, migration and apoptosis) and vascular injury responses.
Role: PI (final year of the award was re-dated due to institutional transfer)

UW-Graduate School (Liu, PI) 7/1/15-6/30/16
Vascular smooth muscle cell apoptosis in intimal hyperplasia.
This individual fall competition proposal functions as a reassurance for NIH R01HL122562-01. The budget for one graduate student is requested.
Role: PI (funded but declined)

10GRNT3020052 Liu (PI) 7/1/2010-6/30/2013
American Heart Associate/Grant-in-Aid
Novel role of apoptosis in aneurysmal dilation

This project is to test a new paradigm in which we hypothesize that apoptosis of vascular smooth muscle cells contributes to aneurysm pathogenesis by stimulating pro-inflammatory signaling.
Role: PI

14UFEL20010034 Assa (PI) 6/1/14-8/31/14
American Heart Association
The Role of PKC-delta in the Regulation of RIP3 Expression in Aortic Smooth Muscle Cells.
This summer research award is to support Miss Carmel Assa's summer research experience in Liu's lab.
Role: Mentor

Lifeline Foundation Award Phan (PI) 7/1/14-8/31/14
Society of Vascular Surgery
RIP3 as a therapeutic target for abdominal aortic aneurysm.
This award is to support Miss Noel Phan, a first year medical student, to gain research experience in Liu's lab over the summer.
Role: Mentor