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### **CURRICULUM VITAE**

**NAME:** Xuejun Wang, M.D., Ph.D.

NICKNAME: "XJ" Wang

CITIZENSHIP: U.S.A.

**AFFILIATION:** Division of Biomedical and Translational Sciences

Sanford School of Medicine University of South Dakota

414 E Clark St., Lee Medical Science Building

Vermillion, SD 57069

USA

Phone: 605 658-6345 Fax: 605 677-6381

E-mail: xuejun.wang@usd.edu

https://www.usd.edu/research-and-faculty/faculty-and-staff/xuejun-wang

RANK AND/OR TITLE: Tenured Full Professor of Basic Biomedical Sciences

Director, the MD/PhD Program

Complete List of Published Work in My Bibliography:

https://www.ncbi.nlm.nih.gov/myncbi/xuejun.wang.1/bibliography/public/

**ORCID**: https://orcid.org/0000-0001-9267-1343

Google Scholar: https://scholar.google.ca/citations?user=ipQguqMAAAAJ&hl=en

### **EDUCATION**

September 1980 to July 1985

Wuhan University College of Medicine, Wuhan, Hubei, China Bachelor of Medicine in Clinical Medicine (M.D. equivalent)

September 1985 to July 1988

Wuhan University College of Medicine, Wuhan, Hubei, China M.S. in Pathophysiology (Advisor: Chuanren Dong, M.D.)

Thesis Title: Hastened Plasma Coagulation and Thrombosis Contribute to The Induction of

Myocardial Infarction/Necrosis by Isoproterenol in Rats.

January 1996 to August 1998

University of South Dakota College of Medicine, Vermillion, South Dakota, USA Ph.D. in Anatomy and Structural Biology (Advisor: A. Martin Gerdes, Ph.D.)

Dissertation Title: Cardiomyocyte Remodeling in Chronic Pressure Overload Cardiac

Hypertrophy and Heart Failure in Guinea Pigs.

### **POSTDOCTORAL TRAINING**

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September 1998 to September 2001

Postdoctoral Fellow

Advisor: Jeffrey Robbins, Ph.D.

Division of Molecular Cardiovascular Biology

Cincinnati Children's Hospital Medical Center

Cincinnati, Ohio

American Heart Association (AHA) Postdoctoral Fellowship project title: Dissecting Desmin-

related Cardiomyopathy with Mouse Transgenesis.

### ACADEMIC/ADMINISTRATIVE APPOINTMENTS

September 2006 – present

Professor and Director

The MD/PhD Program

Sanford School of Medicine

University of South Dakota

Vermillion, SD

September 2010 - July 2016

Director

The Interim PQCD Research Center

USD Sanford School of Medicine

Vermillion, SD

June 2006

Tenure granted by University of South Dakota

June 2005 – August 2006

Associate Professor (Tenure Track/Tenured)

Cardiovascular Research Institute,

Sanford School of Medicine of the University of South Dakota

Sioux Falls, SD

October 2001 – May 2005

Assistant Professor (Tenure Track)

Cardiovascular Research Institute

University of South Dakota School of Medicine

Sioux Falls, SD

September 1998 – September 2001

Research Fellow

Division of Molecular Cardiovascular Biology

Cincinnati Children's Hospital Medical Center

Cincinnati, Ohio

January 1996 – August 1998

Graduate Assistant

Department of Anatomy and Structural Biology

University of South Dakota School of Medicine

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Vermillion, SD

### November 1994 – December 1995

Research Associate Department of Anatomy and Structural Biology University of South Dakota School of Medicine Vermillion, SD

### July 1993 – October 1994

Associate Professor
Department of Pathophysiology
Wuhan University College of Medicine
Wuhan, Hubei, China

### July 1988 – June 1993

Instructor
Department of Pathophysiology
Wuhan University College of Medicine
Wuhan, Hubei, China

### September 1985 – June 1988

Graduate Teaching and Research Assistant Department of Pathophysiology Wuhan University College of Medicine Wuhan, Hubei, China

### **SPECIAL HONORS OR RECOGNITIONS**

1988	Best Original Research Article Award Society of Pathophysiology of Hubei Province, P.R. China
1988	Best Original Research Articles in Natural Sciences (3 <sup>rd</sup> prize) The Science & Technology Association of Hubei Province, P. R. China
1990	Best Original Research Articles in Natural Sciences (2 <sup>nd</sup> prize) The Science and Technology Association of Hubei Province, P. R. China
1991	Best Original Scientific Research Articles (2 <sup>nd</sup> prize) The Science and Technology Association of Wuhan, P.R. China
1993	The Medical Sciences and Technology Advancement Awards (2 <sup>nd</sup> prize) The Department of Health, Hubei Province, China
1995	Best Original Scientific Research Articles (3 <sup>rd</sup> prize) The Science and Technology Association of Wuhan, the Commission of Science and Technology of Wuhan, and the Department of Personnel of Wuhan, China
1995	The Sciences and Technology Advancement Awards (3 <sup>rd</sup> prize)

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	The Government of Hubei Province, China
2000	Postdoctoral Fellowship American Heart Association (AHA) Ohio Valley Affiliate
2000	Young Investigator Award Heart Failure Society of America (HFSA)
2001	Young Investigator Award International Society for Heart Research-North American Section (ISHR-NAS)
2002	Best Abstract Award Finalist ISHR-North American Section Annual Meeting
2002	Scientist Development Award American Heart Association (AHA) National Center
2003	Distinguished Performance Award Vice President for Health Affairs and Office of the Dean, USD School of Medicine
2005	The Protein Folding Scientific Advisory Committee Poster Award "Inaugural Annual Symposium of Protein Folding Disorders" Cambridge Healthtech Institute
2007	AHA Established Investigator Award American Heart Association National Center
2008	President Award for Excellence in Research of the Established Faculty University of South Dakota
2010	Fellow AHA Council on Basic Cardiovascular Sciences
2011	Fellow American Physiological Society: Cardiovascular Section
2012	Distinguished Service Award The Academy of Cardiovascular Research Excellence (ACRE)
2019	Fellow (FISHR) International Society of Heart Research (ISHR)
2020	Professor of the Game University of South Dakota Academic Affairs (Designated at USD Men's basketball game vs. Purdue Fort Wayne, 1/23/2020)
2021	The 2021 USD Sanford School of Medicine Class 1958 Basic Biomedical Sciences Award The Sanford School of Medicine Alumni Relations Council

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(This award was established in 2008 in honor of Dr. W.O. Read, Professor of Physiology. This award recognizes a faculty member in the Division of Basic Biomedical Sciences who has shown excellence in teaching, research and service.)

The Carl J. Wiggers Award (award letter received).

The American Physiological Society (APS)

(This award is presented to a scientist who has made outstanding contributions to cardiovascular research throughout their career, has been an active and committed member of the APS CV section, and who will attract outstanding new members to the

Cardiovascular Section from the US and abroad.)

### **MEMBERSHIPS AND OFFICES IN PROFESSIONAL SOCIETIES**

Membership 2000-	American Heart Association (AHA)
2000-	International Society for Heart Research (ISHR): North American Section
2003-	Academy of Cardiovascular Research Excellence (ACRE), lifetime member
2005-	American Physiological Society (APS)
2018-	Chinese American Heart Association (CNAHA), lifetime member
<b>Offices</b> 2008-2010	Board Director, ACRE
2010	Chair, Nomination/Election Committee, ACRE
2010-2014	Research Committee of AHA Midwest Affiliate
2010-2014	The Committee for Melvin L. Marcus Young Investigator Award in Cardiovascular Sciences
2014	The Committee for the Junior Young Investigator Award, ISHR-North American Section
2013-2015	Nominating Committee of APS Cardiovascular Section
2013-present	Scientific Advisory Board of the International Academy of Cardiology
2016-2022	Awards Committee, APS Cardiovascular Section
2019-2022	Chair, Awards Committee, APS Cardiovascular Section
2019-2022	Steering Committee, APS Cardiovascular Section
2020-2021	President-elect, Midlands Society of Physiological Sciences (a chapter of APS)

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2021-2022	President, Midlands Society of Physiological Sciences (a chapter of APS) <a href="https://msps-online.org/previous-years/">https://msps-online.org/previous-years/</a>
2022-2025	Fellowship Committee, APS Cardiovascular Section
2021-2022	President-elect, Academy of Cardiovascular Research Excellence (ACRE). http://my-acre.org/
2023-2024	President, Academy of Cardiovascular Research Excellence (ACRE). <a href="http://my-acre.org/">http://my-acre.org/</a>
2025-2026	Immediate Past President/Chair of the Long-rang Planning Committee, ACRE, <a href="https://my-acre.org/about/board-of-directors">https://my-acre.org/about/board-of-directors</a>

### **CONSULTING POSITIONS**

#### A. PEER REVIER

Acta Pharmaceutica Sinica B

American Journal of Cardiology

American Journal of Pathology

American Journal of Physiology: Cellular Physiology

American Journal of Physiology: Heart and Circulatory Physiology

Antioxidants & Redox Signaling

Archives of Biochemistry and Biophysics

Autophagy

BBA-Gene Regulatory Mechanisms

BBA-Molecular Basis of Disease

BBA-Molecular Cell Research

**BBRC** 

BioMed Central-Cardiovascular Disorders

Biomolecules

Brain Research Bulletin

Cardiovascular Research

Cardiovascular Toxicology

Cell Physiology & Biochemistry

Cell Motility and Cytoskeleton

Cells

Circulation

Circulation Research

Circulation: Heart Failure

Clinica Chemica Acta

Comprehensive Physiology

Coronary Artery Disease

Current Molecular Medicine

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Developmental Biology

**EBiomedicine** 

eLife

EMBO Molecular Medicine

European Journal of Heart Failure

European Pharmacology Research

Experimental Cell Research

Free Radical Biology and Medicine

Frontiers in Cell and Developmental Biology

Frontiers in Physiology

Frontiers in Public Health

Growth Hormone and IGF Research

**Human Molecular Genetics** 

Hypertension

International Journal of Medicine

International Journal of Molecular Medicine

International Journal of Molecular Science

International Journal of Obesity

International Journal of Nanomedicine

Journal of American College of Cardiology

Journal of American Heart Association

Journal of Cardiac Failure

Journal of Cardiovascular Pharmacology

Journal of Cell Physiology

Journal of Cell Science

Journal of Cellular and Molecular Medicine

Journal of Clinical Investigation

JCI-Insight

Journal of Investigative Medicine

Journal of Molecular and Cellular Cardiology

Journal of Molecular and Cellular Biology

Journal of Physiology

Journal of Translational Medicine

Journal of Vascular Research

Journal of Visualized Experiments

Medical Hypotheses

Metabolism

Molecular Cellular Biochemistry

Molecular and Cellular Biology

Molecular Medicine

Molecular Therapy Nucleic Acids

**Nature Communication** 

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Nature Review of Cardiology

Pharmacology Research

Physiology Reports

PLoS Genetics

PLoS One

**PNAS** 

Protein and Cell

Redox Biology

Scientific Reports

Trends in Cardiovascular Medicine

Trends in Molecular Medicine

# B. EDITORIAL BOARDS

2009-2010	Guest Editor for a Spotlight Issue on "The Ubiquitin-Proteasome Pathway in Cardiovascular Disease" for Cardiovascular Research
2011-7/2023	Associate Editor-in-Chief, American Journal of Cardiovascular Disease
8/2023-present	Editor-in-Chief, American Journal of Cardiovascular Disease
2012-present	American Journal of Physiology- Heart & Circulatory Physiology
2012-present	Review Editor, Frontiers in Clinical and Translational Physiology
2013-2019	Review Editor, Frontiers in Physiology-Striated Muscle Physiology
2013-2017	Circulation Research
2019 – present	Associate Editor, Frontiers in Striated Muscle Physiology
2020 – present	Journal of Molecular and Cellular Cardiology
2020 – 2025	Associate Editor, Frontiers in Ageing - Aging, Metabolism and Redox Biology
2020 - 2021	Co-Guest Editor for <i>Cells</i> Special Issue on "Molecular Mechanisms Underlying Cardiac Dysfunction" <a href="https://www.mdpi.com/journal/cells/special_issues/cardiac_dysfunction_mechanisms">https://www.mdpi.com/journal/cells/special_issues/cardiac_dysfunction_mechanisms</a>
2020 - present	Engineering
2022 - 2024	Co-Topic Editor for Research Topic on "Proteostasis in Cardiac Health and Disease" sponsored by <i>Frontiers in Molecular Biosciences</i> and <i>Frontiers in</i>

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Cellular and Developmental Biology (https://www.frontiersin.org/research-

topics/31026/proteostasis-in-cardiac-health-and-disease)

2024-present *Circulation Research* 

2025-present Journal of Cardiac Aging

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C	NATIONAL	/INTERNATIONAL	COMMITTERS

2003-2020 International Expert Panel

Singapore National Medical Research Council

2005-2007 External Expert Grant Reviewer

Philip Morris External Research Program

National Institutes of Health

National Heart, Lung & Blood Institute; Ad hoc Reviewer for PPG

2007-2009 American Heart Association (AHA) National Center

Cardiac Biology/Regulation Study Section II; Chartered Member

2009 AHA National Center

Cardiac Biology/Regulation Study Section 2; Chairman

2007-2015 China National Natural Science Foundation

Key Research Projects; Oversea Expert Reviewer

2008-2009 National Institutes of Health

Cardiac Contractility & Heart Failure Study Section; Ad hoc Member

2009-2013 National Institutes of Health

Cardiac Contractility & Heart Failure Study Section; Chartered Member

2009-present Abstract Review

AHA Annual Scientific Sessions

2012-2015 AHA National Center

Cardiac Biol. & Regulation – Basic Science Study Section; chartered member

2014-present Abstract Reviewer

AHA Basic Cardiovascular Sciences Annual Scientific Session

2014 International Society for Heart Research North American Section

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	Junior Young Investigator Award; Judge
2015 -present	Grant Reviewer Israel Science Foundation, Israel
2015	Grant Reviewer Fondazione Cariparo, Italy
2015	NIH Special Emphasis Panel Cardiovascular and Respiratory Sciences Member Conflict Applications (ZRG1 CVRS-B 02)
2015	NIH Special Emphasis Panel Cardiovascular and Respiratory Sciences Member Conflict Applications (ZRG1 CVRS-E (02) M)
2015	The Ministry of Science and Technology, China The State Science and Technology Awards of China; Oversea Reviewer
2015	The Ministry of Education, China. The Chang-Jiang Scholar Program; Oversea Reviewer
2015	International Society for Heart Research-North American Section (ISHR-NAS) 2015 Annual Meeting (Seattle, WA) Poster Awards; Judge
2016	NIH National Heart Lung and Blood Institute (NIH/NHLBI) Program Project Grant Peer Review Panel (2016/05 HLBP 1); Ad hoc Reviewer
2017	NIH National Heart Lung and Blood Institute (NIH/NHLBI) Program Project Review Committee (HLBP 1 Workgroup 005, 2017/05 HLBP1); Ad hoc Reviewer
2017 - 2018	AHA National Center Cardiac Biol. & Regulation – Basic Science Study Section; chartered member
2018	NIH Center for Scientific Review ZRG1 F05-U (20) Fellowships: Cell Biology, Developmental Biology, and Bioengineering
2018 -	UK Medical Research Council, Ad Hoc Reviewer
2018	The Netherlands Organization for Scientific Research (NWO/ZonMw), Ad Hoc Reviewer

C	
2020 - 2022	AHA National Center Career Development Awards Cardiac Basic Sciences 2 committee, chartered member
2020	National Institutes of Health Myocardial Ischemia and Metabolism (MIM) Study Section; <i>Ad hoc</i> Member (2020 June meetings)
2020	National Institutes of Health Special Emphasis Panel for the dissolving MIM: ZRG1 MIM-R 01 (meeting date October 29-30, 2020)
2020-2022	International Expert Panel Singapore National Medical Research Council
2020	Judge Panel, Young Investigator Awards Great Wall International Congress of Cardiology 2020 (GW-ICC 2020 virtual)/Asian Heart Society Congress 2020, October 18, 2020
2021	National Institutes of Health Special Emphasis Panel, Fellowship: Cell Biology, Developmental Biology, and Bioengineering (F05-U) (meeting date Feb 18-19, 2021)
2022	National Institutes of Health Myocardial Physiology/Pathophysiology A – MPPA, February 22-23, June 22- 23, and November 7-8, 2022.
2023	National Institutes of Health Myocardial Physiology/Pathophysiology A – MPPA, February 22-23, June 21- 22, 2023
2022-	AHA National Center Established Investigator Awards (EIA) Peer Review Committee, chartered member
2022-	Invited external reviewer for University of Nebraska system internal grants.
2023-2024	Member of the Open Fund – Young Individual Research Grant (OF-YIRG) Review Panel (RP), National Medical Research Council, Singapore
2024	National Institutes of Health Myocardial Physiology/Pathophysiology A – MPPA, Feb 28-29, July 9-10, Oct 30-31, 2024

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2024	National Institutes of Health National Institute of General Medical Sciences Predoctoral T32 SEP, ZGM1 TWD-M (MS), June 6-7, 2024
2024	China Xplorer Prize application reviewer, May 10-June 15, 2024
2024	National Institutes of Health National Heart, Lung and Blood Institute R35 Outstanding Investigator Awards (OIA) Review Panel 2024/10 ZHL1- CSR-I (01), July 24-25, 2024
2025	National Institutes of Health Myocardial Physiology/Pathophysiology A – MPPA, Feb 26-27 (April 2-3), June 25-26, and Oct 29-30 (invitation accepted), 2025.
2025	China Xplorer Prize application reviewer, May 20-June 9, 2025
2025	United Kingdom Research and Innovation (UKRI) grant review (Sept. – Oct.)

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# **COMMITTEE ASSIGNMENTS**

XJ Wang

University of South Dakota (USD) Sanford School of Medicine		
2001-2003	Coordinator, Cardiovascular Research Institute Seminar and Journal Club Series	
2002-2004	Coordinator for Graduate Studies, Cardiovascular Research Institute	
2002-2004	Director, Molecular Biology Core of Cardiovascular Research Institute	
2002-2005	Internal Advisory Committee for the Cardiovascular COBRE	
2003-2009	Research Committee of School of Medicine	
2005-2007	Chair, Research Committee of School of Medicine	
2004-2007	Graduate Committee of USD School of Medicine	
2005-2007	University Senate	
2005-2006	Conference of the Senate	
2005	The Task Force of the USD Senate on USD Conflict of Interest Policy Draft	
2005-2008	Medical Student Research Committee	
2006	The Task Force for the Creation of Medical Student Scholarship Pathway	
2006-2016	Chair, the MD/PhD Admissions Committee	
2016-present	The MD/PhD Admissions Standing Committee, permanent voting member	
2007	Pre-Tenure Review Committee for Dr. Yifan Li	
2007	Pre-Tenure Review Committee for Dr. Alexander Erkine	

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2007	Chair, the Taskforce to Establishing a Graduate Course on Grant and Scientific
	Writing, for Basic Biomedical Sciences Graduate Program
2007	Convener, the Molecular Pathogenesis group SWOT (strength, weakness,
	opportunities, and threat) Analysis for Division of Basic Biomedical Sciences
	Research Retreat 2007.
2007-2014	Research Council of the Division of Basic Biomedical Sciences
2007-2008	Chair, the Search Committee for a tenure-track faculty position in Protein Quality
	Control (PQC) of the Division of Basic Biomedical Sciences
2008-2009	The Search Committee for a tenure-track faculty position in Protein Quality Control
	(PQC) of the Division of Basic Biomedical Sciences
2008	USD Committee investigating alleged research misconduct of a faculty member
2009-2018	Sanford School of Medicine P&T Committee
2009-2014	Chair, Monthly PQC Roundtable Meeting
2009-2010	LCME Task Force Sub-Committee
2010-2011	Chair, the Organizing Committee for the Inaugural Symposium on Ubiquitin,
	Protein Quality Control and Molecular Pathogenesis, Vermillion, SD, June 22-24,
	2011.
2010-2011	The Search Committee for a tenure-track faculty position in Protein Quality Control
	and Degradation (PQCD)
2010-2016	Director, the Interim Center for PQCD Research
2009-2016	Chair, the Finance/Budget Committee for PQCD Research & Development
2011-2012	Task Force for Medical Curriculum Reform (Skin & Musculoskeletal Block)
2011	The Search Committee for VP of Health Affairs/Dean of Sanford School of
	Medicine
2011	Pre-tenure Review Committee of Dr. Victor Huber
2012	Chair, The Organizing Committee for the Second Symposium on Ubiquitin, Protein
	Quality Control and Molecular Pathogenesis, Deadwood, SD, June 13-15, 2012
2012	Pre-tenure Review Committee of Dr. Hongmin Wang
2013	The Primary Committee for Dr. Carlos Telleria's Promotion to Full Professor
2013	Pre-tenure Review Committee of Dr. Khosrow Rezvani
2013	The Search Committee for two tenure-track faculty positions in the Department of
	Biomedical Engineering

XJ Wang	CV Page 14 of 76 9/27/2025
2014	Chair, The Organizing Committee for the Third Symposium on Ubiquitin, Protein
	Quality Control and Molecular Pathogenesis, Deadwood, SD, June 4-6, 2014
2014-2019	Grant Applications Pre-submission Internal Review Committee of Division of Basic
	Biomedical Sciences
2014	Pre-tenure Review Committee of Dr. James S. P.
2016-6/2022	Graduate Committee of USD Sanford School of Medicine, standing member.
7/2023-present	Graduate Committee of USD Sanford School of Medicine, Advisory member.
2018	Member of The Search Committee for a tenure-track Assistant or Associate
	Professor in infectious disease for the Division of Basic Biomedical Sciences
2018	Member of The Primary Committee for Dr. S. N. Sathyanesan's Promotion to Full
	Professor
2019	Member of The Search Committee for a tenure-track Assistant Professor for the
	Division of Basic Biomedical Sciences
2019	Chair, The Primary Committee for Dr. H. Wang's Promotion to Full Professor.
2021-2023	P&T Committee, Sanford School of Medicine, USD.
2023-present	University Graduate Council, USD
2023-present 2024-2025 2024-2025	Advisory Member, Basic Biomedical Sciences Graduate Program Chair, pre-tenure review committee for Dr. William Chen USD Sanford School of Medicine reaccreditation taskforce

COMMUNITY SERVICE				
2002-2006	Judge, Sioux Valley Hospital & Health System Annual Quality Fair			
2003	Volunteer Speaker, AHA Sioux Falls Regional Gala			
2006 - 2017	Faculty Advisor, USD Association of Chinese Students and Scholars			
2015- 2020	Food Server, USD Lee Medical Building Annual Welcome Table Christmas Dinner			

# **TEACHING AND ADVISING**

### A. COURSES TAUGHT

1.	ANAT 511	Gross Anatomy	USD School of Medicine and Health Sciences
2.	<b>ANAT 521</b>	Microanatomy	USD School of Medicine and Health Sciences
3.	<b>BIOCHEM</b>	Medical Biochemistry	USD Sanford School of Medicine
4.	PHPH 792	Genetic Approaches	USD Graduate School (Course Director)
5.	CPHD 740	Protein Quality Control	USD Graduate School (Course Director)
6.	BIOC 798	<b>Heat Shock Proteins</b>	USD Graduate School
7.	PHPH 728	Signal Transduction	USD Graduate School
8.	<b>CPHD</b> 788	Res Basic Biomed Sci	USD Graduate School

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9. CPHD 898	Thesis Research	USD Graduate School
10. CPHD 620	Foundations of Cardiovasc.	Sci. USD Graduate School (Course Director)
11. CPHD 792	Heat Shock Proteins and Di	s. USD Graduate School
12. IMC 601	Skin and Musculoskeletal B	lock USD Sanford School of Medicine
13. IMC 605	Cardiovascular Block	USD Sanford School of Medicine
14. CPHD 792	PQCD Journal Club	USD Graduate School (Course Director)
15. PHGY 792	Physiology Journal Club	USD Graduate School (Course Director)

# B. GRADUATE STUDENTS MENTORING

# 1. Served as the Primary Mentor

Graduate student	Degree obtained Dates		Current positions	
names	(pursued)			
Wei Huang (visiting	Ph.D.	10/2001 -	Professor of Medicine,	
student)		10/2002	Nanjing Medical	
			University, Nanjing,	
			Jiangsu, China	
Assangi R. K.	Ph.D.	9/2002 -	Associate Professor,	
Kumarapeli		8/2006	Department of Pathology,	
			University of Arkansas for	
			Medical Sciences, Little	
			Rock, AR	
Mingxin Tang	M.S.	7/2003 —	Research Scientist	
		8/2006	University of Hawaii,	
			Honolulu, HI, PA	
Jie Li	Ph.D.	9/2003 -	Assistant Professor,	
		12/2008	Medical College of Georgia	
			Augusta University,	
			Augusta, GA, USA	
Qingwen Zheng	Ph.D.	9/2005 —	Physician, Kaiser	
		12/2010	Permanente Roseville	
			Medical Center	
			Roseville, California	
Mark J. Ranek, BS	Ph.D.	9/2006 —	Assistant Professor, Johns	
		5/2012	Hopkins University	
Lei Zhang, MS	Ph.D.	8/2015 —	Postdoc at Medical	
	(co-mentor)	8/2016	University of South	
			Carolina, Charleston, SC	
Hanming Zhang, BS	(PhD)	8/2013 —	Postdoc at Yale University,	
		5/2019	New Haven, Connecticut	
Penglong Wu, BM, MS	Visiting PhD	6/22/2015 —	Postdoctoral fellow,	
	Student from	6/21/2017	Guangzhou Medical	
	Shanghai Jiao		University and USD	
	Tong University		Sanford School of	
			Medicine.	
Chao Suo, DDS	(PhD)	8/2015 —	Taking a 2-year leave of	
		5/2017	absence for a Dentistry	

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			T
			Licensure training program
			in University of Las Vegas,
			Las Vegas, NV.
Megan T. Lewno, BA	M.S.	8/22/2019-	PreClinical Applications
		12/21/2021	Specialist, Scintica Inc.
			Webster, TX
Liuqing Yang, BS, MS	PhD	8/22/2017 —	Postdoctoral fellow,
		8/21/2023	University of Rochester,
			Rochester, NY
Samiksha Giri, BA	PhD	8/22/2017-	Postdoctoral fellow, USD
		8/21/2023	
Mingqi Cai, MBBS	Visiting Graduate	1/22/2020 -	USD PhD student
	Student	1/21/2021	
Mingqi Cai, MBBS, MS	(PhD)	1/06/2021 -	
MdSalim Ahammed, MS	(PhD)	1/06/2021-	
MdGiash Uddin, MS	(PhD)	8/24/2022-	
Ayisha Mahama, MS	(PhD)	8/24/2022-	Transferred to a different
	·	5/21/2024	lab at USD
Jingyi Lin, BS	(PhD)	8/20/2023-	
Yifan Wang, BS	(PhD)	8/27/2024-	

# 2. Served as a Member of the Graduate Study Advisory Committees

2001-2003	James Kuzman, PhD Advisory Committee, BBS
2005-2006	Leah Callahan, MS thesis committee, BBS
2008-2010	Lili Guo, PhD Advisory/Dissertation Committee, BBS
2010-2011	Rui Du, PhD Advisory Committee, BBS
2010-2014	Shuai Li, PhD Advisory/Dissertation Committee, BBS
2013-2016	Lei Zhang, PhD Advisory /Dissertation Committee, BBS
2013-2017	Xianhua Meng, MS/PhD Thesis and Dissertation Committees, Dept. of
	Chemistry, USD
2015-2018	Hongbo Gao, PhD Advisory/Dissertation Committee, BBS
2020-2024	Katherine Aby, PhD Advisory/Dissertation Committee, BBS
2024-	Jin (Jason) Zhang, PhD Advisory/Dissertation Committee, BBS/BaTS
2025-	Sahas Pokharel, PhD Advisory/Dissertation Committee, BBS/BaTS

### C. NON-CLASSROOM TEACHING/ADVISING

# 1. List of Junior Faculty Mentored

2008-2012 H. Su, PhD, Research Assistant Professor; currently R01-funded tenured Associate Professor at Medical College of Georgia of Augusta University, Augusta, Georgia

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- 2009-2015 H. Wang, PhD, Assistant Professor; currently R01-funded tenured Associate Professor at University fo South Dakota Sanford School of Medicine, Vermillion, SD 57069
- 2011-2016 K. Rezvani, PhD, Assistant Professor; currently Tenured Associate Professor at USD Sanford School of Medicine, Vermillion, SD
- 2011-2016 J.S. Pattison, PhD, Assistant Professor
- 2013 -2015 C. Wang, MD, PhD, Research Assistant Professor; currently Professor and Chairman of the Dept. of Pathophysiology, Wuhan University Medical School, Wuhan, Hubei, China
- 2017- 2019 Nirmal Parajuli, PhD, Research Assistant Professor, currently Senior Research Associate at the Immunology Research Program, Henry Ford Health System, Detroit, MI.
- 2019 2022 Xing Liu, PhD, Assistant Professor, Department of Biochemistry, Purdue University, West Lafayette, IN, (secondary mentor for AHA CDA grant, funded on July 1<sup>st</sup>, 2020)
- William Chen, MD, PhD, Assistant Professor, Division of Basic Biomedical Sciences, USD Sanford School of Medicine. Primary mentor, including for his AHA CDA (funded in 2022).
- 2023- Jingrui Chen, PhD, Instructor, Department of Pharmaceutical Sciences, Washington State University College of Pharmacy, Spokane, WA (Secondary mentor for AHA CDA grant, funded).

### 2. List of Postdoctoral Trainees

Name of trainees Training		Current position	
	period		
Quanhai Chen, MD	1/2003 -	Senior Scientist, GlaxoSmithKline, Heart	
	11/2005	Failure (Development Performance Unit),	
		King of Prussia, PA, USA	
Hanqiao Zheng, MD, PhD	8/2003 -	Pathologist, UMass Memorial Medical	
	5/2008	Center, Assistant Professor, UMass Medical	
		School, Worcester, MA, USA	
Jinbao Liu, MD, PhD	11/2003 -	- Professor and Vice President for Research,	
10/2005		Guangzhou Medical University, Guangzhou,	
		Guangdong, China	
Huabo Su, PhD	11/2004 -	Professor (tenured), Vascular Biology	
	6/2008	Center and Department of Pharmacology,	

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	7/2008 —	Medical College of Georgia Augusta
	7/2012	University, Augusta, GA, USA
Daoxiong Lei, MD, PhD	11/2005-	Professor, Tianjin 4 <sup>th</sup> Hospital, Tianjin,
	10/2008	China
Youn-Chul Ryu, PhD	9/2006 —	Professor, Division of Biotechnology, SARI,
-	4/2009	Jeju National University, Jeju 63243, Korea
Wei Huang, MD, PhD	10/2007-	Professor, Nanjing Medical University,
	10/2008	Nanjing, Jiangsu, China
Jie Li, MD, phD	1/2009 —	Assistant Professor, Medical College of
	7/21/2012	Georgia Augusta University, Augusta, GA,
		USA
Zongwen Tian, MD, PhD	8/2009 —	Associate Professor & Chair, Dept. of
	8/21/2012	Anatomy, Wuhan University Medical
		School, Wuhan, Hubei, China
Changhua Wang, MD, PhD	10/2010-	Professor & Chair, Dept. of
	10/2011	Pathophysiology, Wuhan University
		Medical School, Wuhan, Hubei, China
Mark J. Ranek, PhD	6/1/2012-	Assistant Professor at Johns Hopkins
	11/21/2012	University, Baltimore, MD
Hongxin Xu, MD, PhD	11/1/2012-	Associate Professor and Cardiologist,
	11/21/2013	Renming Hospital, Wuhan University
		School of Medicine, Wuhan, Hubei, China
Chengjun Hu, MD, PhD	3/22/2012 —	Associate Professor & Vice-Chair, Dept. of
	3/31/2014	Anatomy, Wuhan University College of
		Basic Biomedical Sciences, Wuhan, Hubei,
		China
Yihao Tian, MD, PhD	3/22/2012 —	Associate Professor, Dept. of Anatomy,
	3/31/2014	Wuhan University College of Basic
		Biomedical Sciences, Wuhan, Hubei, China
Erin J. Terpstra, PhD	2/1/2012 –	Medical Student, USD SSOM
	6/30/2015	
Bo Pan, PhD	12/22/2014 –	Senior Scientist, Zymeron Corporation,
	6/21/2019	Research Triangle Park, NC, USA
Peng Xiao, PhD	1/22/2015 —	Postdoctoral Fellow, The Wistar Institute,
	9/21/2018	Philadelphia, PA 19104
Ammara Abdullah, PhD	6/22/2015 —	Research Scientist II, ONC ODD/Oncology
	6/21/2017	NIBR, Novartis Pharmaceuticals, 3000 Kent
D 1 W 10 N 5	0/0/0015	Ave. Ste. #1950, West Lafayette, IN 47906
Penglong Wu, MD, PhD	8/3/2017-	Physician Scientist, The Cardiovascular
	6/21/2020	Institute of Xiamen University, Xiamen,
W 1 I D 1 7 7	1/0/0001	Fujian, China
Mark J. Bouska, PhD	1/3/2021 –	Assistant Professor, Dept of Biology, USD
G : D' M'S	8/9/2024	A D . C CD! 1
Saima Ejaz, PhD	11/27/2022-	Assistant Professor of Physiology,
	3/21/2025	Dept of Basic Biomedical Sciences
A C : i: M	7/17/2022	University of Pikeville, Pikeville, KY 41501
Ana Cristina Mosena	7/17/2023-	(resigned due to family relocation)
Tomoson, PhD	12/28/2023	

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Samiksha Giri, PhD	8/22/2023-	
Neha Dagar, PhD	3/22/2025-	

# 3. <u>List of Visiting Scientists</u>

Name & Degrees	Training	Parent Institution	
	period		
Changhua Wang, MD,	1/2014 ~	Professor & Chair, Dept. of Pathophysiology,	
PhD	8/21/2015	Wuhan University College of Basic Medical	
		Sciences, Wuhan, Hubei, China	
Maggie Gong, MD, PhD	2/2014 ~	Professor, Harbin Medical University, Harbin,	
	1/21/2015	Heilongjiang, China	
Feng Yao, MD, PhD	4/2009-	Professor & Chair, Dept. of Breast Surgery,	
	11/2009	Wuhan University Medical College, Wuhan,	
		Hubei, China	

# 4. Medical Students and Medical Resident Research

2002	Matt Mahowald, USD medical student of Class 2005, summer research
2002	Louis W. Lim, MD, Internal Medicine Chief Resident, research rotation
2004	Paul King, USD medical student of Class 2007, summer research
2005	Weitian Liu, MD, Inetrnal Medicine Resident, research rotation
2007	Marius Vulcan, USD medical student of Class 2010, summer research
2011, 2012	Sigurd E. Hartnett, USD MD/PhD program student, summer research
2015	Nickolas Pekas, USD MD/PhD student, summer research
2021 - 2023	Andrew L. Guymon, USD medical student of Class 2025, scholarship pathway

# 5. Undergraduate Student Researchers

Name of	School attended	Distinction	Training period
trainees			
Mark List	Augustana	BRIN Summer	2005 & 2006 summer
	College, Sioux	Scholars	
	Falls, SD		
Mark List	Augustana	Part-time undergrad	1/2005-12/2006
	College	researcher	
Lindsey Gerdes	Augustana	COBRE Summer	2005 summer
	College,	Research Scholar	
Andy Nelson	Augustana	Undergrad Summer	2006 summer
	College	Researcher	
Heath Eggleston	Dakota Wesley	BRIN Summer Scholar	2007 summer

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Blake Alberts	USD	The Honors' Thesis	2008-2010
		Research	
Blake Alberts	USD	NIH summer research	2009 summer
		scholarship	
Morgan Hanson	USD	The Honors Thesis	2008-2010
		Research	
Levi Froke	USD	NIH Summer Research	2009 summer
		Scholarship	
Levi Froke	USD	Part-time undergrad.	2009-2011
		researcher and The	
		Honors Thesis	
		Research	
Yun Zou	USD	Part-time undergrad.	12/2009-5/2010
		researcher	
Michael Freitag	USD	Part-time undergrad.	1/2010-4/2010
		researcher	
Michael Freitag	USD	Undergrad summer	2010 summer
		researcher	
Jiwen Li	Rice University	Rice/Baylor Medical	2010 summer
		Scholar, NIH Summer	
		Research Scholarship	
Michael Freitag	USD	Undergrad summer	2011 summer
		researcher	
Levi Froke	USD	Undergrad summer	2011 summer
		researcher	
Lance M. Ranek	USD	Work study (undergrad	2012/2013 school year
		research assist)	
Lance M. Ranek	USD	Work study (undergrad	2013/2014 school year
		research assist)	
Lance M. Ranek	USD	Undergrad summer	2014 summer
		researcher	

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Casey A. Reihe	USD	Undergrad researcher	2015 Spring – 2017
			Spring
Caleb Ray Wenz	USD	Undergrad researcher	2015 Spring-2016 Spring
Andrew V.Y.	USD	Undergrad researcher	2016 Spring- 2017
Yevugah			Spring
Tanner James Redlin	USD	Undergrad researcher	2016 Fall-2017 Spring
Taylor Grace Faw	USD	Undergrad researcher	2016 Fall-2018 Summer
Kasha Merie Shear	USD	Undergrad researcher	2016 Fall-2018 Spring
Wyatt Windhorse	Mount Marty	BRIN Undergrad Scholar	2022 Summer
Katelin Stoebner	USD	Undergrad researcher	2024 fall-
Donnie Arens	USD	The honors thesis research	2024 fall-

# 6. Undergraduate Honors Thesis Advised

2008-2010	Blake Alberts, USD
2008-2010	Morgan Hanson, USD
2009-2011	Levi Froke, USD
2014-2017	Casey A. Reihe, USD
2017-2018	Taylor Grace Faw, USD
2019-2019	Mary Ann Doom, USD

# 7. Research Technicians Mentored

Research Technicians Mentored		
2002-2003	Niels Harden, currently practicing physician	
2003-2005	Joseph W. Glasford, currently Research Operation Manager of Sanford	
	Research/USD	
2004-2008	Kathleen M. Horak, currently homemaker	
2006-2008	Mingxin Tang, currently Director of Physiology Core of University of Hawaii,	
	Honolulu, Hawaii, USA	
2007-2008	Amy J. Stephenson	
2007-2008	John R. Bosch, went to Osteopathic medical school at St Paul, MN	
2008-2010	Emily McDowell, currently Research Associate in USDSSOM	
2011-2012	Travis Bjordahl, went to dental school	
2009-2014	Suleman Said, Research Associate III	
2008-2015	Andrea Jahn, 2008-11/8/2015, Research Associate III; currently Assistant to the	
	Dean of BBS.	
2016-2019	Megan T. Lewno, BS, Research Associate I and II.	
2018-	Jack O. Sternberg, BS, Research Associate I (7/2018-6/2020), II (7/2020-	
	6/2024), and III (7/2024 –).	

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2020 - 2023	Jose Lira, BS, Research Associate I (8/21/2020 – 2/2022) and II (3/2020-
	7/2023)
2021-2021	Renae Sieck, MS, Research Associate I (7/26/21 – 11/10/2021)
2022 - 2023	Addilyn Hillinger, BS, Research Associate I (6/1/2022-4/21/2023)
2023-2024	Jovani Gomez, BS, Research Associate I (8/28/2023 – 5/3/2024)

### D. DEVELOPMENT OF TEACHING STRATEGIES, ASSESSMENTS, METHODS

2004-2005	Developed and directed a graduate course "Genetic Approaches"
2007	Chair, the Working Group on establishing a graduate course on Grant and
	Scientific Writing, USD Sanford School of Medicine Division of Basic
	Biomedical Sciences (2007).
2011	Member, Medical Curriculum Innovation (Skin and musculoskeletal system section)
2012	Developed and directed a graduate course "CPHD 740: Protein Quality Control
	and Degradation (PQCD)"
2013	Chair, Taskforce to develop the curriculum for the Cardiovascular Sciences
	Specialty of the Basic Biomedical Sciences graduate program
2014	Developed and directed a graduate course "CPHD 620: Foundation of
	Cardiovascular Sciences"
2021	Revitalized PQCD and Physiology Journal Clubs.

### **PRESENTATIONS**

### **Invited Seminars/Presentations (National and International)**

- 1. "Cardiac myocyte remodeling in pressure overloaded cardiac hypertrophy and failure"; The Institute of Muscle, Arthritis, and Skin Diseases, NIH, Bethesda, MD. April, 1998.
- 2. "Cardiac myocyte remodeling in chronic pressure overload-induced cardiac hypertrophy and failure"; Gladstone Cardiovascular Institute, University of California at San Francisco, CA, May, 1998.
- 3. "The alteration of intercalated disk-associated proteins during the progression from compensated cardiac hypertrophy to congestive heart failure in pressure overloaded guinea pigs"; Department of Pharmacology in University of Minnesota, Minneapolis, MN. March, 1998.
- 4. "Intercalated disk remodeling in pressure overloaded cardiac hypertrophy and failure"; Division of Molecular Cardiovascular Biology, Children's Hospital Research Foundation, Cincinnati, OH. April, 1998.
- 5. "Cytoskeletal remodeling of cardiac myocytes in pressure overload hypertrophy and failure"; Department of Pharmacology, East Tennessee State University School of Medicine, Johnson City, TN, July, 1999.
- 6. "*In vivo* Modeling Desmin-related Cardiomyopathies with Transgenics"; the 4<sup>th</sup> Annual Scientific Meeting of Heart Failure Society of America, Boca Raton, FL, September

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10-13, 2000.

7. "Transgenic Models of Desmin-related Cardiomyopathies"; South Dakota Health Research foundation-Cardiovascular Research Institute, University of South Dakota, Sioux Falls, SD, October 16, 2000.

- 8. "Desmin filaments and heart diseases"; Department of Biomedical Sciences, Florida Atlantic University, Boca Raton, FL, May 21, 2001.
- 9. "Intermediate Filaments and Cardiac Diseases: Cause and Effects"; Division of Cardiology, University of California at Davis, Davis, CA, May 25, 2001.
- 10. "Intermediate Filaments and Cardiac Diseases: Cause and Effects"; Department of Basic Biomedical Sciences, Mercer University Medical School, Macon, GA, June 14, 2001.
- 11. "Intermediate Filaments and Cardiac Diseases: Cause and Effects"; Center of Excellence in Genomics and Bioinformatics, University of Tennessee, Memphis, TN, June 25, 2001.
- 12. "Intermediate filaments and cardiac diseases: Cause and Effects"; Midwestern University, Glendale, AZ, June 29, 2001.
- 13. "Desmin in cardiac remodeling"; A Symposium on "Remodeling and Progression of Heart Failure" (an official satellite meeting of the 17<sup>th</sup> World Congress of International Society for Heart Research), Minneapolis, MN, July 12-15, 2001.
- 14. "Desmin filaments and cardiac diseases: cause and effects"; University of South Dakota School of Medicine, Vermillion, SD, July 16, 2001.
- 15. "Intermediate filaments and cardiac diseases: cause and effects"; Department of Physiology, University of Taxes Health Science Center, San Antonio, TX, July 23, 2001.
- 16. "Ubiquitin-Proteasome System in Pathogenesis and Therapeutics"; Wuhan University College of Basic Medical Sciences, Wuhan, Hubei, China, September 20, 2002.
- 17. "Ubiquitin-Proteasome System and Cardiovascular Diseases"; South Dakota State University College of Veterinary Science, Brookings, SD, October 4, 2002.
- 18. "Intermediate filaments and cardiac disease: establish causality"; Wuhan University College of Medicine, Wuhan, Hubei, China, Oct. 29, 2002.
- 19. "Ubiquitin-Proteasome System in Pathogenesis and Therapeutics"; Guangzhou Medical College, Guangzhou, Guangdong, China, Nov. 1, 2002.
- 20. "Desmin filaments and cardiac diseases"; the VII Meeting of International Society for Heart Research: China Section, Guangzhou, China, November 1-5, 2002.
- 21. "Modulation of the ubiquitin-proteasome system by an alpha B-crystallin mutant"; The 1<sup>st</sup> Annual COBRE Symposium. Rapid city, SD, June 28-30, 2003.

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22. "In Situ Monitoring Dynamic Changes in the Ubiquitin-Proteasome System in vitro and in vivo"; The 1<sup>st</sup> Symposium of the Academy of Cardiovascular Research Excellency (ACRE), Washington, DC, April 20, 2004.

- 23. "Trashmen and police on strike in Alzheimer's disease of the heart"; The 2<sup>nd</sup> Annual COBRE Symposium. West Yellow Stone, MT, August 4-7, 2004.
- 24. "Trashmen on strike in a mouse model of cardiac Alzheimer's"; Division of Cardiology, University of Utah, Salt Lake City, UT, November 2, 2004.
- 25. "A novel transgenic mouse model reveals deregulation of the ubiquitin-proteasome system in the heart by Doxorubicin"; The 2<sup>nd</sup> ACRE annual scientific meeting, Vancouver, Canada, July 15, 2005.
- 26. "The Ubiquitin-Proteasome System in Cardiac Remodeling and Failure"; Cardiovascular Distinguished Lecture Series, University of California at Los Angeles School of Medicine, LA, CA January 31, 2006.
- 27. "Dissecting the Ubiquitin-Proteasome System in the Heart with Genetic Approaches"; Long Island Jewish Medical Center, New Hyde Park, NY, March 7, 2006.
- 28. "The Ubiquitin-Proteasome System in Cardiac Remodeling and Failure" at the Department of Molecular and Cellular Pharmacology, University of Miami, Miami, FL, March 16, 2006.
- 29. "The Ubiquitin-Proteasome System in Cardiac Physiology and Pathophysiology"; The 5<sup>th</sup> International Ascona Workshop on Cardiomyocyte Cell Biology, Monte Verita, Ascona, Switzerland, April 2-6, 2006.
- 30. "Inadequate Protein Quality Control in Heart Failure"; Division of Molecular Medicine, UCLA School of Medicine, Los Angelis, CA, April 18, 2006.
- 31. "The Ubiquitin-Proteasome System in Cardiac Remodeling and Failure"; Department of Molecular Genetics, University of Cincinnati, Cincinnati, OH May 2, 2006.
- 32. "Inadequate Protein Quality Control in Heart Failure". The Center for Translational Medicine, Jefferson Medical College, Philadelphia, PA, May 10, 2006.
- 33. "The Ubiquitin-Proteasome System in Cardiac Remodeling and Failure"; The Center of Cardiovascular Sciences, Albany Medical College, Albany, NY, May 12, 2006.
- 34. "The Ubiquitin-Proteasome System in Cardiac Remodeling and Failure"; Department of Pharmacology, Loyola University Medical Center, Maywood, IL, May 15, 2006.
- 35. "The COP9 Signalosome and Protein Quality Control", ZOMES IV: The 4<sup>th</sup> International Symposium on COP9 Signalosome, Proteasome, and eIF3: at the interface between signaling & proteolysis. New Haven, CT, June 18-21, 2006.
- 36. "The Ubiquitin-Proteasome System in Cardiac Remodeling and Failure"; University of Texas Houston Medical School, Houston, TX, May 11, 2007.

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37. "Protein quality control in cardiac remodeling and failure"; Wuhan University College of Basic Biomedical Sciences, Wuhan, China, June 4, 2007.

- 38. "The ubiquitin proteasome system in cardiac remodeling and failure"; Marie Curie Symposium on the Ubiquitin-proteasome System in Cardiovascular Disease, Hamburg, Germany, June 9, 2007.
- 39. "Ubiquitin-proteasome system dysfunction in cardiomyopathies"; Heart Failure 2007 (the annual meeting of Heart Failure Association of the European Society of Cardiology), Hamburg, Germany, June 10, 2007.
- 40. "Cardiac remodeling and protein quality control"; The 29<sup>th</sup> Meeting of the North American Section of the International Society for Heart Research (ISHR), Bologna, Italy, June 21-22, 2007.
- 41. "Proteasomal degradation"; The 4<sup>th</sup> Annual Symposium of the American Heart Association Council on Basic Cardiovascular Sciences. Keystone, CO, USA, July 30-August 2, 2007.
- 42. "The Proteasome and Cardiac Disease"; *Sunday Morning Program*, American Heart Association Scientific Sessions, Orlando, Florida, USA, November 5, 2007.
- 43. "Proteasomal degradation in cardiomyopathy"; *Cardiac Seminar*, American Heart Association Scientific Sessions, Orlando, Florida, USA, November 7, 2007.
- 44. "The ubiquitin-proteasome system for protein degradation"; *European Winter Meeting on Translational Cardiology*, organized by the Heart Failure Association (HFA) of the European Society of Cardiology (ESC), Garmisch-Partenkirchen, Germany, January 23-26, 2008.
- 45. "Proteasomes in cardiac remodeling and failure"; Late Breaking Sciences-ISHR-North America Section 2008 meeting, Cincinnati, OH, June 17-21, 2008.
- 46. "The role of the UPS in cardiac disease"; Sunday Morning Program Session on Protein Misfolding, Proteolysis, and Cardiac Disease, AHA Scientific Sessions, New Orleans, LA, November 8, 2008.
- 47. "COP9 Signalosome, Proteasome, and Lysosome"; The Graduate Seminar Series, Guangzhou Medical College, Guangzhou, Guangdong, China, December 18, 2008
- 48. "COP9 Signalosome, Proteasome, and Lysosome: All in the Same Zomes"; Wuhan University College of Basic Medical Sciences, Wuhan, Hubei, China, December 19, 2008.
- 49. "Protein Quality Control in Cardiac Remodeling and Failure"; University of British Columbia, Vancouver, BC, Canada, April 24, 2009.
- 50. "A molecular pathway underlying cardiac pathogenesis of inadequate PQC"; the Division of Basic Biomedical Sciences of Guangzhou Medical College, Guangzhou, Guangdong, China, June 19, 2009.

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51. "Proteasome, lysosome, and signalosome: all in the same ZOME"; Wuhan University College of Medicine, Wuhan, Hubei, China, June 24, 2009

- 52. "COP9 signalosome in the heart"; the Sunday Morning Program on "Protein Quality Control in Heart Disease", AHA Scientific Sessions, Orlando, FL, November 15, 2009.
- 53. "Ubiquitin-proteasome system in heart disease"; the Graduate School of Guangzhou Medical College, Guangzhou, Guangdong, China, December 17, 2009.
- 54. "The ubiquitin-proteasome system in cardiac proteinopathy"; Department of Cellular Physiology and Neurosciences, Loyola University, Maywood, IL, April 20, 2010.
- 55. "Proteasome functional insufficiency in cardiac proteinopathy"; The session on "The Role of the Ubiquitin Proteasome System in Cardiac Disease, Diabetes, and Aging" of the 2010 EB meeting, Anaheim, CA, April 24-28, 2010.
- 56. "The ubiquitin-proteasome system in cardiac proteinopathy"; The Department of Physiology of University of Oklahoma College of Medicine, Oklahoma City, OK, May 10, 2010.
- 57. "COP9 Signalosomes regulate proteolysis in the heart"; a state-of-the-art lecture given to the Symposium "Genes, Proteins, and Translational Medicine" hosted by UCLA in conjunction with the AHA BCVS 2010 meeting, Rancho Mirage, CA, July 18, 2010.
- 58. "The ubiquitin-proteasome system in cardiac remodeling and failure"; Department of Biology, San Diego State University, San Diego, CA, November 4, 2010.
- 59. "The Ubiquitin-Proteasome System in Cardiac Remodeling and Failure"; Department of Molecular and Integrative Physiology University of Illinois at Urbana-Champaign, Urbana, IL, April 28, 2011.
- 60. "Protein Quality Control and Heart Disease"; Molecular Biology and Biotechnology Seminar Series, The Center of Molecular Biology and Biotechnology and College of Medicine, Florida Atlantic University, Boca Raton, FL, November 16, 2011.
- 61. "The COP9 Signalosome Regulates Autophagy"; Sanford Research/USD, Sioux Falls, SD, November 18, 2011.
- 62. "Proteasome Functional Insufficiency in Cardiac Pathogenesis"; Lillehei Heart Institute Lecture, Lillehei Heart Institute at the University of Minnesota Medical School, Minneapolis, MN, December 7, 2011.
- 63. "Can we treat proteinopathy by upregulating 11S proteasomes?" A State-of-the-Art Lecture at the Conference on the Protein Degradation Pathways in Health and Diseases, San Diego, CA., January 23, 2012.
- 64. "The ubiquitin-proteasome system in cardiac pathogenesis"; Department of Pathology, University of Cincinnati, Cincinnati, OH, May 18, 2012.
- 65. "Proteasome functional insufficiency in cardiac pathogenesis"; Department of Cell

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- Biology and Molecular Medicine, UMDNJ New Jersey Medical School, Newark, NJ, May 23, 2012.
- 66. "The ubiquitin-proteasome system in heart disease"; Department of Biomedical Sciences, New York College of Osteopathic Medicine at New York Institute of Technology, Old Westbury, NY, May 25, 2012.
- 67. "Protein Quality Control and Disease: Focus on the COP9 Signalosome"; the Educational Ministry Key Laboratory Seminar Series, Shanghai Jiaotong University, Shanghai, China. June 20, 2012.
- 68. "Intracellular Protein Quality Control and Pathogenesis: the COP9 signalosome"; Pathophysiology Invited Seminars of Wuhan University, Wuhan, Hubei, China. June 25, 2012
- 69. "Ubiquitination and Proteasomes: Mechanism of Heart Failure"; The 2012 Scientific Session of American Heart Association Council on Basic Cardiovascular Sciences (AHA-BCVS): Frontiers in Cardiovascular Science and Novel Therapy. New Orleans, LA, July 24, 2012.
- 70. "The COP9 Signalosome Polices the Heart"; Department of Biological Sciences, University of Illinois at Chicago, Chicago, IL, September 18, 2012.
- 71. "Proteasome Dysfunction in Cardiac Pathogenesis"; the Feinberg Cardiovascular Research Institute, Northwestern University, Chicago, IL, September 19, 2012.
- 72. "Proteasome Dysfunction in Pathogenesis"; the Biochemistry and Molecular Biology Seminar at Mayo Clinic in Rochester, Minnesota, October 2, 2012
- 73. "Protein Quality Control and Pathogenesis"; *University of Wisconsin Department of Pathology and Laboratory Medicine Seminar*, Madison, Wisconsin, October 10, 2012.
- 74. "UPS regulation and dysfunction in heart failure", an invited lecture to a Session on Protein Quality Control and Homeostasis in Cardiac Physiology and Disease, AHA Scientific Sessions, Los Angelis, CA, November 4, 2012.
- 75. "Proteasome dysfunction in cardiac pathogenesis"; Keystone Symposium on Cardiac Remodeling, Signaling, Matrix and Heart Function (D4-2013), Snowbird, UT, April 9, 2013.
- 76. "Interaction of ubiquitin proteasome system and autophagy in the heart"; Cardiac Seminars on Dynamics of Protein Degradation Machinery in Cardiac Function. AHA Scientific Sessions, Dallas, TX, November 18, 2013.
- 77. "Loss of Function of an Extraproteasomal Ubiquitin Receptor Ubiquilin1 in Cardiomyocytes Exacerbates Cardiac Proteotoxicity"; The 35<sup>th</sup> International Society for Heart Research North American Section Meeting, Miami Beach, Florida, USA on May 12-15, 2014.
- 78. "Protein Quality Control and Cell Death"; Department of Anatomy and Cell Biology,

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University of South Carolina School of Medicine, Columbia, SC, USA, May 19, 2014.

- 79. "Inadequate Coupling between Ubiquitination and Proteasomal Degradation in Cardiac Pathogenesis"; Wuhan University College of Basic Medical Sciences, Wuhan, Hubei, China, June 13, 2014.
- 80. "Protein Quality Control and Disease"; the 2nd Affiliated Hospital of Zhongnan University Xiangya Medical School, Changsha, Hunan, China on June 20, 2014.
- 81. "Protein Quality Control and Degradation in Cardiac Disease"; the 2nd Affiliated Hospital of Zhejiang University Medical College, Hangzhou, Zhejiang, China, June 25, 2014.
- 82. "Protein Quality Control in Cardiac Pathogenesis"; the Institute of Molecular Medicine of Peking University, Beijing, China, July 1, 2014.
- 83. "Priming the proteasome by PKG: a novel cardioprotective mechanism of sildenafil"; The 19th World Congress on Heart Disease, Boston, MA, USA on July 28, 2014.
- 84. "Inadequate Protein Quality Control in Cardiac Pathogenesis"; the Invited Seminars at Molecular Medicine, University of Oklahoma Health Science Center, Oklahoma City, OK, August 7, 2014.
- 85. "Inadequate Protein Quality Control in Cardiac Pathogenesis"; the School of Veterinary Medicine and Biomedical Sciences, University of Nebraska, Lincoln, Nebraska, September 29, 2014
- 86. "Protein degradation and heart failure: The NRF2-p62 axis in the cross-talk between proteasomal and lysosomal degradation"; the 36<sup>th</sup> International Society for Heart Research North American Section (ISHR-NAS) Annual Meeting, Seattle, WA, June 9, 2015.
- 87. "Neddylation/Deneddylation, Protein Quantity & Quality Control, and Cardiomyocyte Necroptosis"; the Session on Protein Folding and ER Stress, AHA Scientific Sessions, Orlando, FL, November 9, 2015.
- 88. "The COP9 Coerces Lysosomes and Proteasomes to Police the Heart"; Department of Biomedical Sciences, New York Institute of Technology College of Osteopathic Medicine, Old Westbury NY, March 14, 2016.
- 89. "The Interplay between Autophagy and the Ubiquitin-Proteasome System in Cardiac Proteotoxicity"; American Society for Investigative Pathology (ASIP) 2016 Annual Meeting at Experimental Biology, San Diego, CA, April 2-6, 2016.
- 90. "Inadequate protein quality control and heart failure"; The 4<sup>th</sup> International Conference on Cardio-metabolic Science, Wuhan, Hubei, China, May 11-14, 2016.
- 91. "The COP9 signalosome in the heart"; Department of Pathophysiology at Guangzhou Medical University, Guangzhou, China, May 20, 2016

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92. "The COP9 coerces lysosomes and proteasomes to police the heart"; College of Life Science at Shanghai Ocean University, Shanghai, China, May 23, 2016

- 93. "Proteasome functional insufficiency in cardiac pathogenesis", the Division of Cardiology at the 6<sup>th</sup> People's Hospital of Shanghai, Shanghai, China, May 24, 2016
- 94. "Cardiac protein quality control and necroptosis"; Department of Pathology and Translational Pathobiology, LSU at Shreveport, Shreveport, LA, May 31, 2016.
- 95. "The COP9 Signalosome: A Posttranscriptional Cop in the Heart"; the 2016 Scientific Sessions of American Heart Association and the Council on Basic Cardiovascular Sciences, Phoenix, Arizona, July 18-21, 2016.
- 96. "Cardiac protein quality control in health and disease"; the ADVS/CIB Seminar Series of Utah State University at Logan, UT, September 22, 2016.
- 97. "Proteasome functional insufficiency in pathogenesis"; the Molecular and Cellular Pathology Seminar Series of the Graduate Program of the Department of Pathology at University of Alabama at Birmingham, Birmingham, AL, October 11, 2016.
- 98. "The State-Of-The-Art in Cardiac Protein Misfolding"; Cardiac Seminars on Misfolded Proteins of the 2016 Scientific Sessions of American Heart Association, New Orleans, Louisiana, November 15, 2016.
- 99. "Ubiquitin and ubiquitin-like proteins in the heart: an overview"; to the Symposium entitled "Ubiquitin and ubiquitin-like proteins in cardiovascular physiology and disease" of the Experimental Biology meeting, Chicago, IL, April 22-26, 2017.
- 100. "Protein Degradation in Heart Failure"; the 36th Annual Conference of the North American Section of the International Society of Heart Research (NAS-ISHR), New Orleans, LA, May 30-June 2, 2017.
- 101. "The COP9 Signalosome and the Heart", Wuhan University College of Basic Medical Sciences, Wuhan, Hubei, China, June 17, 2017.
- 102. "Proteasome and Heart Failure", Guangzhou Medical University College of Basic Medical Science and College of Pharmacy, Guangzhou, Guangdong, China, June 20, 2017.
- 103. "Proteasome Functional Insufficiency in Cardiac Pathogenesis", Invited Seminar Series of the Department of Physiology, Peking University Health Science Center, Beijing, China, July 7, 2017.
- 104. "The Pathophysiological Significance of Cardiac Proteasome Functional Insufficiency (PFI)", Department of Pharmacology, Harbin Medical University School of Pharmacy, Harbin, Heilongjiang, China, July 13, 2017.
- 105. "The Ubiquitin-Proteasome System in Cardiac Pathogenesis", The 7<sup>th</sup> Cold Region Cardiology Conference (CRCC) and the 3<sup>rd</sup> China-Russia Jointed Pharmacology Conference, Harbin, Heilongjiang, China, July 13-16, 2017.

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106. "Targeting protein quality control to treat heart disease", Department of Pharmacology and Toxicology, Medical College of Georgia, Augusta University, Augusta, GA, Jan 22 2018.

- 107. "Pathophysiology of cardiac protein quality control", The Seminar Series for Advancing Scientific Research at the No. 1 Affiliated Hospital of Guangxi University of Traditional Chinese Medicine, Nanning, Guangxi, China, August 14, 2018.
- 108. "Pathophysiology of Cardiac Protein Quality Control", Nebraska Physiological Society Annual Scientific Meeting, Omaha, NE, October 20, 2018.
- 109. "Proteinopathies and Heart Disease", the Session entitled: "Proteostasis Meets Protein Trafficking in the Heart" in the AHA Scientific Sessions 2018 to be held in Chicago IL November 12, 2018.
- 110. "Priming the Proteasome to Treat Cardiac Proteotoxicity", Invited Seminar Series of the Department of Cell and Molecular Physiology, Stritch School of Medicine, Loyola University Chicago, Maywood IL, April 18, 2019.
- 111. "Duo-activation of PKG and PKA by PDE Inhibition to Treat Heart Disease with Increased Proteotoxic Stress", Distinguished Lecturer Seminar Series of The Institute of Biosciences & Technology (IBT), the Texas A&M University College of Medicine, in Houston TX, May 6, 2019.
- 112. "Priming the proteasome to treat heart failure", Distinguished Medical Lecturer Seminar Series, Wuhan University School of Basic Medical Sciences, Wuhan, Hubei, China, May 22, 2019
- 113. "Priming the proteasome to treat heart failure", Lectures by Oversea Chinese Medical Elites Session 8, The 13th Oriental Congress of Cardiology (OCC 2019), Shanghai, China, June 2, 2019.
- 114. "Aberrant Protein Aggregation in Cardiac Muscle", a panelist for a Visual Keystone Symposium (VKS) "Intracellular Aggregates: Across the Spectrum of Health and <u>Disease</u>", July 18, 2019. (https://virtual.keystonesymposia.org/ks/live/290/page/1580
- 115. "Dual Activation of PKA and PKG by PDE1 Inhibition Facilitates Proteasomal Degradation of Misfolded Proteins and Protects against Proteinopathy-Based HFpEF", 2019 AHA BCVS Scientific Sessions –Session 1A, Boston, MA, July 29, 2019.
- 116. "Phosphoregulation of the Proteasome", an invited lecture to the Cardiovascular Seminars Session entitled "Maintaining Protein Integrity Under Stress" of 2019 AHA Scientific Sessions (November 18, 2019; Philadelphia, PA).
- 117. "Harness proteasome phosphoregulation to protect against proteotoxicity", Invited Seminar Series, Department of Surgery, The Ohio State University College of Medicine, Columbus, OH, December 10, 2019.

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118. "Interplay between the ubiquitin-proteasome system and autophagy", International Society for Heart Research (ISHR) (Quarantine) Cardiovascular Webinar Series. May 22, 2020. <a href="https://www.youtube.com/watch?v=xiys1qoCMjI&t=45s">https://www.youtube.com/watch?v=xiys1qoCMjI&t=45s</a>

- 119. "Crosswalk between proteasomal and lysosomal degradation", 14<sup>th</sup> Oriental Congress of Cardiology (OCC2020 Virtual Conference), Channel-10 Session 6 WACC/CNAHA Session: Novel Technologies and Translational Medicine in the Diagnosis and Treatment of the Cardiovascular Diseases; June 1, 2020. https://occ.1mice.net/live/play/144818.
- 120. "Priming the proteasome to protect against proteotoxicity", a Keynote Lecture to the 7<sup>th</sup> ACRE-APS Scientific Symposium (virtual), Aug. 8<sup>th</sup>, 2020.
- 121. "Activation of the proteasome by PKA protects the heart under stress", an invited lecture to BCVS@GW-ICC: Kinase Signaling and Cardiac Injury, Great Wall International Congress of Cardiology 2020 (GW-ICC 2020 virtual)/Asian Heart Society Congress 2020, October 19, 2020.
- 122. "Priming the proteasome to treat heart failure", a virtual seminar to Translational Cardiovascular Research Center at the University of Arizona College of Medicine at Phoenix, February 22, 2021.
- 123. "Priming the proteasome to ameliorate cardiac proteotoxic stress", a virtual seminar to the Department of Pathology at the University of Alabama at Birmingham, April 15, 2021.
- 124. "Priming the proteasome to protect against proteotoxic stress", a virtual seminar to the Department of Physiology at the University of Tennessee Health Sciences Center School of Medicine, June 21, 2021.
- 125. "Catecholamine surges cause cardiomyocyte necroptosis via a RIPK1-RIPK3 dependent pathway", an invited lecture to CNAHA@GW-ICC: Basic/Translational Cardiovascular Research and Novel Technologies, Great Wall International Congress of Cardiology 2020 (GW-ICC 2020 virtual)/Asian Heart Society Congress 2020, October 21, 2020.
- 126. "Priming the proteasome to protect against proteotoxic stress", Virtual Seminar Series of the Center for Diagnostics and Therapeutics, Georgia State University, May 25, 2021.
- 127. "Cardiac UCHL1 protects against post-MI remodeling", an invited lecture (virtual) to Session 1 of Chinese International Forum in the 15th Oriental Congress of Cardiology (OCC 2021): Translational Cardiovascular Research: from the bench-side to the bedside (virtual), May 29, 2021.
- 128. "Priming the proteasome to protect against proteotoxicity", an invited lecture (in person) to the 40<sup>th</sup> ISHR-NAS Scientific Conference: "*Novel Mechanisms of Heart Failure: Advancing New Therapies*". September 12-16th 2021 in Denver, Colorado.
- 129. "Priming the proteasome to treat heart failure", an invited lecture (virtual) to BCVS-ACRE@GW-ICC: Molecular Mechanisms and Intervention of Cardiac Injury/Repair,

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- Great Wall International Congress of Cardiology 2021 (GW-ICC 2021)/Asian Heart Society Congress 2021, October 28, 2021.
- 130. "The proteasome in cardiac health and disease", an invited seminar (virtual) to the Seminar Series of the McAllister Heart Institute at the University of North Carolina at Chapel Hill. November 10<sup>th</sup>, 2021.
- 131. "Priming the proteasome to protect against proteotoxicity", an invited seminar (virtual) to the Seminar Series of the Department of Pharmacology at Johns Hopkins University School of Medicine, Baltimore MD. December 1<sup>st</sup>, 2021.
- 132. "Priming the Proteasome by Augmentation of cAMP and cGMP to protect against Proteotoxicity", an invited seminar to the Department of Pharmaceutical Sciences at Washington State University College of Pharmacy and Pharmaceutical Sciences, Spokane, WA, March 30, 2022.
- 133. "The role of cardiomyocyte UCHL1 in post-MI cardiac remodeling and heart failure", an invited lecture (virtual) to the 13<sup>th</sup> Cross-Strait Cardiovascular Symposium and the 7<sup>th</sup> China Wine-City International Congress of Cardiology, Luzhou, Sichuan, China; April 22-25, 2022.
- 134. "Catecholamine surges cause cardiomyocyte necroptosis", an invited lecture (virtual) to Session 1 of Chinese International Forum in the 16th Oriental Congress of Cardiology (OCC 2022): Translational Cardiovascular Research: from the bench-side to the bedside (virtual), May 27, 2022.
- 135. "Genetic mimicry of the activation of 26S proteasomes by cAMP-dependent protein kinase protects against proteotoxicity in animals", an invited lecture (virtual) to The Inaugural Symposium on Protein Modifications: Advances in Methodologies and Applications. Sept. 29 Oct.1, 2022, Guangzhou, China.
- 136. "Assessing Autophagic Flux: Are we Using Right Methods?", an invited lecture (virtual) to AHA/ACRE@GW-ICC: Building Bridges and Working Together to Fight Cardiovascular Diseases, The 33<sup>rd</sup> Great Wall International Congress of Cardiology 2022 (GW-ICC 2021)/Asian Heart Society Congress 2022, October 30, 2022
- 137. "Defect in PKA-mediated proteasome activation is a key pathogenic factor for cardiac proteinopathy", an invited Rapid-Fire lecture to Heart Failure 2023, Prague-Czech Republic May 21, 2023.
- 138. "Phosphoregulation of the Proteasome in Proteotoxicity", an invited lecture to "Session 9: Novel Strategies to Understand Cardiotoxicity and Proteotoxicity" at the 42<sup>nd</sup> International Society for Herat Research North American Section (ISHR-NAS) annual scientific meeting, Madison, WI, June 27-30, 2023
- 139. "Activation of the proteasome by cAMP protects against cardiac proteotoxicity", an invited lecture to The 34<sup>th</sup> Great Wall International Congress of Cardiology (GW-ICC)/Asian Heart Society Congress 2023 (AHS.23), Beijing, China, September 5-9, 2023

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140. "The COP9 signalosome in cardiovascular health and disease", an invited seminar to the Department of Physiology, Peking University College of Basic Medical Sciences, Beijing, China September 11, 2023.

- 141. "Ser14-phosphorylated RPN6 mediates proteasome activation by PKA and alleviates proteinopathy", an invited seminar to Wuhan University College of Basic Medical Sciences, Wuhan, China, September 14, 2023.
- 142. "Priming the Proteasome to Protect against Proteotoxicity", an invited seminar to Department of Medical Pharmacology and Physiology, School of Medicine, University of Missouri, Columbia, MO, October 17, 2023.
- 143. "Proteasome functional insufficiency in cardiac pathogenesis", an invited virtual seminar to Yale Virtual Myocardial Biology Seminar Series. Yale University School of Medicine, November 30, 2023.
- 144. "Ser14-phosphorylated RPN6 mediates proteasome activation by PKA and alleviates proteinopathy", an invited lecture (virtual) to the 24<sup>th</sup> CAAC Saloon organized by Chinese American Academy of Cardiology (CAAC), December 4<sup>th</sup>, 2023.
- 145. "Priming the Proteasome to Protect against Proteotoxicity", an invited seminar to Center for Biotechnology & Genomic Medicine, Augusta University, Augusta, GA, March 22, 2024.
- 146. "Cardiac Pathophysiology of Proteasome Activation by PKA", an invited lecture to The 2nd Scientific Meeting of ACRE Canada, London, Ontario, Canada, July 5, 2024.
- 147. "Fatal Attraction: a novel pathway to proteotoxicity", an invited seminar to New York Institute of Technology College of Osteopathic Medicine Dept. of Biomedical Sciences Seminar Series, Long Island, NY, July 26, 2024.
- 148. "Proteostasis and Heart Failure", an invited seminar to University of Iowa François M. Abboud Cardiovascular Research Center (ACRC) Distinguished Seminar Series, Iowa City, IA, August 9<sup>th</sup>, 2024.
- 149. "Fatal Attraction: a novel pathway to proteotoxicity", an invited lecture to the symposium of "Proteotoxicity and Proteomic Remodeling in the Healthy and Failing Heart" at the ISHR-NAS 43rd Annual Conference "Advancements in Translational Biomedical Sciences: Single Cell Omics and AI in CV Medicine" on August 20th-23rd, 2024.
- 150. "Protein Quality Control and Heart Failure", an invited seminar to the Center for Cardiovascular Research (CCR) in the Department of Internal Medicine, Cardiovascular Division, at Washington University School of Medicine, St. Louis, MO, September 24-25, 2024.
- 151. "PKA-mediated proteasome activation is essential to proteostasis during cardiac hypertrophy", an invited lecture to The International Forum (virtual) of the 35<sup>th</sup> the Great Wall International Congress of Cardiology (GWICC)/Asian Heart Society Congress 2024 (AHS.24), Nov 7-9, 2024.

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152. "Aberrant protein aggregation intersects inflammation and proteostasis", an invited lecture to the International Forum (Virtual) at The 9th China Wine City International Congress of Cardiovascular Medicine (第九届中国酒城国际心血管医学学术大会国际论坛), Luzhou, Sichuan, China, December 1<sup>st</sup>, 2024.

- 153. "The Proteasome Functional Insufficiency (PFI) Theory of Heart Failure", an invited lecture to 2025 Taiwan Circulation Research Society (TCRS) Annual Meeting and the Stanford-Taiwan Symposium on Biomedical Advances, held at the Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan on March 14-15, 2025.
- 154. "Fatal Attraction: a novel mechanism for inflammation to impair proteostasis", an invited seminar to the Dept of Biomedical Engineering, UAB School of Engineering and School of Medicine, Birmingham, AL, March 20-22.
- 155. "Fatal Attraction: a novel mechanism for inflammation to impair proteostasis", an invited seminar to the College of Basic Biomedical Sciences, Wuhan University Health Science Center, Wuhan, Hubei, China May 23, 2025.
- 156. "Sustained but decoyed activation of the JAK-STAT pathway exacerbates proteotoxicity: a new mechanism intersecting inflammation and impaired proteostasis", an invited seminar to the College of Basic Biomedical Sciences, Guangzhou Medical University, Guangzhou, Guangdong, China May 26, 2025.
- 157. "Targeting decoyed JAK-STAT signaling to treat heart failure with increased proteotoxic stress", an invited lecture to the 19th Oriental Congress of Cardiology (OCC 2025) held in Shanghai, China, May 29-June 1, 2025.
- 158. "Probing cAMP/PKA signaling at Proteasome Nanodomains", an invited seminar (virtual) to the Karen M. Swindler Department of Chemical and Biological Engineering, South Dakota School of Mines & Technology, Rapid City, South Dakota. September 9, 2025.
- 159. "Autophagy and cell death in senescence", an invited lecture to the Session entitled "Molecular and Functional Insights in Cardiovascular Aging" during AHA Scientific Sessions 2025, New Orleans, LA, November 7-10, 2025 (invitation accepted).
- 160. "Priming the proteasome to treat heart disease" an invited lecture to "Frontiers in Cardiovascular Sciences" to be held in Honolulu, HI, January 2-6, 2026 (Invitation accepted).

### **Seminars Given in Employer Institutions**

- 161. "Measurement of regional myocardial blood flow with unlabeled microspheres and Coulter Channelyzer" at University of South Dakota School of Medicine, Vermillion, SD. May 8, 1996.
- 162. "Dissecting desmin-related cardiomyopathy with mouse transgenesis"; Division of Pediatric Cardiology, Children's Hospital, Cincinnati, OH, February 7, 2000.
- 163. "Ubiquitin-Proteasome System and Diseases", Division of Basic Biomedical Sciences,

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- University of South Dakota School of Medicine, Vermillion, SD, September 17, 2002.
- 164. "The COP9 Signalosome: A New Initiative from Plants to Mammalian Hearts", Faculty Seminar, Division of Basic Biomedical Sciences, University South Dakota School of Medicine, Vermillion, SD September 27, 2005.
- 165. "Protein turnover, cardiomyopathy and the young"; Pediatric Grand Rounds, Department of Pediatrics, University of South Dakota School of Medicine, Sioux falls, SD, March 17, 2005.
- 166. "Targeted proteolysis in conformational disease"; Faculty Seminar Series, Division of Basic Biomedical Sciences, USD Sanford School of Medicine, October 28, 2008.
- 167. "Protein quality control and degradation in the heart"; The Inaugural Symposium on Ubiquitin, Protein Quality Control and Molecular Pathogenesis hosted by Sanford School of Medicine of University of South Dakota, Vermillion, SD, June 22-24, 2011.
- 168. "Histopathology in the post-genomics era", Faculty Seminar Series of Division of Basic Biomedical Sciences, Sanford School of Medicine of University of South Dakota, Vermillion, SD 57069, March 16, 2012.
- 169. "Can we boost cardiac proteasomes by stimulating PKG?" The 2nd Annual PQCD Symposium, Deadwood, SD, USA. June 14, 2012.
- 170. "The Ubiquitin-Proteasome System in Cardiac Pathogenesis: Beyond the Proteasome", Faculty Seminar Series, USD Sanford School of Medicine, November 30, 2017.
- 171. "Protein quality control and degradation in the heart", Faculty Seminar Series, Department of Biomedical Engineering, University of South Dakota, Sioux Falls, SD, USA, January 18, 2018.
- 172. "Pathophysiological significance of priming the proteasome by PKA", Faculty Seminar Series, USD Sanford School of Medicine, Vermillion, SD, September 17, 2020
- 173. "Fatal attraction: a novel mechanism for inflammation to impair proteostasis. Faculty Seminar Series, USD Sanford School of Medicine, Vermillion, SD, December 5, 2024

### INVITED MODERATOR (National/International)

- 2007 Co-chair, Sunday Morning Program-"Protein Conformation, Degradation and Cardiac Disease", AHA Scientific Sessions 2007, Orlando, FL.
- 2008 Chair, the session on Genetic Models of Human Disease, AHA Scientific Sessions, Nov 8-10, 2008, New Orleans, LA.
- 2009 Co-Chair and invited speaker, Sunday Morning Program "Protein Quality Control in Heart Disease", AHA Scientific Sessions, Orlando, FL Nov 14, 2009

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2010 Co-Chair, the Symposium on "The Role of the Ubiquitin Proteasome System in Cardiac Disease, Diabetes, and Aging" for the Experimental Biology 2010 meeting. April 24-28 in Anaheim, CA.

- 2010 Co-Chair, Melvin L. Marcus Young Investigator Award in Cardiovascular Sciences. AHA Scientific Sessions, Nov. 15, 2010 in Chicago, IL
- 2014 Co-Chair, Session title: "Mitochondrial Biology and Protein Misfolding and/or Proteotoxicity" in the AHA BCVS 2014 "Pathways to Cardiovascular Therapeutics" conference July 14-17, 2014 in Las Vegas, Nevada.
- Co-Chair, Session Title: "Cellular Quality Control Mechanisms" in the AHA 2015
   BCVS Scientific Sessions: Pathway to Cardiovascular Therapeutics. July 13-16, 2015
   New Orleans, Louisiana.
- 2017 Co-Chair, a Symposium entitled: "Ubiquitin and Ubiquitin-Like Proteins in Cardiovascular Physiology and Disease" in 2017 Experimental Biology (EB) meeting, Chicago, IL, April 24, 2017.
- 2018 Co-Moderator, The Symposium 2 on Basic biomedical Science and Translational Medicine in the 11<sup>th</sup> Tongji Cardiovascular Disease Forum/2018China Precision Cardiology 2018/Central China International Congress of Cardiology, Wuhan, Hubei, China, August 11, 2018.
- 2018 Chair, the session entitled "Proteostasis Meets Protein Trafficking in the Heart" in AHA Scientific Sessions 2018, Chicago, IL November 12, 2018.
- 2019 Moderator, Concurrent Session 2B: Beyond Myocytes and Fibroblasts: Forgotten Cells of the Heart. BCVS 2019 Scientific Sessions Integrative Approaches to Complex Cardiovascular Diseases, Boston, Massachusetts, July 29- Aug 1, 2019.
- 2020 Moderator, Channel-10, Session 6 WACC/CNAHA Session: Novel Technologies and Translational Medicine in the Diagnosis and Treatment of the Cardiovascular Diseases (June 1, 2020). The 14th Oriental Congress of Cardiology (OCC2020 Virtual Conference), May 31-June 2, 2020.
- 2021 Co-Chair, 2021 CAAC-ACRE-CNAHA Cardiovascular Research Symposium (virtual), November 12, 2021.
- 2022 Co-Chair, 2022 CAAC-ACRE-CNAHA Cardiovascular Research Symposium (virtual), November 19, 2022.
- 2022 Chair of the Organizing Committee for *The 2022 John H. Lawrence Biomedical Symposium and MSPS Annual Scientific Sessions*, October 7-8, 2022 Vermillion, SD

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2023 Chair of the Organizing Committee for *The Inaugural ACRE@ISHR-NAS Preconference Symposium*, Madison WI, June 26, 2023.

- 2023 Co-Chair of the CNAHA/ACRE/CAAC Joint Symposium and Philly Night @ AHA Scientific Sessions, Philadelphia, PA, November 10, 2023.
- 2024 Co-Chair, Asian Cardiovascular Symposium (ACS)@BCVS-AHA, Chicago IL, July 21, 2024
- 2024 Chair, the Organizing Committee for *The 2nd ACRE@ISHR-NAS Preconference Symposium*, Long Beach CA, August 19, 2024.
- 2025 Moderator, Keynote Lecture, the 7<sup>th</sup> Asian Cardiovascular Symposium at BCVS Scientific Sessions. Baltimore MD, July 22, 2025.
- 2025 Co-Moderator, BCVS 2025 Session 14 Pathophysiologic and Systemic Axes Beyond the Heart. Baltimore MD, July 26, 2025.

## **BIBLIOGRAPHY**

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https://www.ncbi.nlm.nih.gov/myncbi/xuejun.wang.1/bibliography/public/

## A. ORIGINAL ARTICLES IN SCHOLARLY JOURNALS

## (A) In Peer-Reviewed Chinese Journals

- 1. Dong C, **Wang X**, Tu S, and Deng G. Alterations of plasma coagulation and extremity blood flow in erythermalgia. *Natl Med J China* 1988; 68(5): 292-293.
- 2. **Wang X** and Dong C. A preliminary study on the relationship between epidemic erythermalgia and El Niño. *Natl Med J China* 1988; 68(5): 266-268.
- 3. **Wang X**, Dong C, and Xiang J. Effects of ribavirin on coagulation-anticoagulation process in patients with epidemic hemorrhagic fever. *Natl Med J China* 1988; 68(12):699-701.
- 4. Dong C, **Wang X**, Xiang J, and Cosgraff T. The kinetic alterations of coagulation, anticoagulation and fibrinolytic system of patients with epidemic hemorrhagic fever and their significance. *Natl Med J China* 1988; 68(12): 678-681.
- 5. Dong C and **Wang X**. The alterations of coagulation, fibrinolysis, kinin, and complement system in epidemic hemorrhagic fever with DIC and its clinical Value. *Chinese J Pathophysiol* 1989; 5(5): 285-288.

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6. Tu S, **Wang X**, Dong C, and Ling H. The significance of electrocardiogram on the estimation of myocardial infarction size induced by isoproterenol in rats. *Acta Academiniae Medicinae Hubei* 1989; 10(4): 306-308.

- 7. **Wang X**, Dong C, and Xiang J. Effects of ribavirin on hemorrhagic tendency and fatality rate of patients with epidemic hemorrhagic fever. *Acta Academiniae Medicinae Hubei* 1989; 10(3): 193-196.
- 8. **Wang X**, Dong C, and Ling H. The kinetic alterations of plasma prekallikrain and antithrombin 3 in rats following isoproterenol-induced myocardial infarction. *Chinese J Pathophysiol* 1990; 6(2): 100-103.
- 9. **Wang X**, Dong C, and Xiang J. Studies on the anion gap of epidemic hemorrhagic fever (I): The kinetic alterations of anion gap in EHF. *Acta Academiniae Medicinae Hubei* 1990; 11(12): 285-289.
- 10. Dong C, **Wang X**, and Xiang J. Studies on anion gap of epidemic hemorrhagic fever (II): The mechanism and clinical significance of the increase in anion gap in EHF. *Acta Academiniae Medicinae Hubei* 1990; 11(12): 289-293.
- 11. **Wang X**, Dong C, and Xiang J. Studies on anion gap of epidemic hemorrhagic fever (III): The mechanism and clinical significance of the decrease in anion gap in EHF. *Acta Academiniae Medicinae Hubei* 1991; 12(1): 1-4.
- 12. Dong C, **Wang X**, and Xiang J. Studies on the anion gap of epidemic hemorrhagic fever (IV): The significance of simultaneous changes in anion gap, urine volume, and serum concentration of Na+ on the estimations of EHF prognosis. *Acta Academiniae Medicinae Hubei* 1991; 12(1): 5-7.
- Wang X, Dong C, and Ling H. Effects of Agkistrodon Halys on plasma coagulation in rats following isoproterenol-induced myocardial infarction. *Pace and Heart (Chinese)* 1991; 5(1): 29-31.
- 14. **Wang X**, Dong C, and Ling H. The kinetic alterations and pathophysiological significance of plasma coagulation in rats following isoproterenol-induced myocardial infarction. *Acta Academiniae Medicinae Hubei* 1991; 12(4): 299-303.
- 15. **Wang X**, Ouyang J, Liu J, and Dong C. A pathogenesis of isoproterenol-induced occlusion of cardiac microvasculature in rats. *J Microcirculation* 1992; 2(1):8-11.
- 16. Yu X, Dong C, Ouyang J, Li D, and **Wang X**. An experimental study on the protective modification of soybean phospholipid liposomes enclosed superoxide dismutase (SOD) on the membrane of ischemic and reperfused myocardium in rats. *Chinese J Pathophysiol* 1993; 9(7): 804.

- 17. Dong C, Chen X, Wang C, Zhong Y, and **Wang X**. Experimental studies of the effects of soybean phospholipid liposomes against the myocardial membrane injury by ischemia/reperfusion. *Acta Academiae Medicinae Hubei* 1993; 14(4): 323-329.
- 18. **Wang X** and Dong C. Studies on the anion gap of epidemic hemorrhagic fever: V. Effects of intravenous ribavirin therapy on the changes of anion gap of patients with EHF. *Acta Academiae Medicinae Hubei* 1994; 15(3):247-249.
- 19. Dong C, Yu X, and **Wang X**. Myocardial membrane injury of myocardial ischemia and lipoideamia in rats. *Prog Biochem Biophys* 1994; 21:347-350.
- 20. **Wang X**, Dong C, Tu S, Zhang Y, Ouyang J, and Liu Y. Effects of soybean phospholipids liposomes on the left ventricular function and infarct size of ischemic-reperfused hearts in rabbits. *Chinese J Pathophysiol* 1994; 10(6):583-585.
- 21. Huang W, Ma W-Z, and **Wang X**. Intercalated disc remodeling in a transgenic mouse model of desmin-related cardiomyopathy. *Chin J Cardiol* 2003; 31(11):859-864.

## (B) In Peer-Reviewed English Journals

- 22. **Wang X**, Li F, Said S, Capasso JM, and Gerdes AM. Measurement of regional myocardial blood flow in rats by unlabeled microspheres and Coulter Channelyzer. *Am J Physiol* 1996; 271:H1656-1665.
- 23. Li F, **Wang X**, Capasso JM, and Gerdes AM. Rapid transition of cardiac myocytes from hyperplasia to hypertrophy during postnatal development. *J Mol Cell Cardiol* 1996; 28: 1737-1746.
- 24. Gerdes AM, Onodera T, **Wang XJ**, McCune SA, and Capasso JM. Myocyte remodeling during the progression to failure in rats with hypertension. *Hypertension* 1996; 28:609-614.
- 25. Li F, **Wang X**, Bunger PC, and Gerdes AM. Formation of binucleated myocytes in rat heart: I. role of actin-myosin contractile ring. *J Mol Cell Cardiol* 1997; 29:1541-1551.
- 26. Li F, **Wang X**, and Gerdes AM. Formation of binucleated myocytes in rat heart: II. Cytoskeletal organization. *J Mol Cell Cardiol* 1997; 29:1553-1565.
- Wang X, Li F, and Gerdes AM. Chronic pressure overload cardiac hypertrophy and failure in guinea pigs: I. Regional hemodynamics and myocyte remodeling. *J Mol Cell Cardiol* 1999; 31(2):307-317.(cover illustration)
- Wang X, Li F, Campbell SE, and Gerdes AM. Chronic pressure overload cardiac hypertrophy and failure in guinea pigs: II. Cytoskeletal remodeling. *J Mol Cell Cardiol* 1999; 31(2): 318-331. (cover illustration)

- 29. **Wang X** and Gerdes AM. Chronic pressure overload cardiac hypertrophy and failure in guinea pigs: III. Intercalated disk remodeling. *J Mol Cell Cardiol* 1999; 31(2): 332-343. (cover illustration)
- 30. Milner DJ<sup>§</sup>, Taffet GE, <sup>§</sup> Wang X<sup>§</sup>, Pham T, Tamura T, Hartley C, Gerdes AM, and Capetanaki Y. The absence of desmin leads to cardiomyocyte hypertrophy and cardiac dilation with compromised systolic function. *J Mol Cell Cardiol* 1999; 31(11):2063-76.
- 31. Sanbe A, Nelson D, Gulick J, Setser E, Osinska H, **Wang X**, Hewett TE, Klevitsky R, Hayes E, Warshaw D, and Robbins J. In Vivo Analysis of an Essential Myosin Light Chain Mutations Linked to Familial Hypertrophic Cardiomyopathy. *Circ Res* 2000; 87: 296-302.
- 32. Yang Q, Hewett TE, Klevitsky R, Sanbe A, **Wang X**, and Robbins J. PKA dependent phosphorylation of myosin binding protein C in transgenic mice. *Cardiovasc Res* 2001; 51(1): 80-88.
- 33. **Wang X**, Osinska H, Dorn 2<sup>nd</sup> GW, Nieman M, Lorenz JN, Gerdes AM, Witt S, Kimball T, Gulick J, and Robbins J. Transgenic mouse model of desmin related cardiomyopathy. *Circulation* 2001; 103(19): 2402-2407.
- 34. **Wang X**, Osinska H, Klevitsky R, Gerdes AM, Nieman M, Lorenz JN, Hewett T, and Robbins J. Expression of R120G-(-B-crystallin causes aberrant desmin and alpha-B-crystallin aggregation and cardiomyopathy in mice. *Circ Res* 2001; 89(1): 84-91. (*with companion editorial*)
- 35. Wu G, Yussman MG, Barrett TJ, Hahn HS, Osinska H, Hilliard GM, **Wang X**, Toyokawa T, Yatani A, Lynch RA, Robbins J, and Dorn 2<sup>nd</sup> GW. Increased Myocardial Rab GTPase Expression. A Consequence and Cause of Cardiomyopathy. *Circ Res* 2001; 89:1130-1137.
- 36. Yi XP, **Wang X**, Gerdes AM, and Li F. Subcellular redistribution of focal adhesion kinase and its related nonkinase in hypertrophic myocardium. *Hypertension* 2003; 41: 1317-1323.
- 37. **Wang X\***, Klevitsky R, Huang W, Glasford JW, Li F, and Robbins J. αB-Crystallin Modulates Protein Aggregation of Abnormal Desmin. *Circ Res* 2003; 93: 998-1005. (\*corresponding author)
- 38. Dong X, Liu J, Zheng HQ, Glasford JW, Huang W, Chen QH, Harden NR, Li F, Gerdes AM, and **Wang X\*.** *In Situ* Dynamically Monitoring the Proteolytic Function of the Ubiquitin-Proteasome System in Cultured Cardiac Myocytes. *Am J Physiol Heart Circ Physiol* 2004; 287:H1417-H1425.
- 39. Yi XP, Zhou J, Baker J, **Wang X**, Gerdes AM, and Li F. Myocardial expression and redistribution of GRKs in hypertensive hypertrophy and failure. *Anatomic Record* 2005; 282A: 13-23.

- 40. Gard JJ, Yamada K, Green KG, Eloff BC, Rosenbaum DS, **Wang X**, Robbins J, Schuessler RB, Yamada KA, and Saffitz JE. Remodeling of gap junctions and slow conduction in a mouse model of desmin-related cardiomyopathy. *Cardiovasc Res* 2005; 67(3): 539-547.
- 41. Kumarapeli ARK, Horak KM, Glasford JW, Li J, Chen Q, Liu J, Zheng H, **Wang X\***. A novel transgenic mouse model reveals deregulation of the ubiquitin-proteasome system in the heart by doxorubicin. FASEB J. 2005 Dec;19(14):2051-3. doi: 10.1096/fj.05-3973fje. Epub 2005 Sep 27. PubMed PMID: 16188962.
- 42. Tang YD, Kuzman JA, Said S, Anderson BE, **Wang X**, and Gerdes AM. Low thyroid function leads to cardiac atrophy with chamber dilatation, impaired myocardial blood flow, loss of arterioles, and severe systolic dysfunction. *Circulation* 2005; 112: 3122-3130.
- 43. Chen Q, Liu J-B, Horak KM, Zheng H, Kumarapeli ARK, Li J, Li F, Gerdes AM, Wawrousek EF, and **Wang X\***. Intrasarcoplasmic amyloidosis impairs proteolytic function of proteasomes in cardiomyocytes by compromising substrate uptake. *Circ Res* 2005; 97: 1018-1026. (*with companion editorial*)
- 44. Liu J-B, Chen Q, Huang W, Horak KM, Zheng H, Mestril R, and **Wang X\***. Impairment of the ubiquitin-proteasome system in desminopathy mouse hearts. *FASEB J* 2006; 20: 362-364.
- 45. Yi XP, Zhou J, Huber L, Qu J, **Wang X**, Gerdes AM, and Li F. Nuclear compartmentalization of FAK and FRNK in cardiac myocytes. *Am J Physiol Heart Circ Physiol* 2006; 290: H2509-H2515.
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- 75. Zhang, Hanming, Wang, Xuejun. PDE1 inhibition primes the proteasome. Presented at the AHA Basic Cardiovascular Sciences (BCVS) 2016 Scientific Sessions: Pathways to Cardiovascular Therapeutics, Phoenix, AZ. July 18, 2016.
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- 82. **Wu, Penglong**, Wang, Yibin, Liu, Jinbao, Wang, Xuejun. Necroptosis Resulting from Activation of a RIP3-dependent Pathway Contributes to Cardiomyocyte Death Induced by Isoproterenol. Presented at the 2019 Experimental Biology meeting, Orlando, FL. (April 8, 2019)
- 83. **Wu, Penglong**, Li, Yi-Fan, Liu, Jinbao, Wang, Xuejun. Post-MI Cardiac Remodeling and Malfunction in Mice Are Exacerbated by Cardiomyocyte-restricted Ablation of the Uchl1 Gene. Presented at the 2019 Experimental Biology meeting, Orlando, FL. (April 7, 2019)
- 84. Penglong Wu, Bo Pan, Megan Lewno, Nirmal Parajuli, **Xuejun Wang**. In vivo genetic interrogations establish unequivocally the pathophysiological significance of proteasome phosphoregulation by protein kinase A. *J Mol Cell Cardiol*. March 2020; 140:6. DOI: <a href="https://doi.org/10.1016/j.vjmcc.2019.11.010">https://doi.org/10.1016/j.vjmcc.2019.11.010</a> Presented at the 23<sup>rd</sup> World Congress of International Society for Heart Research (ISHR) held in Beijing, China (June 4, 2019).
- 85. Hanming Zhang, Bo Pan, Penglong Wu, Nirmal Parajuli, Mark D. Rekhter, Alfred L Goldberg, **Xuejun Wang**. Dual Activation of PKA and PKG by PDE1 Inhibition Facilitates Proteasomal Degradation of Misfolded Proteins and Protects Against Proteinopathy-Based HFpEF. Oral abstract presentation at Session 1A "HFpEF: Unraveling the Gordian Knot" of 2019 AHA BCVS Scientific Sessions (July 29, 2019; Boston, MA).
- 86. Penglong Wu, Nirmal Parajuli, Megan Lewno, Jinbao Liu, **Xuejun Wang**. Proteasome priming by cyclic AMP signaling protects stressed hearts in mice. Presented at American Heart Association (AHA) Scientific Sessions, Philadelphia, PA, November 16-18, 2019.
- 87. Hanming Zhang, Bo Pan, Penglong Wu, Nirmal Parajuli, Mark D. Rekhter, Alfred L Goldberg, **Xuejun Wang**. Dual Activation of PKA and PKG by PDE1 Inhibition Facilitates Proteasomal Degradation of Misfolded Proteins and Protects Against Proteinopathy-Based HFpEF. Presented at the Session entitled "Best of AHA Specialty Conferences: BCVS 2019 of 2019", AHA Scientific Sessions, Philadelphia, PA, November 17, 2019.
- 88. **Penglong Wu**, Nirmal Parajuli, Megan Lewno, Liuqing Yang, Jinbao Liu, Xuejun Wang. RPN6-Ser14 Phosphorylation Is Responsible for Proteasome Activation by PKA and Protects against Pathological Cardiac Hypertrophy and Malfunction in Mice. *FASEB J* 17 April 2020; 34(S1): 03399. <a href="https://doi.org/10.1096/fasebj.2020.34.s1.03399">https://doi.org/10.1096/fasebj.2020.34.s1.03399</a> (with this work, Dr. Wu won the Runner-up of APS-Cardiovascular Section Outstanding Postdoctoral Trainee Awards).
- 89. **Megan Lewno**, Xuejun Wang. Phenotypic Differences Among Mice with Induced Cardiomyocyte-Restricted Ablation of Cops5, Cops8, or Both. Presented at *Iowa*

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- Physiological Society (IPS) and Midlands Society of Physiological Sciences (MSPS) Scientific Sessions 2020 (virtual), October 30-31, 2020.
- 90. **Samiksha Giri**, Chao Suo, Megan T. Lewno, Douglas S. Martin, Xuejun Wang. Defining molecular mechanism promoting neointimal hyperplasia by CSN8 hypomorphism. Presented at *Iowa Physiological Society (IPS) and Midlands Society of Physiological Sciences (MSPS) Scientific Sessions 2020 (virtual), October 30-31, 2020.*
- 91. **Liuqing Yang**, Nirmal Parajuli, Jack O. Sternburg, Xuejun Wang. Ser14-Psmd11/Rpn6 phosphorylation is required for activation of the 26S proteasome by PKA but is dispensable for cardiac responses to increased proteotoxic stress. Presented at *Iowa Physiological Society (IPS) and Midlands Society of Physiological Sciences (MSPS) Scientific Sessions 2020 (virtual)*, October 30-31, 2020.
- 92. **Mingqi Cai**, Xuejun Wang. Soluble guanylate cyclase activation increases proteasome activities and facilitates degradation of misfolded proteins in cardiomyocytes. Presented at *Iowa Physiological Society (IPS) and Midlands Society of Physiological Sciences (MSPS) Scientific Sessions 2020 (virtual), October 30-31, 2020.*
- 93. **Samiksha Giri**, Chao Suo, Douglas S. Martin, Xuejun Wang. Defining Molecular Mechanism Promoting Neointimal Hyperplasia by CSN8 Hypomorphism. *FASEB J.* 14 May 2021; 35(S1):04143. <a href="https://doi.org/10.1096/fasebj.2021.35.S1.04143">https://doi.org/10.1096/fasebj.2021.35.S1.04143</a> (with this work, PhD student Samiksha Giri won an APS-Cardiovascular Section Research Recognition Award).
- 94. **Megan Lewno**, Xuejun Wang. Phenotypic Differences Among Mice with Induced Cardiomyocyte-Restricted Ablation of Cops5, Cops8, or Both. *FASEB J.* 14 May 2021; 35(S1):05216. <a href="https://doi.org/10.1096/fasebj.2021.35.S1.05216">https://doi.org/10.1096/fasebj.2021.35.S1.05216</a>
- 95. **Mingqi** Cai, Xuejun Wang. Soluble guanylate cyclase activation increases proteasome activities and protects against proteotoxicity in cardiomyocytes. *FASEB J.* 14 May 2021; 35(S1): 05087. https://doi.org/10.1096/fasebj.2021.35.S1.05087
- 96. **Samiksha Giri**, Chao Suo, Douglas S. Martin, Xuejun Wang. CSN5-mediated nuclear exclusion of p27 in vascular smooth muscle cells contributes to the exacerbation of neointimal hyperplasia by CSN8 hypomorphism. *FASEB J.* 2022, (accepted for presentation in EB meeting to be held in Philadelphia PA April 2-5, 2022.)
- 97. Liuqing Yang, Nirmal Parajuli, Penglong Wu, Jinbao Liu, Xuejun Wang. Ser14-Rpn6/PSMD11 Phosphorylation Mediates the Activation of 26S Proteasomes by cAMP and Protects against Cardiac Proteotoxic Stress in Mice. (For this work, graduate student Liuqing Yang was selected the first runner-up of the 2022 APS CV Section Outstanding Graduate Student Trainee Award during the oral presentation competition for the award during the EB meeting to be held in Philadelphia PA April 4, 2022).
- 98. **Mingqi Cai**, Xuejun Wang. Activation of the Soluble Guanylate Cyclase Increases 26S Proteasome Activities and Protects against Proteotoxicity in Cardiomyocytes. (For this work, graduate student Mingqi Cai has been selected as a winner for the Research

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**Recognition** Awards during the EB meeting to be held in Philadelphia PA April 2-5, 2022).

- 99. Wyatt Windhorst\*, Jack Sternburg\*, Daniel Finely, Xuejun Wang. Cardiomyocyterestricted Overexpression of RPN6 Increases Myocardial Proteasome Peptidase Activities in Mice. Selected for Undergraduate Student Oral Presentation Award at The 2022 John H. Lawrence Biomedical Symposium and MSPS Annual Scientific Sessions, October 7-8, 2022 Vermillion, SD.
- 100. Liuqing Yang, Nirmal Parajuli, Jinbao Liu, Xuejun Wang. GENETIC MIMICRY OF THE ACTIVATION OF 26S PROTEASOMES BY CAMP-DEPENDENT PROTEIN KINASE PROTECTS AGAINST PROTEOTOXICITY. Selected for Graduate Student Oral Presentation Award at The 2022 John H. Lawrence Biomedical Symposium and MSPS Annual Scientific Sessions, October 7-8, 2022 Vermillion, SD.
- 101. Samiksha Giri, Chao Suo, Douglas S. Martin, Xuejun Wang. THE COP9 SIGNALOSOME PROMOTES NEOINTIMAL HYPERPLASIA THROUGH CULLIN DENEDDYLATION DEPENDENT AND INDEPENDENT MECHANISMS. Selected for Graduate Student Oral Presentation Award at The 2022 John H. Lawrence Biomedical Symposium and MSPS Annual Scientific Sessions, October 7-8, 2022 Vermillion, SD.
- 102. Mingqi Cai, Bo Pan, Peng Xiao, Megan T. Lewno, Xuejun Wang. SUSTAINED BUT DECOYED ACTIVATION OF THE JAK1-STAT PATHWAY BY EXPRESSION OF MISFOLDED PROTEINS EXACERBATES PROTEOTOXICITY. Selected for Graduate Student Oral Presentation Award at The 2022 John H. Lawrence Biomedical Symposium and MSPS Annual Scientific Sessions, October 7-8, 2022 Vermillion, SD.
- 103. Mark Bouska, Mingqi Cai, Yu July Xing, Erliang Zeng, Xiang Gao, Xuejun Wang. RNA SEQUENCING ACROSS LIFESPAN OF THE CARDIAC SPECIFIC CRYABR120G PROTEOTOXIC STRESS MOUSE MODEL. Selected for Postdoctoral Oral **Presentation Award** at The 2022 John H. Lawrence Biomedical Symposium and MSPS Annual Scientific Sessions, October 7-8, 2022, Vermillion, SD.
- 104. Samiksha Giri, Chao Suo, Ruggero Pardi, Gregory Fishbein, Xuejun Wang. The COP9 Signalosome Promotes Neointimal Hyperplasia through Cullin Deneddylation Dependent and Independent Mechanisms. Oral Presentation at the Inaugural ACRE@ISHR-NAS Preconference Symposium, Madison, WI, June 26, 2023
- 105. Md Salim Ahammed, Penglong Wu, Liuqing Yang, Jack O. Sternburg, Huiyun Liang, Faqian Li, Jinbao Liu, Xuejun Wang. PKA-mediated Phosphoregulation and Activation of 26S Proteasomes Protects Against Cardiac Hypertrophy and Heart Failure Induced by Systolic Overload. Oral Presentation at the Inaugural ACRE@ISHR-NAS Preconference Symposium, Madison, WI, June 26, 2023
- 106. Mark Bouska, Mingqi Cai, Yu Xing, Erliang Zeng, Xiang Gao, Xuejun Wang. Ubiquitin Ligase Fbxo36 Dysregulation Under Cardiac Specific Proteotoxic Stress. Poster presentation at the 42nd International Society for Herat Research North American Section (ISHR-NAS) annual scientific meeting, June 27-30, 2023, Madison, WI.

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107. **Md Salim Ahammed**, Penglong Wu, Liuqing Yang, Jack O. Sternburg, Huiyun Liang, Faqian Li, Jinbao Liu, Xuejun Wang. PKA-mediated Phosphoregulation and Activation of 26S Proteasomes Protects Against Cardiac Hypertrophy and Heart Failure Induced by Systolic Overload. Poster presentation at the 42nd International Society for Herat Research North American Section (ISHR-NAS) annual scientific meeting, June 27-30, 2023, Madison, WI.

- 108. **Jose Lira**, Andrew Guymon, Liuqing Yang, Jack Sternburg, Samiksha Giri, Xuejun Wang. Myocardial Ubiquitin-proteasome System Performance is Impaired in a Mouse Model of Heart Failure with Preserved Injection Fraction (HFpEF). Poster presentation at the 42nd International Society for Herat Research North American Section (ISHR-NAS) annual scientific meeting, June 27-30, 2023, Madison, WI.
- 109. **Jack Sternburg**, Wyatt Windhorst, Daniel Finley, Xuejun Wang. Cardiomyocyterestricted Overexpression of Rpn6/Psmd11 Increases Myocardial Proteasome Peptidase Activities in Mice. Poster presentation at the 42nd International Society for Herat Research North American Section (ISHR-NAS) annual scientific meeting, June 27-30, 2023, Madison, WI.
- 110. Liuqing Yang, Nirmal Parajuli, Jose Lira, Jinbao Liu, Xuejun Wang. Genetic Correction of Impaired Ser14-RPN6 Phosphorylation Protects against Proteotoxicity in Mice. Poster presentation at the 42nd International Society for Herat Research North American Section (ISHR-NAS) annual scientific meeting, June 27-30, 2023, Madison, WI. (For this work, PhD Student Liuqing Yang won an ISHR-NAS Travel Award).
- 111. **Mingqi Cai**, Bo Pan, Peng Xiao, Megan Lewno, Xuejun Wang. Sustained but Decoyed Activation of the JAK1-STAT Pathway by Expression of Misfolded Proteins Exacerbates Proteotoxicity. Poster presentation at the 42nd International Society for Herat Research North American Section (ISHR-NAS) annual scientific meeting, June 27-30, 2023, Madison, WI.
- 112. **Samiksha Giri**, Chao Suo, Ruggero Pardi, Gregory Fishbein, Xuejun Wang. The COP9 Signalosome Promotes Neointimal Hyperplasia through Cullin Deneddylation Dependent and Independent Mechanisms. Poster presentation at the 42nd International Society for Herat Research North American Section (ISHR-NAS) annual scientific meeting, June 27-30, 2023, Madison, WI.
- 113. **Mingqi Cai**, Bo Pan, Peng Xiao, Megan Lewno, Xuejun Wang. Sustained but Decoyed Activation of the JAK1-STAT Pathway by Expression of Misfolded Proteins Exacerbates Proteotoxicity. Poster presentation at the 2023 Annual Meeting of The Midlands Society of Physiological Sciences (MSPS), Oct 21, 2023, Omaha, NE.
- 114. Md Salim Ahammed, Penglong Wu, Liuqing Yang, Jack O. Sternburg, Huiyun Liang, Faqian Li, Jinbao Liu, Xuejun Wang. PKA-mediated phosphoregulation and activation of 26S proteasomes protects against cardiac hypertrophy and heart failure induced by systolic overload. Oral presentation at the 2023 Annual Meeting of The Midlands Society of Physiological Sciences (MSPS), Oct 21, 2023, Omaha, NE. (Oral presentation award in the graduate student category)

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115. **Mark Bouska,** Mingqi Cai, Yu July Xing, Erliang Zeng, Xiang Gao, Xuejun Wang. DISSECTING THE ROLE OF SBK2 KINASE IN DESMIN RELATED CARDIOMYOPATHY. Poster presentation at the 2023 Annual Meeting of The Midlands Society of Physiological Sciences (MSPS), Oct 21, 2023 Omaha, NE.

- 116. Md. Salim Ahammed, Penglong Wu, Liuqing Yang, Jack O. Sternburg, Huiyun Liang, Faqian Li, Jinbao Liu, Xuejun Wang. RPN6-Serine14 Phosphorylation by PKA Protects Against Systolic Overload-Induced Cardiac Remodeling and Heart Failure. Poster presentations at ACS@BCVS and BCVS Scientific Sessions, July 21-25, 2024, Chicago, IL.
- 117. Saima Ejaz, Jack O. Sternburg, Hongmin Wang, Khosrow Rezvani, Xuejun Wang. Genetic blockade of PKA-mediated phosphoregulation of 26S proteasomes exacerbates pathology in both the brain and heart of an Alzheimer's disease model. Poster presentations at ACS@BCVS and BCVS Scientific Sessions, July 21-25, 2024, Chicago, IL.
- 118. Samiksha Giri, Chao Suo, Ruggero Pardi, Gregory A. Fishbein, Khosrow Rezvani, Yabing Chen, Taixing Cui, Xuejun Wang. Nuclear export by COPS5/CSN5/JAB1 mediates vascular smooth muscle cell dedifferentiation in neointimal hyperplasia. Poster presentation at the 2024 Annual Meeting of The Midlands Society of Physiological Sciences (MSPS), Oct 19, 2024, Vermillion, SD.
- 119. **Mingqi Cai**, Bo Pan, Peng Xiao, Mark Bouska, Megan T. Lewno, Yue Xing, Erliang Zeng, Huiyun Liang, Faqian Li, Xiang Gao, Xuejun Wang. Sustained but Decoyed Activation of the JAK1-STAT Pathway by Aberrant Protein Aggregation Exacerbates Proteotoxicity. Poster presentation at the 2024 Annual Meeting of The Midlands Society of Physiological Sciences (MSPS), Oct 19, 2024, Vermillion, SD.
- 120. **Md. Salim Ahammed**, Penglong Wu, Liuqing Yang, Jack O. Sternburg, Huiyun Liang, Faqian Li, Jinbao Liu, Xuejun Wang. The activation of 26S proteasomes by protein kinase A during systolic overload is a compensatory response. Poster presentation at the 2024 Annual Meeting of The Midlands Society of Physiological Sciences (MSPS), Oct 19, 2024, Vermillion, SD.
- 121. **Md. Giash Uddin**, Liuqing Yang, Xuejun Wang. PKA-mediated proteasome activation is required for PDE4 inhibition to slow down cardiac function deterioration in mice with desmin-related cardiomyopathy. Poster presentation at the 2024 Annual Meeting of The Midlands Society of Physiological Sciences (MSPS), Oct 19, 2024, Vermillion, SD.
- 122. Saima Ejaz, Jack O. Sternburg, Hongmin Wang, Khosrow Rezvani, Xuejun Wang. Genetic blockade of PKA-mediated phosphoregulation of 26S proteasomes exacerbates pathology in both the brain and heart of an Alzheimer's disease model. Oral presentation award in the postdoc category at the 2024 Annual Meeting of The Midlands Society of Physiological Sciences (MSPS), Oct 19, 2024, Vermillion, SD.
- 123. **Mingqi Cai**, Xuejun Wang. Jak1 kinase activity is required for dysregulated JAK-STAT pathway to impair proteostasis in mouse hearts. **Winner of the 2025 APS CV Section Outstanding Graduate Student Trainee Award** competition and also presented as a poster at the conference. Baltimore MD, April 24-27, 2025.

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# PATENTS and PROVISIONAL PATENTS



(19) United States

(12) Patent Application Publication (10) Pub. No.: US 2021/0261936 A1 Wang (43) Pub. Date: Aug. 26, 2021

(54) COMPOSITIONS AND METHODS FOR ENHANCING THE UBIQUITIN PROTEASOME SYSTEM

(71) Applicant: South Dakota Board of Regents, Pierre, SD (US)

(72) Inventor: Xuejun Wang, Vermillion, SD (US)

(21) Appl. No.: 17/184,187

(22) Filed: Feb. 24, 2021

Related U.S. Application Data

(60) Provisional application No. 62/980,654, filed on Feb. 24, 2020.

**Publication Classification** 

(51) Int. Cl.

(52) U.S. Cl.

(57) ABSTRACT

Disclosed herein is a method of enhancing the ubiquitin proteasome system ("UPS") in a subject in need thereof, comprising administering an effective amount of a composition comprising neprilysin and a cell targeting moiety, wherein administration of the composition delivers the composition into the intracellular space of one or more cells of the subject and wherein the subject suffers from a condition associated with a LIPS deficiency.

## **GRANT/CONTRACT SUPPORT**

## **Current Grant Support**

2R01 HL153614-05 Wang 8/1/20-4/30/29 NIH/NHLBI \$475,000 (annual direct)

Cardiac Pathophysiology of Proteasome Phosphoregulation

The goal of this project is to determine in vivo (patho)physiological significance of phosphoregulation of the 26S proteasome by PKA.

Role: PI

4R01AG072510-02 Wang H, Wang X (Contact) 7/1/2022 – 6/30/2027 NIH/NIA \$342,000 (annual direct)

Priming the proteasome to protect against aging and Alzheimer's disease.

The goal of this project is to determine in vivo pathophysiological and pharmacological significance of phosphoregulation of the 26S proteasome by PKA in Alzheimer's disease

Role: Duo-PI, Contact PI

2R01 HL072166-18 Wang 7/1/03 - 6/30/2026

NIH/NHLBI NCE

PKG and PKA Duo-Activation to Treat Cardiac Proteotoxicity

The goal of this project is to exploit proteasome activation by PKG and PKA duo-activation to treat cardiac proteinopathy.

Role: PI

(Competitive renewal application submitted, discussed but needs revision).

# **Pending**

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2R01HL072166-19 Wang 7/1/2026-6/30/2030 NIH/NHLBI \$499,000 (annual direct)

Proteasome Malfunction in HFpEF

The goal of this project is to establish the pathogenic role of proteasome malfunction in HFpEF.

Role: PI

(IRG review completed, discussed/scored, but needs revision)

## **Previous Grant Support**

AHA Postdoctoral Fellowship Wang (PI) 7/1/2000 – 6/30/2002 American Heart Association (AHA) Ohio Affiliate \$70,000 (total direct)

Dissecting Desmin-related Cardiomyopathy with Transgenesis

Role: PI

(Terminated upon assistant professor appointment on October 1, 2001)

AHA 0235099N Wang (PI) 7/1/2002 – 6/30/2007

American Heart Association (AHA) National Center SDG \$260,000 (total direct)

Ubiquitin-Proteasome System in the Pathogenesis of Crystallinopathy

Role: PI

1P20RR17662-019003 Wang (PI) 9/20/2002 - 6/30/2007 NIH/NCRR \$100,000 (annual direct)

Mechanisms of Cardiovascular Remodeling: Molecular Biology Core

Role: Core Director

1P20RR17662-010001 Wang (PI) 9/20/2002 - 6/30/2007 NIH/NCRR \$200,000 (annual direct)

Mechanisms of Cardiovascular Remodeling: Project 1-Ubiquitin-Proteasome System

Dysfunction in Cardiac Remodeling and Failure

Role: PI of Project 1.

Reference # 0740025N Wang (PI) 1/1/2007- 12/31/2012 AHA Established Investigator Award \$500,000 (total cost)

Inadequate Protein Quality Control in Heart Failure

Role: PI

R01HL068936-04~05 Powell (contact), Wang 12/1/2008-6/30/2014 NIH/NHLBI \$280,000 (annual direct)

Proteasome, protein oxidation, and cardiomyocyte function

Role: Duo-PI, PI #2

AHA 0510069Z Kumarapeli (PI) 1/1/2005-12/31/2006 AHA Predoctoral Fellowship \$52,000 (total cost)

Alpha B-crystallin modulates cardiac hypertrophic response to mechanical overload.

Role: Sponsor and Primary Mentor

AHA 0620032Z H. Zheng (PI) 1/1/2006-12/31/2007 AHA Postdoctoral Fellowship Grant \$100,000 (total cost) XJ Wang CV Page 71 of 76 9/27/2025

Genetic Inhibition of Proteasomal Function in the Heart.

Role: Sponsor and Primary Mentor

Postdoctoral fellowship Su (PI) 7/1/2006 - 6/30/2008 AHA Greater Midwest Affiliate \$100,000 (total cost)

Physiological Significance of COP9 Signalosome in Adult Hearts.

Role: Sponsor and Primary Mentor

Reference # 0815571G Q. Zheng (PI) 7/1/2008-6/30/2010 AHA Predoctoral Fellowship \$52,000 (total cost)

Autophagy is activated by and compensates for proteasome malfunction in desminopathy

Role: Sponsor and Primary Mentor

11PRE5730009 Ranek (PI) 1/1/2011-12/31/2012 AHA Predoctoral Fellowship \$52,000 (total cost) The Role of PKG in the Stimulation of the UPS by the Muscarinic 2 Receptor Role: Sponsor and Primary Mentor

 11SDG6960011
 Su (PI)
 07/01/2011-06/30/2015

 AHA Scientist Development Grant (National Center)
 \$280,000 (total direct)

The Ubiquitin Proteasome System in Diabetic Cardiomyopathy

Role: Collaborator and Mentor

1 F32 HL122045-01 Terpstra (PI) 07/01/2014 – 6/30/2017

NIH National Research Service Award (Postdoc Fellowship) \$162,000 (total direct)

Direct proteasomal enhancement contributes to PKG-triggered cardioprotection

Role: Sponsor and Primary Mentor;

(Terminated on 8/2015 upon the PI's matriculation to medical school)

 16UFEL29640003
 Reihe (PI)
 06/01/2016 - 8/31/2016

 AHA Undergraduate Student Research Program
 \$4000 (scholarship)

Effect of Neddylation Inhibition on Autophagic Flux in Cardiomyocytes

Role: Sponsor and Primary Mentor

16PRE27790059 Zhang (PI) Wang (Sponsor) 01/01/2016 – 12/31/2017

AHA Predoctoral Fellowship \$52,000 (total direct)

PDE1 inhibition improves cardiac protein quality control

Role: Sponsor and Primary Mentor

R01 HL085629-01~13 Wang 7/1/06 - 6/30/21

NIH/NHLBI \$4,684,110 (total cost)

The COP9 Signalosome in the Heart

Role: PI

R01 HL131667-04 Cui, Wang (Contact) 4/1/17 - 3/31/22

NIH/NHLBI \$1,414,250 (total cost)

The NRF2-p62 Axis in the Cross-Talk between Proteasomal and Lysosomal Degradation

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The goal of this project is to test the role of the NRF2-p62 pathway in the impact of autophagy insufficiency on UPS performance.

Role: Duo-PI (contact PI)

1 R41 HL152919-01A1 Shaffer (Contact); Wang 2/16/21 -1/31/23

NIH/NHLBI \$320,198 (\$251,774 to Wang lab)

VAL-0914 Decreases PAO to Protect Against Cardiac Proteinopathies

The goal of this STTR project is to test a novel proprietary compound (VAL-0914) in a mouse model of cardiac proteinopathy.

Role: Duo-PI

3 P20GM103443-21S2 Huber (PI)/Wang X (PL) 9/1/2022 – 8/31/2024 NIH/NIGMS/NIA \$250,000 (direct)

AD Supplement to SD BRIN \$369,177 (total cost for this

suppl)

Role: Project Leader for the AD Supplement

23POST1018909 Bouska (PI) 1/1/2023 – 8/31/2024

AHA Postdoc Fellowship \$140,558

Defining the mechanistic role of SBK2 in proteotoxic cardiomyopathy progression

Role: Mentor/Sponsor

(Terminated because the postdoc took a faculty job).

20TPA35490091 Wang 1/1/21-12/31/24

American Heart Association (AHA) \$300,000

JAK1-STAT Pathway Promotes Cardiac Proteotoxicity

This AHA transformative project award will support a research project to investigate the role of the JAK1-STAT signaling pathway in the pathogenesis of cardiac proteinopathy.

Role: PI

23PRE1023108 Cai (PI) 1/1/2023 – 6/30/2025

AHA Predoc Fellowship \$65,106

JAK1 inhibition protects against cardiac proteotoxicity

Role: Mentor/Sponsor

## **CONTRIBUTIONS TO SCIENCE**

1. Discoveries of novel mechanisms by which proteasome function is regulated, establishment of their pathophysiological significance, and identification of new strategies to prime or activate the proteasome. It is well known that proteasome-mediated proteolysis requires ATP, but we have discovered that physiological levels of ATP above a relatively low threshold (50μM) suppress proteasome activity, serving to maintain a proteasome functional reserve for normal cells (Huang 2010). We also have discovered that protein kinase G (**PKG**) activates or primes the proteasome (Ranek 2013). PKG activation by either genetic or pharmacological (e.g., PDE5 inhibition) means promotes proteasome-dependent degradation of misfolded proteins in cardiomyocytes and slows down disease progression in a well-established mouse model of cardiac proteinopathy. This discovery has been confirmed recently by others in other cell types (PMID: 32513741, 34382059).

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Our discovery that M2 receptor activation enhances cardiac proteasomal function in a PKG dependent manner was the first to unveil the physiological requirement of kinase-elicited proteasome activation (PMID: 24508699). In 2019, we demonstrated duo-activation of PKA and PKG by PDE1 inhibition confers striking therapeutic benefit in a mouse model of proteinopathy-based HFpEF. More recently, we have established for the first time in animals that Ser14-phosphorylated RPN6 mediates proteasome activation by PKA and ameliorates proteinopathy. These findings also demonstrate the feasibility of using pharmacological methods to enhance proteasomal degradation of misfolded proteins and thereby improve PQC in the heart.

- a. Yang L, Parajuli N, Wu P, Liu J, Wang X\*. S14-phosorylated RPN6 mediates proteasome activation by PKA and alleviates proteinopathy. *Circ Res.* 2023;133(7):572-587.PMCID: PMC10502926.
- b. Zhang H, Pan B, Wu P, Parajuli N, Rekhter MD, Goldberg AL, **Wang X\***. PDE1 inhibition facilitates proteasomal degradation of misfolded proteins and protects against cardiac proteinopathy. **Sci Adv.** 2019; 5(5):eaaw5870. PMCID: PMC6531002.
- c. Ranek MJ, Terpstra EJ, Li J, Kass DA, **Wang X\***. Protein kinase g positively regulates proteasome-mediated degradation of misfolded proteins. *Circulation*. 2013; 128(4):365-76. PMCID: <u>PMC3761383</u>.
- d. Huang H, Zhang X, Li S, Liu N, Lian W, McDowell E, Zhou P, Zhao C, Guo H, Zhang C, Yang C, Wen G, Dong X, Lu L, Ma N, Dong W, Dou QP, Wang X\*, Liu J\*. Physiological levels of ATP negatively regulate proteasome function. *Cell Res*. 2010; 20(12):1372-85. PMCID: PMC2996470.
- 2. Dissecting the crosstalk between UPS and ALP pathways in cardiac PQC. We have elucidated a pivotal role of the calcineurin-TFEB-p62/SQSTM1 pathway in this crosstalk. We have shown that proteasomal malfunction activates autophagy in the heart while ALP inhibition hinders the degradation of ubiquitinated proteins by the proteasome in a p62-dependent manner, contributing to the dark side of Nrf2 activation in both hypertensive and diabetic cardiomyopathies. We are the first to report the upregulation of p62 at both transcript and protein levels in proteinopathic hearts which are known to have UPS insufficiency and demonstrate that this upregulation plays an important role in promoting autophagic removal and aggresomal sequestration of toxic misfolded proteins. More recently we documented the mediating role of the calcineurin-TFEB axis in the upregulation of p62 by proteasome malfunction. These discoveries have improved our understanding of cardiac PQC mechanisms, helping devise new therapeutic strategies for heart disease with increased proteotoxic stress, a highly prevalent category of heart diseases.
  - a. Pan B, Li J, Parajuli N, Tian Z, Wu P, Lewno MT, Bedford L, Mayer RJ, Fang J, Liu J, Cui T, Su H, **Wang X\***. The calcineurin-TFEB-p62 pathway mediates the activation of cardiac macroautophagy by proteasomal malfunction. *Circ Res.* 2020; 127(4):502–518. PMCID: PMC7416491
  - b. Zang H, Wu W, Qi L, Tan W, Nagarkatti P, Nagarkatti M, **Wang X**, Cui T. Autophagy inhibition enables Nrf2 to exaggerate the progression of diabetic cardiomyopathy in mice. *Diabetes* 2020;69(12):2720-2734. PMCID: PMC7679777.
  - c. Wang C, **Wang X\***. The interplay between autophagy and the ubiquitin-proteasome system in cardiac proteotoxicity. *Biochim Biophys Acta*. 2015; 1852(2):188-94. PMCID: <u>PMC4277934</u>
  - d. Zheng Q, Su H, Ranek MJ, **Wang X\***. Autophagy and p62 in cardiac proteinopathy. *Circ Res*. 2011; 109(3):296-308. PMCID: PMC3142307.

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3. Established the necessity of PFI and inadequate ubiquitination-proteasome coupling in pathogenesis. Although UPS malfunction was proposed first by neuroscientists to play a role in neurodegeneration, the necessity of PFI in pathogenesis was not demonstrated until 2011 when we published that genetic enhancement of the proteasome protects against protein pathy and I/R injury in mice. Our discovery that PA28\alpha overexpression enhances proteasome function identifies the 1st method to achieve proteasome gain-of-function, allowing us to generate the first animal model of proteasome function enhancement. This also represents the first demonstration that the proteasome can also be a rate-limiting step in the UPS-mediated degradation of at least a subset of proteins. We also created the first cardiomyocyte-restricted proteasome inhibition (CR-PsmI) and ubiquitinationproteasome uncoupling (Ubiquilin1 conditional knockout) mouse models. These unique genetic tools are essential to, and have remarkably facilitated, defining the pathophysiological significance of cardiac UPS malfunction. Using them, we have established a major pathogenic role for PFI in I/R injury, pressure overloaded cardiac maladaptive remodeling, and diabetic cardiomyopathy, three major causes of heart failure. These studies are also strongly indicative of improving proteasome function as a potentially novel therapeutic strategy for a large subset of heart diseases, providing compelling rationale to study the regulation of the UPS.

- a. Hu C, Tian Y, Xu H, Pan B, Terpstra EM, Wu P, Wang H, Li F, Liu J, Wang X\*. Inadequate ubiquitination-proteasome coupling contributes to myocardial ischemia-reperfusion injury. J Clin Invest. 2018; 128(12):5294-06. PMCID: PMC6264645.
- b. Li J, Ma W, Yue G, Tang Y, Kim IM, Weintraub NL, Wang X, Su H. Cardiac proteasome functional insufficiency plays a pathogenic role in diabetic cardiomyopathy. *J Mol Cell Cardiol*. 2017; 102:53-60. PMCID: PMC5316366.
- c. Tian Z, Zheng H, Li J, Li Y, Su H, **Wang X\***. Genetically induced moderate inhibition of the proteasome in cardiomyocytes exacerbates myocardial ischemia-reperfusion injury in mice. *Circ Res*. 2012; 111(5): 532-42. PMCID: PMC3426260.
- d. Li J, Horak KM, Su H, Sanbe A, Robbins J, **Wang X\***. Enhancement of proteasomal function protects against cardiac proteinopathy and ischemia/reperfusion injury in mice. *J Clin Invest*. 2011; 121(9): 3689-700. PMCID: PMC3163952.
- 4. Elucidation of physiological roles of the COP9 signalosome (CSN) in the heart and liver. Ub ligases or E3s confer substrate specificity and attach Ub to substrate proteins. The Cullin-RING ligases (CRLs) are the largest family of Ub E3s, known to regulate a variety of cellular processes including cell cycle control. CRLs are activated by cullin neddylation, inhibition of which via MLN4924 is in clinical trials for treating cancers. The CSN holo-complex consisting of 8 unique protein subunits (COPS1 ~ COPS8) functions as a deneddylase for cullins, indispensable to CRLs catalytic dynamics. The CSN was rarely studied for its role in terminally differentiated organs of vertebrates. Through cardiac targeting *Cops8*, we demonstrate that COPS8/CSN is required for cardiomyocyte survival and functioning, COPS8/CSN regulates not only the UPS but also the ALP, the latter was not known before our discovery that COPS8/CSN is required for autophagosome fusion with lysosomes. More recently, our studies revealed for the first time that CRLs contribute to degradation of misfolded cytosolic proteins and that Cops8/CSN suppresses the RIPK1-RIPK3 mediated cardiomyocyte necroptosis in mice.
  - a. Xiao P, Wang C, Li J, Su H, Yang L, Wu P, Lewno MT, Liu J, Wang X\*. COP9 signalosome suppresses RIPK1-RIPK3-mediated cardiomyocyte necroptosis in mice. Circ Heart Fail. 2020; 13(8): e006996. PMCID: PMC7438278.

b. Su H, Li J, Zhang H, Ma W, Wei N, Liu J, Wang X\*. COP9 signalosome controls the degradation of cytosolic misfolded proteins and protects against cardiac proteotoxicity. *Circ Res*. 2015; 117(11):956-66. PMCID: PMC4636927.

- c. Su H, Li F, Ranek MJ, Wei N, **Wang X\***. COP9 signalosome regulates autophagosome maturation. *Circulation*. 2011; 124(19):2117-28. PMCID: <a href="mailto:pmc3211066">PMC3211066</a>.
- d. Su H, Li J, Menon S, Liu J, Kumarapeli AR, Wei N, Wang X\*. Perturbation of cullin deneddylation via conditional Csn8 ablation impairs the ubiquitin-proteasome system and causes cardiomyocyte necrosis and dilated cardiomyopathy in mice. *Circ Res*. 2011; 108(1):40-50. PMCID: PMC3017673.
- 5. Discovery of UPS functional insufficiency in mouse models of heart disease using innovative tools generated in my lab. UPS-mediated protein degradation, initially discovered in 1980s, had not attracted the attention of a broader spectrum of cell biologists until mid-1990s. The attention to the UPS from general biomedical scientists outside the cell biology field was drawn by the award of the 2004 Nobel Prize in Chemistry to 3 scientists for their contributions to the discovery of the UPS. As a pioneer for studying UPS dysfunction in cardiac pathogenesis, my lab has worked on the UPS since its inception in 2001. By then, research into health and disease of most organs/systems, including the heart, had emphasized primarily changes in gene expression at the transcription or, in some cases, protein synthesis level, although changes in protein degradation can have equal or even greater impact on the level and functioning of a protein. A major hurdle then was lacking tools to monitor UPS function in vivo. We first developed stable cell lines, adenoviruses, and stable transgenic (tg) mouse lines expressing a modified GFP (GFPu or GFPdgn) that is a proven surrogate substrate of the UPS, allowing monitoring the dynamics of UPS performance in situ and in vivo. These new tools are distributed to researchers around the world and enabled my lab to demonstrate in intact animals for the first time in the world that increases in misfolded proteins and resultant aberrant protein aggregation impair UPS function and cause proteasome functional insufficiency (PFI). Similarly, we were also the first to document cardiac UPS functional insufficiency in acute ischemia/reperfusion (I/R) injury, chronic pressure overload, and diabetic cardiomyopathy, which prompted investigations into the pathogenic role of cardiac UPS dysfunction. More recently, we have discovered that aberrant protein aggregation hijacks phosphorylated STATs into the aggregates, which decoys and sustains the activation of the JAK1-STATs pathway, forming a vicious circle. This discovery identifies the first mechanistic and druggable link between inflammation and proteostasis impairment in the cell (Cai M et al. 2024), unveiling a new pathogenic cause of proteotoxicity and PFI in common and lethal diseases.
  - a. Cai M, Pan B, Xiao P, Bouska M, Lewno MT, Xing Y, Zeng E, Liang H, Li F, Gao X, **Wang X\***. Sustained but decoyed activation of the JAK1-STAT pathway by aberrant protein aggregation exacerbates proteotoxicity. *Circulation*. 2024;150(16):1302-1305. PMCID: PMC11483158.
  - b. Liu J, Chen Q, Huang W, Horak KM, Zheng H, Mestril R, **Wang X\***. Impairment of the ubiquitin-proteasome system in desminopathy mouse hearts. *FASEB J*. 2006; 20(2):362-4. PMID: 16371426.
  - c. Chen Q, Liu JB, Horak KM, Zheng H, Kumarapeli AR, Li J, Li F, Gerdes AM, Wawrousek EF, Wang X\*. Intrasarcoplasmic amyloidosis impairs proteolytic function of proteasomes in cardiomyocytes by compromising substrate uptake. *Circ Res*. 2005; 97(10):1018-26. PMID: 16210548.
  - d. Kumarapeli AR, Horak KM, Glasford JW, Li J, Chen Q, Liu J, Zheng H, **Wang X\***. A novel transgenic mouse model reveals deregulation of the ubiquitin-proteasome system in the heart by doxorubicin. *FASEB J*. 2005; 19(14):2051-3. PMID: 16188962.

<sup>\*</sup>Corresponding author

# Complete List of Published Work in My Bibliography: https://www.ncbi.nlm.nih.gov/myncbi/xuejun.wang.1/bibliography/public/

**References** (will be provided upon request)