

CURRICULUM VITAE

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

NICKNAME: “XJ” Wang

CITIZENSHIP: U.S.A.

AFFILIATION: Division of Basic Biomedical Sciences
Sanford School of Medicine
University of South Dakota
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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>

Scopus Profile: <https://www.scopus.com/authid/detail.uri?authorId=35235510300>

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

EDUCATION

September 1980 to July 1985

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

September 1985 to July 1988

Hubei Medical University (now 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

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
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
Hubei Medical University (now Wuhan University College of Medicine)
Wuhan, Hubei, China

July 1988 – June 1993

Instructor
Department of Pathophysiology
Hubei Medical University (now Wuhan University College of Medicine)
Wuhan, Hubei, China

September 1985 – June 1988

Graduate Teaching Assistant
Department of Pathophysiology
Hubei Medical University (now 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 (3rd prize)
The Science & Technology Association of Hubei Province, P. R. China
- 1990 Best Original Research Articles in Natural Sciences (2nd prize)
The Science and Technology Association of Hubei Province, P. R. China
- 1991 Best Original Scientific Research Articles (2nd prize)
The Science and Technology Association of Wuhan, P.R. China
- 1993 The Medical Sciences and Technology Advancement Awards (2nd prize)
The Department of Health, Hubei Province, China
- 1995 Best Original Scientific Research Articles (3rd 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 (3rd prize)
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
(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.)

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

Offices

- 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)
- 2021-2022 President, Midlands Society of Physiological Sciences (a chapter of APS)
<https://msps-online.org/society-leadership/>
- 2021- President-elect, Academy of Cardiovascular Research Excellence (ACRE).

<http://my-acre.org/>

CONSULTING POSITIONS

A. PEER REVIEWER

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
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
Molecular Cellular Biochemistry
Molecular and Cellular Biology
Molecular Medicine
Molecular Therapy Nucleic Acids
Nature Communication
Nature Review of Cardiology
Pharmacology Research
Physiology Reports
PLoS Genetics
PLoS One
Protein and Cell
Redox Biology
Scientific Reports
Trends in Cardiovascular Medicine
Trends in Molecular Medicine

B. EDITORIAL BOARDS

- 2008-present *International Journal of Physiology, Pathophysiology and Pharmacology*
- 2009-present *American Journal of Translational Research*
- 2009-2010 Guest Editor for a Spotlight Issue on “The Ubiquitin-Proteasome Pathway in Cardiovascular Disease” for *Cardiovascular Research*
- 2011-present Associate 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 – present Associate Editor, *Frontiers in Ageing - Aging, Metabolism and Redox Biology*
- 2020 - 2021 Co-Guest Editor for *Cells* Special Issue on “Molecular Mechanisms Underlying Cardiac Dysfunction”
https://www.mdpi.com/journal/cells/special_issues/cardiac_dysfunction_mechanisms
- 2020 - *Engineering*
- 2022 - Co-Topic Editor for Research Topic on “Proteostasis in Cardiac Health and Disease” sponsored by *Frontiers in Molecular Biosciences* and *Frontiers in Cellular and Developmental Biology* (<https://www.frontiersin.org/research-topics/31026/proteostasis-in-cardiac-health-and-disease>)

C. NATIONAL/INTERNATIONAL COMMITTEES

- 2003-2020 International Expert Panel
Singapore National Medical Research Council
- 2005-2007 External Expert Grant Reviewer
Philip Morris External Research Program

2006	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 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
- 2020 - 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; *Ad hoc* 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- 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 (invite accepted), 2022.
- 2022- AHA National Center Established Investigator Awards (EIA) Peer Review Committee, chartered member
- 2022 Invited external reviewer for University of Nebraska system internal grants

COMMITTEE ASSIGNMENTS

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
- 2007 Pre-Tenure Review Committee for Dr. Yifan Li
- 2007 Pre-Tenure Review Committee for Dr. Alexander Erkin
- 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
- 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.
- 2016-2022 Graduate Committee of USD Sanford School of Medicine
- 2016-present The MD/PhD Admissions Standing Committee
- 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-present P&T Committee, Sanford School of Medicine, USD.

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 | <i>Gross Anatomy</i> | USD School of Medicine and Health Sciences |
| 2. ANAT 521 | <i>Microanatomy</i> | USD School of Medicine and Health Sciences |
| 3. BIOCHEM | <i>Medical Biochemistry</i> | USD Sanford School of Medicine |
| 4. PHPH 792 | <i>Genetic Approaches</i> | USD Graduate School (Course Director) |
| 5. CPHD 740 | <i>Protein Quality Control</i> | USD Graduate School (Course Director) |
| 6. BIOC 798 | <i>Heat Shock Proteins</i> | USD Graduate School |
| 7. PHPH 728 | <i>Signal Transduction</i> | USD Graduate School |
| 8. CPHD 788 | <i>Res Basic Biomed Sci</i> | USD Graduate School |
| 9. CPHD 898 | <i>Thesis Research</i> | USD Graduate School |
| 10. CPHD 620 | <i>Foundations of Cardiovasc. Sci.</i> | USD Graduate School (Course Director) |
| 11. CPHD 792 | <i>Heat Shock Proteins and Dis.</i> | USD Graduate School |
| 12. IMC 601 | <i>Skin and Musculoskeletal Block</i> | USD Sanford School of Medicine |
| 13. IMC 605 | <i>Cardiovascular Block</i> | USD Sanford School of Medicine |

B. GRADUATE STUDENTS MENTORING

1. Served as the Primary Mentor

Graduate student names	Degree obtained (pursued)	Dates	Current positions
Wei Huang (visiting student)	Ph.D.	10/2001 – 10/2002	Professor of Medicine, Nanjing Medical University, Nanjing, Jiangsu, China
Assangi R. K. Kumarapeli	Ph.D.	9/2002 - 8/2006	Associate Professor, Department of Pathology, University of Arkansas for

			Medical Sciences, Little Rock, AR
Mingxin Tang	M.S.	7/2003 – 8/2006	Research Scientist University of Hawaii, Honolulu, HI, PA
Jie Li	Ph.D.	9/2003 - 12/2008	Assistant Professor, Medical College of Georgia Augusta University, Augusta, GA, USA
Qingwen Zheng	Ph.D.	9/2005 – 12/2010	Physician, Kaiser Permanente Roseville Medical Center Roseville, California
Mark J. Ranek, BS	Ph.D.	9/2006 – 5/2012	Assistant Professor, Johns Hopkins University
Lei Zhang, MS	Ph.D. (co-mentor)	8/2015 – 8/2016	Postdoc at Medical University of South Carolina, Charleston, SC
Hanming Zhang, BS	(PhD)	8/2013 – 5/2019	Postdoc at Yale University, New Haven, Connecticut
Penglong Wu, BM, MS	Visiting PhD Student from Shanghai Jiao Tong University	6/22/2015 – 6/21/2017	Postdoctoral fellow, Guangzhou Medical University and USD Sanford School of Medicine.
Chao Suo, DDS	(PhD)	8/2015 – 5/2017	Taking a 2-year leave of absence for a Dentistry Licensure training program in University of Las Vegas, Las Vegas, NV.
Megan T. Lewno, BA	M.S.	8/22/2019- 12/21/2021	PreClinical Applications Specialist, Scintica Inc. Webster, TX
Liuqing Yang, BS, MS	PhD	8/22/2017 -	
Samiksha Giri, BA	PhD	8/22/2017-	
Mingqi Cai, MBBS	Visiting Graduate Student	1/22/2020 - 1/21/2021	USD PhD student
Mingqi Cai, MBBS	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-	

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/Thesis Committee, BBS

- 2010-2011 Rui Du, PhD Advisory Committee, BBS
- 2010-2014 Shuai Li, PhD Advisory/Thesis Committee, BBS
- 2013-2016 Lei Zhang, PhD Advisory Committee, BBS
- 2013-2017 Xianhua Meng, MS/PhD Thesis Committees, Dept. of Chemistry, USD
- 2015-2018 Hongbo Gao, PhD Advisory/Thesis Committee, BBS

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
- 2009-2015 H. Wang, PhD, Assistant Professor; currently R01-funded tenured Associate Professor at University of 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 1st, 2020)
- 2021- 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).

2. List of Postdoctoral Trainees

Name of trainees	Training period	Current position
Quanhai Chen, MD	1/2003 - 11/2005	Senior Scientist, GlaxoSmithKline, Heart Failure (Development Performance Unit),

		King of Prussia, PA, USA
Hanqiao Zheng, MD, PhD	8/2003 - 5/2008	Res. Scientist, Harvard University School of Public Health, Boston, MA, USA
Jinbao Liu, MD, PhD	11/2003 - 10/2005	Professor and Vice President for Research, Guangzhou Medical University, Guangzhou, Guangdong, China
Huabo Su, PhD	11/2004 – 6/2008 7/2008 – 7/2012	Associate Professor (tenured), Vascular Biology Center and Department of Pharmacology, Medical College of Georgia Augusta University, Augusta, GA, USA
Daoxiong Lei, MD, PhD	11/2005- 10/2008	Professor, Tianjin 4 th Hospital, Tianjin, China
Youn-Chul Ryu, PhD	9/2006 – 4/2009	Associate Professor, Jeju National University, Jeju-si, Jeju-do, Korea
Wei Huang, MD, PhD	10/2007- 10/2008	Professor, Nanjing Medical University, Nanjing, Jiangsu, China
Jie Li, MD, PhD	1/2009 – 7/21/2012	Assistant Professor, Medical College of Georgia Augusta University, Augusta, GA, USA
Zongwen Tian, MD, PhD	8/2009 – 8/21/2012	Associate Professor & Chair, Dept. of Anatomy, Wuhan University Medical School, Wuhan, Hubei, China
Changhua Wang, MD, PhD	10/2010- 10/2011	Professor & Chair, Dept. of Pathophysiology, Wuhan University Medical School, Wuhan, Hubei, China
Mark J. Ranek, PhD	6/1/2012- 11/21/2012	Assistant Professor at Johns Hopkins University, Baltimore, MD
Hongxin Xu, MD, PhD	11/1/2012- 11/21/2013	Associate Professor and Cardiologist, Renming Hospital, Wuhan University School of Medicine, Wuhan, Hubei, China
Chengjun Hu, MD, PhD	3/22/2012 – 3/31/2014	Associate Professor & Vice-Chair, Dept. of Anatomy, Wuhan University College of Basic Biomedical Sciences, Wuhan, Hubei, China
Yihao Tian, MD, PhD	3/22/2012 – 3/31/2014	Associate Professor, Dept. of Anatomy, Wuhan University College of Basic Biomedical Sciences, Wuhan, Hubei, China
Erin J. Terpstra, PhD	2/1/2012 – 6/30/2015	Medical Student, USD SSOM
Bo Pan, PhD	12/22/2014 – 6/21/2019	Senior Postdoctoral Research Associate, Department of Physiology, Wayne State University College of Medicine, Detroit, MI
Peng Xiao, PhD	1/22/2015 – 9/21/2018	Postdoctoral Fellow, The Wistar Institute, Philadelphia, PA 19104
Ammara Abdullah, PhD	6/22/2015 – 6/21/2017	Research Scientist II, ONC ODD/Oncology NIBR, Novartis Pharmaceuticals, 3000 Kent Ave. Ste. #1950, West Lafayette, IN 47906

Penglong Wu, MD, PhD	8/3/2017- 6/21/2020	Physician Scientist, The Cardiovascular Institute of Xiamen University, Xiamen, Fujian, China
Mohamed Hussain, PhD	9/22/2020 - 6/21/2021	(Unknown)
Mark J. Bouska, PhD	1/3/2021 -	
Saima Ejaz, PhD	11/1/2022-	

3. List of Visiting Scientists

Name & Degrees	Training period	Parent Institution
Changhua Wang, MD, PhD	1/2014 ~ 8/21/2015	Professor & Chair, Dept. of Pathophysiology, Wuhan University College of Basic Medical Sciences, Wuhan, Hubei, China
Maggie Gong, MD, PhD	2/2014 ~ 1/21/2015	Professor, Harbin Medical University, Harbin, Heilongjiang, China
Feng Yao, MD, PhD	4/2009- 11/2009	Professor & Chair, Dept. of Breast Surgery, 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, Internal 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
9/2021 -	Andrew L. Guymon, USD medical student of Class 2025, scholarship pathway

5. Undergraduate Student Researchers

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

Andy Nelson	Augustana College	Undergrad Summer Researcher	2006 summer
Heath Eggleston	Dakota Wesley	BRIN Summer Scholar	2007 summer
Blake Alberts	USD	The Honors' Thesis Research	2008-2010
Blake Alberts	USD	NIH summer research scholarship	2009 summer
Morgan Hanson	USD	The Honors Thesis Research	2008-2010
Levi Froke	USD	NIH Summer Research Scholarship	2009 summer
Levi Froke	USD	Part-time undergrad. researcher and The Honors Thesis Research	2009-2011
Yun Zou	USD	Part-time undergrad. researcher	12/2009-5/2010
Michael Freitag	USD	Part-time undergrad. researcher	1/2010-4/2010
Michael Freitag	USD	Undergrad summer researcher	2010 summer
Jiwen Li	Rice University	Rice/Baylor Medical Scholar, NIH Summer Research Scholarship	2010 summer
Michael Freitag	USD	Undergrad summer researcher	2011 summer
Levi Froke	USD	Undergrad summer researcher	2011 summer
Lance M. Ranek	USD	Work study (undergrad research assist)	2012/2013 school year
Lance M. Ranek	USD	Work study (undergrad research assist)	2013/2014 school year

Lance M. Ranek	USD	Undergrad summer researcher	2014 summer
Casey A. Reihe	USD	Undergrad researcher	2015 Spring – 2017 Spring
Caleb Ray Wenz	USD	Undergrad researcher	2015 Spring-2016 Spring
Andrew V.Y. Yevugah	USD	Undergrad researcher	2016 Spring- 2017 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

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

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

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”

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 4th Annual Scientific Meeting of Heart Failure Society of America, Boca Raton, FL, September 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 17th 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 Texas 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 1st Annual COBRE Symposium. Rapid city, SD, June 28-30, 2003.
 22. “In Situ Monitoring Dynamic Changes in the Ubiquitin-Proteasome System in vitro and in vivo”; The 1st 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 2nd 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 2nd 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 5th 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 Angeles, 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 4th 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.
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 29th Meeting of the North American Section of the International Society for Heart Research (ISHR), Bologna, Italy, June 21-22, 2007.
41. “Proteasomal degradation”; The 4th 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.
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 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 Angeles, 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 35th 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, 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 36th 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 4th 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
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 6th 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 7th Cold Region Cardiology Conference (CRCC) and the 3rd China-Russia Jointed Pharmacology Conference, Harbin, Heilongjiang, China, July 13-16, 2017.
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 Disease](#)”, 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.
118. “Interplay between the ubiquitin-proteasome system and autophagy”, International Society for Heart Research (ISHR) (Quarantine) Cardiovascular Webinar Series. May 22, 2020. <https://www.youtube.com/watch?v=xiys1qoCMjI&t=45s>
119. “Crosswalk between proteasomal and lysosomal degradation”, 14th 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 7th ACRE-APS Scientific Symposium (virtual), Aug. 8th, 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 40th 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, 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 10th, 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 1st, 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 13th Cross-Strait Cardiovascular Symposium and the 7th 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.

Seminars Given in Employer Institutions

135. “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.
136. “Dissecting desmin-related cardiomyopathy with mouse transgenesis”; Division of Pediatric Cardiology, Children’s Hospital, Cincinnati, OH, February 7, 2000.
137. “Ubiquitin-Proteasome System and Diseases”, Division of Basic Biomedical Sciences, University of South Dakota School of Medicine, Vermillion, SD, September 17, 2002.
138. “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.
139. “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.
140. “Targeted proteolysis in conformational disease”; Faculty Seminar Series, Division of Basic Biomedical Sciences, USD Sanford School of Medicine, October 28, 2008.
141. “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.
142. “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.

143. “Can we boost cardiac proteasomes by stimulating PKG?” The 2nd Annual PQCD Symposium, Deadwood, SD, USA. June 14, 2012.
144. “The Ubiquitin-Proteasome System in Cardiac Pathogenesis: Beyond the Proteasome”, Faculty Seminar Series, USD Sanford School of Medicine, November 30, 2017.
145. “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.
146. “Pathophysiological significance of priming the proteasome by PKA”, Faculty Seminar Series, USD Sanford School of Medicine, Vermillion, SD, September 17, 2020

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
- 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.
- 2015 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-Modulator, The Symposium 2 on Basic biomedical Science and Translational Medicine in the 11th 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 Modulator, 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 Modulator, Modulator, 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.

BIBLIOGRAPHY

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E. ABSTRACTS AND CONFERENCE PRESENTATIONS

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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)
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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. <https://doi.org/10.1096/fasebj.2020.34.s1.03399> (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 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-Psm11/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. <https://doi.org/10.1096/fasebj.2021.35.S1.04143> (with

this work, PhD student Samiksha Giri won an APS-Cardiovascular Section Research Recognition Award).

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

PATENTS and PROVISIONAL PATENTS



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(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**

(52) **U.S. CL**
 CPC *C12N 9/50* (2013.01); *A61K 47/6815* (2017.08); *A61K 38/00* (2013.01); *C07K 2319/33* (2013.01); *C07K 2319/10* (2013.01); *C12Y 304/24011* (2013.01)

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(57) **ABSTRACT**

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

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Publication Classification

(51) **Int. Cl.**

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 UPS deficiency.

GRANT/CONTRACT SUPPORT**Current Grant Support**

- 1 R01 HL153614-03 Wang 8/1/20-6/30/24
NIH/NHLBI \$250,000 (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
- 2 R01 HL072166-17 Wang 7/1/03 – 6/30/24
NIH/NHLBI \$336,902 (annual direct)
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
- 20TPA35490091 Wang 1/1/21-12/31/23
American Heart Association (AHA) \$90,909 (annual direct)
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
- 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
- 1RF1AG072510-01A1 Wang H (Contact), Wang X 7/1/2022 – 6/30/2027
NIH/NIA \$375,000 (annual direct)
Priming the proteasome to protect against aging and Alzheimer's disease.
Role: Duo-PI
(NOA has been issued for the first 3 years. Subsequent years will follow RF1 procedures for non-competitive renewal.)
- 3 P20GM103443-21S1 Goodman (PI)/Wang X, Wang H (PL) 9/1/2022 – 8/31/2023
NIH/NIA \$250,000 (annual direct)
AD Supplement to SD BRIN
Role: one of the 2 Project Leaders for the AD Supplement

Pending Grant Support

- 23POST1018909 Bouska (PI) 1/1/2023 – 12/31/2024

AHA Postdoc Fellowship \$140,558
 Defining the mechanistic role of SBK2 in proteotoxic cardiomyopathy progression
 Role: Mentor/Sponsor

23PRE1023108 Cai (PI) 1/1/2023 – 12/31/2024
 AHA Predoc Fellowship \$65,106
 JAK1 inhibition protects against cardiac proteotoxicity
 Role: Mentor/Sponsor

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 Genetic Inhibition of Proteasomal Function in the Heart. Role: Sponsor and Primary Mentor		\$100,000 (total cost)
Postdoctoral fellowship AHA Greater Midwest Affiliate Physiological Significance of COP9 Signalosome in Adult Hearts. Role: Sponsor and Primary Mentor	Su (PI)	7/1/2006 – 6/30/2008 \$100,000 (total cost)
Reference # 0815571G AHA Predoctoral Fellowship Autophagy is activated by and compensates for proteasome malfunction in desminopathy Role: Sponsor and Primary Mentor	Q. Zheng (PI)	7/1/2008-6/30/2010 \$52,000 (total cost)
11PRE5730009 AHA Predoctoral Fellowship The Role of PKG in the Stimulation of the UPS by the Muscarinic 2 Receptor Role: Sponsor and Primary Mentor	Ranek (PI)	1/1/2011-12/31/2012 \$52,000 (total cost)
11SDG6960011 AHA Scientist Development Grant (National Center) The Ubiquitin Proteasome System in Diabetic Cardiomyopathy Role: Collaborator and Mentor	Su (PI)	07/01/2011-06/30/2015 \$280,000 (total direct)
1 F32 HL122045-01 NIH National Research Service Award (Postdoc Fellowship) Direct proteasomal enhancement contributes to PKG-triggered cardioprotection Role: Sponsor and Primary Mentor; <i>(Terminated on 8/2015 upon the PI's matriculation to medical school)</i>	Terpstra (PI)	07/01/2014 – 6/30/2017 \$162,000 (total direct)
16UFEL29640003 AHA Undergraduate Student Research Program Effect of Neddylation Inhibition on Autophagic Flux in Cardiomyocytes Role: Sponsor and Primary Mentor	Reihe (PI)	06/01/2016 – 8/31/2016 \$4000 (scholarship)
16PRE27790059 AHA Predoctoral Fellowship PDE1 inhibition improves cardiac protein quality control Role: Sponsor and Primary Mentor	Zhang (PI) Wang (Sponsor)	01/01/2016 – 12/31/2017 \$52,000 (total direct)
R01 HL085629-01~13 NIH/NHLBI The COP9 Signalosome in the Heart Role: PI	Wang	7/1/06 - 6/30/21 \$4,684,110 (total cost)
R01 HL131667-04 NIH/NHLBI	Cui, Wang (Contact)	4/1/17 - 3/31/22 \$1,414,250 (total cost)

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

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)

CONTRIBUTION TO SCIENCE

1. 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 begun to attract a broader spectrum of cell biologists until mid-1990s. The attention to the UPS from general biomedical scientists outside the cell biology field was likely drawn by the award of a 2004 Nobel Prize 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 been working on the UPS in the heart since 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, although changes in protein degradation could 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 have been distributed to researchers around the world and also 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 proteolytic 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. These publications have prompted investigations into cardiac pathogenic role of UPS dysfunction.
 - a. Chen Q, Liu JB, Horak KM, Zheng H, Kumarapeli AR, Li J, Li F, Gerdes AM, Wawrousek EF, **Wang X**. Intracellular amyloidosis impairs proteolytic function of proteasomes in cardiomyocytes by compromising substrate uptake. *Circ Res*. 2005; 97(10):1018-26. PMID: [16210548](#).
 - b. 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](#).
 - c. Liu J, Chen Q, Huang W, Horak KM, Zheng H, Mestral R, **Wang X**. Impairment of the ubiquitin-proteasome system in desminopathy mouse hearts. *FASEB J*. 2006; 20(2):362-4. PMID: [16371426](#).
 - d. 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. PMID: [PMC5316366](#).
2. Demonstration of the necessity of proteasome functional insufficiency (PFI) and inadequate ubiquitination-proteasome coupling in pathogenesis. We have established that PFI plays an essential pathogenic role in proteinopathy and I/R injury, as well as pressure overload right heart failure and diabetic cardiomyopathy (by collaboration). Although UPS malfunction had been 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 proteinopathy and I/R injury in mice. Our discovery that PA28 α overexpression enhances proteasome function, which identifies the 1st measure to achieve

proteasome gain-of-function, allowing us to generate the first animal model with forced proteasome function enhancement. We also created the first cardiomyocyte-restricted proteasome inhibition (CR-PsmI) and ubiquitination-proteasome uncoupling mouse models. These unique genetic models are essential to, and have remarkably facilitated, defining the pathophysiological significance of cardiac UPS malfunction. Using these tools, 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 also strongly indicative of improving proteasome function as a potentially novel therapeutic strategy for a large subset of heart diseases, providing compelling rationale for studies on the regulation of the UPS in the heart.

- 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](#).

3. Discovery of novel mechanisms by which proteasome function is regulated and identification of new strategies to prime or activate the proteasome. We discovered that cGMP-dependent kinase (PKG) positively regulate proteasome function in cardiomyocytes, PKG activation by either genetic or pharmacological (e.g., PDE5 inhibition) means promotes proteasome-dependent degradation of a surrogate and a bona fide misfolded protein in cardiomyocytes, and PDE5 inhibition by sildenafil reduces misfolded protein abundance and aggregation and slows sown disease progression in a well-established mouse model of cardiac proteinopathy, which represents the first demonstration that proteasome function can be pharmacologically enhanced to treat disease. Our discovery that muscarinic receptor 2 activation enhances cardiac proteasomal function in a PKG dependent manner was the first to unveil the physiological requirement of kinase-elicited proteasome activation. More recently, we demonstrated duo-activation of PKA and PKG by PDE1 inhibition confers striking therapeutic benefit in a mouse model of proteinopathy-based HFpEF. These findings also demonstrate the feasibility to use pharmacological method to enhance proteasomal degradation of misfolded proteins and thereby improve PQC in the heart.

- a. 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](#).
- b. 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: [PMC3761383](#).
- c. 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](#).

- d. **Wang X** and Wang H. Priming the proteasome to protect against proteotoxicity. *Trends in Molecular Medicine*. 25 March 2020 (Online First); DOI:<https://doi.org/10.1016/j.molmed.2020.02.007>. (PMC in progress).
4. Elucidation of physiological roles of the COP9 signalosome (CSN) in the heart and liver. Ub ligases or E3s confer substrate specificity and catalyze the Ub ligation to substrates, the final and rate-limiting step in ubiquitination. 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 thru COPS8) functions as a deneddylase for cullins, indispensable to CRLs catalytic dynamics. The CSN was rarely studied for its role in a terminally differentiated organ of vertebrates. Through cardiac targeting the Cops8 gene, we demonstrate that COPS8/CSN is required for cardiomyocyte survival and functioning, COPS8/CSN regulates not only the UPS but also the autophagic-lysosomal system (ALP), the latter was not known before our discovery that COPS8/CSN is required for autophagosome fusion with lysosomes. More recently, our studies reveal 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](https://pubmed.ncbi.nlm.nih.gov/32444444/).
- 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](https://pubmed.ncbi.nlm.nih.gov/26144444/).
- c. Su H, Li F, Ranek MJ, Wei N, **Wang X**. COP9 signalosome regulates autophagosome maturation. *Circulation*. 2011; 124(19):2117-28. [PMCID: PMC3211066](https://pubmed.ncbi.nlm.nih.gov/21111111/).
- 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](https://pubmed.ncbi.nlm.nih.gov/20111111/).
5. Dissecting the crosstalk between cardiac 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 including for example ischemic heart disease, some of the familial cardiomyopathies, and even pressure overload 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](https://pubmed.ncbi.nlm.nih.gov/3416491/)

- 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](https://pubmed.ncbi.nlm.nih.gov/37679777/).
- c. Zheng Q, Su H, Ranek MJ, **Wang X**. Autophagy and p62 in cardiac proteinopathy. *Circ Res*. 2011; 109(3):296-308. PMCID: [PMC3142307](https://pubmed.ncbi.nlm.nih.gov/3142307/).

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