

**CURRICULUM VITAE**

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

**NICKNAME:** “X-J” Wang

**PLACE OF BIRTH:** P. R. China

**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

**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

AHA Postdoctoral Fellowship project title: Dissecting Desmin-related Cardiomyopathy with Mouse Transgenesis.

**ACADEMIC/ADMINISTRATIVE APPOINTMENTS**

December 2008 – 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

September 2006 – November 2008

Professor and Co-Director  
The MD/PhD Program  
Sanford School of Medicine  
University of South Dakota  
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 (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)  
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)

### **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 Excellency (ACRE)/Chinese American Heart Association (CNAHA), lifetime member

2005- American Physiological Society (APS)

### **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-present Awards Committee, APS Cardiovascular Section

2019- Chair, Awards Committee, APS Cardiovascular Section

### **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  
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  
Oncotarget  
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	<i>International Journal of Physiology, Pathophysiology and Pharmacology</i>
2009-present	<i>American Journal of Translational Research</i>
2009-2010	Guest Editor for a Spotlight Issue on “The Ubiquitin-Proteasome Pathway in Cardiovascular Disease” for <i>Cardiovascular Research</i>
2011-present	Associate Editor-in-Chief, <i>American Journal of Cardiovascular Disease</i>
2012-present	<i>American Journal of Physiology- Heart &amp; Circulatory Physiology</i>
2012-present	Review Editor for <i>Frontiers in Clinical and Translational Physiology</i>
2013-2019	Review Editor for <i>Frontiers in Striated Muscle Physiology</i>
2013-2017	<i>Circulation Research</i>
2019 – present	Associate Editor for <i>Frontiers in Striated Muscle Physiology</i>
2020 – present	<i>Journal of Molecular and Cellular Cardiology</i>

## C. NATIONAL/INTERNATIONAL COMMITTEES

2003-present	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-present	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

### **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 <i>Grant and Scientific Writing</i> , 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. J Scott Pattison
2016-present	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.

### **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- Food Server, USD Lee Medical Building Annual Welcome Table Christmas Dinner

**TEACHING AND ADVISING****A. COURSES TAUGHT**

1. ANAT 511	<b><i>Gross Anatomy</i></b>	USD School of Medicine and Health Sciences
2. ANAT 521	<b><i>Microanatomy</i></b>	USD School of Medicine and Health Sciences
3. BIOCHEM	<b><i>Medical Biochemistry</i></b>	USD School of Medicine
4. PHPH 792	<b><i>Genetic Approaches</i></b>	USD Graduate School ( <b>Course Director</b> )
5. CPHD 740	<b><i>Protein Quality Control</i></b>	USD Graduate School ( <b>Course Director</b> )
6. BIOC 798	<b><i>Heat Shock Proteins</i></b>	USD Graduate School
7. PHPH 728	<b><i>Signal Transduction</i></b>	USD Graduate School
8. CPHD 788	<b><i>Res Basic Biomed Sci</i></b>	USD Graduate School
9. CPHD 898	<b><i>Thesis Research</i></b>	USD Graduate School
10. CPHD 620	<b><i>Foundations of Cardiovasc. Sci.</i></b>	USD Graduate School ( <b>Course Director</b> )
11. CPHD 792	<b><i>Heat Shock Proteins and Dis.</i></b>	USD Graduate School
12. CPHD 700	<b><i>Grant Writing</i></b>	USD Graduate School

**B. GRADUATE STUDENTS MENTORING**

## 1. Served as the Primary Mentor

<b>Graduate student names</b>	<b>Degree obtained (pursued)</b>	<b>Dates</b>	<b>Current positions</b>
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	Assistant 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	Medical Resident of Interfaith Medical Center, New York, NY.
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.
Liuqing Yang, BS, MS	PhD	8/22/2017 -	
Samiksha Giri, BA	PhD	8/22/2017-	
Megan T. Lewno, BA	PhD	8/22/2019-	

## 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 - Xing Liu, PhD, Assistant Professor, Department of Biochemistry, Purdue University, West Lafayette, IN

## 2. List of Postdoctoral Trainees

<b>Name of trainees</b>	<b>Training period</b>	<b>Current position</b>
Quanhai Chen, MD	1/2003 - 11/2005	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 <sup>th</sup> 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, Dept. of Anatomy, Wuhan University College of Basic Biomedical Sciences, Wuhan, Hubei, China
Yihao Tian, MD, PhD	3/22/2012 – 3/31/2014	Assistant 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	Postdoctoral Research Associate, Purdue University, Indiana <abdulla6@purdue.edu>
Penglong Wu, MD, PhD	8/3/2017-pres.	

## 3. List of Visiting Scientists

<b>Name &amp; Degrees</b>	<b>Training period</b>	<b>Parent Institution</b>
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, 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

## 5. Undergraduate Student Researchers

<b>Name of trainees</b>	<b>School attended</b>	<b>Distinction</b>	<b>Training period</b>

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

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- 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 Lewno, BS, Research Associate I and II.
- 2018- Jack Sternberg, BS, Research Associate I.

#### 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 4<sup>th</sup> 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 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 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 1<sup>st</sup> 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 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 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 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.

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.

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 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,

- 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 Univeristy 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. “Neddylolation/Deneddylolation, 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



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.

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](https://virtual.keystonesymposia.org/ks/live/290/page/1580)”, 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”, 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>.

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

120. “Measurement of regional myocardial blood flow with unlabeled microspheres and Coulter Channelyzer” at University of South Dakota School of Medicine, Vermillion, SD. May, 1996.
121. “Dissecting desmin-related cardiomyopathy with mouse transgenesis”; Division of Pediatric Cardiology, Children’s Hospital, Cincinnati, OH, February 7, 2000.
122. “Ubiquitin-Proteasome System and Diseases”, Division of Basic Biomedical Sciences, University of South Dakota School of Medicine, Vermillion, SD, September 17, 2002.
123. “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.
124. “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.
125. “Targeted proteolysis in conformational disease”; Faculty Seminar Series, Division of Basic Biomedical Sciences, USD Sanford School of Medicine, October 28, 2008.
126. “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.
127. “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.
128. “Can we boost cardiac proteasomes by stimulating PKG?” The 2nd Annual PQCD Symposium, Deadwood, SD, USA. June 14, 2012.
129. “The Ubiquitin-Proteasome System in Cardiac Pathogenesis: Beyond the Proteasome”, Faculty Seminar Series, USD Sanford School of Medicine, November 30, 2017.
130. “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.

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 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 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.

## **BIBLIOGRAPHY**

### **NCBI Bibliography Link:**

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

**ResearchGate:** [https://www.researchgate.net/profile/Xuejun\\_Wang3](https://www.researchgate.net/profile/Xuejun_Wang3)

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

### **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 erythralgia. *Natl Med J China* 1988; 68(5): 292-293.
2. **Wang X** and Dong C. A preliminary study on the relationship between epidemic erythralgia 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.
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 Academiae 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 Academiae 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 Academiae 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<sup>+</sup> on the estimations of EHF prognosis. *Acta Academiae Medicinae Hubei* 1991; 12(1): 5-7.
13. **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 Academiae 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**

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44. Huabo Su, Jie Li, Suchithra Menon, Kathleen Horak, Faqian Li, Ning Wei, Xuejun Wang. Perinatal Cardiomyocyte-Restricted Knockout of the COP9 Signalosome Subunit 8 Gene Compromises Proteasome Proteolytic Function, Triggers Necrosis, and Causes Heart Failure in Mice. Circ Res 2008; 103:e35-e70.
45. Kumarapeli AR, Tang M, Zheng H, Horak KM, Li M, Molkenin JD, Wang X. Protein Quality Control Inadequacy Activates NFAT Signaling in Cardiomyocytes. Circulation 2008; 118: S\_393. Oral presentation, AHA Scientific Sessions 2008; Nov 8-12, New Orleans, LA.
46. Hanqiao Zheng; Mingxin Tang; Asangi R. K. Kumarapeli; Kathleen M. Horak; Xuejun Wang. Doxycycline Attenuates Protein Aggregation in Cardiomyocytes and Improves Survival of a Mouse Model of Cardiac Conformational Disease. Poster presentation at ISHR North American Section Meeting: New Discoveries for Prevention and Treatment of Heart Disease May 26-29, 2009 Baltimore, MD.
47. Ranek MJ, Wang X. Activation of muscarinic receptor 2 stimulates proteasome function in cardiomyocytes. Experimental Biology Meeting April 24-28, 2010 Anaheim, CA.
48. Ranek MJ, Wang X. Stimulation of adrenergic receptors regulates proteasome function in cardiomyocytes. Experimental Biology Meeting April 24-28, 2010 Anaheim, CA.
49. Davis F, Predmore J, Wang P, Li J, Su H, Converso K, Allen A, Jones R, Powell SR, Wang X, Day SM. Activation of the ubiquitin proteasome system after myocardial

infraction. Presented at the AHA Scientific Sessions, November 2010, Chicago, IL. *Circulation* 2010; 122(21): A18730.

50. Li J, Horak KM, Su H, Sanbe A, Robbins J, Wang X. Enhancement of Proteasomal Function Protects Against Proteinopathy and Myocardial Ischemia-Reperfusion Injury in Mice. AHA Basic Cardiovascular Sciences 2011 Scientific Sessions, New Orleans, LA July 18-21, 2011
51. Tian Z, Zheng H, Wang X. Genetically Induced Moderate Inhibition of the Proteasome in Cardiomyocytes Exacerbates Myocardial Ischemia-Reperfusion Injury in Mice (Poster 271). AHA Basic Cardiovascular Sciences 2011 Scientific Sessions, New Orleans, LA July 18-21, 2011
52. Wang C, Tian Z, Zheng Q, Su H, Li J, Wang X. Interplay Between the Ubiquitin-Proteasome System and Autophagy in the Heart. AHA Basic Cardiovascular Sciences 2011 Scientific Sessions, New Orleans, LA July 18-21, 2011
53. Su H, Tian Z, Wang C, Said S, Ranek MJ, Wang X. Impaired Autophagosome Removal in Cardiomyocytes Triggers Programmed Necrosis in Mouse Hearts. AHA Basic Cardiovascular Sciences 2011 Scientific Sessions, New Orleans, LA July 18-21, 2011
54. Zheng Q, Su H, Ranek MJ, Wang X. The Role of p62 in Cardiac Protein Quality Control. AHA Basic Cardiovascular Sciences 2011 Scientific Sessions, New Orleans, LA July 18-21, 2011
55. Su H, Li F, Ranek MJ, Wei N, Wang X. The COP9 Signalosome Regulates Autophagy. AHA Basic Cardiovascular Sciences 2011 Scientific Sessions, New Orleans, LA July 18-21, 2011
56. Ranek MJ, Wang X. Protein Kinase G Regulates the UPS in Cardiomyocytes. Presented at the Protein Degradation Pathways in Health and Diseases, San Diego, CA, USA, January 2012.
57. Ranek MJ, Martin D, Kost C, Wang X. Activation of Protein Kinase G Enhances Proteasome-Mediated Degradation of Misfolded Proteins. Presented at the AHA Basic Cardiovascular Sciences Scientific Sessions, New Orleans, LA, July 22-24, 2012.
58. Ranek MJ, Terpstra EJM, Li J, Wang X. Protein kinase G regulates proteasome-mediated degradation of misfolded proteins. the AHA Scientific Sessions, Los Angeles, CA. November 3-8, 2012
59. Su H., Li J., Wei N., Wang X. The COP9 signalosome subunit 8 hypomorphism impairs deneddylation and exacerbates desmin-related cardiomyopathy. Poster presentation at Experimental Biology 2013, April 20-24, Boston, MA, USA.
60. Ranek MJ, Terpstra EJM, Li J, Kass DA, Wang X. Protein kinase G positively regulates proteasome-mediated degradation of misfolded proteins. Presented at the AHA Basic Cardiovascular Sciences Scientific Sessions, Las Vegas, Nevada, July 22-25, 2013.

61. Terpstra EJM, Ranek MJ, Callegari E, Wang X. The Proteasome is a Target of Protein Kinase G. Presented at the AHA Scientific Sessions, Dallas TX, November 16-20, 2013.
62. Day S M, Yob J, Davis F, Wang P, Converso K L, Wang X, Powell, S R. Selective Inhibition of the Immunoproteasome Attenuates Adverse Left Ventricular Remodeling, Improves Cardiac Function, and Prevents Heart Failure After Myocardial Infarction. Presented at the AHA Scientific Sessions, Dallas TX, November 16-20, 2013.
63. Ranek MJ, Terpstra EJM, Li J, Kass DA, Wang X. Protein kinase G positively regulates proteasome-mediated degradation of misfolded proteins. Presented at the AHA Scientific Sessions, Dallas TX, November 16-20, 2013.
64. Tian Z, Wang C, Hu C, Tian Y, Liu J, Wang X. Autophagic-Lysosomal Inhibition Compromises Ubiquitin-1 Proteasome System Performance in a p62 Dependent Manner in Cardiomyocytes. Presented at the 35th International Society for Heart Research North American Section Meeting: "NOVEL STRATEGIES TO COMBAT HEART FAILURE", Miami Beach, Florida, May 12 -15, 2014
65. Hu, C., Wang, X., Wang, H., Tian, Y. Inadequate Coupling between Ubiquitination and the Proteasome is a Major Pathogenic Factor of Myocardial Ischemia/Reperfusion Injury. Presented at the The First Annual ACRE/APS Symposium, Las Vegas, NV. (2014, July 13).
66. Wang, X., Hu, C., Tian, Y., Wang, H. Inadequate Coupling between Ubiquitination and the Proteasome is a Major Pathogenic Factor of Myocardial Ischemia/Reperfusion Injury. Presented at the Basic Cardiovascular Sciences 2014 Scientific Sessions: Pathway to Cardiovascular Therapeutics, Las Vegas, NV. (2014, July 16).
67. Wang, C., Jahn, A., Su, H., Wang, X. Duo-impairment of the Ubiquitin-Proteasome System and Autophagy by Ablation of COP9 Signalosome Subunit 8 Activates a Programmed Necrosis Pathway Mediated by RIP1-RIP3 Kinases but not Cyclophilin D-regulated Mitochondrial Membrane Permeability . Presented at the Basic Cardiovascular Sciences 2014 Scientific Sessions: Pathway to Cardiovascular Therapeutics, Las Vegas, NV. (2014, July 16).
68. Su, H., Li, J., Zhang, H., Wei, N., Wang, X. The COP9 signalosome controls the degradation of cytosolic misfolded proteins and protects against cardiac proteotoxicity. Presented at the 36th International Society for Heart Research North American Section (ISHR-NAS) Meeting, Seattle, WA. (June 8, 2015)
69. Li, J., Ma, W., Li, H., Hou, N. Wang, X., Kim I-M., Li, F., Su, H. NEDD8 ultimate buster-1 long (NUB1L) protein regulates atypical neddylation and protects against myocardial ischemia-reperfusion injury. Presented at the AHA Basic Cardiovascular Sciences 2015 Scientific Sessions: Pathway to Cardiovascular Therapeutics, New Orleans, LA. July 13-16, 2015.
70. Wang, X., Terpstra, E.J., Callegari, E., Hu, C., Zhang, H. Wang, X. Proteasome priming by protein kinase G protects against myocardial ischemia-reperfusion injury. Presented

at the AHA Basic Cardiovascular Sciences 2015 Scientific Sessions: Pathway to Cardiovascular Therapeutics, New Orleans, LA. July 13-16, 2015.

71. Wang, X., Wang, C., Terpstra, E.J., Wang, Y., Wang, X. Activation of the p38 branch of mitogen activated protein kinase pathway stimulates proteasome proteolytic function. Presented at the AHA Basic Cardiovascular Sciences 2015 Scientific Sessions: Pathway to Cardiovascular Therapeutics, New Orleans, LA. July 13-16, 2015.
72. Wang C, Li J, Su H, Xiao P, Wang X. COPS8 inhibits cardiomyocyte necroptosis in mouse hearts via suppressing the RIPK1-RIPK3 pathway. Presented at American Heart Association (AHA) Scientific Sessions, Orlando, FL, November 9; 2015.
73. Zhang, Hanming, Wang, Xuejun. PDE1 inhibition improves cardiac protein quality control. Presented at the 3rd ACRE/APS symposium, Phoenix, AZ. July 17, 2016.
74. Wu, Penglong, Zhu, Wei, Li, Jinbo, Wang, Xuejun. Cathepsin D haploinsufficiency exacerbates post-MI cardiac remodeling and malfunction by impairing autophagosome removal. Presented at the 3rd ACRE/APS symposium, Phoenix, AZ. July 17, 2016.
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.
76. Wu, Penglong, Zhu, Wei, Li, Jinbo, **Wang, Xuejun**. Cathepsin D haploinsufficiency exacerbates post-MI cardiac remodeling and malfunction by impairing autophagosome removal. Presented at the AHA Basic Cardiovascular Sciences 2016 Scientific Sessions: Pathways to Cardiovascular Therapeutics, Phoenix, AZ, July 19, 2016.
77. Abdullah, Ammara; Eyeter, Kathleen M; Bjordahl, Travis; Xiao, Peng; Zeng, Erliang; **Wang, Xuejun**. Cardiac transcriptome analysis reveals a critical role for the COP9 signalosome in transcriptional regulation of the substrate receptors of cullin-RING ligases in mice. Presented at The 12th International Conference on Pathways, Networks, and Systems Medicine, Aegean Conference, Crete, Greece, June 29 ~ Jul 4, 2017.
78. **Zhang, Hanming**; Wang, Xuejun. Inhibition of phosphodiesterase 1 confers striking therapeutic benefit to HFpEF in mice. Presented at the AHA Basic Cardiovascular Sciences 2017 Scientific Sessions. (New Investigator Travel Award), Portland, OR, July 10-13, 2017.
79. **Zhang, Hanming**, Rekhater, Mark D., Wang, Xuejun. Inhibition of Type 1 Phosphodiesterase Confers Therapeutic Benefit to Proteinopathy-based HFpEF in Mice. Presented at the 2018 Experimental Biology Meeting, San Diego, CA. (April 25, 2018)
80. **Wu, Penglong**, Wang, Yibin, Wang, Xuejun. EXCESSIVE BETA-ADRENERGIC RECEPTOR STIMULATION INDUCES CARDIOMYOCYTE NECROPTOSIS VIA A RIP3-DEPENDENT PATHWAY. Presented at the 2018 Experimental Biology Meeting, San Diego, CA. (April 22, 2018)
81. **Wang, Xuejun**, Wu, Penglong, Parajuli, Nirmal, Pan, Bo, Lewno, Megan, Liu, Jinbao. Proteasome phosphorylation and activation by PKA protects against cardiac

remodeling in mice subjected to myocardial infarction. Presented at the 2019 Experimental Biology meeting, Orlando, FL. (April 9, 2019)

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. 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 AAMP 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.

## **GRANT/CONTRACT SUPPORT**

### **Current Grant Support**

R01 HL085629-13	Wang (PI)	1.8 Cal.	7/1/06 - 6/30/21
NIH/NHLBI			(no cost extension)

The COP9 Signalosome in the Heart

The goal of this project is to elucidate the (patho)physiological significance of the COP9 signalosome in the heart with the emphasis on its regulation on the ubiquitin proteasome system in early postnatal hearts.

Role: PI

R01 HL131667-04 Cui, Wang (Contact) 1.0 Cal. 4/1/17 - 3/31/21  
 NIH/NHLBI \$250,000  
 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)

RO1 HL072166-14 Wang (PI) 1.8 Cal. 7/1/03 – 6/30/20  
 Ubiquitin Receptors and Proteotoxicity (No cost extension)  
 This study investigates the pathogenic roles of uncoupling between ubiquitination and proteasomal degradation in cardiac proteinopathy and myocardial ischemia-reperfusion injury in mice.  
 Role: PI (A1 competitive renewal received 10.0% rank from IRG on Feb 20, 2020)

### **Pending**

2 R01 HL072166-15A1 Wang (PI) 2.4 Cal. 7/1/20 – 6/30/24  
 NIH/NHLBI \$343,921  
 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 cardiac proteinopathy.  
 Role: PI (Scored a top 10% rank, NIH intends to fund).

1 R01 HL153614-01 Wang (PI) 1.8 Cal. 7/1/20-6/30/24  
 NIH/NHLBI \$250,000  
 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 (Scored a top 3% rank, NIH intends to fund)

20TPA35490091 Wang (PI) 0.5 Cal. 7/1/20-6/30/23  
 American Heart Association (AHA) \$90,909  
 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 (Scored top 0.22% rank)

1 R35 HL155674-01 Wang (PI) 6.0 Cal. 12/1/20 – 11/30/27  
 NIH/NHLBI \$600,000  
 Phosphoregulation of Cardiac Proteasomes  
 The goal of this R35 research program is to study the molecular biology, physiology, pathophysiology, and pharmacology of the regulation of cardiac proteasomes by key kinases such as PKA and PKG.  
 Role: PI

1 R41 HL152919-01A1 Shaffer (Contact); Wang 1.2 Cal. 12/1/20 -11/30/21  
 NIH/NHLBI \$320,198  
 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 (Received a priority score of 23 from study section on July 16; current NHLBI pay zone for R41: 10~40)

1 R01 AG072510-01 Wang, H (Contact); Wang, X 1.2 Cal. 04/01/21 – 3/31/26  
NIH/NIA \$300,000

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

The goals of this project are to determine the role of proteasome phosphoregulation by protein kinase A in brain aging and Alzheimer's disease as well as the contribution of RPN6-Ser14 phosphorylation to the protective effect of PDE4 inhibition on Alzheimer's disease.

Role: MPI

### **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)
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;		
<i>(Terminated on 8/2015 upon the PI's matriculation to medical school)</i>		
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		



## CONTRIBUTION TO SCIENCE

1. Discovery of ubiquitin (Ub)-proteasome system (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 most likely drawn by the award of a 2004 Nobel Prize to 3 scientists for their contributions to the discovery of the UPS. Regarded as a pioneer for studying UPS dysfunction in cardiac pathogenesis, my lab has been working on the UPS in the heart 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, 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 UPS functional insufficiency. 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 Nov 11;97(10):1018-26. PubMed 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 Dec;19(14):2051-3. PubMed PMID: [16188962](#).
  - c. Liu J, Chen Q, Huang W, Horak KM, Zheng H, Mestrlil R, Wang X. Impairment of the ubiquitin-proteasome system in desminopathy mouse hearts. *FASEB J*. 2006 Feb;20(2):362-4. PubMed PMID: [16371426](#).
  - d. Liu J, Tang M, Mestrlil R, Wang X. Aberrant protein aggregation is essential for a mutant desmin to impair the proteolytic function of the ubiquitin-proteasome system in cardiomyocytes. *J Mol Cell Cardiol*. 2006 Apr;40(4):451-4. PubMed PMID: [16481005](#).
2. Demonstration of the necessity of proteasome functional insufficiency (PFI) in pathogenesis. We have established that PFI plays an essential pathogenic role in proteinopathy and I/R injury, as well as diabetic cardiomyopathy and pressure overload right heart failure (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 proteasome enhancement protects against proteinopathy and I/R injury in mice. What enabled this study is our discovery that PA28 $\alpha$  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) mouse model. These unique genetic models are essential to, and have remarkably facilitated, defining the pathophysiological significance of

cardiac proteasome dysfunction. Using these tools, we have established a major pathogenic role for PFI in I/R injury, pressure overloaded cardiac maladaptive remodeling, and diabetic cardiomyopathy. These studies also demonstrate that improving proteasome function can be 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 Sep 11. pii: 98287. doi: [10.1172/JCI98287](https://doi.org/10.1172/JCI98287) [Epub ahead of print] PMID: 30204128
  - b. Li J, Ma W, Yue G, Johnson J, Kim I-M, Weintraub N, Wang X, and Su H. Cardiac proteasome functional insufficiency plays a pathogenic role in diabetic cardiomyopathy. *J Mol Cell Cardiol* 2016 102:53-60. PubMed PMID: 27913284; NIHMS ID: [NIHMS837534](https://doi.org/10.1016/j.yjmcc.2016.11.013) DOI: <http://dx.doi.org/10.1016/j.yjmcc.2016.11.013>
  - 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 Aug 17;111(5):532-42. PubMed PMID: [22740087](https://pubmed.ncbi.nlm.nih.gov/22740087/); PubMed Central PMCID: [PMC3426260](https://pubmed.ncbi.nlm.nih.gov/PMC3426260/).
  - d. Li J, Powell SR, Wang X. Enhancement of proteasome function by PA28alpha overexpression protects against oxidative stress. *FASEB J*. 2011 Mar;25(3):883-93. PubMed PMID: [21098724](https://pubmed.ncbi.nlm.nih.gov/21098724/); PubMed Central PMCID: [PMC3042837](https://pubmed.ncbi.nlm.nih.gov/PMC3042837/).
  - e. 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 Sep;121(9):3689-700. PubMed PMID: [21841311](https://pubmed.ncbi.nlm.nih.gov/21841311/); PubMed Central PMCID: [PMC3163952](https://pubmed.ncbi.nlm.nih.gov/PMC3163952/).
3. Discovery of novel mechanisms by which proteasome function is regulated and identification of new strategies to prime 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 increases proteasome activities and 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 down disease progression in a well-established mouse model of cardiac proteinopathy. Muscarinic receptor activation can enhance cardiac proteasomal function in a PKG dependent manner. These findings demonstrate the feasibility to use pharmacological method to enhance proteasomal degradation of misfolded proteins and thereby improve PQC in the heart. Duo-activation of PKG and PKA by PDE1 inhibition (IC86430) increases proteasome activities and improves UPS performance in vitro and in vivo and protects against proteinopathy-based heart failure with preserved ejection fraction (HFpEF) in mice.
- 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 Dec;20(12):1372-85. PubMed PMID: [20805844](https://pubmed.ncbi.nlm.nih.gov/20805844/); PubMed Central PMCID: [PMC2996470](https://pubmed.ncbi.nlm.nih.gov/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 Jul 23;128(4):365-76. PubMed PMID: [23770744](https://pubmed.ncbi.nlm.nih.gov/23770744/); PubMed Central PMCID: [PMC3761383](https://pubmed.ncbi.nlm.nih.gov/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. *Science Advances* 2019 May 22; 5(5):eaaw5870. DOI: [10.1126/sciadv.aaw5870](https://doi.org/10.1126/sciadv.aaw5870) PMID: 31131329. PMCID: [PMC6531002](https://pubmed.ncbi.nlm.nih.gov/PMC6531002/).
  - d. **Wang X\***, Wang H. Priming the proteasome to protect against proteotoxicity. *Trends in Molecular Medicine*. 2020 March 25, DOI: [10.1016/j.molmed.2020.02.007](https://doi.org/10.1016/j.molmed.2020.02.007).
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. Additionally, our study on Cops8 hypomorphism reveals for the first time that CRLs contribute to degradation of misfolded cytosolic proteins.
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    - b. Su H, Li F, Ranek MJ, Wei N, Wang X. COP9 signalosome regulates autophagosome maturation. *Circulation*. 2011 Nov 8;124(19):2117-28. PubMed PMID: [21986281](https://pubmed.ncbi.nlm.nih.gov/21986281/); PubMed Central PMCID: [PMC3211066](https://pubmed.ncbi.nlm.nih.gov/PMC3211066/).
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  5. Dissecting the crosstalk between cardiac UPS and ALP pathways in cardiac PQC. We have elucidated a pivotal role of the calcineurin-TFEB-p62 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. We are the first to report the upregulation of p62 at both transcript and protein levels in proteinopathic hearts that 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. 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.

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