CURRICULUM VITAE

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

PLACE OF BIRTH: Hubei, P.R. China

CITIZENSHIP: U.S.A.

AFFILIATION: Division of Basic Biomedical Sciences
Sanford School of Medicine
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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 (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 Hypertrophy and 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)
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)

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), 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 Award Committee, APS Cardiovascular Section

CONSULTING POSITIONS

A. PEER REVIER

American Journal of Pathology
American Journal of Physiology
Antioxidants & Redox Signaling
Archives of Biochemistry and Biophysics
Autophagy
BBA-Gene Regulatory Mechanisms
BBA-Molecular Basis of Disease
BBA-Molecular Cell Research
BioMed Central-Cardiovascular Disorders
Biomolecules
Brain Research Bulletin
Cardiovascular Research
Cardiovascular Toxicology
Cell Motility and Cytoskeleton
Circulation
Circulation: Heart Failure
Clinica Chemica Acta
Comprehensive Physiology
Coronary Artery Disease
Current Molecular Medicine
Developmental Biology

EBiomedicine
eLife
European Journal of Heart Failure
European Pharmacology Research
Experimental Cell Research
Free Radical Biology and Medicine
Frontiers in Physiology
Growth Hormone and IGF Research
Human Molecular Genetics
Hypertension
International Journal of Medicine
International Journal of Molecular Medicine
International Journal of Obesity
International Journal of Nanomedicine
Journal of American College of Cardiology
Journal of Cardiac Failure
Journal of Cardiovascular Pharmacology
Journal of Cell Science
Journal of Cellular and Molecular Medicine
Journal of Clinical Investigation
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
Oncotarget
Pharmacology Research
PLoS Genetics
PLoS One
Protein and Cell
Scientific Reports
Trends in Cardiovascular 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 Physiology- Heart & Circulatory Physiology*
2012-present	*Frontiers in Clinical and Translational Physiology*
2013-present	Review Editor for *Frontiers in Striated Muscle Physiology*
2013-2017	*Circulation Research*

C. NATIONAL/INTERNATIONAL COMMITTEES

2003-present	External Expert Grant Reviewer 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 -	AHA National Center Cardiac Biol. & Regulation – Basic Science Study Section; chartered 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 Erkine
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-present	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-present	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 School of Medicine
2016-present	The MD/PhD Admissions Standing Committee

COMMUNITY SERVICE

2002-2006	Judge, Sioux Valley Hospital & Health System Annual Quality Fair
2003	Volunteer Speaker, AHA Sioux Falls Regional Gala
2015-	Food Server, USD Lee Medical Building Annual Welcome Table Christmas Dinner

TEACHING AND ADVISING

A. COURSES TAUGHT

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

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	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	Research Scientist, Medical College of Georgia, Georgia Regents University, Augusta, GA
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	Postdoctoral fellow, 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 - present	
Penglong Wu, BM, MS	Visiting PhD Student from Shanghai Jiao	6/22/2015 – 6/21/2017	Postdoctoral fellow, Guangzhou Medical University and USD Sanford

	Tong University		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-	

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-present 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 tenure-track Assistant Professor at Medical College of Georgia Augusta University, Augusta, Georgia

2009-2015 H. Wang, PhD, Assistant Professor; currently R01-funded Tenured Associate Professor at USD Sanford School of Medicine, Vermillion, SD

2011-2016 K. Rezvani, PhD, Assistant Professor; currently Tenured Associate Professor at USD Sanford School of Medicine, Vermillion, SD

2011- J.S. Pattison, PhD, Assistant Professor

2. List of Postdoctoral Trainees

Name of trainees	**Training period**	**Current position**
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 -	Professor and Vice President, Guangzhou

	10/2005	Medical University, Guangzhou, Guangdong, China
Huabo Su, PhD	11/2004 – 6/2008 7/2008 – 7/2012	Assistant Professor (tenure-track), Vascular Biology Center and Department of Pharmacology, Georgia Regents University, Medical College of Georgia, Augusta, GA, USA
Daoxiong Lei, MD, PhD	11/2005-10/2008	Professor, Tianjin 4th Hospital, Tianjin, China
Youn-Chul Ryu, PhD	9/2006 – 4/2009	Associate Professor, Jeju Natioanl 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	Research Scientist, Georgia Regents University, Medical College of Georgia Augusta, GA, USA
Zongwen Tian, 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	6/1/2012-11/21/2102	Postdoc 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 – pres.	
Peng Xiao, PhD	1/22/2015 – pres.	
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

Name & Degrees	**Training period**	**Parent Institution**
Changhua Wang, MD, PhD	1/2014 ~ 8/21/2015	Professor, 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, Inetrnal Medicine Resident, research rotation
2007 Marius Vulcan, USD medical student of Class 2010, summer research
2011, 2012 Sigurd E. Hartnett, USD MD/PhD program student, summer research
2015 Nickolas Pekas, USD MD/PhD student, summer research

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-
Tanner James Redlin	USD	Undergrad researcher	2016 Fall-
Taylor Grace Faw	USD	Undergrad researcher	2016 Fall-
Kasha Merie Shear	USD	Undergrad researcher	2016 Fall-

6. Undergraduate Honors Thesis Advised
   - 2008-2010 Blake Alberts, USD
   - 2008-2010 Morgan Hanson, USD
   - 2009-2011 Levi Froke, USD
   - 2014-2017 Casey A. Reihe, USD

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- Megan Lewno, 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 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 Taxes Health Science Center, San Antonio, TX, July 23, 2001.

16. "Ubiquitin-Proteasome System in Pathogenesis and Therapeutics"; Wuhan University

College of Basic Medical Sciences, Wuhan, Hubei, China, September 20, 2002.

17. "Ubiquitin-Proteasome System and Cardiovascular Diseases"; South Dakota State University College of Veterinary Science, Brookings, SD, October 4, 2002.

18. "Intermediate filaments and cardiac disease: establish causality"; Wuhan University College of Medicine, Wuhan, Hubei, China, Oct. 29, 2002.

19. "Ubiquitin-Proteasome System in Pathogenesis and Therapeutics"; Guangzhou Medical College, Guangzhou, Guangdong, China, Nov. 1, 2002.

20. "Desmin filaments and cardiac diseases"; the VII Meeting of International Society for Heart Research: China Section, Guangzhou, China, November 1-5, 2002.

21. "Modulation of the ubiquitin-proteasome system by an alpha B-crystallin mutant"; The 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 Angelis, CA, April 18, 2006.

31. "The Ubiquitin-Proteasome System in Cardiac Remodeling and Failure"; Department of Molecular Genetics, University of Cincinnati, Cincinnati, OH May 2, 2006.

32. "Inadequate Protein Quality Control in Heart Failure". The Center for Translational Medicine, Jefferson Medical College, Philadelphia, PA, May 10, 2006.

33. "The Ubiquitin-Proteasome System in Cardiac Remodeling and Failure"; The Center of Cardiovascular Sciences, Albany Medical College, Albany, NY, May 12, 2006.

34. "The Ubiquitin-Proteasome System in Cardiac Remodeling and Failure"; Department of Pharmacology, Loyola University Medical Center, Maywood, IL, May 15, 2006.

35. "The COP9 Signalosome and Protein Quality Control", ZOMES IV: The 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 Angelis, CA, November 4, 2012.

75. "Proteasome dysfunction in cardiac pathogenesis"; Keystone Symposium on Cardiac Remodeling, Signaling, Matrix and Heart Function (D4-2013), Snowbird, UT, April 9, 2013.

76. "Interaction of ubiquitin proteasome system and autophagy in the heart"; Cardiac Seminars on Dynamics of Protein Degradation Machinery in Cardiac Function. AHA Scientific Sessions, Dallas, TX, November 18, 2013.

77. "Loss of Function of an Extraproteasomal Ubiquitin Receptor Ubiquilin1 in Cardiomyocytes Exacerbates Cardiac Proteotoxicity"; The 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 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 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.

Seminars Given in Employer Institutions

106. "Measurement of regional myocardial blood flow with unlabeled microspheres and Coulter Channelyzer" at University of South Dakota School of Medicine, Vermillion, SD. May, 1996.

107. "Dissecting desmin-related cardiomyopathy with mouse transgenesis"; Division of Pediatric Cardiology, Children's Hospital, Cincinnati, OH, February 7, 2000.

108. "Ubiquitin-Proteasome System and Diseases", Division of Basic Biomedical Sciences, University of South Dakota School of Medicine, Vermillion, SD, September 17, 2002.

109. "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.

110. "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.

111. "Targeted proteolysis in conformational disease"; Faculty Seminar Series, Division of Basic Biomedical Sciences, USD Sanford School of Medicine, October 28, 2008.

112. "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.

113. "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.

114. "Can we boost cardiac proteasomes by stimulating PKG?" The 2nd Annual PQCD Symposium, Deadwood, SD, USA. June 14, 2012.

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, scheduled for April 24, 2017.

BIBLIOGRAPHY

NCBI Bibiogrpahy Link:
http://www.ncbi.nlm.nih.gov/sites/myncbi/collections/public/1buzcylVbHr7_zlaKmmTxHiAy/?sort=date&direction=descending

ResearchGate: https://www.researchgate.net/profile/Xuejun_Wang3

A. ORIGINAL ARTICLES IN SCHOLARLY JOURNALS

(A) **In Peer-Reviewed Chinese Journals**

1. Dong C, **Wang X**, Tu S, and Deng G. Alterations of plasma coagulation and extremity blood flow in erythermalgia. ***Natl Med J China*** 1988; 68(5): 292-293.

2. **Wang X** and Dong C. A preliminary study on the relationship between epidemic erythermalgia and El Niño. ***Natl Med J China*** 1988; 68(5): 266-268.

3. **Wang X**, Dong C, and Xiang J. Effects of ribavirin on coagulation-anticoagulation process in patients with epidemic hemorrhagic fever. ***Natl Med J China*** 1988; 68(12):699-701.

4. Dong C, **Wang X**, Xiang J, and Cosgraff T. The kinetic alterations of coagulation, anticoagulation and fibrinolytic system of patients with epidemic hemorrhagic fever and their significance. ***Natl Med J China*** 1988; 68(12): 678-681.

5. Dong C and **Wang X**. The alterations of coagulation, fibrinolysis, kinin, and complement system in epidemic hemorrhagic fever with DIC and its clinical Value. ***Chinese J Pathophysiol*** 1989; 5(5): 285-288.

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

7. **Wang X**, Dong C, and Xiang J. Effects of ribavirin on hemorrhagic tendency and fatality rate of patients with epidemic hemorrhagic fever. ***Acta Academiniae Medicinae Hubei*** 1989; 10(3): 193-196.

8. **Wang X**, Dong C, and Ling H. The kinetic alterations of plasma prekallikrain and antithrombin 3 in rats following isoproterenol-induced myocardial infarction. ***Chinese J Pathophysiol*** 1990; 6(2): 100-103.

9. **Wang X**, Dong C, and Xiang J. Studies on the anion gap of epidemic hemorrhagic fever (I): The kinetic alterations of anion gap in EHF. ***Acta Academiniae Medicinae Hubei*** 1990; 11(12): 285-289.

10. Dong C, **Wang X**, and Xiang J. Studies on anion gap of epidemic hemorrhagic fever (II): The mechanism and clinical significance of the increase in anion gap in EHF. ***Acta Academiniae Medicinae Hubei*** 1990; 11(12): 289-293.

11. **Wang X**, Dong C, and Xiang J. Studies on anion gap of epidemic hemorrhagic fever (III): The mechanism and clinical significance of the decrease in anion gap in EHF. ***Acta Academiniae Medicinae Hubei*** 1991; 12(1): 1-4.

12. Dong C, **Wang X**, and Xiang J. Studies on the anion gap of epidemic hemorrhagic fever (IV): The significance of simultaneous changes in anion gap, urine volume, and serum concentration of Na+ on the estimations of EHF prognosis. ***Acta Academiniae Medicinae Hubei*** 1991; 12(1): 5-7.

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 Academiniae Medicinae Hubei*** 1991; 12(4): 299-303.

15. **Wang X**, Ouyang J, Liu J, and Dong C. A pathogenesis of isoproterenol-induced occlusion of cardiac microvasculature in rats. ***J Microcirculation*** 1992; 2(1):8-11.

16. Yu X, Dong C, Ouyang J, Li D, and **Wang X**. An experimental study on the protective modification of soybean phospholipid liposomes enclosed superoxide dismutase (SOD) on the membrane of ischemic and reperfused myocardium in rats. ***Chinese J Pathophysiol*** 1993; 9(7): 804.

17. Dong C, Chen X, Wang C, Zhong Y, and **Wang X**. Experimental studies of the effects of soybean phospholipid liposomes against the myocardial membrane injury by ischemia/reperfusion. ***Acta Academiae Medicinae Hubei*** 1993; 14(4): 323-329.

18. **Wang X** and Dong C. Studies on the anion gap of epidemic hemorrhagic fever: V. Effects of intravenous ribavirin therapy on the changes of anion gap of patients with EHF. ***Acta Academiae Medicinae Hubei*** 1994; 15(3):247-249.

19. Dong C, Yu X, and **Wang X**. Myocardial membrane injury of myocardial ischemia and lipoideamia in rats. ***Prog Biochem Biophys*** 1994; 21:347-350.

20. **Wang X**, Dong C, Tu S, Zhang Y, Ouyang J, and Liu Y. Effects of soybean phospholipids liposomes on the left ventricular function and infarct size of ischemic-reperfused hearts in rabbits. ***Chinese J Pathophysiol*** 1994; 10(6):583-585.

21. Huang W, Ma W-Z, and **Wang X**. Intercalated disc remodeling in a transgenic mouse model of desmin-related cardiomyopathy. ***Chin J Cardiol*** 2003; 31(11):859-864.

(B) **<u>In Peer-Reviewed English Journals</u>**

22. **Wang X**, Li F, Said S, Capasso JM, and Gerdes AM. Measurement of regional myocardial blood flow in rats by unlabeled microspheres and Coulter Channelyzer. ***Am J Physiol*** 1996; 271:H1656-1665.

23. Li F, **Wang X**, Capasso JM, and Gerdes AM. Rapid transition of cardiac myocytes from hyperplasia to hypertrophy during postnatal development. ***J Mol Cell Cardiol*** 1996; 28: 1737-1746.

24. Gerdes AM, Onodera T, **Wang XJ**, McCune SA, and Capasso JM. Myocyte remodeling during the progression to failure in rats with hypertension. ***Hypertension*** 1996; 28:609-614.

25. Li F, **Wang X**, Bunger PC, and Gerdes AM. Formation of binucleated myocytes in rat heart: I. role of actin-myosin contractile ring. ***J Mol Cell Cardiol*** 1997; 29:1541-1551.

26. Li F, **Wang X**, and Gerdes AM. Formation of binucleated myocytes in rat heart: II. Cytoskeletal organization. ***J Mol Cell Cardiol*** 1997; 29:1553-1565.

27. **Wang X**, Li F, and Gerdes AM. Chronic pressure overload cardiac hypertrophy and failure in guinea pigs: I. Regional hemodynamics and myocyte remodeling. ***J Mol Cell Cardiol*** 1999; 31(2):307-317.(cover illustration)

28. **Wang X**, Li F, Campbell SE, and Gerdes AM. Chronic pressure overload cardiac hypertrophy and failure in guinea pigs: II. Cytoskeletal remodeling. ***J Mol Cell Cardiol*** 1999; 31(2): 318-331. (cover illustration)

29. **Wang X** and Gerdes AM. Chronic pressure overload cardiac hypertrophy and failure in guinea pigs: III. Intercalated disk remodeling. ***J Mol Cell Cardiol*** 1999; 31(2): 332-343. (cover illustration)

30. Milner DJ[§], Taffet GE,[§] **Wang X[§]**, Pham T, Tamura T, Hartley C, Gerdes AM, and Capetanaki Y. The absence of desmin leads to cardiomyocyte hypertrophy and cardiac dilation with compromised systolic function. ***J Mol Cell Cardiol*** 1999; 31(11):2063-76.

31. Sanbe A, Nelson D, Gulick J, Setser E, Osinska H, **Wang X**, Hewett TE, Klevitsky R, Hayes E, Warshaw D, and Robbins J. In Vivo Analysis of an Essential Myosin Light Chain Mutations Linked to Familial Hypertrophic Cardiomyopathy. ***Circ Res*** 2000; 87: 296-302.

32. Yang Q, Hewett TE, Klevitsky R, Sanbe A, **Wang X**, and Robbins J. PKA dependent phosphorylation of myosin binding protein C in transgenic mice. ***Cardiovasc Res*** 2001; 51(1): 80-88.

33. **Wang X**, Osinska H, Dorn 2nd GW, Nieman M, Lorenz JN, Gerdes AM, Witt S, Kimball T, Gulick J, and Robbins J. Transgenic mouse model of desmin related cardiomyopathy. ***Circulation*** 2001; 103(19): 2402-2407.

34. **Wang X**, Osinska H, Klevitsky R, Gerdes AM, Nieman M, Lorenz JN, Hewett T, and Robbins J. Expression of R120G-(-B-crystallin causes aberrant desmin and alpha-B-crystallin aggregation and cardiomyopathy in mice. ***Circ Res*** 2001; 89(1): 84-91. (*with companion editorial*)

35. Wu G, Yussman MG, Barrett TJ, Hahn HS, Osinska H, Hilliard GM, **Wang X**, Toyokawa T, Yatani A, Lynch RA, Robbins J, and Dorn 2nd GW. Increased Myocardial Rab GTPase Expression. A Consequence and Cause of Cardiomyopathy. ***Circ Res*** 2001; 89:1130-1137.

36. Yi XP, **Wang X,** Gerdes AM, and Li F. Subcellular redistribution of focal adhesion kinase and its related nonkinase in hypertrophic myocardium. ***Hypertension*** 2003; 41: 1317-1323.

37. **Wang X*,** Klevitsky R, Huang W, Glasford JW, Li F, and Robbins J. αB-Crystallin Modulates Protein Aggregation of Abnormal Desmin. ***Circ Res*** 2003; 93: 998-1005. (*corresponding author)

38. Dong X, Liu J, Zheng HQ, Glasford JW, Huang W, Chen QH, Harden NR, Li F, Gerdes AM, and **Wang X*.** *In Situ* Dynamically Monitoring the Proteolytic Function of the Ubiquitin-Proteasome System in Cultured Cardiac Myocytes. ***Am J Physiol Heart Circ Physiol*** 2004; 287:H1417-H1425.

39. Yi XP, Zhou J, Baker J, **Wang X**, Gerdes AM, and Li F. Myocardial expression and redistribution of GRKs in hypertensive hypertrophy and failure. ***Anatomic Record*** 2005; 282A: 13-23.

40. Gard JJ, Yamada K, Green KG, Eloff BC, Rosenbaum DS, **Wang X**, Robbins J, Schuessler RB, Yamada KA, and Saffitz JE. Remodeling of gap junctions and slow conduction in a mouse model of desmin-related cardiomyopathy. ***Cardiovasc Res*** 2005; 67(3): 539-547.

41. Kumarapeli ARK, Horak KM, Glasford JW, Li J, Chen Q, Liu J, Zheng Q, and **Wang X***. A novel transgenic mouse model reveals deregulations of the ubiquitin-proteasome system in the heart by doxorubicin. ***FASEB J*** express article 10.1096/fj.05-3973. Published online October. 7, 2005.

42. Tang YD, Kuzman JA, Said S, Anderson BE, **Wang X**, and Gerdes AM. Low thyroid function leads to cardiac atrophy with chamber dilatation, impaired myocardial blood flow, loss of arterioles, and severe systolic dysfunction. ***Circulation*** 2005; 112: 3122-3130.

43. Chen Q, Liu J-B, Horak KM, Zheng H, Kumarapeli ARK, Li J, Li F, Gerdes AM, Wawrousek EF, and **Wang X*.** Intrasarcoplasmic amyloidosis impairs proteolytic function of proteasomes in cardiomyocytes by compromising substrate uptake. ***Circ Res*** 2005; 97: 1018-1026. (*with companion editorial*)

44. Liu J-B, Chen Q, Huang W, Horak KM, Zheng H, Mestril R, and **Wang X***. Impairment of the ubiquitin-proteasome system in desminopathy mouse hearts. ***FASEB J*** 2006; 20: 362-364.

45. Yi XP, Zhou J, Huber L, Qu J, **Wang X**, Gerdes AM, and Li F. Nuclear compartmentalization of FAK and FRNK in cardiac myocytes. ***Am J Physiol Heart Circ Physiol*** 2006; 290: H2509-H2515.

46. Liu J-B, Tang M, Mestril R, and **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; 40(4): 451-454. (*with companion editorial*)

47. Lindsten K, Menendez-Benito V, Masucci MG, Dantuma NP, Kumarapeli AR, Horak KM, Zheng H, and **Wang X***. GFP reporter mouse models of UPS proteolytic function. ***FASEB J*** 2006; 20(7):1027-1028.

48. Zhou J, Qu J, Yi XP, Graber K, Huber L, **Wang X**, Gerdes AM, and Li F. Up-regulation of gamma-catenin compensates for the loss of beta-catenin in adult cardiac myocytes. ***Am J Physiol Heart Circ Physiol***. 2007; 292(1):H270-276.

49. Kobayashi S, Mao K, Zheng H, **Wang X**, Patterson C, O'Connell TD, and Liang Q. Diminished GATA4 protein levels contribute to hyperglycemia-induced cardiomyocyte injury. ***J Biol Chem*** 2007; 282:21945-52.

50. Qu J, Zhou J, Ping Yi X, Dong B, Zheng H, Miller LM, **Wang X**, Schneider MD, and Li F. Cardiac-specific haploinsufficiency of beta-catenin attenuates cardiac hypertrophy but enhances fetal gene expression in response to aortic constriction. ***J Mol Cell Cardiol*** 2007; 43:319-26. (cover illustration)

51. Powell SR, Samuel SM, Wang P, Divald A, Thirunavukkarasu M, Koneru S, **Wang X**, and Maulik N. Upregulation of myocardial 11S-activated proteasome in experimental hyperglycermia. ***J Mol Cell Cardiol*** 2008; 44(3):618-21.

52. Kumarapeli ARRK, Su H, Huang W, Horak MK, Tang M, Zheng H, Li M, and **Wang X***. Alpha B-Crystallin suppresses pressure overload cardiac hypertrophy. ***Circ Res*** 2008; 103(12): 1473-1482. (*with editorial*)

53. Liu J, Zheng H, Tang M, Ryu Y-C, and **Wang X***. A therapeutic dose of doxorubicin activate ubiquitin-proteasome system mediated proteolysis by acting on both ubiquitination apparatus and the proteasome. ***Am J Physiol Heart Circ Physiol*** 2008; 295 (6): H2541-2550.

54. Tydlacka S, Li S, **Wang X**, Li S, and Li X-J. Differential activities of the ubiquitin-proteasome system in neurons and glia may account for the preferential accumulation of misfolded proteins in neurons. ***J Neuroscience*** 2008; 28(49): 13285-13295.

55. Su H, Huang W, and **Wang X***. The COP9 signalosome negatively regulates proteasome proteolytic function and is essential to transcription. ***Int J Biochem Cell Biol*** 2009; 41(3):615-24.

56. Yang H, Zhou P, Huang H, Ma N, Shen S, Dong W, **Wang X**, Dou Q, Liu J. Shikonin exerts antitumor activity via proteasome inhibition and cell death induction in vitro and in vivo***. Int J Cancer*** 2009; 124(10): 2450-2459. (cover illustration).

57. Kumarapeli AR, Horak KM, **Wang X***. Protein quality control in protection against systolic overload cardiomyopathy: the long term role of small heat shock proteins. ***Am J Transl Res*** 2010; 2(4):390-401.

58. Zheng H[§], Tang M[§], Zheng Q, Kumarapeli ARK, Horak KM, Tian Z, **Wang X*.** Doxycycline Attenuates Protein Aggregation in Cardiomyocytes and Improves Survival of a Mouse Model of Cardiac Proteinopathy. ***J Am Coll Cardiol*** 2010; 56(17):1418-26. (*with companion editorial*)

59. Tang M[§], Huang W[§], Li J[§], Su H, Horak KM, Liang Q, Molkentin JD, and **Wang X*.** Proteasome Functional Insufficiency Activates the Calcineurin-NFAT Pathway in Cardiomyocytes and Mouse hearts. ***Cardiovasc Res*** 2010; 88(3):424-33. (*with companion editorial*)

60. Lei D, Li F, Su H, Ye B, Wei N, and **Wang X*.** COP9 Signalosome subunit 8 is essential to postnatal hepatocyte survival and effective proliferation. ***Cell Death Diff*** 2010; 18(2): 259-270.

61. 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***, and Liu J*. Physiological levels of ATP negatively regulate proteasome function. ***Cell Res*** 2010; 20(12):1372-85.

62. Su H, Li J, Menon S, Liu J-B, Kumarapeli AR, Wei N, and **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.

63. Li J, Powell SR, and **Wang X***. Enhancing proteasome function via overexpressing PA28α protects against oxidative stress. ***FASEB J*** 2011; 25(3):883-893. PMID: 21098724

64. Lu L, Qin A, Huang H, Zhou P, Zhang C, Liu N, Li S, Wen G, Zhang C, Dong W, **Wang X**, Dou QP, and Liu J. Shikonin extracted from medicinal Chinese herbs exerts anti-inflammatory effect via proteasome inhibition. ***Eur J Pharmacol*** 2011; 658(2-3): 242-7.

65. Huang H, Liu N, Zhao K, Zhu C, Lu X, Li S, Lian W, Zhou P, Dong X, Zhao C, Guo H, Zhang C, Yang C, Wen G, Lu L, Li X, Guan L, Liu C, **Wang X**, Dou QP, and Liu J. Sanggenon C decreases tumor cell viability associated with proteasome inhibition. ***Front Biosci (Elite Ed)***. 2011; 3:1315-25.

66. Zheng Q, Su H, Ranek MJ, and **Wang X***. Autophagy and p62 in cardiac proteinopathy. ***Circ Res*** 2011; 109 (3): 296-308.

67. Li J, Horak KM, Su H, Sanbe A, Robbins J, and **Wang X***. Enhancement of proteasomal function protects against cardiac proteinopathy and ischemia/reperfusion injury in mice. ***J Clin Invest*** 2011; 121(9):3689-700.

68. Zheng Q, Su H, Tian Z, **Wang X***. Proteasome malfunction activates macroautophagy in the heart. ***Am J Cardiovasc Dis*** 2011; 1(3):214-226.

69. Su H, Li F, Ranek MJ, Wei N, **Wang X***. The COP9 signalosome regulates autophagosome maturation. ***Circulation*** 2011; 124(19): 2117-2128.

70. Tian Z[§], Zheng H[§], Li J, Li YF, Su H, and **Wang X***. Genetically Induced Moderate Inhibition of the Proteasome in Cardiomyocytes Exacerbates Myocardial Ischemia-Reperfusion Injury in Mice. ***Circ Res*** 2012; 111(5): 532-542. (*with companion editorial*)

71. Huang H, Liu N, Guo H, Liao S, Li X, Yang C, Liu S, Song W, Liu C, Guan L, Li B, Xu L, Zhang C, **Wang X**, Dou QP, and Liu J. L-Carnitine Is an Endogenous HDAC Inhibitor Selectively Inhibiting Cancer Cell Growth In Vivo and In Vitro. ***PLoS One*** 2012; 7(11):e49062. doi: 10.1371/journal.pone.0049062.

72. Li X, Liu S, Huang H, Liu N, Zhao C, Liao S, Yang C, Liu Y, Zhao C, Li S, Lu X, Liu C, Guan L, Zhao K, Shi X, Song W, Zhou P, Dong X, Guo H, Wen G, Zhang C, Jiang L, Ma N, Li B, Wang S, Tan H, **Wang X**, Dou QP, and Liu J. Gambogic acid is a tissue-specific proteasome inhibitor in vitro and in vivo. ***Cell Reports*** 2013; 3(1): 211-22.

73. Rajagopalan V, Zhao M, Reddy S, Fajarado G, **Wang X**, Dewey S, Gomes AV, Bernstein D. Altered ubiquitin-proteasome signaling in right ventricular hypertrophy and failure. ***Am J Physiol Heart Circ Physiol*** 2013; 305(4):H551-62. doi: 10.1152/ajpheart.00771.2012.

74. Ranek MJ, Terpstra EJ, Li J, Kass DA, and **Wang X***. Protein kinase G positively regulates proteasome-mediated degradation of misfolded proteins. ***Circulation*** 2013; 128: 365-376. *(with companion editorial*).

75. Liu C, Guo L, Menon S, Jin D, Pick E, **Wang X**, Deng XW, and Ning W. COP9 signalosome subunit Csn8 is required to prevent premature G1 to S phase transition. ***J Biol Chem*** 2013; 288(28): 20443-52. doi: 10.1074/jbc.M113.468959.

76. Lei D, Li F, Su H, Wei N, and **Wang X*.** Hepatic Deficiency of COP9 Signalosome Subunit 8 Induces Ubiquitin-Proteasome System Impairment and Bim-mediated Apoptosis in Murine Livers. ***PLoS ONE*** 2013; 8(7): e67793. doi:10.1371/journal.pone.0067793.

77. Zhao C[§], Liu S[§], Yang C, Li S, Huang H, Liu N, Li S, **Wang X***, and Liu J*. Gambogic acid moderates cardiac responses to chronic hypoxia likely by acting on the proteasome and NF-κB pathway. ***Am J Cardiovasc Dis*** 2013; 3(3): 135-145.

78. Su H, Li J, Osinska H, Li F, Robbins J, Wei N, and **Wang X***. The COP9 signalosome is required for autophagy, proteasome-mediated proteolysis, and cardiomyocyte survival in adult mice. ***Circ Heart Fail*** 2013; 6(5): 1049-1057.

79. Li S, **Wang X**, Li Y, Kost CK Jr., and Martin DS. Bortezomib, a proteasome inhibitor, attenuates angiotensin II-induced hypertension and aortic remodeling in rats. ***PLoS ONE*** 2013; 8(10): e78564. doi:10.1371/journal.pone.0078564.

80. Liu S[§], Zhao C[§], Yang C, Li X, Huang H, Liu N, Li S, **Wang X***, and Liu J*. Gambogic acid suppresses pressure overload cardiac hypertrophy in rats. ***Am J Cardiovasc Dis*** 2013; 3(4): 227-238.

81. Shi X, Chen X, Li X, Lan X, Zhao C, Liu S, Huang H, Liu N, Liao S, Song W, Zhou P, Wang S, **Wang X**, Dou QP, and Liu J. Gambogic acid induces apoptosis in chronic myeloid leukemia cells resistant to imatinib via inducing proteasome inhibition and caspase-dependent Bcr-Abl cleavage. ***Clin Cancer Res*** 2014; 20(1):151-63. doi: 10.1158/1078-0432.CCR-13-1063.

82. Liu Y, Hettinger CL, Zhang D, Rezvani K, **Wang X**, Wang H. The Proteasome Function Reporter GFPu Accumulates in Young Brains of the APPswe/PS1dE9 Alzheimer's Disease Mouse Model. ***Cell Mol Neurobiol*** 2014; 34(3):315-322.

83. Liu Y, Hettinger CL, Zhang D, Rezvani K, **Wang X**, and Wang H. Sulforaphane enhances proteasomal and autophagic activities in mice and is a potential therapeutic reagent for Huntington's disease. ***J Neurochem*** 2014; 129(3):539-47. doi: 10.1111/jnc.12647.

84. Liu Y, Lü L, Hettinger C, Dong G, Zhang D, Rezvani K, **Wang X**, and Wang H. Ubiquilin-1 protects cells from oxidative stress and ischemic stroke caused tissue injury in mice. ***J Neurosci*** 2014; 34(8):2813-21. doi: 10.1523/JNEUROSCI.3541-13.2014.

85. Ranek MJ, Kost CK, Martin DS, and **Wang X***. Muscarinic 2 receptors modulate cardiac proteasome function in a protein kinase G-dependent manner. ***J Mol Cell Cardiol*** 2014; 69:43-51. doi: 10.1016/j.yjmcc.2014.01.017.

86. Liu N, Li X, Liao S, Huang H, Zhao C, Yang C, Liu S, Song W, Lu X, Xu L, Jiang L, Zhao C, Dong X, Zhou P, Wang S, **Wang X**, Dou QP, and Liu J. A novel proteasome inhibitor inhibits tumor growth *in vitro, in vivo* and *ex vivo via* targeting both 19S proteasome deubiquitinases and 20S proteolytic peptidases. ***Sci Rep*** 2014; 4:5240. doi: 10.1038/srep05240.

87. Tian Z, Wang C, Hu C, Tian Y, Liu J, and **Wang X***. Autophagic-lysosomal inhibition impairs cardiac ubiquitin-proteasome system performance in a p62 dependent manner. ***PLoS ONE*** 2014; 9(6):e100715. doi: 10.1371/journal.pone.0100715.

88. Liu N[§], Li X[§], Huang H[§], Zhao C[§], Liao S[§], Yang C[§], Liu S[§], Song W, Lu X, Lan X, Chen X, Xu L, Jiang L, Zhao C, Dong X, Zhou P, Li S, Wang S, Shi X, Dou QP, **Wang X**, and Liu J. Clinically used antirheumatic agent auranofin is a proteasomal deubiquitinase inhibitor and inhibits tumor growth. ***Oncotarget*** 2014; 5(14):5453-71.

89. Gupta MK, Gulick J, Liu R, **Wang X**, Molkentin JD, and Robbins J. SUMO E2 enzyme UBC9 is required for efficient protein quality control in cardiomyocytes. ***Circ Res***. 2014; 115(8):721-9. doi: 10.1161/CIRCRESAHA.115.304760. *(with companion editorial*)

90. Chen X, Shi X, Zhao C, Li X, Lan X, Liu S, Huang H, Liu N, Liao S, Zang D, Song W, Liu Q, Carter BZ, Dou QP, **Wang X**, and Liu J. Anti-rheumatic agent auranofin induced apoptosis in

chronic myeloid leukemia cells resistant to imatinib through both Bcr/Abl-dependent and -independent mechanisms. ***Oncotarget.*** 2014 Oct 15; 5(19):9118-32.

91. Shi X, Lan X, Li X, Chen X, **Wang X**, and Liu J. 2-tert-butyl-1,4-benzoquinone induces apoptosis in chronic myeloid leukemia cells resistant to imatinib via inducing caspase-dependent Bcr-Abl downregulation. ***Med Chem*** 2014; 4 (12): 784-790. doi:10.4172/2161-0444.1000231

92. Shi X, Lan X, Chen X, Zhao C, Li X, Liu S, Huang H, Liu N, Zhang D, Liao Y, Zhang P, **Wang X**, Liu J. Gambogic acid induces apoptosis in diffuse large B-cell lymphoma cells via inducing proteasome inhibition. ***Sci Rep.*** 2015 Apr 8; 5:9694.

93. Ranek MJ[§], Zheng H[§], Huang W[§], Kumarapeli AR, Li J, Liu J, and **Wang X***. Genetically induced moderate inhibition of 20S proteasomes in cardiomyocytes facilitates heart failure in mice during systolic overload. ***J Mol Cell Cardiol.*** 2015; 85 (8):273-81. *(with companion editorial*)

94. Li J, Ma W, Li H, Hou N, **Wang X**, Kim IM, Li F, and Su H. NEDD8 Ultimate Buster-1 Long (NUB1L) Protein Suppresses Atypical Neddylation and Promotes Proteasomal Degradation of Misfolded Proteins. ***J Biol Chem*** 2015; 290(39):23850-62.

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

96. Qin Q, Qu C, Niu T, Zang H, Qi L, Lyu L, **Wang X**, Janicki J, Wang XL, Cui T. Nrf2-mediated cardiac maladaptive remodeling and dysfunction in a setting of autophagy insufficiency. ***Hypertension*** 2016 Jan; 67(1):107-17. doi: 10.1161/HYPERTENSIONAHA.115.06062.

97. Huang H[§], Liao Y[§], Liu N, Hua X, Cai J, Yang C, Zhao C, Chen X, Lan X, Zang D, Wu J, Li X, Shi X, **Wang X**, and Liu J. Two clinical drugs deubiquitinase inhibitor auranofin and aldehyde dehydrogenase inhibitor disulfiram trigger synergistic anti-tumor effects in vitro and in vivo. ***Oncotarget*** 2016; 7(3): 2098-2808. doi: 10.18632/oncotarget.6425.

98. Jiang L[§], Zang D[§], Yi S[§], Li X[§], Yang C, Dong X, Zhao C, Lan X, Chen X, Liu S, Liu N, Huang H, Shi X, **Wang X***, and Liu J*. A microRNA-mediated decrease in eukaryotic initiation factor 2α promotes cell survival during endoplasmic reticulum stress. ***Sci Rep***. 2016; 6:21565.

99. Zhao C[§], Chen X[§], Zang D, Lan X, Liao S, Yang C, Zhang P, Wu J, Li X, Liu N, Liao Y, Huang H, Shi X, Jiang L, Liu X, Dou QP, **Wang X**, and Liu J. A novel nickel complex works as a proteasomal deubiquitinase inhibitor for cancer therapy. ***Oncogene*** 2016; 35(45):5916-5927. doi: 10.1038/onc.2016.114.

100. Zhang L, Hapona MB, Goyeneche AA, Srinivasan R, Carlos D. Gamarra-Luques CD, Callegari EA, Drappeau DD, Terpstra EJ, Knapp J, Chien J, **Wang X**, Eyster KM, and Telleria CM. Mifepristone induces endoplasmic reticulum stress, triggers the unfolded protein response, increases autophagic flux, and kills ovarian cancer cells in combination with bortezomib or chloroquine. ***Molecular Oncology*** 2016; 10(7):1099-1117. doi: 10.1016/j.molonc.2016.05.001.

101. Hou N[§], Ye B[§], Li X, Margulies KB, Xu H, **Wang X**, and Li F. TCF7L2 Mediates Canonical Wnt/β-Catenin Signaling and c-Myc Upregulation in Heart Failure. ***Circ Heart Fail*** 2016 Jun; 9(6). pii: e003010. doi: 10.1161/CIRCHEARTFAILURE.116.003010. Epub 2016 Jun 14

102. Zhao C, Chen X, Zang D, Lan X, Liao S, Yang C, Zhang P, Wu J, Li X, Liu N, Liao Y, Huang H, Shi X, Jiang L, He Z, Liu X, **Wang X***, and Liu J*. Platinum-containing compound platinum pyrithione is stronger and safer than cisplatin in cancer therapy. ***Biochemical Pharmacology*** 2016; 116: 22-38.

103. Liao Y, Liu N, Hua X, Cai J, Xia X, **Wang X**, Huang H, and Liu J. Proteasome-associated deubiquitinase ubiquitin-specific protease 14 regulates prostate cancer proliferation by deubiquitinating and stabilizing androgen receptor. ***Cell Death Dis*** 2017 Feb 2; 8(2):e2585. DOI: 10.1038/cddis.2016.477.

104. Lan X, Zhao C, Chen X, Zhang P, Zang D, Wu J, Chen J, Long H, Yang L, Huang H, Carter BZ, **Wang X**, Shi X*, Liu J*. Nickel pyrithione induces apoptosis in chronic myeloid leukemia cells resistant to imatinib via both Bcr/Abl-dependent and -independent mechanisms. ***J Hematol Oncol*** 2016 Nov 25; 9(1):129. DOI: 10.1186/s13045-016-0359-x.

105. 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 Nov 30;102:53-60. DOI: http://dx.doi.org/10.1016/j.yjmcc.2016.11.013

106. Zhao C[§], Chen X[§], Yang C[§], Zang D, Lan X, Liao S, Zhang P, Wu J, Li X, Liu N, Liao Y, Huang H, Shi X, Jiang L, Liu X, **Wang X***, and Liu J*. Repurposing an antidandruff agent to treating cancer: zinc pyrithione inhibits tumor growth via targeting proteasome-associated deubiquitinases. ***Oncotarget***. 2017 Feb 21; 8(8):13942-13956. doi: 10.18632/oncotarget.14572.

107. Liao Y, Liu N, Hua X, Cai J, Xia X, **Wang X**, Huang H, Liu J. Proteasome-associated deubiquitinase ubiquitin-specific protease 14 regulates prostate cancer proliferation by deubiquitinating and stabilizing androgen receptor. ***Cell Death Dis***. 2017 Feb 2; 8(2):e2585. DOI: 10.1038/cddis.2016.477

108. Balla C, Assenza GE, Subramanian K, **Wang X**, Volpe M, Dec GW, del Monte F. Presenilin-2, a Novel Excitation Contraction Coupling Protein, Modulates Both Ca2+ Release and Ca2+ Reuptake in Cardiomyocytes. 2015 (revised)

109. Xiao L, Lan X, Shi X, Zhao K, **Wang X**, Li F, Huang H, Liu J. Cytoplasmic RAP1 mediates cisplatin resistance of non-small cell lung cancer. ***Cell Death Dis.*** 2017 May 18; 8(5):e2803. (DOI: 10.1038/cddis.2017.210). PubMed PMID: 28518145.

110. Huang H[§], Guo M[§], Liu N[§], Zhao C[§], Chen H, Wang X, Liao S, Zhou P, Liao Y, Chen X, Lan X, Xu D, Li X, Shi X, **Wang X***, Zhang C-E*, and Liu J*. Bilirubin neurotoxicity is associated with proteasome inhibition. ***Cell Death Dis***. 2017; 8(6): e2877 (DOI: 10.1038/cddis.2017.274)

111. Cai J[§], Xia X[§], Liao Y[§], Liu N, Guo Z, **Wang X**, Huang H*, Liu J*. A novel deubiquitinase inhibitor b-AP15 triggers apoptosis in both androgen receptor-dependent and -independent prostate cancers. ***Oncotarget*** 2017 (in press)

112. Chen X, Wu J, Zhang P, Liao S, Lan X, Chen J, Li X, Huang H, Liao Y, Zhang X, Yang Q, Shi X, Jiang L, Liu N, He Z, **Wang X**, Zhao C, and Liu J. Cadmium pyrithione suppresses tumor growth in vitro and in vivo through inhibition of deubiquitinase. 2016 (submitted).

113. Chen X, Zhang X, Chen J, Yang Q, Yang L, Xu D, Zhang P, Lan X, Liao Y, Long H, Cai J, Li X, Huang H, Jiang L, **Wang X**, Liu J. Hinokitiol copper complex inhibits proteasomal deubiquitination and induces paraptosis-like cell death in human cancer cells. ***European J Pharmacol*** 2017 (in press)

114. Lan X, Zhao C, Chen X, Zhang P, Zang D, Wu J, Chen J, Long H, Yang L, Huang H, **Wang X**, Shi X, Liu J. Platinum pyrithione induces apoptosis in chronic myeloid leukemia cells resistant to imatinib via DUB inhibition-dependent caspase activation and Bcr-Abl down-regulation. ***Cell Death Dis***. 2017; 8(7): e2913. (DOI: 10.1038/cddis.2017.284).

115. Hou N, Xu H, **Wang X**, Li F, Ye B. Activation of Yap1/Taz signaling in ischemic heart disease and dilated cardiomyopathy. 2017 (submitted)

116. Wu P, Yuan X, Li F, Zhang J, Zhu W, Wei M, Li J*, **Wang X***. Myocardial upregulation of cathepsin D by ischemic heart disease promotes autophagic flux and protects against cardiac remodeling and heart failure. ***Circ Heart Fail*** 2017; 10(7) (DOI: 10.1161/CIRCHEARTFAILURE.117.004044)

117. Abdullah A, Eyster KM, Bjordahl T, Xiao P, Zeng E, **Wang X***. Murine myocardial transcriptome analysis reveals a critical role of COPS8 in the gene expression of Cullin-RING ligase substrate receptors and redox and vesicle trafficking pathways. ***Frontiers in Physiology-System Biology*** 17 August 2017 | https://doi.org/10.3389/fphys.2017.00594.

118. Pan B, Zhang H, Cui T, **Wang X***. TFEB activation protects against cardiac proteotoxicity via increasing autophagic flux. 2017 (in revision).

B. REVIEW ARTICLES

119. **Wang X**, Dong C. Apoptosis and ischemic-reperfused injury. ***Foreign Medical Sciences (Physiology, Pathology, and Clinic)*** 1997; 17(2): 125-127.

120. **Wang X*,** Osinska H, Gerdes AM, and Robbins J. Desmin and cardiac diseases: establishing causality. ***J Card Failure*** 2002; 8: S287-S292. (*correspondence)

121. Li F, **Wang X**, Yi XP, and Gerdes AM. Structural Basis of Ventricular Remodeling: Role of the Myocyte. ***Current Heart Failure Reports*** 2004; 1(1): 5-8.

122. Kumarapeli A, **Wang X***. Genetic Modification of the Heart: Chaperones and the Cytoskeleton. ***J Mol Cell Cardiol*** 2004; 37: 1097-1109.

123. **Wang X** and Robbins J. Heart Failure and Protein Quality Control. ***Circ Res*** 2006; 99: 1315-1326.

124. **Wang X**, Su H, and Ranek M. Protein quality control and degradation in cardiomyocytes (Invited Review). ***J Mol Cell Cardiol*** 2008; 45(1):11-27.

125. Zheng Q, Li J, and **Wang X***. Interplay between the ubiquitin-proteasome system and autophagy in proteinopathy. ***Int J Physiol Pathophysiol Pharmacol*** 2009; 1(2):127-142.

126. Ranek M and **Wang X***. Activation of the ubiquitin-proteasome system in doxorubicin cardiomyopathy. ***Curr Hypertens Rep*** 2009; 11(6):389-95.

127. Su H and **Wang X***. The ubiquitin-proteasome system in cardiac proteinopathy: a quality control perspective. ***Cardiovasc Res*** 2010; 85(2):253-62.

128. Depre C, Powell SR, and **Wang X**. The role of the ubiquitin-proteasome pathway in cardiovascular disease. ***Cardiovasc Res*** 2010; 85(2):251-2.

129. Zheng Q and **Wang X***. Autophagy and the ubiquitin-proteasome system in cardiac dysfunction. ***Panminerva Med***. 2010; 52(1):9-25.

130. Li Y-F and **Wang X***. The Role of the Proteasome in Heart Disease. ***Biochim Biophys Acta*** 2011;1809(2):141-149.

131. **Wang X***, Li J, Zheng H, Su H, and Powell SR. Proteasome functional insufficiency in cardiac pathogenesis. ***Am J Physiol Heart Circ Physiol*** 2011; 301(6): H2207-2219.

132. Su H and **Wang X***. p62 stages an interplay between the ubiquitin-proteasome system and autophagy in the heart of defense against proteotoxic stress. ***Trends Cardiovasc Med*** 2011; 21(8): 224-228.

133. Powell SR, Herrmann J, Lerman A, Patterson C, and **Wang X**. The ubiquitin-proteasome system and cardiovascular disease. ***Prog Mol Biol Transl Sci*** 2012; 109: 295-346.

134. Klionsky DJ, many others, **Wang X**, *et al*. Guidelines for the use and interpretation of assays for monitoring autophagy. ***Autophagy*** 2012; 8(4):445-544. (Contributed a full figure)

135. **Wang X*** and Terpstra EJ. Ubiquitin Receptors and Protein Quality Control. ***J Mol Cell Cardiol*** 2013; 55(2):73-84. doi: 10.1016/j.yjmcc.2012.09.012. Epub 2012 Oct 6.

136. **Wang X*,** Pattison JS, and Su H. Posttranslational modification and protein quality control (Invited Review). ***Circ Res*** 2013; 112(2): 367-81.

137. Chen X, Shi X, **Wang X**, and Liu J. Novel use of old drug: Anti-rheumatic agent auranofin overcomes imatinib-resistance of chronic myeloid leukemia cells. ***Can Cell Microenviron*** 2014; 1: e415. doi: 10.14800/ccm.415.

138. **Wang X*** and Robbins J. Proteasomal and lysosomal protein degradation and heart disease (Invited Review). ***J Mol Cell Cardiol*** 2014; 71C:16-24. doi: 10.1016/j.yjmcc.2013.11.006.

139. Wang C and **Wang X***. The interplay between autophagy and the ubiquitin-proteasome system in cardiac proteotoxicity (invited review). ***BBA-Mol Basis Dis*** 2015; 1852(2):188-94.

140. Zhang H and **Wang X***. Priming the proteasome: a novel mechanism for cardioprotection by sildenafil. ***Future Cardiology*** 2015; 11(2):177-89. doi: 10.2217/fca.15.3.

141. **Wang X*** and Martin DS. The COP9 signalosome and cullin RING ligases in the heart. ***Am J Cardiovasc Dis*** 2015; 5(1):1-18.

142. Martin DS***** and **Wang X*.** The COP9 signalosome in vascular function. ***Am J Cardiovasc Dis*** 2015; 5(1):33-52.

143. Klionsky DJ, many others, **Wang X**, *et al*. Guidelines for the use and interpretation of assays for monitoring autophagy. ***Autophagy*** 2016; 12(1):1-222. (Contributed a full figure).

144. Cui T*, Lai Y, Janicki JS, and **Wang X***. Nrf2-mediated protein quality control in cardiomyocytes. ***Frontiers in Bioscience*** (Landmark Ed). 2016 Jan 1; 21:192-202. PubMed PMID: 26709769.

145. **Wang X***, Cui T*. Modulation of autophagy – a potential therapeutic approach for cardiac hypertrophy (Invited review). ***Am J Physiol-Heart Circ Physiol*** 2017 Aug 1; 313(2):H304-H319. doi: 10.1152/ajpheart.00145.2017. Epub 2017 Jun 2. Review. PubMed PMID: 28576834.

C. <u>INVITED EDITORIALS</u>

146. **Wang X***, Su H. Unraveling Enigma in the Z-disk. ***Circ Res*** 2010; 107:321-3.

147. Su H, **Wang X***. Autophagy and p62 in cardiac protein quality control. ***Autophagy*** 2011; 7(11): 1382-1383.

148. **Wang X***, Su H. FoxO3 hastens autophagy and shrinks the heart but does not curtail pathological hypertrophy in adult mice. ***Cardiovasc Res*** 2011; 91 (4):561-62.

149. **Wang X***. Repeated Intermittent Administration of a Ubiquitous Proteasome Inhibitor Leads to Restrictive Cardiomyopathy. ***Eur J Heart Fail*** 2013; 15(6): 597-598.

150. Liu J*, Su H, **Wang X**.* The COP9 signalosome coerces autophagy and the ubiquitin-proteasome system to police the heart. ***Autophagy*** 2016; 12(3):601-602.

151. **Wang X***. Entangled in a heart-ailing quandary: could modified cofilin-2 be a culprit of Alzheimer's disease of the heart? ***J Am Coll Cardiol*** 2015 65(12):1215-7.

152. **Wang X***. Vascular Spasm: A Newly Unraveled Cause for Cardiovascular Adversity of Proteasome Inhibition. EBioMedicine, 2017. (DOI: 10.1016/j.ebiom.2017.06.010)

D. CHAPTERS IN BOOKS

153. **Wang X** and Dong C. Chapter 21. Prostaglandins. in Yang G, eds. *Endocrinal Physiology and Pathophysiology*. Tianjing: Tianjing Science and Technology Press 1995; 819-851.

154. Zhen XH, Xia ZP, Xia ZX, and **Wang X**, co-eds. *Advanced Education Self-Study Examination Review Guide: Pathophysiology and Pharmacology*. 1st ed. Wuhan: Hubei Science and Technology Press 1993; pp1-609.

155. Gerdes AM and **Wang X**. Structural remodeling of cardiac myocytes in hypertrophy and progression to failure. In: "Cardiovascular Remodeling and failure". Eds. PK Singal, IMC Dixon, LA Kirshenbaum, NS Dhalla. Klewer Academic Publishers, Boston, MA, 2003; pp183-193.

156. **Wang X** and Patterson C. Chapter 27. Protein quality control in cardiomyocytes; In: Hill JA, Olson EN, eds. ***Muscle: Fundamental Biology and Mechanisms and Disease***. Elsevier 2012; pp. 353-368.

157. Su H and **Wang X***. Chapter 13, Defense against proteotoxic stress in the heart: role of p62, autophagy, and ubiquitin-proteasome system. In: M. A. Hayat, eds. ***Autophagy: Cancer, Other Pathologies, Inflammation, Immunity, Infection, and Aging***. Elsevier 2014; Vol 3, pp. 188-202.

158. **Wang X***. Chapter 12. Desmin Filaments and Desmin-Related Myopathy. In: Schatten H, eds. ***The Cytoskeleton in Health and Disease***. Springer Science+Business Media New York 2015; 281-306.

159. Cui T and **Wang X***. Chapter 3, Interplay among oxidative stress, redox signaling, ER-stress, autophagy and protein ubiquitination. In Ren, Sowers, Zhang, eds. ***Autophagy and Cardiometabolic Diseases: From Mechanisms to Molecules to Medicine***. Academic Press, May 1, 2018 - Medical - 224 pages.

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E. ABSTRACTS AND CONFERENCE PRESENTATIONS

1. Dong, C., X. Wang, and J. Xiang. The kinetic changes of coagulation and anti-coagulation of patients with epidemic hemorrhagic fever. FASEB J 1991; 5(6): 1628.

2. Gerdes A. M., T. Onodera, F. Li, X. Wang, S. A. McCune, and J. M. Capasso. Regional changes in cardiac myocyte shape during the progression to failure in rats. J Mol Cell Cardiol 1996; 28:A200.

3. Li F, X. Wang, AM Gerdes. Cellular mechanism of binucleation in neonatal rat cardiocytes. Circulation 1996; 94(8): No.3544.

4. Wang X, S.E. Campbell, A.M. Gerdes. Regional alterations of microtubule density in cardiac myocytes following chronic aortic stenosis in guinea pigs. Circulation 1997;96(8): I-254.

5. Wang X, and Gerdes AM. Altered expression and distribution of intercalated disks associated proteins in ventricular myocytes from guinea pigs with chronic pressure overloaded cardiac hypertrophy and failure. Journal of Cardiac Failure 1998; 3(2 Suppl. 1): 58.

6. Wang X, Gulick J, Oscinska H, Hewett T, Robbins J. A desminopathy-associated desmin mutation causes aberrant desmin aggregation and early cardiac hypertrophy in transgenic mice. A Keystone Symposia: Molecular Biology of the Cardiovascular System, January 12-17, 2000, Snowbird, UT.

7. Wang X., H. Osinska, G.W. Dorn II, A.M. Gerdes, R. Klevisky, J. Gulick, J. Robbins. In vivo modeling desmin-related cardiomyopathies with transgenics. Journal of Cardiac Failure 2000; 5(Young Investigator Award 2nd prize at the 4th Annual Scientific Meeting of the Heart Failure Society of America, September 10-13, 2000, Boca Raton, FL.

8. Schwartzbauer, G.T., J.D. Molkintin, M.A. Sussman, X. Wang, J. Robbins. Differential protein expression among four models of cardiomyopathy identified by high throughput screening of cardiac polysome fractions. Circulation 2000; 102(18): II-33.

9. Wang X., H. Osinska, R. Klevitsky, A. Sambe, J. Robbins. R120G-alpha-B-crystallin causes desmin-related cardiomyopathy in transgenic mice. Circulation 2000; 102(18): II-201.

10. Wang X., R. Klevitsky, T.E. Hewett, A. M. Gerdes, T. R. Kimball, J. Robbins. Aberrant desmin aggregation disrupts desmin filament networks and leads to early concentric cardiac hypertrophy in transgenic mice. Circulation 2000; 102(18): II-290.

11. Wang X., H. Osinska, G.W. Dorn II, R. Klevisky, J. Gulick, J. Robbins. A transgenic mouse model of desmin related cardiomyopathy. Circulation 2000; 102(18): II-218.

12. Wang X., R. Klevisky, J. Robbins. J. Robbins. Loss of function of alpha B-crystallin enhances the pathogenesis of a desmin mutation. FASEB J 2001; 15(5): A1158.

13. Wang X, Klevitsky R, Robbins J. □B-crystallin is essential to keeping desmin from aggregating adversely. J Mol Cell Cardiol 2001; 33(6): A129.

14. Hahn HS, Lin G, Wu G, Barrett T, Wang X, Robbins J, Lorenz JN, Mochly-Rosen D, Dorn II GW. □PKC Inhibition lead
with mutant attenuated promoters. Circulation 2001; Publishing ID: 402

15. Wang X, Klevistsky R, Grupp IL, Robbins J. Cardiac a-B-crystallin Is protective against ischemia/reperfusion injury and essential in cardiac preconditioning: genetic studies. Circulation 2001; Publishing ID: 485

16. Wang X, Huang W, Andersen SM, Gerdes AM, Robbins J. Expression of R120G-□B-crystallin impairs proteolytic function of the proteasomes. J Mol Cell Cardiol 2002; 34(7):A15.

17. Saffitz JE, Green KG, Wang X, Robbins J. Down-regulation of intercellar junction proteins in a mouse model of desmin-related cardiomyopathy. Circulation 2002; 106(19):II-206.

18. Dong X, Huang W, Glasford JW, Harden NR, Li F, Gerdes AM, Wang X. Dynamic monitoring of the proteolytic function of the ubiquitin-proteasome system in cultured cardiomyocytes. J Mol Cell Cardiol 2003; 35 (6):A50. The 25th Annual Meeting ISHR-North American Section, 6/28-7/1/2003, Mystic, CT.

19. Huang W, Glasford JW, Harden NR, Dong X, Gerdes AM, Robbins J, Wang X. Remodeling of the intercalated disks in desmin-related cardiomyopathy caused by an alpha B-crystallin mutation in mice. J Card Fail 2003; 9(5): S27.

20. Chen QH, Huang W, Dong X, Glasford JW, Li F, Gerdes AM, Robbins J, Wang X. Modulation of the ubiquitin-proteasome system by R120G-αB-crystallin in vivo and in vitro. Circulation 2003; 108(17): IV-177.

21. Wang X, Kumarapeli AR, Glasford J, Liu J, Chen QH, Horak K, Zheng H, Dong X. In vivo monitoring dynamic changes in the proteolytic function of the ubiquitin-proteasome system. (A late-breaking abstract presented in 1st Annual Symposium of the AHA Council on Basic Cardiovascular Sciences. July 14-18, 2004, Stevenson, WA.)

22. Liu J, Chen QH, Wang X. Impairment of the ubiquitin-proteasome system in cardiac myocytes by reactive oxygen species revealed by a surrogate substrate. Circ Res 2004, 94(12):data supplement on abstracts of 1st Annual Symposium of the AHA Council on Basic Cardiovascular Sciences. July 14-18, 2004, Stevenson, WA.

23. Kumarapeli AR, Liu J, Glasford JW, Chen QH, Horak K, Dong X, Wang X. Myocardial ischemia/reperfusion impairs the ubiquitin-proteasome system: role of reactive oxygen species. Circulation 2004; 110(17): III-237. Oral presentation at AHA Scientific Sessions 2004, New Orleans, LA, November 7-10, 2004.

24. Wang X, Liu J, Chen QH, Dong X, Wawrousek EF, Li F, Horak K. Impairment of the ubiquitin-proteasome system by misfolded cytoplasmic protein in cardiac myocytes. Circulation 2004; 110 (17):III-160. Oral presentation at AHA Scientific Sessions 2004, New Orleans, LA, November 7-10, 2004.

25. Wang X, Chen Q, Liu J, Kumarapeli ARK, Zheng H, Horak K, Glasford JW, Gerdes AM, Li F. A novel functional indicator mouse model reveals impairment of the ubiquitin-proteasome system by misfolded proteins in the heart. The Inaugural Annual Symposium on Protein Folding Disorders. San Diego, CA, Jan 11-13, 2005.

26. Liu J, Tang M, Chen Q, Wang X. H2O2 inhibits proteolytic function of the ubiquitin-proteasome system by activating caspases. Experimental Biology/IUPS 2005 Late Breaking Abstracts, LB15. San Diego, CA, March 31-April 5, 2005.

27. Liu J, Chen Q, Huang W, Horak K, Zheng H, Mestril R, Wang X. Aberrant protein aggregation impairs the ubiquitin-proteasome system by affecting the entry of ubiquitinated proteins into the 20S proteasomes: A novel pathogeneic pathway in cardiac remodeling and failure. Second Annual Symposium of the AHA Council on Basic Cardiovascular Sciences. July 24-27, 2005, Keystone, CO.

28. Li F, Zhou J, Yi XP, Graber, K, Qu J, Huber L, Wang X. Remodeling of the intercalated disk in cardiac specific -catenin knockout mice. Second Annual Symposium of the AHA Council on Basic Cardiovascular Sciences. July 24-27, 2005, Keystone, CO.

29. Zhou J, Yi XP, Huber L, Qu J, Graber K, Wang X, Gerdes AM, Li F. Serine phosphorylation and nuclear redistribution of FAK and FRANK in cardiac myocytes. Second Annual Symposium of the AHA Council on Basic Cardiovascular Sciences. July 24-27, 2005, Keystone, CO.

30. Liu J-B, Chen Q, Wang X. Aberrant protein aggregation impairs protein degradation in mouse heart. AHA Research Symposium, November 12, 2005, Dallas, TX.

31. Chen Q, Liu J-B, Horak KM, Zheng H, Li J, Tang M, Su H, Kumarapeli AR, Li F, Gerdes AM, Wang X. Cytoplasmic aberrant protein aggregation impairs protein degradation in the heart by compromising the entry of ubiquitinated proteins into the 20S proteasomes. Circulation 2005 Oct 25; 112(17): II-188. AHA Scientific Sessions, November 12-16, 2005, Dallas, TX.

32. Zheng H, Horak KM, Robbins J, Wang X. Genetic inhibition of 20S proteasome in the heart. Late-breaking abstract in Experimental Biology 2006, April 1-5, 2006, San Francisco, CA

33. Kumarapeli ARK, Wang X. Alpha B-crystallin modulates pressure overload cardiac hypertrophy. Late-breaking abstract in Experimental Biology 2006, April 1-5, 2006, San Francisco, CA

34. Zheng H, Su H, Horak KM, Wang X. The ubiquitin-proteasome system in cardiac remodeling and failure. J Mol Cell Cardiol 2006; 41(4):748. The 28th Meeting of the North American Section of ISHR, June12-15 2006, Toronto, Canada.

35. Su H, Menon S, Horak KM, Li J, Li F, Wei N, Wang X. Postnatal cardiomyocyte-restricted knockout of a COP9 signalosome gene compromises proteolytic function of the ubiquitin proteasome system and causes congestive heart failure in mice. Late-breaking basic science abstracts of the AHA Scientific Sessions 2006, November 12-15, 2006, Chicago, IL.

36. Liu JB, Zheng H, Tang M, Wang X. Doxorubicin activates ubiquitin-proteasome system mediated proteolysis by acting on both ubiquitination apparatuses and the proteasome. FESAB J 2007:A1024; Abstract 808.4 in the Abstract Book PART II of Experimental Biology 2007, April 28-May 2, Washington, DC.

37. Su H, Li JB, Osinska H, Menon S, Li F, Robbins J, Wei N, Wang X. Genetic inhibition of cullin based ubiquitin ligase dynamics in adult mouse hearts suffices to cause heart failure. FESAB J 2007: A870; Abstract 747.11 in the Abstract Book PART II of Experimental Biology 2007, April 28-May 2, Washington, DC.

38. Lei D-X, Li F, Menon S, Su H, Horak KM, Wei N, Wang X. Ablation of a COP9 signalosome gene in liver causes cirrhosis and dysplastic changes. 2007 Abstract Book of Keystone Symposium on Ubiquitin and Siganling, Feb 4-9, 2007, Big Sky, Montana.

39. Zheng Q, Mizushima N, Wang X. Proteasome malfunction increases autophagosomes in cardiomyocytes and mouse hearts. FASEB J. 2008 22:605.8 Experimental Biology Meeting 2008

40. Zheng H, Li M, Horak KM, Huang W, Sanbe A, Robbins J, Li F, Wang X. Moderate cardiomyocyte-restricted proteasome inhibition exacerbates diastolic malfunction in desmin-related cardiomyopathy mice. J Mol Cell Cardiol 2008; 44:S50.

41. Su H, Li J, Osinska H, Menon S, Horak KM, Li F, Molkentin JD, Robbins J, Wei N, Wang X. Cardiac ablation of CSN8 perturbs proteasomal proteolysis, activates autophagy, and causes fatal heart failure in adult mice. J Mol Cell Cardiol 2008; 44:S51.

42. Li J, Horak KM, Sanbe A, Jeffrey Robbins J, Wang X. A transgenic mouse model of benign enhancement of cardiac proteasomal function. J Mol Cell Cardiol 2008; 44:S53.

43. Ryu Y-C, Wang X. Hyper-phosphorylation of proteasome subunits increases proteasome peptidase activities in desminopathy mouse hearts. J Mol Cell Cardiol 2008; 44:S60.

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, Molkentin 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 fnction 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.

GRANT/CONTRACT SUPPORT

Current Grant Support

RO1 HL072166-01~14 Wang (PI) 7/1/2003 – 10/31/2018
NIH/NHLBI $250,000 (annual direct)
Ubiquitin receptors and cardiac proteotoxicity
Role: PI

R01 HL085629-01~14 Wang (PI) 7/1/2006 - 6/30/2020
NIH/NHLBI $250,000 (annual direct)
The COP9 signalosome in the heart
Role: PI

R01HL131667-01A Cui, Wang (contact) 4/1/2017 - 3/31/2021
NIH/NHLBI $250,000 (annual direct)
The NRF2-p62 axis in the cross-talk between proteasomal and lysosomal degradation
Role: Contact PI, MPI

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 Mentor

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

16UFEL29640003 Reihe (PI) 06/01/2016 – 8/31/2016
AHA Undergraduate Student Research Program $4000 (scholarship)

Effect of Neddylation Inhibition on Autophagic Flux in Cardiomyocytes
Role: Sponsor and Primary Mentor

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. Intrasarcoplasmic 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, Mestril 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, Mestril 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 PA28α 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. 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; PubMed Central PMCID: PMC3042837.

b. 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; PubMed Central PMCID: PMC3163952.

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; PubMed Central PMCID: PMC3426260.

d. Rajagopalan V, Zhao M, Reddy S, Fajardo G, Wang X, Dewey S, Gomes AV, Bernstein D. Altered ubiquitin-proteasome signaling in right ventricular hypertrophy and failure. Am J Physiol Heart Circ Physiol. 2013 Aug 15;305(4):H551-62. PubMed PMID: 23729213; PubMed Central PMCID: PMC3891246.

e. 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 DOI: http://dx.doi.org/10.1016/j.yjmcc.2016.11.013

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 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.

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; PubMed Central 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 Jul 23;128(4):365-76. PubMed PMID: 23770744; PubMed Central PMCID: PMC3761383.

c. Ranek MJ, Kost CK Jr, Hu C, Martin DS, Wang X. Muscarinic 2 receptors modulate cardiac proteasome function in a protein kinase G-dependent manner. J Mol Cell Cardiol. 2014 Apr;69:43-51. PubMed PMID: 24508699; PubMed Central PMCID: PMC3977985.

d. Zhang H, Wang X. Priming the proteasome by protein kinase G: a novel cardioprotective mechanism of sildenafil. Future Cardiol. 2015 Mar;11(2):177-89. PubMed PMID: 25760877; PubMed Central PMCID: PMC4370174.

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.

a. 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 Nov 6;117(11):956-66. PubMed PMID: 26383969; PubMed Central PMCID: PMC4636927.

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; PubMed Central PMCID: PMC3211066.

c. Lei D, Li F, Su H, Tian Z, Ye B, Wei N, Wang X. COP9 signalosome subunit 8 is required for postnatal hepatocyte survival and effective proliferation. Cell Death Differ. 2011 Feb;18(2):259-70. PubMed PMID: 20689553; PubMed Central PMCID: PMC2976840.

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 Jan 7;108(1):40-50. PubMed PMID: 21051661; PubMed Central PMCID: PMC3017673.

5. Dissecting the crosstalk between cardiac UPS and ALP pathways in cardiac PQC. We have elucidated a pivotal role of p62/SQSTM1 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 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. 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. Cui T, Lai Y, Janicki JS, Wang X. Nuclear factor erythroid-2 related factor 2 (Nrf2)-mediated protein quality control in cardiomyocytes. Front Biosci (Landmark Ed). 2016 Jan 1;21:192-202. PubMed PMID: 26709769; PubMed Central PMCID: PMC4723105.

b. Tian Z, Wang C, Hu C, Tian Y, Liu J, Wang X. Autophagic-lysosomal inhibition compromises ubiquitin-proteasome system performance in a p62 dependent manner in cardiomyocytes. PLoS One. 2014;9(6):e100715. PubMed PMID: 24959866; PubMed Central PMCID: PMC4069113.

c. Zheng Q, Su H, Ranek MJ, Wang X. Autophagy and p62 in cardiac proteinopathy. Circ Res. 2011 Jul 22;109(3):296-308. PubMed PMID: 21659648; PubMed Central PMCID: PMC3142307.

d. Zheng Q, Su H, Tian Z, Wang X. Proteasome malfunction activates macroautophagy in the heart. Am J Cardiovasc Dis. 2011;1(3):214-26. PubMed PMID: 22081794; PubMed Central PMCID: PMC3211094.