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陈亚兵教授是美国阿拉巴马大学伯明翰分校(University of Alabama at Birmingham, UAB)病理系终身教授及系副主任，并担任 UAB 研究生院生物医学分部病理分子医学主任。陈教授的主要研究方向为动脉粥样硬化、血管硬化和钙化、糖尿病血管病变以及血管老化的分子机制和信号转导。陈教授的研究项目一直受到美国国家卫生院（NIH),美国老兵总属(VA),以及美国心脏学会（AHA）的资助,主持了多项的重大研究项目。陈教授最近被美国老兵总属科研部授予杰出科学家成就奖。她被聘请为学术期刊《Circulation Research》、《Arteriosclerosis, Thrombosis, and Vascular Biology》和《Journal of Biological Chemistry》编委。自2006 年以来, 陈教授担任美国NIH, VA 及 AHA 科研基金评审委员会成员;当选为美国心脏学会 fellow 和美国心脏学会年会主席团成员。

Dr. Yabing Chen is currently Professor and Vice Chair in the Department of Pathology at the University of Alabama at Birmingham, as well as Principal Investigator at the Birmingham Veterans Affairs (VA) Medical Center. Dr. Chen's research program focuses on understanding the molecular mechanisms of vascular smooth cell regulation and contribution to the pathogenesis of vascular disease, including vascular calcification in atherosclerosis, arterial stiffness, diabetic vasculopathy and vascular aging. Her research has been continuously supported by the National Institutes of Health (NIH), VA and American Heart Association (AHA). She recently received a Research Career Scientist Award from the Veterans Affairs Research Department. Dr. Chen is a Fellow of the American Heart Association (FAHA), and has continuously contributed to AHA, particularly, the Council on Arteriosclerosis, Thrombosis and Vascular Biology (ATVB) by serving on the ATVB Early Career Committee from 2009 to 2011, and ATVB Committee on Scientific Sessions Program of the AHA since 2011. She is currently the Chair of the ATVB Scientific & Clinical Education Lifelong Learning (SCILL) committee; and has been an editorial board member for Circulation Research, Arteriosclerosis, Thrombosis and Vascular Biology and the Journal of Biological Chemistry. Dr. Chen has also served as a regular member or chair on grant review panels for the NIH, VA and AHA, including the NIH Vascular Cell and Molecular Biology (VCMB) and Atherosclerosis and Inflammation of the Cardiovascular System (AICS) study sections, VA Cardiology review panel and AHA Vascular Biology and Vascular Wall Biology grant review committees.

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Yabing Chen	**Professor and Vice Chair** **Department of Pathology**
eRA COMMONS USER NAME **CHENYA**	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
Fudan University, Shanghai, P.R. China	B.Sc.	1988	Biochemistry
Xiamen University, Xiamen, P.R. China	Ph.D.	1996	Cell & Molecular Biology
University of Vermont, Burlington, VT	M.B.A.	2001	Business Administration

A. Personal Statement

My research programs are focused on studying the molecular and cellular mechanisms underlying phenotypic modulation of vascular smooth muscle cells (VSMC) and their contributions to the pathogenesis of vascular diseases, including atherosclerosis, arterial stiffness, diabetic vasculopathy, and other major vascular complications during aging. I have 16 years of experience in vascular biology and have expertise in using primary cell culture, ex vivo organ culture, and genetically modified mouse models to study cardiovascular diseases. Over the years, we have generated several unique mouse models with tissue-specific gene ablation; and accumulate experience using cutting-edge technologies to evaluate vascular cells and their functions during development and in the pathogenesis of vascular disease. Our work in the past few years has determined a definitive role of SMC-specific Runx2 in regulating vascular calcification and stiffness in animal models of atherosclerosis and diabetes.

B. Positions and Honors

Professional Positions

1988-1992	Assistant Engineer and Team Leader, Fuzhou Pharmaceutical Factory, JX, P.R.China.
1992-1996	Graduate Research Fellow, State Lab at Xiamen University. Xiamen, P.R.China.
1997-1998	Postdoctoral Research Associate, Department of Botany and Agricultural Biochemistry, The University of Vermont (UVM), Burlington, VT.
1998-2001	Research Associate, Center for Cardiovascular Research, Department of Medicine, UVM
2001-2004	Instructor, Center for Cardiovascular Research, Department of Medicine, UVM
2004-2010	Assistant Professor, Department of Pathology, The University of Alabama at Birmingham (UAB), Birmingham, AL.
2005-Present	Scientist, UAB Center for Aging, Birmingham, AL.
2005-Present	Scientist, UAB Comprehensive Diabetes Center, Birmingham, AL.
2005-Present	Scientist, UAB Center for Metabolic Bone Disease, Birmingham, AL.
2007-Present	Scientist, UAB Center for Free Radical Biology, Birmingham, AL.
2008-present	Scientist, UAB Nephrology Research Training Center, Birmingham, AL.
2005-2009	Co-Investigator (IPA), Birmingham VA, Research Department, Birmingham AL
2009-present	VA Investigator (6/8), Birmingham VA, Research Department, Birmingham AL
2010-2014	Associate Professor, Department of Pathology, The University of Alabama at Birmingham
2014-present	Professor (tenured), Department of Pathology, The University of Alabama at Birmingham
2016-present	VA Research Career Scientist, Research Department, Birmingham VA Medical Center
2017-present	Vice Chair for Faculty Development and Education, Department of Pathology, The University of Alabama at Birmingham

Awards and Honors

1992	Excellent New Product Awards (Jiangxi Province)
1993-1996	The Guanghua Prize (1st Prize, 4 consecutive years), Xiamen University
1994	The 1st Prize, Graduate Research Papers of Natural Sciences
1995	Excellent Research Paper of Young Scientists, Fujian Science & Technology Asso.
1997	Outstanding Thesis of the Year, Fujian Province
2006-present	Member, VA Research Safety Committee, Birmingham VA Medical Center
2008	American Heart Association Grant Review Committee (Vascular Biology)
2009-10	American Heart Association Grant Review Committee (Vascular Wall Biology)

2009 NIH Grant Review Study Section, special panel for vascular biology (ZRG1 VH-D8)
2009-present Editorial Board Member, *Atherosclerosis Thrombosis and Vascular Biology*
2009 Fellow of American Heart Association
2009-2010 AHA/ATVB Early Career Committee, Member and Editor for Newsletter
2010-2012 NIH Grant Review Study Sections (AICS and VCMB), *Ad Hoc* Reviewer
2011 NIH Grant Review Study Section, Special Panel for P01 (Vascular Smooth Muscle Biology)
2012 NIH Grant Review Study Section, Special Panel for P01 (Bone Biology)
2012-present AHA Committee on Scientific Sessions Program, Representative of ATVB council
2013-present Editorial Board Member, *Journal of Biological Chemistry*
2013-present NIH Grant Review Study Section (VCMB), regular member
2014-present Editorial Board Member, *Circulation Research*
2015-present Chair, UAB Faculty Senate Governance & Operation Committee
2016-present Co-Chair, AHA Grant Review Committee on Vascular Wall Biology
2006-present Vice Chair, VA Research Safety Committee, Birmingham VA
2016 UAB Graduate School Dean's Award for Excellence in Mentorship
2016 Research Career Scientist Award, United States Department of Veterans Affairs
Member, Birmingham VA Research and Development Committee
2016 VA, Research Career Scientist and Promotion Review Committee
2016, 2017 ATVB journal Top 10 Reviewer Award
2017-present Chair, Birmingham VA Mentoring and Career Development Committee
2017 AHA Strategically Focused Research Network (SFRN) - Vascular Disease Review Committees (Phase I and Phase II)
2017 VA Scientific Review Committee on Shared Equipment Evaluation Program (shEEP)
2017 VA Scientific Review Panel, CARDIOLOGY- B
2017 AHA Strategically Focused Research Network (SFRN) - Vascular Disease Review Committees (Phase I and Phase II)
2018 *Ad Hoc* Reviewer, NIH Grant Review Study Sections (VCMB)
2018 Chair, NIH Grant Review Study Section (Special Emphasized Panel)

C. Contribution to Science

Our major contributions in vascular biology have been enhancing our understanding of molecular mechanisms of vascular calcification. We have determined an integrated role of the osteogenic transcription factor Runx2 and Runx2 regulation in pathogenesis of vascular calcification in atherosclerosis and diabetes; uncovered novel mechanisms underlying Runx2 upregulation in the vasculature by oxidative stress and hyperglycemia; and discovered a novel crosstalk between VSMC, macrophages and stem cells in the development of atherosclerotic calcification. Our studies have not only revealed novel molecular insights into vascular calcification, but also support that Runx2-mediated osteogenic signals are potential new targets amenable to drug discovery for vascular disease and aging.

C.1 *Elucidate an essential role of oxidative stress-induced Runx2 in regulating vascular smooth muscle cell osteogenic differentiation and vascular calcification in atherosclerosis.* VSMC exhibit an extraordinary capacity to undergo phenotypic change during development, in cultures and with diseases. Previously considered as passive calcium deposition, vascular calcification is now well established as an active differentiation process of vascular cells, resembling osteogenesis and mineralization of bones. Our group was the first one to establish a mouse primary VSMC calcification model induced by oxidative stress, a key inducer for atherosclerosis and diabetes. We found that oxidative stress induces Runx2 expression via the PI3K/AKT signaling pathways. With gene knockout and gain-of-function system, we demonstrated an essential and sufficient role of Runx2 in oxidative stress-induced VSMC calcification (*JBC* 2008). Our report was selected as a featured article by the North American Vascular Biology Society in 2008 and has been cited over 350 times. This work laid the foundation for the research programs to elucidate the function of Runx2 in regulating vascular calcification in atherosclerosis *in vivo* (*Circ Res* 2012), which was a top downloaded article in Circulation Research in 2012 and selected in the journal highlights. We further identified a direct interaction between Runx2 and serum response factor, a key SMC transcription regulator (*JBMR* 2012); and demonstrated that AKT-regulated FOXO signaling in regulating Runx2 ubiquitination and stability (*ATVB 2015*). These studies in a preclinical atherosclerotic model clearly indicated that Runx2 and Runx2-regulated signals are potential new targets amenable to drug discovery. Recently, we demonstrated dietary potassium regulates Runx2 expression in atherosclerosis, and thus vascular calcification (*JCI Insight 2017*). This work has been well received as a top-read article and highlighted in over 60

news outlets.

a. Byon CH, Javed A, Dai Q, Kappes JC, Clemens TL, Darley-Usmar VM, McDonald JM, **Chen Y**. Oxidative stress induces vascular calcification through modulation of the osteogenic transcription factor RUNX-2 by AKT signaling. ***J Biol Chem.*** **(2008)** 283:15319-15327. PMCID:PMC2397455 (*a featured article in vascular biology, selected by the North American Vascular Biology Organization in 2008, over 350 citation to date)*

b. Sun Y, Byon CB, Yuan K, Chen JF, Mao X, Heath JM, Javed A, Zhang, K, Anderson PG, and **Chen Y**. Smooth muscle cell-specific Runx2 deficiency inhibits vascular calcification. ***Circulation Research.*** **(2012)** 111(5):543-52. PMID:22773442. PMCID:PMC3678289 *(a top downloaded paper in Circ Res in 2012; highlighted in Kidney International in 2012 and Circ Res Thematic Synopsis: Atherosclerosis in 2013)*

c. Deng L*, Huang L*, Sun Y*, Heath JM, Wu H and **Chen Y**. Inhibition of FOXO1/3 promotes vascular calcification. ***Arterioscle Thromb Vasc Biol.*** **(2015)** 35(1):175-83. PMCID:PMC4270841.

d. Sun Y*, Byon CH*, Yang Y, Bradley WE, Dell'Italia LJ, Sanders PW, Agarwal A, Wu H and **Chen Y**. Dietary potassium regulates vascular calcification and arterial stiffness. ***JCI Insight. (2017)*** 5;2(19). pii: 94920. doi: 10.1172/jci.insight.94920. [Epub ahead of print] PMID: 28978809 PMCID:PMC5841863 (*published as An Editor's pick, A top read paper in JCI Insight with a total view over 11,500 in the first week of its publication; Highlighted in JCI This Month in November 2017; Highlighted in over 60 news outlets, including ScienceDaily, Newsweek, USA Today, NIH Research Matters and many others)*

C.2 *Discover the novel mechanisms underlying vascular osteoclasts in atherosclerotic vascular calcification* One of the most intriguing discoveries we made is the identification of a positive correlation of vascular osteoclasts with vascular calcification in atherosclerosis (*ATVB* 2011, *Circ Res* 2012), representing a novel paradigm that atherosclerotic calcification resembles bone remodeling. Osteoclast-like cells were observed in atherosclerotic lesions of human and mouse. However, the regulation and origin of the vascular osteoclast-like cells were unknown. We found that calcified SMC Runx2- dependently increased the expression of receptor activator for nuclear factor κB ligand (RANKL) (*ATVB* 2011), the key osteoclast inducer that we have reported (*JBC* 2008, *JBC* 2010). RANKL has also been shown to promote VSMC calcification but VSMC from RANKL deficient mice still undergo calcification, suggesting that RANKL is not essential for VSMC calcification and it plays a more complex role in regulating vascular calcification. We discovered that VSMC-derived RANKL promoted macrophage migration and differentiation into osteoclasts (*ATVB 2011, Circ Res 2012*). These findings lead to a new direction for us to investigate the Runx2/RANKL-dependent formation of vascular osteoclasts and their function as an emerging novel mechanism of vascular calcification in atherosclerosis.

a. **Chen Y**, Wang X, Di L, Fu G, Chen Y, Bai L, Liu J, Feng X, McDonald JM, Michalek S, He Y, Yu M, Fu YX, Wen R, Wu H, Wang D. Phospholipase Cgamma2 mediates RANKL-stimulated lymph node organogenesis and osteoclastogenesis. ***J Biol Chem.*** **(2008)** 283 (43):29593-601. PMID: 18728019. PMCID:PMC2570883.

b. Chen JF, Sun Y, Mao X, Liu Q, Wu H and **Chen Y**. RANKL Up-regulates Brain-type Creatine Kinase *via* Poly(ADP-ribose) Polymerase-1 during Osteoclastogenesis**.** ***J. Biol. Chem.*** **(2010)** 19;285(47):36315-21. PMCID:PMC2978559.

c. Byon CB, Sun Y, Chen JF, Mao X, Heath JM, Anderson PG, Tintut Y, Demer LL, Wang D and **Chen Y**. Runx2-depedent expression of RANKL during calcification of vascular smooth muscle cells promotes migration and osteoclastic differentiation of macrophages. ***Arterioscle Thromb Vasc Biol.*** **(2011)** 31(6):1387-96. PMID:21454810. PMCID:PMC3098301 (*published with accompanying editorial*)

d. Sun Y, Byon CB, Yuan K, Chen JF, Mao X, Heath JM, Javed A, Zhang, K, Anderson PG, and **Chen Y**. Smooth muscle cell-specific Runx2 deficiency inhibits vascular calcification. ***Circulation Research.*** **(2012)** 111(5):543-52. PMCID:PMC3678289 *(a top downloaded paper in Circ Res in 2012; highlighted in Kidney International in 2012 and Circ Res Thematic Synopsis: Atherosclerosis in 2013)*

C.3 *Discover an important role of protein O-GlcNAcylation in regulating vascular calcification in diabetes.* Our studies in uncovering molecular mechanisms underlying vascular calcification have led to the discovery of the high glucose and oxidative stress *(JBC 2008, ATVB 2011)* and chronic protein O-GlcNAcylation (*Circ Res* 2014) promotes vascular calcification, by enhancing AKT activation through O-GlcNAcylation of AKT that leads to elevation of the Runx2 transactivity. Using constitutively activated AKT, we further demonstrated that AKT activation regulated FOXO1/3-mediated Runx2 ubiquitination that upregulates Runx2 and promotes VSMC calcification (*ATVB 2015*). This line of research has been recognized by an accompanying editorial, a best basic science paper in the AHA scientific sessions (2013) and a most-often read paper in *Circ Res* (August 2014).

a. Byon CH, Javed A, Dai Q, Kappes JC, Clemens TL, Darley-Usmar VM, McDonald JM, **Chen Y**. Oxidative stress induces vascular calcification through modulation of the osteogenic transcription factor RUNX-2 by AKT signaling. J Biol Chem. **(2008)** 283:15319-15327. PMID: 18378684. PMCID:PMC2397455 (*a featured article in vascular biology, selected by the North American Vascular Biology Organization in 2008, over 350 citation to date)*

b. Byon CB, Sun Y, Chen JF, Mao X, Heath JM, Anderson PG, Tintut Y, Demer LL, Wang D and **Chen Y**. Runx2-depedent expression of RANKL during calcification of vascular smooth muscle cells promotes migration and osteoclastic differentiation of macrophages. ***Arterioscle Thromb Vasc Biol.*** **(2011)** 31(6):1387-96. PMID:21454810. PMCID:PMC3098301 (*published with accompanying editorial*)

c. Heath J, Sun Y, Yuan K, Bradley WE, Litovsky S, Dell'Italia LJ, Chatham JC, Wu H and **Chen Y**. O-GlcNAc modification and activation of AKT induces diabetic vascular calcification. ***Circulation Research.*** **(2014)** 28;114(7):1094-102. PMCID:PMC4030422. (*published with accompanying editorial; Editor's pick of the March 28, 2014 issue; a most often read paper in Circ Res in August 2014)*

d. Deng L*, Huang L*, Sun Y*, Heath JM, Wu H and **Chen Y**. Inhibition of FOXO1/3 promotes vascular calcification. *equal contribution. ***Arterioscle Thromb Vasc Biol.*** **(2015)** 35(1):175-83. PMID:25378413. PMCID:PMC4270841.

A List of Published Work in My NCBI
http://www.ncbi.nlm.nih.gov/sites/myncbi/yabing.chen.2/bibliography/41141662/public/?sort=date&direction=ascending.

D. Research Support

Ongoing Research support

NIH/NHLBI R01 **(Chen, PI)** 07/01/17-06/30/22

Novel regulator of vascular smooth muscle cell function

The specific aims are to 1) determine the role of Phospholipase C gamma in regulating vascular smooth muscle cell calcifiction in vivo; and 2) determine Phospholipase C gamma-dependent molecular signals that regulate VSMC matrix vesicle secreation and mineralization.

1IK6BX003617-03 **(Chen, PI)** 10/01/16-09/30/21

VA Research Career Scientist Award

This is a research career scientist award, which recognizes research accomplishments and service to the VA, and provides 5 years' salary support for the PI.

5R01HL092215-08 **(Chen, PI)** 06/24/15-04/30/19

NIH/NHLBI

Molecular Regulation of Vascular Calcification in Atherosclerosis

The specific aims are to: 1) characterize vascular osteoclasts in regulating vascular calcification in atherosclerosis *in vivo*; and 2) define the molecular mechanisms underlying vascular osteoclast-regulated VSMC calcification.

1R01DK100847 **(Chen, PI)** 04/01/14-02/28/19 (NCE)

NIH/NIDDK

O-GlcNAcylation regulates vascular smooth muscle cells in diabetic vasculopathy

The specific aims are to 1) determine the role of protein O-GlcNAcylation in diabetic vascular calcification; and 2) determine O-GlcNAcylation-dependent molecular signals that regulate medial calcification in diabetes.

Completed Research Support (last three years)

1I01BX002296-04 **(Chen, PI)** 04/01/14-3/31/18

VA merit review

Death Receptor Signaling in Pancreatic Cancer: Mechanisms and Therapeutic Targets

The aims are to characterize the function of PARP1 in 1) regulating death receptor-mediated apoptotic signals; 2) regulating death receptor- mediated survival signals; and 3) TRA-8 therapy in mouse models of pancreatic cancer.

1IP1BX001595 (Sanders, contact PI) 10/01/12-09/30/16

VA Program Projects Award **(Chen, Project 2 PI & Director of Molecular Pathology SubCore)**

Novel regulators for vascular disease

The program projects include a series of 3 inter-related projects and a state-of-the-art animal vascular phenotyping core facility. The PPA will focus on the common theme of vascular dysfunction associated with increased arterial stiffness. The objective of Project 2 is to determine the role of mechanisms underlying high salt-induced aortic calcification.

14POST20450117 (Yang, Awardee) 07/01/14-06/30/16

AHA Post-doctoral Fellowship Award **(Chen, Mentor)**

Function of STIM1 in regulating Vascular Calcification

The specific aims are to characterize the function of STIM1 in regulating vascular calcification in vivo; and to determine molecular mechanisms underlying STIM1-regulated VSMC calcification.

5R01HL092215 **(Chen, PI)** 04/01/09-03/31/15

NIH/NHLBI

Molecular Signaling in Oxidative Stress-Induced Vascular Calcification

The specific aims are to: 1) characterize Runx2 dependent vascular calcification in atherosclerosis *in vivo*; and 2) define Runx2 dependent signals in oxidative stress-induced VSMC calcification.