BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Yibing Qyang, PhD	Associate Professor of Medicine and Pathology
eRA COMMONS USER NAME (credential, e.g., agency login) yqyang	

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Nanjing University, Nanjing, China	B.S.	1988-1992	Biochemistry
Institute of Microbiology, CAS, Beijing, China	M.S.	1992-1995	Microbiology
University of Texas M.D. Anderson Cancer Center, Houston, TX	M.S.	1995-1999	Molecular Genetics
University of Texas M.D. Anderson Cancer Center, Houston, TX	Ph.D.	1999-2002	Molecular Genetics

A. Personal Statement

Our research laboratory is interested in employing induced pluripotent stem (iPS) and embryonic stem (ES) cells to develop novel experimental models of human genetic diseases for the purpose of elucidating causative mechanisms and identifying potential therapeutic interventions to treat those diseases. Through a close collaboration with several clinicians at Yale, we are able to obtain cells from a variety of tissues procured from patients with cardiovascular diseases. These cells include dermal fibroblast cells derived from skin punch biopsies or peripheral mononuclear blood cells, which are isolated and reprogrammed into iPS cells in our laboratory before being re-differentiated into functional cardiovascular cells. In this way, we have the ability to derive an unlimited amount of cardiovascular cells containing disease-causing genetic errors for use in our investigations into the specifics of cardiovascular disease mechanisms. In addition to identification of the mechanisms responsible for disease phenotypes, we have interest and experience in producing candidate molecular intervention strategies using small molecule screening and homologous recombination-mediated gene correction.

Another focus of our lab is to derive functional cardiomyocytes, vascular smooth muscle cells, endothelial cells and cardiovascular stem cells from ES and iPS cells, generate engineered cardiac or vascular tissues, and test their cardiovascular repair and regeneration in small and large animal models. Using a multidisciplinary approach to the study of stem cell biology, cardiac development, cardiac physiology, tissue engineering and small molecule screening, we hope to contribute to the understanding of cardiovascular disease mechanisms as well as the development of novel therapeutic interventions for these diseases.

B. Positions and Honors

Positions and Employment

8/02-8/03 Postdoctoral, Huffington Center on Aging, Baylor College of Medicine, Houston.
8/03-8/05 Postdoctoral, Institute of Molecular Medicine, University of California, San Diego.
8/05-9/08 Research Fellow, Cardiovascular Research Center, Massachusetts General Hospital, Harvard Medical School, Harvard Stem Cell Institute, Boston, MA
10/08-6/10 Instructor, Section of Cardiovascular Medicine, Dept. of Internal Medicine, Yale Stem Cell Center, Yale University School of Medicine, New Haven, CT
3/10- Director of Yale Stem Cell Research Forum, Yale Stem Cell Center
7/10-6/16 Assistant Professor of Medicine, Section of Cardiovascular Medicine, Dept. of Internal Medicine, Yale University School of Medicine, New Haven, CT
7/16- Associate Professor of Medicine, Section of Cardiovascular Medicine, Dept. of Internal Medicine, Yale University School of Medicine, New Haven, CT

Other Experience and Professional Membership

2007- The International Society for Stem Cell Research Member (ISSCR)

2009 Reviewer for British Heart Foundation
2011 Reviewer for American Heart Association CVD2 Study Section
2011- Editorial board, Journal of Clinical and Experimental Cardiology
2011- American Heart Association Member
2012 Reviewer for NIH VCMB Study Section
2013 Reviewer for NHLBI Progenitor Cell Biology Consortium
2014 Reviewer for NHLBI PPG
2015 Reviewer for NHLBI NHLBI Cardiovascular Development Consortium
2016 Reviewer for NHLBI PPG

Awards and Honors

2002 Presidents' Research Scholarship Awarded by the Presidents of UT M.D. Anderson Cancer Center and UT Health Science Center at Houston (*Only 4 awards given to over 100 graduate students*).
2002 Alfred G. Knudson Best Dissertation Award by UT M.D. Anderson Cancer Center (*Only 2 awards given to over 50 graduate students).*
2005-08 Ruth L. Kirschstein National Research Service Award (NRSA), Massachusetts General Hospital, Harvard Medical School.
2007 Best Abstract Award in the 2007 Retreat of Harvard Stem Cell Institute, Harvard Medical School (*1 of the 4 winners amongst over 100 competitors*).
2010-12 Scholar award from Yale Center for Clinical Investigation, Yale University.

C. Contribution to Science

1. **Novel role of the ubiquitous transcription factor USF in cellular proliferation and new findings of the p21-activated kinase, Shk1, in modulating microtubule dynamics.** My early publications as a graduate student at The University of Texas M.D. Anderson Cancer Center were focused on studying the novel mechanism of the cell-type-dependent activity of the ubiquitous transcription factor USF in cellular proliferation and transcriptional activation. Through studying its protein expression, subcellular localization and DNA-binding activity, and performing mutational analysis and transcriptional domain swapping experiments, a highly conserved USF-specific region (USR) was proven to be responsible for the inactivity of USF in the osteosarcoma cell line (Saos-2). Furthermore, I investigated the cellular and molecular functions of the p21-activated kinase, Shk1, in the fission yeast. By showing malformed microtubules in *shk1* mutant cells, tight correlation between Shk1 kinase activity and microtubule polymerization and colocalization of Shk1 with microtubules, I established a novel role of this kinase as a microtubule regulator. The above research has contributed significantly to our understanding of transcriptional regulation of cellular proliferation and microtubule dynamics during cell cycle.
   a. **Qyang, Y.,** X. Luo, T. Lu, P.M. Ismail, D. Krylov, C. Vinson & M. Sawadogo. (1999). Cell-type-dependent activity of the ubiquitous transcription factor USF in cellular proliferation and transcriptional activation. *Mol. Cell. Biol.* 19, 1508-17. PMID:9891084. PMCID:PMC116079
   b. *Kim, H., *Yang, P., *__Qyang, Y.__, H. Lai, H. Du, J.S. Henkel, K. Kumar, S. Bao & S. Marcus. Genetic and molecular characterization of Skb15, a highly conserved inhibitor of the Fission Yeast PAK, Shk1. (2001). *Mol. Cell* 7, 1095-1101. (*contributed equally.) PMID:11389855.
   c. *Bao, S., ***Qyang, Y**., *Yang, P., H. Kim, H. Du, G. Bartholomeusz, R. Pimental, F. Verde & S. Marcus**.** (2001). The highly conserved protein methyltransferase, Skb1, is a mediator of hyperosmotic stress response in the fission yeast, *Schizosacchromyces pombe. J. Biol. Chem.* 276, 14549-14552. (*contributed equally.) PMID:11278267.
   d. **Qyang, Y.,** P. Yang, H. Kim, H. Du, H. Lai & S. Marcus. (2002). The p21-Activated Kinase, Shk1, is required for proper regulation of microtubule dynamics in the fission yeast, *Schizosaccharomyces pombe*. *Mol. Microbiol.* 44, 325-334. PMID:11972773.

2. **First demonstration that Wnt/β-catenin signaling pathway plays a key role during pre-specification, self-renewal and cardiac differentiation of *Isl1*$^{+}$ cardiovascular progenitor cells (ISL1-CPCs), as well as showing for the first time robust myocardial regeneration potential of human ISL1-CPCs using a rapid 3D methylcellulose approach.** I performed my postdoctoral research in Dr. Kenneth Chien's laboratory at The Harvard Stem Cell Institute and Harvard Medical School. I isolated a novel population of cardiovascular progenitor cells (CPC) marked by ISL1—a LIM-Homeo domain transcription factor, from rodent and human tissues as well as from murine ES cells. Using a high-throughput small molecule screen, coupled with murine embryonic heart developmental and ES cell-based assays, I discovered that the Wnt/β-catenin

pathway promotes the renewal of these CPC, while negating the pre-specification of mesodermal precursors into CPC and differentiation of these CPC into cardiomyocytes. In my independent group at Yale Univerisity, I discovered a cardiomyogenic role for Bmp4 directly on a pure population of Isl1-CPCs, which could lead to enhancement of cardiac differentiation and engraftment, holding a therapeutic value for cardiac repair. Moreover, we have established highly efficient approaches to derive ISL1-CPCs from human pluripotent stem cells and to enhance the cellular engraftment after implantation into injured hearts, and uncovered novel function of ISL1-CPCs during cardiac repair and regeneration.

a. Moretti, A., Caron, L., Nakano, A., Lam, J.T., Bernshausen, A., Chen, Y., **Qyang, Y.,** Bu, L., Sasaki, M., Martin-Puig, S., Sun, Y., Evans, S.M., Laugwitz, K.L. and Chien, K.R. (2006) Multipotent embryonic isl1+ progenitor cells lead to cardiac, smooth muscle, and endothelial cell diversification. *Cell* 127, 1151-1165. PMID:17123592.
b. **Yibing Qyang**, Silvia Martin-Puig, Murali Chiravuri, Susanna Chen, Huansheng Xu, Lei Bu, Xin Jiang, Lizhu Lin, Anne Granger, Alessandra Moretti, Leslie Caron, Xu Wu, Jonathan Clarke, Makoto M. Taketo, Karl-Ludwig Laugwitz, Randall T. Moon, Peter Gruber, Sylvia M. Evans, Sheng Ding, and Kenneth R. Chien (2007). The Renewal and Differentiation of *Isl1*$^{+}$ Cardiovascular Progenitors Are Controlled by a Wnt/β-Catenin Pathway. *Cell Stem Cell* 1, 165-179. PMID: 18371348.
c. Esra Cagavi, Oscar Bartulos, Carol Y. Suh, Baonan Sun, Zhichao Yue, Zhengxin Jiang, Lixia Yue, **Yibing Qyang** (2014). Functional cardiomyocytes derived from Isl1 cardiac progenitors via Bmp4 stimulation. *PLOS ONE* 9(12):e110752. PMID:25522363. PMCID:PMC4270687
d. Oscar Bartulos, PhD, Zhen Wu Zhuang, MD, Yan Huang, PhD, Nicole Mikush, BS, Carol Suh, MS, Alda Bregasi, MD, Lin Wang, MS, William Chang, MD, PhD, Diane S. Krause, MD, PhD, Lawrence H. Young, MD Jordan S. Pober, MD, PhD, **Yibing Qyang**, PhD (2016). ISL1 Cardiovascular Progenitor Cells for Cardiac Repair after Myocardial Infarction. *JCI Insight* (Accepted).

3. **First report of investigating Supravalvular aortic stenosis (SVAS) using patient-specific induced pluripotent stem cells (iPSCs) and first development of functional 3D tissue rings and tissue-engineered blood vessels using human iPSC-derived vascular smooth muscle cells (VSMCs).** Having patient-specific VSMCs available may facilitate the study of disease mechanisms and development of novel therapeutic interventions. We were the first to describe the development of a human induced pluripotent stem cell (iPSC) line from a patient with SVAS. SVAS iPSC-VSMCs recapitulate key pathological features of patients with SVAS and may provide a promising strategy to study disease mechanisms and to develop novel therapies. Furthermore, the availability of unlimited supply of ESC- or iPSC-derived VSMCs has allowed us for the first time to generate 3D tissue rings for disease mechanism studies in a physiologically more relevant model, as well as to develop tissue-engineered blood vessels for vascular disease treatment.
   a. X. Ge, Y. Ren, Z. Yue, K. Kim, M. Lee, W. Li, P. Amos, E. Bozkulak, W. Zheng, H. Zhao, K. Martin, D. Kotton, G. Tellides, I. Park, L. Yue, **Y. Qyang** (2012). Modeling Supravalvular Aortic Stenosis Syndrome Using Human Induced Pluripotent Stem Cells. *Circulation* 126 (14):1695-1704. PMID: 22914687. PMCID:PMC3586776
   b. Biraja C. Dash, Zhengxin Jiang, Carol Suh, **Yibing Qyang** (2015). Induced Pluripotent Stem Cell-derived Vascular Smooth Muscle Cells: Methods and Application. *Biochemical Journal* 465(2):185-94. PMID:25559088
   c. Biraja C. Dash, Karen Levi, Jonas Schwan, Jiesi Luo, Oscar Bartulos, Hongwei Wu, Caihong Qiu, Ting Yi, Yongming Ren, Stuart Campbell, Marsha W. Rolle, **Yibing Qyang** (2016). Tissue-Engineered Vascular Rings from Human iPSC-Derived Smooth Muscle Cells. *Stem Cell Reports* (Accepted).
   d. Liqiong Gui, Biraja C. Dash, Jiesi Luo, Lingfeng Qin, Liping Zhao, Kota Yamamoto, Takuya Hashimoto, Hongwei Wu, Alan Dardik, George Tellides, Laura E. Niklason, **Yibing Qyang** (2016). Implantable Tissue-Engineered Blood Vessels from Human Induced Pluripotent Stem Cells. *Biomaterials* 102:120-129 (Available online 14 June 2016).

4. **Novel application of small molecule Wnt inhibitor in promoting cardiomyocyte differentiation of ESC and iPSCs.** Human iPSC potentially provide a unique resource for generating patient-specific cardiomyocytes to study cardiac disease mechanisms and treatments. We were the first group to report that small molecule Wnt inhibitors IWP1 or IWP4, instead of costly growth factors, lead to highly efficient production of cardiomyocytes from ESCs or iPSCs with typical electrophysiological function and pharmacologic responsiveness, thereby offering highly affordable platforms for studying cardiac disease mechanisms and therapeutics. We also established robust cardiac differentiation approach in murine ESCs, providing a model system for cardiovascular repair and regeneration research.

a. Ren Y, Lee MY, Schliffke S, Paavola J, Amos PJ, Ge X, Ye M, Zhu S, Senyei G, Lum L, Ehrlich BE, **Qyang Y** (2011). Small molecule Wnt inhibitors enhance the efficiency of BMP-4-directed cardiac differentiation of human pluripotent stem cells. *J Mol Cell Cardiol* 51(3): 280-7. PMID: 21569778. PMCID:PMC3334336
b. Min Young Lee, Esra Cagavi Bozkulak, Simon Schliffke, Peter J. Amos, Yongming Ren, Xin Ge, Barbara E. Ehrlich, **Yibing Qyang** (2011). High density cultures of embryoid bodies enhanced cardiac differentiation of murine embryonic stem cells**.** *Biochemical and Biophysical Research Communications* 416(1-2):51-7. PMID: 22079290. PMCID:PMC3237870
c. Min Young Lee, Baonan Sun, Simon Schliffke, Zhichao Yue, Mingyu Ye, Jere Paavola, Esra Cagavi Bozkulak, Peter J. Amos, Yongming Ren, Rong Ju, Yong Woo Jung, Xin Ge, Lixia Yue, Barbara E. Ehrlich, **Yibing Qyang** (2012). Derivation of functional ventricular cardiomyocytes using endogenous promoter sequence from murine embryonic stem cells. *Stem Cell Research* 8(1):49-57. PMID: 22099020. PMCID:PMC3222859
d. A. Alcon, E. Bozkulak, **Y. Qyang** (2012). Regenerating functional heart tissue for myocardial repair. *Cellular and Molecular Life Sciences* 69(16):2635-56. PMID: 22388688. PMCID:PMC3400705

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/yibing.qyang.1/bibliograpahy/45849661/public/?sort=date&direction=ascending

D. Research Support
Ongoing Research Support

12-SCB-YALE-06 Qyang (PI) 10/15/2012 – 10/14/2016
Connecticut Regenerative Medicine Research Program
Human tissue-engineered blood vessels using induced pluripotent stem cells
The goals of this project are to generate induced pluripotent stem cells (iPSCs) from primary vascular smooth muscle cells, to develop tissue-engineered blood vessels using human umbilical vein endothelial cells (HUVEC) and iPSC-derived smooth muscle cells, and to investigate the function of the engineered vessels 6 weeks after implanting them as aortic interposition grafts in nude rats.

1R01HL114820-01 Jin (PI; Qyang co-I) 04/01/2013 – 03/31/2017
NIH/NHLBI
Bone Morphogenic Protein Signaling in Lymphatic Endothelial Cells
The goal of this project is to delineate the role of BMP2 signaling in negatively regulating the emergence of lymphatic lineage during development.

1R01HL116705-01 Qyang (PI) 09/01/2013 – 08/31/2018
NIH/NHLBI
Human tissue-engineered blood vessels (TEBVs) using induced pluripotent stem cells
The goals of this project are to derive iPSCs from skin fibroblasts, to generate vascular smooth muscle cells and endothelial cells from iPSCs for TEBV production, and to investigate the function of TEBVs 12 and 24 weeks after implantation into nude rats. 25% of the Aim 2 of the 12-SCB-YALE-06 grant is covered by the Aim 2 of this NIH grant, and the overlapped part of the 12-SCB-YALE-06 grant has been removed from the award.

1R01HL125815 Greif (PI; Qyang co-I) 11/17/2014 – 10/31/2018
NIH/NHLBI
Pathological arterial muscularization and the role of integrins
This work utilizes elastin deficient mice, murine smooth muscle cells and human supravalvular aortic stenosis-derived smooth muscle cells, to elucidate the origins of excess smooth muscle cells and the Gax and integrin beta3-mediated mechanisms, which link elastin deficiency to aortic hypermuscularization.

R21 HL126025 Campbell (PI; Qyang co-I) 12/01/2014 – 11/30/2016
NIH/NHLBI
Engineered Tissue for Biomechanical Phenotyping of Cardiomyopathy Patients
The major goal of this study are to are to (a) test the reproducibility of phenotypic measurements made in engineered heart tissue (EHT) produced using the decellularized tissue sheet method and (b) determine the maximum possible sensitivity of this system by assessing phenotypes of EHTs made from patients with clinically mild mutations (MYH7 and CSRP3 genes).

1R01HL122596-01A1 Chan (PI; Qyang co-I) 08/01/2015 – 07/31/2017

NIH/NHLBI
Iron-Sulfur Deficiency is a Critical Pathogenic Lynchpin of Exercise-Induced Pulmonary Hypertension
The major goal of this study is to delineate the role of miR-210, ISCU, and FXN in controlling iron-sulfur expression, mitochondrial metabolism, and pulmonary hypertension.

15-RMB-YALE-08 Qyang (PI) 12/01/2015 – 11/30/2019
Connecticut Regenerative Medicine Research
Targeted Investigation into the Causes and Amelioration of Vascular Proliferative Disease Using Patient-derived Induced Pluripotent Stem Cells
The purpose of this project is to unravel the pathological mechanism of the devastating vascular proliferative diseases and to discover novel therapies using patient-specific induced pluripotent stem cells in conjunction with high-throughput small molecule screening from a library enriched with FDA-approved drugs.

1R01HL132130-01 Qyang (PI) 07/01/2016 – 06/30/2020
NIH/NHLBI
Biomechanical Signaling in Human Familial Hypertrophic Cardiomyopathy
The goal of this project is to elucidate the pathogenesis of hypertrophic cardiomyopathy by determining the mechanism by which the βMHC and MLP pathways synergistically interact with each other in modulating the disease severity using cellular models and engineered heart tissue constructs.

DOD 11959515 Qyang (PI) 06/1/2016 – 12/31/2017
Department of Defense
Engineering of Pulsatile Conduits from Human Pluripotent Stem Cell-derived Cardiomyocytes
The goal of this project is to seed human induced pluripotent stem cell-derived cardiomyocytes and/or cardiac progenitor cells into biodegradable polyglycolic acid (PGA) scaffolds, to culture cells within PGA scaffolds in a pulsatile bioreactor, and to develop a tissue-engineered pulsatile conduit to pump blood through the pulmonary circulation in a rat model in order to set foundation for establishing a curative, reconstructive surgical option for patients born with single ventricle anomalies.

Completed Research Support

PI (Han); Subcontract Investigator (Qyang) 10/01/2012 – 12/31/2015
Cardiovascular Medical Research and Education Fund
Targeting metabolism to reverse RV dysfunction in PAH
The goal of this project is to use molecular, cellular and imaging approaches to unravel whether right ventricular (RV) cardiomyocyte-intrinsic defects contributes to RV failure in patients with Pulmonary arterial hypertension (PAH).

1K02HL101990-01 Qyang (PI) 07/15/2010 – 05/31/2015
NIH Independent Scientist Award
Derivation and Functional Characterization of Heart Cells from Human Embryonic (ES) and Induced Pluripotent Stem (iPS) Cells
The goals of this award are to derive and characterize heart cells from human ES and iPS cells.

11SCA33 Amos (PI; Qyang co-PI) 03/01/2012 – 07/31/2014
Connecticut Regenerative Medicine Research Program
The role of endocardial cells in human Down syndrome-related heart defects
The goal of this study is to derive and characterize a pure population of endocardial cells for the purpose of developing a means of modeling atrioventricular septal defects in Down syndrome patients.

09SDG2080420 Qyang (PI) 07/01/2009 – 06/30/2014
American Heart Association Scientist Development Grant (National)
Wnt signaling and Functional Characterization of *Isl*$^{+}$ Cardiovascular Progenitor Cells
The goal of this study is to study murine Isl^{+} Cardiovascular Progenitor Cells.

11SCB18 Qyang (PI; Breuer co-PI) 11/01/2011 – 10/31/2013
Connecticut Regenerative Medicine Research Program
Pulsatile tissue-engineered grafts for surgical correction of single ventricle cardiac anomalies
The goals of this award are to characterize ventricular cardiomyocytes (VCMs) derived from human embryonic and induced pluripotent stem cells, to establish cell sheet from human VCMs, to develop pulsatile tissue-engineered grafts by wrapping VCM sheets around tubular scaffolds, and to implant pulsatile grafts as inferior vena cava interposition grafts in murine hearts.