BIOGRAPHICAL SKETCH

NAME: **Joseph C. Wu, MD, PhD**

eRA COMMONS USER NAME (credential, e.g., agency login): **wujos2**

POSITION TITLE: **Professor & Director of Stanford Cardiovascular Institute**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of California, Los Angeles	B.S.	06/1993	Biology
Yale School of Medicine, New Haven	M.D.	06/1997	Medicine
University of California, Los Angeles	Ph.D.	06/2004	Molecular Pharmacology

A. PERSONAL STATEMENT

I am the Simon Stertzer Professor of Medicine and Radiology and Director of Stanford Cardiovascular Institute. My research career has been dedicated to making fundamental discoveries in cardiovascular medicine. We use a combination of multi-omics, molecular & cellular biology, tissue engineering, cardiovascular physiology, and imaging technologies to answer key biological questions. We have made seminal discoveries in the areas of **(i)** disease modeling, (ii) genomics-epigenomics, (iii) pharmacogenomics & drug discovery, (iv) regenerative medicine, and (v) precision medicine (see Section C on "Contributions to Science").

My scholarly work consists of >600 publications with H-index of 130 on Google Scholar and recognition as top 0.1% of highly cited researchers in Web of Science for past 6 years (2018, 2019, 2020, 2021, 2022, 2023). To date, >50 of my former postdoctoral fellows are now faculty in the US and abroad. I have received several awards, including the NIH Director's New Innovator Award, NIH Roadmap Transformative Award, Presidential Early Career Award for Scientists and Engineers given at the White House by President Obama, Burroughs Wellcome Foundation Innovation in Regulatory Science Award, American Heart Association (AHA) Merit Award, and AHA Distinguished Scientist Award.

I also serve on the FDA Cellular, Tissue, and Gene Therapies Advisory Committee and the Keystone Symposia Scientific Board of Directors. I am an elected member of the American Institute for Medical and Biological Engineering (AIMBE), Association of University Cardiologists (AUC), American Association of Physicians (AAP), American Association for Advancement of Science (AAAS), National Academy of Inventors (NAI), and National Academy of Medicine (NAM). I currently serve as President of the American Heart Association (July 2023 – June 2024).

Representative research covered in the following reviews. Detailed research manuscripts are listed in section C.

a) Kim H, Kamm RD, Vunjak-Novakovic G, **Wu JC**. Progress in multicellular human cardiac organoids for clinical applications. ***Cell Stem Cell*** 2022;29(4):503-514. PMID: 35395186
b) Zhang A, Xing L, Zou J, **Wu JC**. The new wave of artificial intelligence in healthcare: shifting from development to deployment and from models to data. ***Nature Biomed Eng*** 2022;6(12):1330-1345. PMID: 35788685
c) Cho S, Discher DE, Leong KW, Vunjak-Novakovic G, **Wu JC.** Challenges and opportunities for the next generation of cardiovascular tissue engineering. ***Nature Methods*** 2022;19(9):1064-1071. PMID: 36064773.
d) Tan WLW, Seow WQ, Zhang A, Rhee S, Wong WH, Greenleaf WJ, **Wu JC**. Current and future perspectives of single-cell multi-omics technologies in cardiovascular research. ***Nature Cardiovasc Res*** 2023;2:20-34.

Ongoing projects to highlight:

T32 EB009035 Wu, Pauly, Nieman (multi-PI) 07/01/2015 – 06/30/2024
NIH/NIBIB
Multi-Disciplinary Training Program in Cardiovascular Imaging at Stanford
This project seeks to train the next generation of scientists in applications of multi-modality cardiovascular imaging.

R25 HL147666 Red-Horse, Wu, Perez (multi-PI) 09/19/2019 – 08/31/2024
NIH/NHLBI
Stanford Undergraduate URM Summer Cardiovascular Research Program
This program invites and trains under-represented minority students from across the country for a summer research program at the Stanford Cardiovascular Institute. Overlap: none

P01 HL141084 Wu, Mercola, Bers (multi-PI) 09/01/2019 – 08/31/2024
NIH/NHLBI
Elucidating the Electro-Mechanical Dysfunction in Heart Failure with Human Stem Cell Models
This project seeks to understand the mechanisms by which altered Na+ and Ca^{2+} signaling contribute to electromechanical dysfunction in heart failure using human stem cell model.

75N92020D00019 Wu (PI) 09/01/2020 – 08/30/2025
NIH/NHLBI
Biorepository of Human Induced Pluripotent Stem Cells for Cardiovascular Diseases (BHIPSC-CVD)
This project will generate iPSCs from cardiovascular disease patients for usage by the broader scientific community.

R01 HL141371-05 Wu, Qi, Wong (multi-PI) 06/01/2022 – 03/30/2026
NIH/NHLBI
Human iPSCs for Elucidating Intercellular Crosstalk Signaling in Dilated Cardiomyopathy
This project will characterize cell type-specific secretomes and elucidate cell-cell crosstalk signaling in LMNA cardiomyopathy.

R01 HL130020 Mercola, Liao, Wu (multi-PI) 07/01/2023 – 04/30/2027
NIH/NHLBI
Human iPSC Model to Elucidate Metabolic Interplay in Diabetic Cardiomyopathy
This project will elucidate cell-type specific mechanisms of SGLT2i in T2D.

B. POSITIONS, SCIENTIFIC APPOINTMENTS & HONORS

Positions and Employment

2015-	Simon H. Stertzer, MD, Endowed Professorship, Stanford University
2013-	Director, Stanford Cardiovascular Institute, Stanford University
2013-	Professor, Dept of Medicine & Radiology, Stanford University
2012-2013	Co-Director, Stanford Cardiovascular Institute, Stanford University
2010-2012	Associate Professor, Dept of Medicine & Radiology, Stanford University
2007-2010	Assistant Professor, Dept of Medicine & Radiology, Stanford University
2004-2006	Instructor, Dept of Medicine & Radiology, Stanford University
2000-2004	PhD in Molecular & Medical Pharmacology (Advisor: Sanjiv S. Gambhir, MD, PhD)
1999-2004	Cardiology Fellowship, UCLA Medical Center
1997-1999	Medicine Internship & Residency, UCLA Medical Center

Editorial Board: *Journal Clinical Investigation* (2012-current); *Circulation Research* (2011-2015; Associate Editor 2015-2022); *Nature Review Cardiology* (2017-current); *Cardiovascular Research* (Senior Advising Editor 2018-current); *Circulation: CV Imaging* (2008-current); *Human Gene Therapy* (2009-current); *Molecular Therapy* (2011-current); *Stem Cell Research* (2012-current); *Scientific Report* (2015-current), *Current Opinion in Physiology* (2020-current), *Journal of Nanobiotechnology* (2021-current).

Professional Services:

2023	President, American Heart Association
2022	President-Elect, American Heart Association
2022-2025	Board of Directors, Keystone Symposia
2021-2022	Member, National Academies Committee on Life and Physical Sciences Research in Space
2021-2023	Member, National Academies Committee on New Approach Methods in Toxicology
2018-2022	Member, NHLBI Program Project Grant (PPG) Review Committee
2018-2020	Chair, AHA Basic Cardiovascular Science (BCVS) Council

2017-2023 FDA Cellular, Tissue, and Gene Therapies Advisory Committee Member
2017-2021 National Board of Directors, American Heart Association
2017-2021 Chair, National Research Committee for American Heart Association (AHA)
2014-2021 Scientific Advisory Board, Keystone Symposia
2014-2017 Councilor, American Society of Clinical Investigation (ASCI)
2012-2016 Member, Cardiac Contractility, Hypertrophy and Failure (CCHF) Study Section

Awards and Honors:

2023 Gill Heart & Vascular Institute Cardiovascular Research Award ($25,000 prize)
2022 Elected to National Academy of Inventors (NAI)
2022 Elected to Academician, Academia Sinica (Taiwan)
2021 Honorary Lifetime Membership, Society of Toxicology (SOT)
2019 Elected to National Academy of Medicine (NAM)
2019 Elected to Fellow of American Association for Advancement of Science (AAAS)
2019 British Society of CV Research Bernard and Joan Marshall Distinguished Investigator Lecture
2018-2022 Top 0.1% of Highly Cited Researchers in Web of Science (2018, 2019, 2020, 2021, 2022)
2018 Elected to Fellow of American Institute for Medical and Biological Engineering (AIMBE)
2018 American Heart Association Distinguished Scientist Award
2017 American Heart Association Merit Award
2015 Elected to American Association of Physicians (AAP)
2015 Inaugural recipient of the Joseph A. Vita Award from the American Heart Association
2015 Burroughs Wellcome Foundation Innovation in Regulatory Science Award
2014 Academy for Radiology & Biomedical Imaging Research Distinguished Investigator Award
2013-2017 American Heart Association Established Investigator Award
2013 Elected to Association of University Cardiologists (AUC)
2012, 17, 18 Best Manuscript Award in *Circ Res* (2012;111:882-893; 2017;120:1561-71; 2018;123:443-450)
2012 Elected to American Society of Clinical Investigation (ASCI)
2010 Presidential Early Career Award for Scientists & Engineers (PECASE) given at the White House by President Barack Obama
2009 American Heart Association (AHA) National Innovative Research Award
2009-2015 NIH Roadmap Transformative Award (TR01)
2008-2013 NIH Director's New Innovator Award (DP2)
2007-2012 Burroughs Wellcome Foundation Career Award for Medical Scientists
2006, 13 Best Basic Science Manuscript Award in *Circulation* (2006;113;1005-14 & 2013;127;1677-91)

C. CONTRIBUTION TO SCIENCE

Total Publications: >600 papers; H-index = 128; i10-index >540; citations >58,000 (Google scholar)
Top 0.1% Highly Cited Researchers in Web of Science from Clarivate Analytics past 6 years (2018-2023)
Complete List of Published Work in: https://www.ncbi.nlm.nih.gov/pubmed/?term=wu+jc+and+stanford
ORCID # 0000-0002-6068-8041

1) Disease Modeling: My lab has made seminal discoveries on how human induced pluripotent stem cells (iPSCs) can be used to model mechanisms of inherited cardiomyopathies, channelopathies, and other acquired cardiovascular diseases. iPSCs can also be used to identify loci or pathways related to disease predisposition via genome editing techniques (e.g., CRISPR/Cas9), thus enabling genotype-phenotype correlations, and improve risk stratification and disease management. Representative publications include:

a) Burridge PW, Li YF, Matsa E, Wu H, Ong SG, Sharma A, Chang AC, Coronado MJ, Ebert AD, Knowles JW, Telli ML, Witteles RM, Blau HM, Bernstein D, Altman RB, **Wu JC**. Human induced pluripotent stem-derived cardiomyocytes recapitulate the predilection of breast cancer patients to doxorubicin-induced cardiotoxicity. ***Nature Medicine*** 2016;22(5):547-56. PMID: 27089514. PMCID: 5086256 (*Accompanied Editorial)
b) Davis J, Davis LC, Correll RN, Makarewich CA, Wang D, York AJ, Wu H, Houser SR, Seidman CE, Seidman JG, Regnier M, Metzger JM, **Wu JC**, Molkentin JD. A tension-based model distinguishes hypertrophic versus dilated cardiomyopathy. ***Cell*** 2016;165(5):1147-59. PMID: 27114035. PMCID: 4874838
c) Wilson KD, Ameen M, Guo H, Abilez OJ, Tian L, Mumbach MR, Diecke S, Qin X, Liu Y, Yang H, Ma N, Gaddam S, Cunningham N, Gu M, Neofytou E, Prado M, Hildebrandt TB, Karakikes I, Chang HY, **Wu JC**.

Endogenous retroviral-derived lncRNA *BANCR* promotes cardiomyocyte migration in humans and non-human primates. ***Developmental Cell*** 2020; S1534-5807(20)30580-3. PMID: 32763147

d) Guo H, Yu X, Liu Y, Paik DT, Justesen JM, Chandy M, Jahng JW, Zhang T, Wu W, Rwere F, Zhao SR, Pokhrel S, Shivnaraine R, Mukherjee S, Simon DJ, Manhas A, Zhang A, Chen CH, Rivas MA, Gross ER, Mochley-Rosen D, **Wu JC**. SGLT2i inhibitor ameliorates endothelial dysfunction associated with the common *ALDH2* alcohol flushing variant. ***Sci Transl Med*** 2023;15(680):eabp9952. PMID: 36696485

2) Genomics & Epigenomics: Human ESCs and iPSCs are defined by their self-renewal and pluripotency potential. My lab has been working on human ESCs since 2004 and on human iPSCs since 2008. We have made several seminal contributions to the field. We are interested in understanding the genomic and epigenetic landscape changes during reprogramming, differentiation, development, and in response to various stress factors or environmental stimuli. Representative publications include:

a) Kodo K, Ong SG, Jahanbani F, Termglinchan V, Hirono K, Inanloo Rahatloo K, Ebert AD, Shukla P, Abilez OJ, Churko JM, Karakikes I, Jung G, Ichida F, Wu SM, Snyder MP, Bernstein D, **Wu JC**. Abnormal activation of TGFβ signaling as a pathogenesis of left ventricular non-compaction cardiomyopathy. ***Nature Cell Biology*** 2016;18(10):1031-42. PMID: 27642787. PMCID: 5042877

b) Churko JM, Lee J, Ameen M, Gu M, Venkatasubramanian M, Diecke S, Sallam K, Im H, Wang G, Gold JD, Salomonis N, Snyder MP, **Wu JC**. Transcriptomic and epigenomic differences in human induced pluripotent stem cells generated from six reprogramming methods. ***Nature Biomed Eng*** 2017;1(10):826-837. PMID: 30263871. PMCID: 6155993 (*Editorial by TF Allison & WE Lowry)

c) Lee J, Shao NY, Paik DT, Wu H, Guo H, Termglinchan V, Churko J, Kim Y, Kitani T, Zhao MT, Zhang Y, Wilson KD, Karakikes I, Snyder MP, **Wu JC**. Dynamic role of SETD7 as a transcriptional activator of cardiac lineage commitment. ***Cell Stem Cell*** 2018;22(3):428-444. PMID: 29499155. PMCID: 5929163

d) Ameen M, Sundaram L, Shen M, Banerjee A, Kundu S, Nair S, Shcherbina A, Gu M, Wilson KD, Varadarajan A, Vadgama N, **Wu JC,** Engreitz JM, Farh K, Karakikes I, Wang KC, Quertermous T, Greenleaf WJ, Kundaje A. Integrative single-cell analysis of cardiogeneis identifies developmental trajectories and non-coding mutations in congenital heart disease. ***Cell*** 2022;185(26):4937-4953. PMID: 36563664

3) Pharmacogenomics & Drug Discovery: Drug discovery is an arduous and expensive process. On average, new drug requires more than $1.8 billion and 12 years from the time of discovery to commercial launch. Taking a cue from the Precision Medicine Initiative, my lab has been focusing on how we can use human iPSCs combined with human genomics to better understand pharmacogenomics and hence accelerate drug discovery. Representative publications include:

a) Matsa E, Burridge PW, Yu KH, Ahrens JH, Termglinchan V, Wu H, Liu H, Shukla P, Sayed N, Churko JM, Shao N, Woo NA, Chao AS, Gold JD, Karakikes I, Snyder MP, **Wu JC**. Transcriptome profiling of patient-specific human iPSC-cardiomyocytes predicts individual drug safety and efficacy responses in vitro. ***Cell Stem Cell*** 2016;19:311-325. PMID: 27545504. PMCID: 5087997

b) Sharma A, Burridge PW, McKeithan WL, Serrano R, Shukla P, Sayed N, Churko JM, Kitani T, Wu H, Holmstrom A, Matsa E, Zhang Y, Kumar A, Fan AC, del Alamo JC, Wu SM, Moslehi JJ, Mercola M, **Wu JC**. High-throughput screening of tyrosine kinase inhibitor-induced cardiotoxicity using human induced pluripotent stem cells. ***Science Transl Med*** 2017;9(377). PMID: 28202772. PMCID: 5409837

c) Sayed N, Liu C, Ameen M, Himmati F, Zhang JZ, Khanamiri S, Moonen JR, Wnorowski A, Cheng L, Rhee JW, Gaddam S, Wang KC, Sallam K, Boyd JH, Woo YJ, Rabinovitch M, **Wu JC**. Clinical trial in a dish using iPSCs shows lovastatin improves endothelial dysfunction and cellular crosstalk in LMNA cardiomyopathy. ***Science Transl Med*** 2020;12(554):eaax9276. PMID: 32727917.

d) Wei TT, Chandy M, Nishiga M, Zhang A, Kumar KK, Thomas D, Manhas A, Rhee S, Justesen JM, Chen IY, Wo HT, Khanamiri S, Yang JY, Seidl FJ, Burns NZ, Liu C, Sayed N, Shie JJ, Yeh CF, Yang KC, Lau E, Lynch KL, Rivas M, Kobilka BK, **Wu JC**. Cannabinoid receptor 1 antagonist genistein attenuated marijuana-induced vascular dysfunction. ***Cell*** 2022;185(10):1676-1693. PMID: 35489334.

4) Regenerative Medicine: Clinical trials using adult stem cells (e.g., BMSCs, MSCs, CPCs) for post-myocardial infarction patients have been actively investigated. However, the challenges for using ESC- or iPSC-based cardiac therapies are significantly greater given the hurdles of tumorigenicity, immunogenicity, safety monitoring, and cost-effectiveness. Over the past 10 years, we have performed several seminal studies addressing these specific areas ranging from basic to clinical arenas. Representative publications include:

a) Burridge PW, Matsa E, Shukla P, Lin ZC, Churko JM, Ebert AD, Lan F, Diecke S, Huber B, Mordwinkin NM, Plews JR, Abilez OJ, Cui B, Gold JD, **Wu JC**. Chemically defined generation of human cardiomyocytes. ***Nature Methods*** 2014;11(8):855-860. PMID: 24930130. PMCID: 4169698
b) Lee AS, Inayathullah M, Lijkwan MA, Zhao X, Sun W, Parekh MB, Kooreman N, Malkovskiy AV, Lau E, Qin X, Pothineni VR, Park S, Hong WX, Sanchez-Freire V, Zhang WY, Ebert AD, Chan CK, Nguyen PK, Rajadas J, **Wu JC**. A novel slow release collagen matrix cross-linked with pro-survival factor analogs promotes stem cell survival for treatment of ischemic cardiovascular disease. ***Nature Biomed Eng*** 2018;2: 104-113. PMID: 29721363. PMCID: 5927627 (highlighted in *Sci Transl Med* 2018;10:431:eaar7536)
c) Zhang JZ, Termgilnchan V, Shao NY, Itzhaki I, Liu C, Ma N, Tian L, Wang VY, Chang ACY, Guo H, Kitani T, Wu H, Lam Ck, Kodo K, Sayed N, Blau HM, **Wu JC**. A human iPSC double-reporter system enables purification of cardiac lineage subpopulations with distinct function and drug response profiles. ***Cell Stem Cell*** 2019;24(5):802-811. PMID: 30880024. PMCID: 6499654.
d) Tu C, Caudal A, Liu Y, Gorgodze N, Zhang H, Lam CK, Dai Y, Zhang A, Wnorowsk A, Wu MA, Yang H, Abilez OJ, Lyu X, Narayan SM, Mestroni L, Taylor MRG, Recchia FA, **Wu JC**. Tachycardia-induced metabolic rewiring as a driver of contractile dysfunction. ***Nature Biomed Eng*** 2023;doi: 10.1038/s41551-023-01134-x

5) Precision Medicine: Precision medicine seeks to link molecular data with the clinical disease phenotypes and to identify patient subpopulations that differ in their disease susceptibility, progression, and prognosis. Instead of one-drug-fits-all model, the ultimate goal is to customize prevention and treatment tailored for individual patient. My lab has been integrating genomics, transcriptomics, proteomics, metabolomics, bioinformatics, and imaging to exactly answer this question. Representative publications include:

a) Wu H, Lee J, Vincent JG, Wang Q, Gu W, Lan F, Churko J, Sallam K, Matsa E, Sharma A, Gold JD, Engler AJ, Xiang YK, Bers DM, **Wu JC**. Epigenetic regulation of phosphodiesterases 2A and 3A underlies compromised β-adrenergic signaling in iPSC model of dilated cardiomyopathy. ***Cell Stem Cell*** 2015;17(1): 89-100. PMID: 26095046. PMCID: 4546705
b) Churko JM, Garg P, Treutlein B, Venkatasubrmanian M, Wu H, Lee J, Wessells QN, Chen SY, Chen WY, Chetal K, Mantalas G, Neff N, Jabar E, Sharma A, Nolan GP, Salomonis N, **Wu JC**. Defining human cardiac transcription factor hierarchies using integrated single-cell heterogeneity analysis. ***Nature Comm*** 2018;9(1): 4906. PMID: 30464173. PMCID: 6249224
c) Lee J, Termglinchan V, Diecke S, Itzhaki I, Lam CK, Garg P, Lau E, Greenhaw M, Seeger T, Wu H, Zhang JZ, Chen X, Gil IP, Ameen M, Sallam K, Rhee JW, Churko J, Chaudhary R, Yi SA, Nam KH, Chour T, Wang PJ, Snyder MP, Chang HY, Karakikes I, **Wu JC**. Activation of PDGF pathway links LMNA mutation to dilated cardiomyopathy. ***Nature*** 2019;572(7769):335-340. PMID: 31316208. PMCID: 6779479
d) Liu C, Shen M, Tan WLW, Chen IY, Liu Y, Yu X, Yang H, Zhang A, Liu Y, Zhao MT, Ameen M, Zhang M, Gross ER, Qi LS, Sayed N, Wu JC. Statins improve endothelial function via suppression of epigenetics driven-EndMT. ***Nature Cardiovasc Res*** 2023;2:467-485