BIOGRAPHICAL SKETCH

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

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

POSITION TITLE: **Director of Stanford Cardiovascular Institute & Professor of Medicine and Radiology**

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of California, Los Angeles	B.S.	1989-93	Biology
Yale School of Medicine, New Haven	M.D.	1993-97	Medicine
University of California, Los Angeles	Ph.D.	2000-04	Molecular Pharmacology

A. Personal Statement

I am the Director of the Stanford Cardiovascular Institute and Professor in the Department of Medicine (Cardiology) and Radiology (Molecular Imaging). My research career has been dedicated to making fundamental discovers in stem cell biology and molecular imaging technologies for the cardiovascular system. My lab currently works on biological mechanisms of adult stem cells, embryonic stem cells (ESCs), and induced pluripotent stem cells (iPSCs). We use a combination of molecular/cellular biology, genomic/epigenomic profiling, tissue engineering, physiological testing, and molecular imaging technologies to better understand stem cell biology *in vitro* and *in vivo*. We have made seminal discoveries in the areas of cardiac iPSCs for **(i)** disease modeling, **(ii)** drug discovery, and **(iii)** regenerative medicine. I have also received numerous prestigious research awards, including the Burroughs Wellcome Foundation Career Award for Medical Scientists (2007), the NIH Director's New Innovator Award (2008), the NIH Roadmap Transformative R01 Award (2009), AHA Innovative Research Award (2009), and the Presidential Early Career Award for Scientists and Engineers from President Obama (2010) for my research. I am also a Council member of the American Society of Clinical Investigation (2014-2017) and a Scientific Advisory Board member for the Keystone Symposia (2014-2017).

1. Sun N, Yazawa M, Liu J, Han L, Abilez O, Navarette EG, Hu S, Wang L, Lee A, Pavlovic A, Lin S, Chen R, Hajjar RJ, Snyder MP, Dolmetsch RE, Butte MJ, Ashley EA, Longaker MT, Robbins RC, **Wu JC**. Patient-specific induced pluripotent stem cells as a model for familial dilated cardiomyopathy. ***Science Transl Med*** 2012;4(130):130ra47. PMID: 22517884. (*Journal cover)
2. Lister R, Mukamel EA, Nery JR, Urich M, Puddifoot CA, Johnson ND, Lucero J, Huang Y, Dwork AJ, Schultz MD, Yu M, Tonti-Filippini J, Pastor WA, Heyne H, Hu S, **Wu JC**, Rao A, Esteller M, He C, Haghighi FG, Sejowski TJ, Behrens MM, Ecker JR. Global epigenomic reconfiguration during mammalian brain development. ***Science*** 2013;341(6146):1237905. PMID: 2382889
3. 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
4. Matsa E, Burridge PW, Wu JC. Human stem cells for modeling heart disease and drug discovery. ***Science Transl Med*** 2014;6(239):239ps6. PMID: 24898747

B. Positions and Honors

Positions and Employment

1997-1998 Medicine Internship, UCLA Medical Center
1998-1999 Medicine Residency, UCLA Medical Center
1999-2004 Cardiology Fellowship, UCLA Medical Center
2000-2004 PhD Graduate Student in Molecular & Medical Pharmacology, Advisor: Sanjiv Gambhir
2004-2006 Instructor, Dept of Medicine & Radiology, Stanford University
2007-2010 Assistant Professor, Dept of Medicine & Radiology, Stanford University
2010-2012 Associate Professor, Dept of Medicine & Radiology, Stanford University
2012-2013 Co-Director, Stanford Cardiovascular Institute, Stanford University
2013- Professor, Dept of Medicine & Radiology, Stanford University
2013- Director, Stanford Cardiovascular Institute, Stanford University

Other Experience and Professional Membership & Activities:

2008- Editorial Board, *Circulation: Cardiovascular Imaging*
2008 Senior Guest Editor, *JACC: Cardiovascular Imaging*
2009- Editorial Board, *Journal Nuclear Cardiology, Human Gene Therapy*
2010- Editorial Board, *Cytotherapy, Current Cardiovascular Imaging Reports*
2011- Editorial Board, *Stem Cell Research, Molecular Therapy, Circulation Research*
2012- Editorial Board, *Journal Clinical Investigation, Current Protocols in Stem Cell Research*
2013- Editorial Board, *Physiological Genomics*
2015- Editorial Board, *Scientific Report*
2015- Associate Editor, *Circulation Research*

Honors and Awards:

1989 Salutatorian, South Pasadena High School
1989-1993 University of California Regents Scholarship, UCLA
1993 *Summa Cum Laude*, UCLA
1993-1997 Yale University School of Medicine Scholarship
1997 *Alpha Omega Alpha*, Yale
2003-2005 GlaxoSmithKline Young Investigator Grant Award
2005-2009 NHLBI K08 Clinician Scientist Award
2006-2008 American College of Cardiology (ACC) Career Award in Cardiovascular Imaging
2006 William Guy Forbeck Scholar Award ("Focus on Stem Cells")
2006 Best Basic Science Manuscript Award (*Circulation* 2006;113;1005-1014)
2007-2012 Burroughs Wellcome Foundation (BWF) Career Award for Medical Scientists
2008 Baxter Foundation Faculty Award
2008-2011 Edward Mallinckrodt Jr. Foundation Junior Faculty Award
2008-2013 NIH Director's New Innovator Award (DP2)
2009 American Heart Association National Innovative Research Award,
2009 Douglas Zipes Distinguished Young Scientist Award, American College of Cardiology
2009-2014 NIH Roadmap Transformative Award (TR01)
2010 Presidential Early Career Award for Scientists & Engineers (PECASE) given by President Obama at the White House
2011 Bernard and Joan Marshall Research Excellence Prize, British Society of CV Research
2012 Elected to American Society of Clinical Investigation (ASCI)
2013 Best Manuscript Award (*Circulation Research* 2012;111:882-893)
2013 American Heart Association Established Investigator Award (EIA)
2013 Elected to Association of University Cardiologists (AUC)
2014 Academy of Radiology Research Distinguished Investigator Award
2014-2017 Elected as Councilor for American Society of Clinical Investigation (ASCI)
2014-2017 Scientific Advisory Board, Keystone Symposia
2014 Best Basic Science Manuscript Award (*Circulation* 2013;127;1677-1691)
2015 Elected to American Association of Physicians (AAP)

C. Contributions to Science
A total of >250 publications of importance to the field.

1. Cardiovascular molecular imaging: My early research focused on the field of cardiovascular molecular imaging. During my PhD, I was trained by one of the early pioneers in this field (Sanjiv S. Gambhir, MD, PhD) and published seminal findings on how we can use molecular imaging to understand cardiac gene & stem cell therapy. This field uses multimodality imaging approaches such as positron emission tomography (PET), magnetic resonance imaging (MRI), magnetic resonance spectroscopy (MRS), optical bioluminescence, optical fluorescence, and ultrasound to probe fundamental biological questions in living subjects.

Representative publication:

a) **Wu JC**, Chen IY, Sundaresan G, Min JJ, De A, Qiao JH, Fishbein MC, Gambhir SS. Molecular imaging of cardiac cell transplantation in living animals using optical bioluminescence and positron emission tomography. ***Circulation*** 2003;108:1302-1305. PMID: 12963637. (*Journal cover)

b) Cao F, Lin S, Xie X, Ray P, Patel M, Drukker M, Dylla SJ, Connolly AJ, Chen X, Weissman IL, Gambhir SS, **Wu JC**. In vivo visualization of embryonic stem cell survival, proliferation, and migration after cardiac delivery. ***Circulation*** 2006;113(7):1005-14. PMID: 16476845 (*Best Basic Science paper in *Circulation* 2006)

c) Nguyen PK, Riegler J, **Wu JC**. Stem cell imaging: from bench to bedside. ***Cell Stem Cell*** 2014;14(4):431-444. PMID: 24702995. PMCID: 4024441

d) Kooreman NG, Ransohoff JD, **Wu JC**. Tracking gene and cell fate for therapeutic gain. ***Nature Materials*** 2014;13(2):106-9. PMID: 24452344

2. Pluripotent stem cell biology: Pluripotent stem cells (PSCs), which include both embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs), are defined by their self-renewal and pluripotent potential. My lab has been working on human ESCs since 2004 and on human iPSCs since 2008. We have made seminal contributions to the field, including the first description of reprogramming using adipose stromal cells and first description of reprogramming using non-viral minicircle vector. Currently, we are interested in understanding the molecular, cellular, and epigenetic landscape changes during the reprogramming process.

Representative publications:

a) Sun N, Panetta NJ, Gupta DM, Wilson KD, Lee A, Jia F, Hu S, Cherry AM, Robbins RC, Longaker MT, **Wu JC**. Feeder-free derivation of induced pluripotent stem cells from adult human adipose stem cells. ***Proc Natl Acad Sci*** 2009;106:15720-15725. PMID: 19805220

b) Jia F, Wilson KD, Sun N, Gupta DM, Huang M, Li Z, Robbins RC, Chen ZY, Kay MA, Longaker MT, **Wu JC**. A nonviral minicircle vector for inducing human iPS cells. ***Nature Methods*** 2010;7(3):197-9. PMID: 20139967

c) Narsinh KH, Sun N, Sanchez-Freire V, Lee AS, de Almeida PE, Hu S, Jan T, Wilson KD, Leong D, Rosenberg J, Yao M, **Wu JC**. Increased heterogeneity of human induced pluripotent stem cells by single cell transcriptional profiling. ***J Clin Invest*** 2011;121(3):1217-21. PMID: 21317531

d) Tang C, Lee AS, Peter-Volkmer J, Sahoo D, Mosley A, van de Rijn M, Inlay MA, Ardehali R, **Wu JC**, Weissman IL, Drukker M. Removal of residual teratoma-forming cells via a surface antibody panel ensures transplantation safety of human pluripotent stem cell derivatives. ***Nature Biotech*** 2011;29(9):829-34. PMID: 21841799 (*Journal cover)

3. Regenerative medicine: Clinical trials using adult stem cells (e.g., BMSCs,MSCs, CPCs) for post-myocardial infarction patients are already underway. Similarly, ESC- and iPSC-derived retinal pigment epithelial cells are now being tested for treatment of patients with macular degeneration. However, the challenges for using ESC- or iPSC-based cardiac therapies are significantly greater given the potential issue of tumorigenicity, immunogenicity, and safety monitoring. Over the past 10 years, we have performed several seminal studies addressing these specific areas as outlined below:

Representative publications:

a) Swijnenburg RJ, Schrepfer S, Govaert JA, Cao F, Sheikh AY, Haddad M, Connolly AJ, Davis MD, Robbins RC, **Wu JC**. Immunosuppressive therapy mitigates immunological rejection of human embryonic stem cell xenografts. ***Proc Natl Acad Sci*** 2008;105(35):12991-6. PMID: 18728188 (*Editorial in *Cell Stem Cell*)

b) Pearl JI, Lee A, Leveson-Gower DB, Sun N, Ghosh Z, Lan F, Ransohoff J, Negrin RS, Davis MM, **Wu JC**. Short-term blockade of leukocyte costimulatory molecules promotes engraftment of embryonic and induced pluripotent stem cells. ***Cell Stem Cell*** 2011;8(3):309-17. PMID: 21362570. PMCID: 3061351 (*Editorial)

c) Lee AS, Tang C, Rao MS, Weissman IL, **Wu JC**. Tumorigenicity as a clinical hurdle for pluripotent stem cells. ***Nature Med*** 2013;19(8):998-1004. PMID: 23921754

d) Vrtovec B, Poglajen G, Lezaic L, Sever M, Cernelc P, Socan A, Schrepfer S, Torre-Amione G, Haddad F, **Wu JC**. Effects of intracoronary $CD34^+$ stem cell transplantation in non-ischemic dilated cardiomyopathy patients: 5-year follow up. ***Circulation Res*** 2013;112:165-173. PMID: 23065358 (*Journal cover and editorial)

4. Pharmacogenomics: Drug discovery is an arduous and expensive process. For example, the average new drug requires more than $1.8 billion and 12 years from the time of discovery to commercial launch. To reduce the high costs and high attrition rates, novel technologies capable of predicting and identifying potential efficacy and safety issues early in the discovery process is needed. Taking a cue from President Obama's Precision Medicine initiative, my lab is focusing on how we can use patient-specific and disease-specific of iPSC derivatives to accelerate the drug discovery process, which will benefit our patients tremendously.

Representative publications:

a) Burridge PW, Keller G, Gold JD, **Wu JC**. Production of de novo cardiomyocytes: human pluripotent stem cell differentiation and direct reprogramming. ***Cell Stem Cell*** 2012;10(1):16-28. PMID: 2226352

b) Liang P, Lan F, Lee AS, Gong T, Sanchez-Freire V, Wang Y, Diecke S, Sallam K, Knowles JW, Nguyen PK, Wang PJ, Bers DM, Robbins RC, **Wu JC**. Drug screening using a library of human induced pluripotent stem cell-derived cardiomyocytes reveals disease specific patterns of cardiotoxicity. ***Circulation*** 2013;127:1677-1691. PMID: 23519760 (*Accompanied Editorial; 2013 Best Basic Science Paper in *Circulation*)

c) Asimaki A, Kapoor S, Plovie E, Arndt AK, Adams E, Liu ZZ, James CA, Judge DP, Calkins H, Churko J, **Wu JC**, MacRae CA, Kleber AG, Saffitz JE. Identification of a new modulator of the intercalated disc in a zebrafish model of arrhythmogenic cardiomyopathy. ***Science Transl Med*** 2014:6(240): p240ra74. PMID: 24920660.

d) Wilson KD, **Wu JC**. Induced pluripotent stem cells. ***JAMA*** 2015;313(16):1613-4. PMID: 25919522.

5. Cardiovascular disease modeling: My lab has made seminal discoveries on how investigators can use iPSC-derived cardiomyocytes to model mechanisms of inherited cardiomyopathies, channelopathies, and other acquired cardiovascular disease conditions. Beyond these capabilities, iPSCs can also be used to identify loci or pathways related to predisposition toward cardiac disorders via genome editing techniques (eg, TALEN and CRISPR/Cas), thus enabling refinement of phenotype-to-genotype correlations, and hence improve risk stratification and disease management.

Representative publications:

a) Sharma A, Marceau CD, Hamaguchi R, Burridge P, Rajarajan K, Churko J, Wu H, Sallam K, Matsa E, Sturzu A, Che Y, Ebert A, Diecke S, Liang P, Red-Horse K, Carette JE, Wu SM, **Wu JC**. Human induced pluripotent stem cell-derived cardiomyocytes as an in vitro model for coxsackievirus B3-induced myocarditis and antiviral drug screening platform. ***Circulation Res*** 2014;115:556-566. PMID: 25015077. PMCID: 4149868 (*Journal cover & 2 accompanied editorials)

b) Lan F, Lee AS, Liang P, Sanchez-Freire V, Nguyen PK, Wang L, Han L, Yen M, Wang Y, Sun N, Abilez OJ, Navarrete EG, Simons CS, Wheeler M, Pruitt B, Lewis R, Ashley EA, Bers DB, Robbins RC, Longaker MT, **Wu JC**. Abnormal calcium handling properties underlie pathogenesis of familial hypertrophic cardiomyopathy in patient-specific induced pluripotent stem cells. ***Cell Stem Cell*** 2013;12(1):101-13. PMID: 23290139 (*Faculty 1000 Must Read Paper)

c) Ebert AD, Kodo K, Liang P, Wu H, Huber BC, Riegler J, Churko J, Lan F, Diecke S, Burridge PW, Gold JD, Mochly-Rosen D, **Wu JC**. Characterization of the molecular mechanisms underlying increased ischemic damage in the aldehyde dehydrogenase 2 genetic polymorphism using a human induced pluripotent stem cell model system. ***Science Transl Med*** 2014;6:255ra130. PMID: 25253673. PMCID: 4215699

d) 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; in press.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/pubmed/?term=wu+jc+and+stanford