BIOGRAPHICAL SKETCH

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NAME: **Oscar J. Abilez, MD, PhD**

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

POSITION TITLE: **Senior Scientist, Stanford University**

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 Texas, Austin, TX	BS	1992	Mechanical Engineering
Cornell University, New York, NY	MD	2002	Medicine
Stanford University Medical Center, Stanford, CA	Residency	2002-2004	Surgery
Stanford University, Stanford, CA	Postdoctoral	2004-2007	Stem Cell Biology
Stanford University, Stanford, CA	PhD	2007-2012	Bioengineering
Stanford University, Stanford, CA	Postdoctoral	2012-2013	Stem Cell Biology

A. Personal Statement.

My role in the proposed project is that of PD/PI. My research interests are aimed at elucidating how various biophysical and bioengineered perturbations regulate early cardiovascular development across time and length scales that span several orders of magnitude, using human pluripotent stem cells (hPSCs) as a model system.

During my research training from 2008-2016 my career was interrupted due to family care responsibilities, and I was constrained to living in the Bay Area. Because of this constraint, in 2012 I declined a tenure-track assistant professor position at a major academic institution outside the Bay Area. In 2016, I was again able to increase my research effort and was also awarded an NIH-NHLBI K01 Mentored Career Development Award that spanned from 2016 to 2022.

My extensive training in cardiovascular hPSC biology and bioengineering informs my current research on applying geometric, biochemical, electrical, mechanical, and optogenetic perturbations to control and manipulate the directed differentiation, maturation, and organization of hPSC-derived cardiovascular cells, engineered heart tissue, and organoids. My long-term goal is to elucidate fundamental mechanisms of human cardiac development and vascularization and to use this knowledge to pursue diagnostics and therapies for congenital and adult heart disease.

The research support and selected publications listed below serve as the basis for my proposed project as they highlight my expertise in hPSC biology, bioengineering, and transcriptomics to create and characterize multicellular tissues, and organoids. I have not published or created research products under another name.

<u>Ongoing Research Support</u>:

Seed Grant — Lee (PI) — Dec 01, 2021-Nov 30, 2022
Stanford Cardiovascular Institute (CVI)
“Understanding Ventricular Tachycardia: A Wholistic Approach Using Porcine and Isolated Perfused Human Heart Models"
The goal of this project is to investigate ventricular tachycardia using perfused heart models.
Role: Collaborator

Loan Repayment Program (LRP) Renewal — Abilez (PI) — Jul 01, 2022 – Jun 30, 2024
National Institutes of Health / NHLBI
“Modeling the Earliest Stages of Cardiac Development using Human Pluripotent Stem Cells”

The goal of this program is to repay my educational loans while modeling the earliest stages of cardiac development.
Role: PI

Completed Research Support:

K01 HL130608 Abilez (PI) Feb 01, 2016-Jan 31, 2022
National Institutes of Health / NHLBI
"Optogenetic Engineered Heart Muscle for Disease Modeling"
The goal of this mentored career award is to use optogenetic engineered heart muscle to elucidate the mechanisms of dilated cardiomyopathy.
Role: PI

Seed Grant Bernstein (PI) Jul 01, 2020-Jun 30, 2022
Stanford Maternal & Child Health Research Institute (MCHRI) Transdisciplinary Initiatives Program (TIP)
"Modeling the Earliest Developmental Stages of Human Cardiac Vascularization using Pluripotent Stem Cells"
The goal of this project is to model the earliest developmental stages of human cardiac vascularization using geometric micropatterning of human pluripotent stem cells.
Role: Co-Investigator

5R25HL145817, Subaward 703992 Abilez (PI) Feb 01, 2020-Jul 31, 2021
NIH / NHLBI Small Research Project
"Elucidating the Role of NOTCH1 in Impaired Cardiogenesis in Hypoplastic Left Heart Syndrome Using Vascularized Cardiac Tissue Derived from Human Pluripotent Stem Cells"
The goal of this project is to elucidate the role of NOTCH1 in Hypoplastic Left Heart Syndrome (HLHS)
Role: PI

Selected Publications:

1. ***Abilez OJ**, Yang H, Tian L, Wilson KD, Lyall EH, Shen M, Bhoi R, Zhuge Y, Jia F, Wo HT, Zhou G, Guan Y, Aldana B, Obal D, Peltz G, Zarins CK, Wu JC.* Micropatterned organoids enable modeling of the earliest stages of human cardiac vascularization. **bioRxiv**. 2022:2022.07.08.499233.

2. *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 NJ, Gu M, Neofytou E, Prado M, Hildebrandt TB, Karakikes I, Chang HY, Wu JC*. Endogenous retrovirus-derived lncRNA BANCR promotes cardiomyocyte migration in humans and non-human primates. **Developmental Cell**. 2020 Sep 28;54(6):694-709. PMID: 32763147.

3. ***Abilez OJ**, Tzatzalos E, Yang H, Zhao MT, Jung G, Zöllner AM, Tiburcy M, Riegler J, Matsa E, Shukla P, Zhuge Y, Chour T, Chen VC, Burridge PW, Karakikes I, Kuhl E, Bernstein D, Couture LA, Gold JD, Zimmermann WH, Wu JC*. Passive stretch induces structural and functional maturation of engineered heart muscle as predicted by computational modeling. **Stem Cells**. 2018 Feb;36(2):265-277. PMID: 29086457.

4. *Myers FB, Silver JS, Zhuge Y, Beygui RE, Zarins CK, Lee LP, **Abilez OJ***. Robust pluripotent stem cell expansion and cardiomyocyte differentiation via geometric patterning. **Integrative Biololgy** (Camb). 2013 Oct 18. PMID: 24141327.

B. Positions, Scientific Appointments, and Honors.

Positions and Employment:

2021-present Senior Scientist, Stanford, CA
2022-present Consultant, Rosebud Biosciences, San Carlos, CA
2013-2021 Instructor, Stanford University Medical Center, Stanford, CA
2012-2013 Postdoctoral Scholar, Stanford University, Stanford, CA
2007-2012 PhD Bioengineering Graduate Student, Stanford University, Stanford, CA
2004-2007 Postdoctoral Scholar, Stanford University, Stanford, CA
2002-2004 Surgery Resident, Stanford University Medical Center, Stanford, CA
1998-2000 Medical Student Research Fellow, Cornell University, New York, NY
1994-1996 MS Bioengineering Graduate Student, University of Texas, Austin, TX

1993-1996 Engineering Staff, CarboMedics, Inc., Austin, TX
1991-1991 Engineering Co-op, General Motors Desert Proving Ground, Mesa, AZ
1989-1990 Engineering Co-op, General Motors Assembly Plant, Shreveport, LA

Professional Memberships and Activities:

2022-present Associate Editor, Frontiers in Physiology, Cardiac Electrophysiology
2020-present International Society for Stem Cell Research (ISSCR)
2020-present Society for Biomaterials (SFB)
2020-present International Society for Applied Cardiovascular Biology (ISACB)
2010-2012 Biophysical Society (BPS)
2006-2012 Biomedical Engineering Society (BMES)
2005-2012 Tissue Engineering & Regenerative Medicine International Society (TERMIS)
2005-2006 American College of Surgery (ACS)
2000-2002 President, Stimson Surgical Society, Cornell University Medical School
1999-1999 American Society for Cell Biology (ASCB)
1995-2000 American Society of Artificial Internal Organs (ASAIO)
1996-1998 Class President, Cornell University Medical School

Honors and Awards:

2022 Stanford Andrew Olson Scientific Image Award
2020 UC San Diego Future Faculty of Cardiovascular Sciences (FOCUS) Summer Institute Scholar
2019 Stanford-Penn Cardiovascular Meeting-1st Place Poster
2016-2021 NIH-NHLBI K01 Mentored Career Development Award
2011 New York Stem Cell Foundation 6th Annual Meeting-1st Place Poster
2011 Siebel Scholar
2011 Gordon Research Conference Scholarship
2011 Keystone Conference Scholarship and Research Competition Finalist
2007-2011 Advanced Residency Training at Stanford (ARTS) Fellowship, Stanford
2010 California Institute for Regenerative Medicine (CIRM) Travel Award
2005-2006 Dean's Postdoctoral Fellowship, Stanford
2002 Franklyn Ellenbogen Prize in Hematology/Oncology, Cornell
2002 Student Leadership Award-Class President, Cornell
2002 US-European Medical Education Exchange (US-EUMEE) Fellowship, Cornell
2002 American Austrian Foundation/Max Kade Foundation Fellowship, Cornell
1999-2000 NIH-NHLBI Predoctoral Research Training Fellowship, Cornell
1998-1999 Lucille P. Markey Foundation Predoctoral Research Training Fellowship, Cornell
1996-1997 NIH Molecular Mechanism-Neural Disease Predoctoral Training Fellowship, Cornell
1995 Biomedical Engineering Scholarship, University of Texas
1991 Pi Tau Sigma Mechanical Engineering Honor Society, University of Texas
1989 General Motors Scholarship, University of Texas
1988-1991 Engineering Honor Roll, University of Texas
1988-1991 Dean's List, University of Texas
1987-1992 Texas Achievement Award, University of Texas
1987 Valedictorian, Junction High School

C. Contributions to Science.

A total of > 40 publications of importance to the field.

1. Pluripotent stem cell biology: Human pluripotent stem cells (hPSCs), which include both embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs), are defined by their self-renewal and pluripotent potential. I have been working on mouse ESCs since 2005, human ESCs since 2006, and on human iPSCs since 2008. I have made contributions to the field in differentiation, sorting, and patterning of hPSC-derived cardiomyocytes to understand their function. Currently, I am interested in understanding the molecular, cellular, and epigenetic landscape changes during the differentiation process.

Representative publications:

a) *Yang H, Shao N, Holmström A, Zhao X, Chour T, Chen H, Itzhaki I, Wu H, Ameen M, Cunningham NJ, Tu C, Zhao MT, Tarantal AF,* ***Abilez OJ****, Wu JC*. Transcriptome analysis of non-human primate induced

pluripotent stem cell-derived cardiomyocytes in 2D monolayer culture versus 3D engineered heart tissue. **Cardiovascular Research.** 2021 Jul 27;117(9):2125-2136. PMID: 33002105.

b) *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 Aug;11(8):855-60. PMID: 24930130.

c) *Myers FB, Zarins CK, **Abilez OJ***, Lee LP**.* Label-free electrophysiological cytometry for stem cell-derived cardiomyocyte clusters. **Lab Chip**. 2013 Jan 21;13(2):220-8. PMID: 23207961. (*co-corresponding authors) (cover article)

d) ***Abilez OJ**, Wu JC*. Stem cell isolation: Differential stickiness. **Nature Materials**. 2013 Jun;12(6):474-6. PMID: 23695740.

2. Cardiac optogenetics/electrophysiology: One of my main research areas has focused on cardiac optogenetics. Optogenetics was pioneered in the neural field by Karl Deisseroth, MD, PhD at Stanford (2005, Boyden et al., Nature Neuroscience). Optogenetics is the targeted genetic introduction of light-sensitive channels and pumps into cells that enables their high spatiotemporal control by optical actuation, leading to downstream generation and inhibition of electrical action potentials. With Professor Deisseroth as a collaborator, we were the first to report the optogenetic pacing of hiPSC-derived cardiomyocytes in 2011.

Representative publications:

a) *Zhuge Y, Patlolla B, Ramakrishnan C, Beygui RE, Zarins CK, Deisseroth K, Kuhl E, **Abilez OJ**.* Human pluripotent stem cell tools for cardiac optogenetics. **Conf Proc IEEE Eng Med Biol Soc**. 2014:6171-6174.

b) ***Abilez OJ***. Optogenetic LED array for perturbing cardiac electrophysiology. **Conf Proc IEEE Eng Med Biol Soc**. 2013 Jul;2013:1619-22. PMID: 24110013.

c) ***Abilez O***. Cardiac optogenetics. **Conf Proc IEEE Eng Med Biol Soc**. 2012:1386-9. PMID: 2336615.

d) ***Abilez O**, Wong J, Prakash R, Deisseroth K, Zarins CK, Kuhl E*. Multiscale computational models for optogenetic control of cardiac function. **Biophysical Journal**. 2011 Sep 21;101(6):1326-34. PMID: 21943413

3. Cardiovascular disease modeling: With my former mentor Joseph Wu, MD, PhD, I have contributed to the seminal discoveries on how investigators can use hPSC-derived cardiomyocytes to model mechanisms of inherited cardiomyopathies, channelopathies, and other acquired cardiovascular disease conditions. Beyond these capabilities, hPSCs can also be used to identify loci or pathways related to predisposition toward cardiac disorders via genome editing techniques (CRISPR/Cas9), thus enabling refinement of phenotype-to-genotype correlations, and hence improve risk stratification and disease management.

Representative publications:

a) *Kodo K, Ong SG, Jahanbani F, Termglinchan V, Hirono K, InanlooRahatloo K, Ebert AD, Shukla P, **Abilez OJ**, Churko JM, Karakikes I, Jung G, Ichida F, Wu SM, Snyder MP, Bernstein D, Wu JC.* iPSC-derived cardiomyocytes reveal abnormal TGF-β signaling in left ventricular non-compaction cardiomyopathy. **Nature Cell Biology**. 2016 Oct;18(10). PMID: 27642787.

b) *Ardehali R, Ali SR, Inlay MA, **Abilez OJ**, Chen MQ, Blauwkamp TA, Yazawa M, Gong Y, Nusse R, Drukker M, Weissman IL*. Prospective isolation of human embryonic stem cell-derived cardiovascular progenitors that integrate into human fetal heart tissue. **Proc Natl Acad Sci USA**. 2013 Feb 7. PMID: 23391730.

c) *Lan F, Lee AS, Liang P, Sanchez-Freire V, Nguyen PK, Wang L, Han L, Yen M, Wang Y, Sun N, **Abilez OJ**, Hu S, Ebert AD, Navarrete EG, Simmons CS, Wheeler M, Pruitt B, Lewis R, Yamaguchi Y, Ashley EA, Bers DM, Robbins RC, Longaker MT, Wu JC.* Abnormal calcium handling properties underlie familial hypertrophic cardiomyopathy pathology in patient-specific induced pluripotent stem cells. **Cell Stem Cell**. 2013 Jan 3;12(1):101-13. PMID: 23290139.

d) *Sun N, Yazawa M, Liu J, Han L, Sanchez-Freire V, **Abilez OJ**, Navarrete 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 Translational Med**. 2012; 4 (130): 130ra47. PMID: 22517884.

4. Regenerative medicine/bioengineering: The challenges for using hESC- or hiPSC-based regenerative therapies are significant given the potential issue of tumorigenicity, immunogenicity, and safety monitoring. In addition, issues such as vascularization, cellular composition, and scale-up also pose challenges to effectiveness. Over the past 16 years, I have contributed to several studies addressing these specific areas as outlined below.

Representative publications:

a) *Tzatzalos E*, **Abilez OJ***, Shukla P, Wu JC*. Engineered heart tissues and induced pluripotent stem cells: Macro- and microstructures for disease modeling, drug screening, and translational studies. **Adv Drug Deliv Rev**. 2016 Jan 15;96:234-44. PubMed PMID: 26428619. (*equal contribution)

b) *Chang EI, Galvez MG, Glotzbach JP, Hamou CD, El-ftesi S, Rappleye CT, Sommer K, Rajadas J, **Abilez OJ**, Fuller GG, Longaker MT, Gurtner GC*. Vascular anastomosis using controlled phase transitions in poloxamer gels. **Nature Medicine**. 2011 Aug 28;17(9):1147-52. doi: 10.1038/nm.2424.

c) ***Abilez O**, Benharash P, Miyamoto E, Gale A, Xu C, Zarins CK*. P19 progenitor cells progress to organized contracting myocytes after chemical and electrical stimulation: implications for vascular tissue engineering. **J Endovasc Ther**. 2006 Jun;13(3):377-88. PMID: 16784327.

d) ***Abilez O**, Benharash P, Mehrotra M, Miyamoto E, Gale A, Picquet J, Xu C, Zarins C*. A novel culture system shows that stem cells can be grown in 3D and under physiologic pulsatile conditions for tissue engineering of vascular grafts. **J Surg Res**. 2006 May 15;132(2):170-8. PMID: 16542683.

5. Computational modeling of cardiovascular function: Using the fundamental laws of physics, I have assisted my collaborators in creating interactive simulation tools to predict the physiology and pathology of cardiovascular systems. Our goal is to understand the mechanisms by which cardiovascular systems grow, develop, evolve, and adapt.

Representative publications:

a) *Böl M, **Abilez O**, Assar AN, Zarins CK, Kuhl E*. Active and passive stresses in electro-active cardiac muscle-a robust in vitro/in silico model to study isometric contractions. **International Journal for Multiscale Computational Engineering**. 2012: 10(2):171-188.

b) *Rausch MK, Dam A, Göktepe S, **Abilez O**, Kuhl E*. Computational modeling of growth: systemic and pulmonary hypertension in the heart. **Biomechanics and Modeling in Mechanobiology**. 2011 Dec; 10(6):799-811. PMID: 21188611).

c) *Göktepe S, **Abilez O**, Kuhl E*. A generic approach towards finite growth with examples of athlete's heart, cardiac dilation, and cardiac wall thickening. **Journal of the Mechanics and Physics of Solids**. 2010 Oct;58:1661-1680.

d) *Göktepe S, **Abilez O**, Parker KK, Kuhl E*. A multiscale model for eccentric and concentric cardiac growth through sarcomerogenesis. **J Theor Biol**. 2010 Aug 7;265(3):433-42. Epub 2010 May 4. PMID: 20447409.

Inventions/Disclosures:

1. ***Abilez OJ**, Yang H, Wu JC*, Stanford University. "Creation of Vascularized Biological Structures." USA. 2022. (Disclosed to Stanford Office of Technology Licensing, Docket S22-080, USPTO Patent Pending US 63/314,958).
2. *Lee L, Myers FB, Silver JS, Zarins CK, **Abilez OJ***, UC Berkeley and Stanford University. "Stencil Patterning Method for Generating Highly Uniform Stem Cell Colonies." USA. 2012. (Disclosed to UC Berkley Office of Technology Licensing, Docket BK-2012-020-1 and Stanford Office of Technology Licensing, Docket S11-387, USPTO Patent Pending 61/585,097).
3. ***Abilez O**, Kuhl E, Zarins C*, Stanford University. "Optical Biological Pacemaker and Defibrillator." USA. 2011. (Disclosed to Stanford Office of Technology Licensing, Docket S11-204).
4. ***Abilez O**, Myers F, Lee L, Zarins C*, Stanford University. "Systems and Methods for Electrophysiological Cell Sorting and Cytometry." USA. 2010. (Disclosed to Stanford Office of Technology Licensing, Docket S10-370, USPTO Patent Pending 61/474,213).
5. ***Abilez O**, Benharash P, Zarins C*, Stanford University. "Cell Sorter and Culture System." USA. 2005. (Disclosed to Stanford Office of Technology Licensing, Docket S05-377, USPTO Patent Pending 11/732,911, Filed 4/05/2007).
6. ***Abilez O***, Stanford University. "Tools and Instruments with Locking Mechanism that Allows Both Left and Right Handed Use." USA. 2004. (Disclosed to Stanford Office of Technology Licensing, Docket S04-303).
7. ***Abilez O***, Stanford University. "Systems, Methods, and Apparatus Configurations Using Genetic Algorithms to Design Cells, Tissues, and Tissue Systems." USA. 2004. (Disclosed to Stanford Office of Technology Licensing, Docket S04-293).

Complete List of Published Work in MyBibliography:
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