BIOGRAPHICAL SKETCH

NAME: Kitchener D. Wilson

eRA COMMONS USER NAME: WILSON.KITCH

POSITION TITLE: Instructor, Pathology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Stanford University, Stanford, CA	B.S.	12/1997	Mechanical Engineering
Duke University, Durham, NC	M.D.	05/2006	Medicine
Stanford University, Stanford, CA	M.S.	06/2007	Bioengineering
Stanford University, Stanford, CA	Ph.D.	06/2010	Bioengineering
Stanford University, Stanford, CA (residency)		06/2014	Clinical Pathology
Stanford University, Stanford, CA (fellowship)		06/2013	Molecular Genetic Pathology

A. Personal Statement

My goal for my clinical practice and research pursuits is Precision Medicine that takes advantage of 21st century technologies. This includes not just "–omic" data (genomic, epigenomic, etc.), but also knowledge gained from patient-specific and disease-specific human induced pluripotent stem cells (iPSCs). These cells present an opportunity to *rapidly phenotype the genome*, and have given scientists a relatively quick and inexpensive method for discovering patient-specific therapies. I am therefore developing myself into both a stem cell scientist and genomic scientist/clinician, with the goal of combining these two fields into a career as an NIH-funded independent investigator (note that I was awarded a K08 in 2016). These goals are a natural synthesis of my clinical background (Attending Physician in Molecular Pathology) and my stem cell research under my longtime mentor Dr. Joseph Wu (Director, Cardiovascular Institute) at Stanford. After completion of residency and fellowship in 2014, I returned to the lab and am now using a variety of tools for interrogating the genome-phenotype interplay in the human heart.

In my basic research I am merging next generation sequencing (NGS) with iPSCs in order to discover and study long noncoding RNAs (lncRNAs) that regulate cardiac development and disease. Interestingly, one lncRNA that we identified, BANCR, is a known driver of migration and metastasis in cancer but exhibits fetal heart-specific expression in its wildtype state, suggesting a role in heart development. Through knockdown and over-expression studies, we have found that BANCR regulates cardiomyocyte migration, similar to its function in cancer cells. Although BANCR originated from a primate endogenous retrovirus more than 30 million years ago and is thus not expressed in mouse, transgenic BANCR knock-in murine embryos do exhibit a mild increase in heart size. Using RNA-seq, ChIP-seq, ChIRP-seq, and ChIRP-mass spectrometry, we have found that TBX5 regulates BANCR expression, and BANCR itself directly targets cardiac development and oncogenic pathways, as well as cell adhesion proteins. This study is the first to describe a primate lncRNA with striking effects on human cardiomyocyte development that has implications for cardiogenesis, oncogenesis and even primate evolution. I expect to submit this work for publication in 2017.

In my clinical research I have been developing custom NGS assays for identifying the DNA mutations that underlie cardiomyopathies, channelopathies, congenital heart disease, and sudden cardiac death. This includes a project that I lead at the Stanford Genome Technology Center (Director, Dr. Ron Davis) to develop a novel assay for inherited cardiomyopathies and congenital heart disease using double-stranded complementary padlock probes (cLPPs). Having secured seed funding from multiple sources, in 2015 we published the first paper describing this technology and its application for cardiovascular genetic testing (Wilson et al. Circ Res 2015, *journal cover*).

B. Positions and Honors

Positions and Employment

1998-1999	Research and Design Engineer, Medtronic Inc., Goleta, CA
2001	Remote Area Medical health volunteer, Aishalton District Hospital, Aishalton, Guyana
2002-2006	Medical Student, Duke University School of Medicine, Durham, NC
2006-2010	Graduate Student, Bioengineering, Stanford University, Stanford, CA
2010-2014	Resident, Clinical Pathology, and Fellow, Molecular Genetic Pathology, Stanford University School of Medicine, Stanford, CA
2014-	Instructor, Department of Pathology, Stanford University, Stanford, CA

Other Experience and Professional Memberships

2006-	International Society for Stem Cell Research
2010-	College of American Pathologists
2010-	Stanford Society of Physician Scholars
2011-	Medical licensure, The Medical Board of California
2012-	Association for Molecular Pathology

Honors

1993	Valedictorian, San Marcos High School, Santa Barbara, CA
2005	Medical School Thesis (received Honors): "Quantitation of Male Mononuclear Cells Transplanted to Female Myocardium Using Real-time PCR Analysis of Y Chromosome, in Swine."
2007	Genomics and Proteomics Workshop Travel Award, National Jewish Medical and Research Center, Denver, CO
2007	Society of Nuclear Medicine Student Fellowship
2008	Stanford University Bio-X Travel Award
2007-2010	Stanford University Bio-X Graduate Student Fellowship: "Investigating the Cardiac Stem Cell Niche Using Genomic, Proteomic and Molecular Imaging Tools".
2012	Mass Spectrometry Applications to the Clinical Lab (MSACL) 2012 Trainee Travel Award
2013-2019	NIH Clinical Loan Repayment Program Awardee
2013	Stanford Cardiovascular Institute Seed Grant
2014	Steven M. Gootter Foundation Seed Grant
2016	NIH K08 (1K08HL119251)

C. Contribution to Science

1. In my graduate research I was primarily focused on measuring and manipulating the molecules – messenger RNA and microRNA - that regulate human embryonic stem cells (hESCs) and iPSCs. For example, I was the first to publish the "microRNA-ome" of iPSCs and show that there are subtle differences when compared to hESCs. Manipulation of one microRNA cluster in particular, miR-302, increased the reprogramming efficiency of somatic cells into iPSCs. This work led to an NIH Director's New Innovator Award for Dr. Wu in 2008. In other work, I demonstrated that novel non-viral minicircle DNA vectors could reprogram adult cells to iPSCs, thus bypassing the transgene integration difficulties that confound standard viral reprogramming methods.
    a. **Wilson KD**, Wu JC. Induced pluripotent stem cells. JAMA. 2015: Apr 28;313(16):1613-4. (PMID: 25919522)
    b. Hu S, **Wilson KD**, Ghosh Z, Han L, Wang Y, Lan F, Ransohoff KJ, Levi B, Longaker MT, Wu JC. MicroRNA-302 increases reprogramming efficiency via repression of NR2F2. Stem Cells. 2012: 31(2): 259-68. (PMCID: PMC3572288)
    c. **Wilson KD**, Sun N, Huang M, Zhang WY, Lee AS, Li Z, Wang SX, Wu JC. Effects of ionizing radiation on self renewal and pluripotency of human embryonic stem cells. Cancer Research. 2010; 70(13): 5539-48. (PMCID: PMC3014320)
    d. Jia F, **Wilson KD**, Sun N, Gupta DM, Huang M, Li Z, Panetta NJ, Robbins RC, Kay MA, Longaker MT, Wu JC. A non-viral minicircle vector for deriving human iPS cells. Nature Methods. 2010; 7(3):197-9. (PMCID: PMC2892897)
    e. **Wilson KD**, Venkatasubrahmanyam S, Jia F, Sun N, Butte AJ, Wu JC. MicroRNA profiling of human induced pluripotent stem cells. Stem Cells and Development. 2009; 18(5): 749-58. (PMCID: PMC3135181)

2. In addition to basic pluripotent cell derivation and biology, much of my work has focused on cardiovascular applications. I published the first study of the microRNA-ome in hESC-derived cardiomyocytes, and discovered that a novel microRNA, miR-499, could enhance cardiac differentiation via regulation of several key transcription factors. I have also performed detailed transcriptomic analyses of hESC-derived cardiomyocytes and endothelial cells, and assessed their regenerative applications in mouse models of myocardial infarction.
    a. He C*, Hu H*, **Wilson KD***, Wu H, Feng J, Xia S, Churko J, Qu K, Chang HY, Wu JC. Systematic characterization of long noncoding RNAs reveals the contrasting coordination of cis- and trans-molecular regulation in human fetal and adult hearts. Circulation: Cardiovascular Genetics. 2016; 9(2):110-8. (PMCID: PMC4862831) * Contributed equally.
    b. **Wilson KD**, Hu S, Venkatasubrahmanyam S, Fu JD, Sun N, Abilez OJ, Baugh JJA, Jia F, Li RA, Butte AJ, Wu JC. Dynamic microRNA expression programs during cardiac differentiation of human embryonic stem cells: Role for miR-499. Circulation: Cardiovascular Genetics. 2010; 3(5): 426-35. (PMCID: PMC3057038)
    c. Li Z, **Wilson KD**, Smith B, Kraft D, Jia F, Huang M, Xie X, Robbins RC, Gambhir SS, Weissman IL, Wu JC. Transcriptional and functional profiling of human embryonic stem cell-derived endothelial cells for treatment of myocardial infarction. PLoS ONE. 2009; 4(12): e8443. (PMCID: PMC2795856)
    d. Cao F*, Wagner RA*, **Wilson KD***, Xie X, Fu JD, Drukker M, Lee AS, Li RA, Gambhir SS, Weissman IL, Robbins RC, Wu JC. Transcriptional and functional profiling of human embryonic stem cell-derived cardiomyocytes. PLoS ONE. 2008; 3(10): e3474. (PMCID: PMC2565131) * Contributed equally.
    e. **Wilson KD**, Li Z, Wagner RA, Yue P, Tsao P, Nestorova G, Huang M, Hirschberg DL, Yock PG, Quertermous T, Wu JC. Transcriptome alteration in the diabetic heart by Rosiglitazone: implications for cardiovascular mortality. PLoS ONE. 2008; 3(7): e2609. (PMCID: PMC2481284)

3. I developed an interest in DNA mutation detection and interpretation during my clinical training, which has lead to a number of projects that use NGS. Thousands of mutations across more than 50 genes have been implicated in inherited cardiomyopathies, however options for sequencing this rapidly evolving gene set are often limited to commercial services and off-the-shelf kits that suffer from slow turnaround, inefficient capture of genomic DNA, and/or high cost. I thus sought to develop a custom high throughput, clinical- grade NGS assay for detecting cardiac disease gene mutations with improved accuracy, flexibility, turnaround, and cost. I employed double-stranded complementary long padlock probes, an inexpensive and customizable capture technology, to efficiently capture and amplify the entire coding region and flanking intronic and regulatory sequences of 88 genes and 40 microRNAs associated with inherited cardiomyopathies, congenital heart disease (CHD), and cardiac development. This format is vastly superior to standard whole exome sequencing and allows facile insertion of additional probes as more cardiomyopathy- and CHD-related genes are discovered, giving researchers a powerful new tool for DNA mutation detection and discovery.
    a. **Wilson KD** (*corresponding author*), Shen P, Zhang A, Fung E, InanlooRahatloo K, Odegaard J, Sallam K, Davis RW, Lui GK, Ashley EA, Scharfe C, Wu JC. A rapid, high-quality, cost-effective, comprehensive and expandable targeted next-generation sequencing assay for inherited heart diseases. Circulation Research. 2015 (*Journal Cover*)
    b. **Wilson KD**, Schrijver I. Transitioning diagnostic molecular pathology to the genomic era: cancer somatic mutation panel testing. Jothy S, Yousef GM (Eds.), Molecular Testing in Cancer. 2014. Springer Science + Business Media

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1hmNCQrvN8zAN/bibliography/40216608/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

K08 HL119251 Wilson (PI) 05/15/2016 - 04/30/2021

Defining the Molecular Mechanism of Hypertrophic Cardiomyopathy with Human Induced Pluripotent Stem Cells

This project will create iPSCs that carry the same HCM-causing gene mutations as the patients from which they are derived. The goal is to dramatically enhance our understanding of the genetics underlying HCM, and will ultimately lead to novel clinical diagnostics and possibly therapies.

Steven M. Gootter Foundation Grant Wilson (PI) 09/14-present

Early Detection Of Sudden Cardiac Death Using Novel Gene Sequencing Technology

This award is supporting the development of a clinical-grade NGS assay for identifying DNA mutations in sudden cardiac death.

Completed Research Support

Stanford CVI Seed Grant Wilson (I) 10/13-10/2015

A Clinical-Grade Next Generation Sequencing Assay For Targeting DNA Mutations In Inherited Non-Syndromic Cardiomyopathies

This seed grant supported the development of novel “padlock” double-stranded DNA probes for identifying DNA mutations in cardiomyopathies and congenital heart disease.

Bio-X Fellowship Wilson (PI) 09/07-05/10

Application of genomic and molecular imaging tools for cardiac regenerative medicine.

This fellowship fully supported my graduate studies, during which I published four first-author original research articles.