

**BIOGRAPHICAL SKETCH**

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NAME Bruce R. Conklin	POSITION TITLE Gladstone Institutes, Senior Investigator UCSF, Professor of Genomic Medicine, and Cellular and Molecular Pharmacology		
eRA COMMONS USER NAME (credential, e.g., agency login) BCONKLIN			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
University of California, Berkeley, CA	A.B.	1982	Public Health
Case Western Reserve U., Cleveland, OH	M.D.	1988	Medicine

**A. Personal Statement**

Dr. Conklin's research focuses on human genetics that lead to cardiovascular diseases, such as cardiac arrhythmias and cardiomyopathy. His major model system is induced pluripotent (iPS) cells that are engineered to test the role of specific genetic changes on disease. Dr. Conklin began his research career by working for two years with Julius Axelrod, Ph.D., (Nobel Laureate) at the National Institutes of Health. He then completed his residency at Johns Hopkins Hospital and a postdoctoral fellowship in the laboratory of Henry Bourne, M.D. at UCSF. In 1995 Dr. Conklin joined the Gladstone Institutes and the UCSF faculty where he has advanced to become a Senior Investigator at Gladstone, and a Professor at UCSF. Dr. Conklin is also the Gladstone Scientific Officer for Technology and Innovation. Dr. Conklin is the founder of several public stem cell and genomics projects including BayGenomics, GenMAPP, AltAnalyze and WikiPathways. Dr. Conklin pioneered the field of using designer G protein coupled receptors (RASSLs) for tissue engineering. He was the founding director of the Gladstone Genomics Core and the Gladstone Stem Cell Core. Dr. Conklin leads the Gladstone Stem Cell Training Program, is the principle investigator on multiple research grants from NIH and serves on multiple advisory boards. He is a member of several honorary societies including the American Society for Clinical Investigation, and is a Fellow in the California Academy of Sciences. Dr. Conklin's expertise in the field of stem cell biology, genomics, regulatory signaling and bioinformatics is essential for the success of his research projects.

**B. Positions and Honors**Positions and Employment

1986–1988 Howard Hughes Medical Institute–NIH Research Scholar, Preceptor: Julius Axelrod, Ph.D., Nobel Laureate, Bethesda, MD

1988–1990 Internal Medicine Internship and Residency, Johns Hopkins Hospital, Baltimore, MD

1990–1994 Postdoctoral Fellow with Henry R. Bourne, M.D., Department of Pharmacology, UCSF

1995–2006 Founder, Gladstone Genomics Core and Gladstone Stem Cell Core Laboratories

1995– Assistant, (2001) Associate, (2007) Senior Investigator, Gladstone Institute of Cardiovascular Disease, San Francisco, CA

1995– Assistant, (2001) Associate, (2007) Full Professor of Medicine, Division of Medical Genetics and Cellular and Molecular Pharmacology, UCSF

Board Certifications and Affiliations

1992– Medical Board of California, License #A49977, Internal Medicine Boards, 1992

1995– Member UCSF Graduate Programs: Program in Biological Sciences (PIBS), Biomedical Sciences (BMS), Pharmacogenomics (PSPG), Biological and Medical Informatics (BMI), California Institute for Quantitative Biomedical Research (QB3), Scientific Advisory Board: Cytoscape Consortium, Cellogy, Assay Depot,

Selected Honors

1990 Medical Resident Research Award, NIH-NIDDK

2003 American Society for Clinical Investigation

2008 Scientific American 50 Award

2011 Fellow, California Academy of Sciences

**C. Selected Peer-reviewed Publications (15 of >90)**

1. **Conklin BR**, Brann MR, Buckley NJ, Ma AL, Bonner TI, Axelrod J. Stimulation of arachidonic acid release and inhibition of mitogenesis by cloned genes for muscarinic receptor subtypes stably expressed in A9 L cells. *Proc Natl Acad Sci U S A*. 1988;85(22):8698-702. PMID: PMC282528
2. **Conklin BR**, Bourne HR. (1993) Structural elements of G alpha subunits that interact with G beta gamma, receptors, and effectors. *Cell* 73:631-41
3. **Conklin BR**, Farfel Z, Lustig KD, Julius D, Bourne HR. (1993) Substitution of three amino acids switches receptor specificity of Gq alpha to that of Gi alpha. *Nature* 363:274-6
4. Coward P, Wada HG, Falk MS, Chan SD, Meng F, Akil H, **Conklin BR**. (1998) Controlling signaling with a specifically designed Gi-coupled receptor. *Proc Natl Acad Sci U S A* 95:352-7
5. Redfern CH, Coward P, Degtyarev MY, Lee EK, Kwa AT, Hennighausen L, Bujard H, Fishman GI, **Conklin BR**. (1999) Conditional expression and signaling of a specifically designed Gi-coupled receptor in transgenic mice. *Nat Biotechnol* 17:165-9
6. Dahlquist KD, Salomonis N, Vranizan K, Lawlor SC, **Conklin BR**. (2002) GenMAPP, a new tool for viewing and analyzing microarray data on biological pathways. *Nat Genet* 31:19-20
7. Tingley WG, Pawlikowska L, Zaroff JG, Kim T, Nguyen T, Young SG, Vranizan K, Kwok PY, Whooley MA, **Conklin BR**. (2007) Gene-trapped mouse embryonic stem cell-derived cardiac myocytes and human genetics implicate AKAP10 in heart rhythm regulation. *Proc Natl Acad Sci U S A* 104:8461-6. PMID: 1866184
8. **Conklin BR**, Hsiao EC, Claeysen S, Dumuis A, Srinivasan S, Forsayeth JR, Guettier JM, Chang WC, Pei Y, McCarthy KD, Nissenson RA, Wess J, Bockaert J, Roth BL. (2008) Engineering GPCR signaling pathways with RASSLs. *Nat Methods* 5:673-8. PMID: 2267039
9. Aalto-Setälä K, **Conklin BR**, Lo B. (2009) Obtaining consent for future research with induced pluripotent cells: opportunities and challenges. *PLoS Biol* 7:e42. PMID: 2652391
10. Salomonis N, Nelson B, Vranizan K, Pico A, Hanspers K, Kuchinsky A, Ta L, Mercola M, **Conklin BR**. Alternative splicing in the differentiation of human embryonic stem cells into cardiac precursors. *PLoS Computational Biology* 2009;5(11):e1000553. PMID: 2764345
11. Salomonis N, Schlieve CR, Pereira L, Wahlquist C, Colas A, Zambon AC, Vranizan K, Spindler MJ, Pico AR, Cline MS, Clark TA, Williams A, Blume JE, Samal E, Mercola M, Merrill BJ, **Conklin BR** (2010) Alternative splicing regulates mouse embryonic stem cell pluripotency and differentiation. *Proc Natl Acad Sci U S A* 107:10514-10519. PMID: 2764345
12. Tomoda K, Takahashi K, Leung K, Okada A, Narita M, Yamada NA, Eilertson KE, Tsang P, Baba S, White MP, Sami S, Srivastava D, **Conklin BR**, Panning B, Yamanaka S. Derivation conditions impact X-inactivation status in female human induced pluripotent stem cells. *Cell Stem Cell*. 2012 Jul 6;11(1):91-9. PMID: 3396435
13. Kreitzer FR, Salomonis N, Sheehan A, Huang M, Park JS, Spindler MJ, Lizarraga P, Weiss WA, So PL, **Conklin BR**. A robust method to derive functional neural crest cells from human pluripotent stem cells. *Am J Stem Cells*. 2013 Jun 30;2(2):119-31. PMID: 3708511
14. Miyaoka Y, Chan AH, Judge LM, Yoo J, Huang M, Nguyen TD, Lizarraga PP, So PL, **Conklin BR**, Isolation of single-base genome-edited human iPS cells without antibiotic selection, *Nature Methods*, 2014 Mar;11(3):291-3. PMID: 24509632, PMID: 4063274
15. Spencer CI, Baba S, Nakamura K, Hua, EA, Sears MFA, Fu CC, Zhang J, Balijepalli S, Tomoda K, Hayashi Y, Lizarraga P, Wojciak J, Scheinman MM, Aalto-Setälä K, Makielski JC, January CT, Healy KE, Kamp TJ, Yamanaka S, and **Conklin BR**, Calcium Transients Closely Reflect Prolonged Action Potentials in iPSC Models of Inherited Cardiac Arrhythmia. *Stem Cell Reports*, 2014, Aug 12 (3) 269–281 PMID pending

## D. Research Support

### ACTIVE

U01 HL100406 (Srivastava, Conklin MPI)

10/1/09–04/30/16

NIH/NHLBI

#### Induced Pluripotent Stem Cells in the Understanding and Treatment of Heart Disease

The major goal of this project is to develop efficient directed differentiation of human iPS cells and methods of direct reprogramming into cell types relevant for disease models and cell-based therapies for cardiovascular disease.

U01 HL098179 (Bruneau, Conklin MPI)

9/1/09–07/31/15

NIH

#### The Epigenetic Landscape of Heart Development

The major goal of this project is to identify genome-wide targets of transcription factors with known roles in cardiac development and human disease, and epigenetic regulators of transcription.

U01 GM094614 (Fletterick)

09/30/2010–06/30/15

UCSF/NIH

#### Structure of Protein Complexes that Regulate Transcription in Embryonic Stem Cells

The major goal of this grant is to reveal molecular mechanisms underlying formation and function of critical transcriptional assemblies essential to embryonic stem (ES) cells and cells with induced pluripotency.

P01 HL089707 (Srivastava)

09/01/08–07/31/18

NIH/NHLBI

#### Transcriptional Networks During Cardiac Differentiation

As a Core Director, Dr. Conklin oversees Core C: Cell Production Core. The overall goal of this PPG is to decipher the complex protein-protein interaction (PPI) networks through which major cardiac transcription factors function to regulate cardiac differentiation and cardiac reprogramming.

CL1-00514-1 (Srivastava)

01/02/08–12/31/14

California Institute for Regenerative Medicine

#### The Gladstone CIRM Shared Human Embryonic Stem Cell Core Laboratory – Part I

These funds will help develop a laboratory for hESC tissue culture with specialized microscopy, and an animal holding and procedure space for in vivo-pre-clinical studies for hESCs in mouse models of disease.

CIRM Training Program TG2-01160 (Mahley, Conklin Associate Director)

04/01/09–04/30/15

California Institute of Regenerative Medicine

The goal of the training program is to use stem cell and related research to develop new therapies for disease.

(Miller, PI)

10/01/13–06/30/14

UCSF/The Bluefield Project

#### Isogenic iPS Cells With Progranulin Disease Mutations

We will use genome engineering to produce three isogenic iPS cell lines that have key mutations in the GNR genes that are associated with Frontal Temporal Dementia. Cell lines and reagents will be provided to the FTD consortium.

Role: Consortium PI

### OVERLAP

None

### COMPLETED IN THE LAST THREE YEARS

R01HL108677 (Healy, Conklin MPI)

09/05/11–05/31/15

UCB/NIH

Disease Specific Cardiac Tissue Models

The major goal of this subcontract is to provide iPS cells from patients with cardiac disease models for analysis in cardiac tissue models.

R01 HL060664 (Conklin)

07/01/03–06/30/13

NIH/NHLBI

Tissue Engineering with a Modular RASSL Toolbox

The major goal of this project is to determine how G protein coupled receptors (GPCR) control a wide variety of physiologic responses and develop Receptors Activated Solely by Synthetic Ligands (RASSLs) for tissue engineering.

RL1-00639-1 (Conklin)

02/01/09–04/30/12

California Institute for Regenerative Medicine

Induced Pluripotent Stem Cells for Cardiovascular Diagnostic

The major goals of this project are: 1) to determine if iPS cell lines from LQTS patients are truly pluripotent, 2) to differentiate iPS cells into cardiac myocytes to determine if iPS cells with genetically defined LQTS can be distinguished from control iPS cells by electrophysiological tests, and 3) to adapt the culture conditions of iPS cell-derived myocytes for high-throughput preclinical screening of drugs.

3R01 GM080223-06S1 Supplement (Conklin, PI)

09/30/09–07/31/11

NIH/NIGMS

GenMAPP-CS, a dynamic resource of pathway analysis

The major goals of this project are: 1) to build GenMAPP-CS, a client-server version of GenMAPP, to provide a dynamic environment for visualizing and analyzing genomic data on biological pathways, 2) to dynamically integrate GenMAP-CS with major gene and pathway databases for over 20 major model organisms, and 3) to enable GenMAPP-CS to visualize and analyze genome-wide splicing, polymorphism, and interaction datasets.

(Conklin, PI)

03/01/10–02/28/11

Takeda Pharmaceuticals

Personalized Stem Cell Medicine:

A Canada-California-Japan Workshop

At this workshop, top stem cell researchers from three major international centers of regenerative medicine research, Canada, California, and Japan, along with industry representatives, will discuss the science of iPS cells and its application to personalized medicine.