

**BIOGRAPHICAL SKETCH**

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NAME Bruce R. Conklin	POSITION TITLE Gladstone, Senior Investigator UCSF, Professor of Medical Genetics, 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 Univ., Cleveland, OH	M.D.	1988	Medicine

**A. Personal Statement:** Bruce R. Conklin, M.D. utilizes receptor engineering, high-throughput genomics and stem cell biology to understand basic pharmacological responses, with a particular emphasis on the largest known family of receptors for hormones and drugs, called G protein-coupled receptors (GPCRs). During his last two years of medical school, Dr. Conklin had the privilege of working under the tutelage of Nobel Laureate Julius Axelrod, Ph.D., 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. From 1995 to 2001, Dr. Conklin was the Associate Director of the General Clinical Research Center at San Francisco General Hospital. He is a member of several honorary societies including the American Society for Clinical Investigation. Dr. Conklin is the founder of several public stem cell and genomics projects including BayGenomics, GenMAPP, AltAnalyze and WikiPathways. Dr. Conklin was the founding director of the Gladstone Genomics Core and the Gladstone Stem Cell Core. Dr. Conklin is the Associate Director of the Gladstone CIRM Scholars Training Program, serves on the board of directors for the Cytoscape consortium and is the principle investigator on multiple research grants from NIH and the CIRM (California Institute for Regenerative Medicine). Dr. Conklin's expertise in the field of stem cell biology, genomics, regulatory signaling and bioinformatics will aid in the successful completion of this project.

**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  
 1995–2001 Associate Director, General Clinical Research Center and Founder, Genomics Core Laboratory, San Francisco General Hospital, San Francisco, CA  
 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– Board Certified, Internal Medicine, Medical Board of California, License #A49977  
 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),  
 2008- Cytoscape Consortium Board of Directors; iPierian Inc, ShrinkNano, Scientific Advisory Board

**Selected Honors**

1988 Harry Resnick Award, Case Western Reserve School of Medicine  
 1990 Medical Resident Research Award, NIH-NIDDK  
 2003 American Society for Clinical Investigation  
 2008 Scientific American 50 Award

### C. Selected Peer-reviewed Publications (15 of >80)

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. Conklin BR. (2007) New tools to build synthetic hormonal pathways. *Proc Natl Acad Sci U S A* 104:4777-8. PMID: PMC1829213
8. 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: PMC1866184
9. **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: PMC2267039
10. Hsiao EC, Boudignon BM, Chang WC, Bencsik M, Peng J, Nguyen TD, Manalac C, Halloran BP, **Conklin BR**, Nissenson RA. (2008) Osteoblast expression of an engineered Gs-coupled receptor dramatically increases bone mass. *Proc Natl Acad Sci U S A* 105:1209-14. PMID: 2234117
11. Kelder T, Pico AR, Hanspers K, van Iersel MP, Evelo C, **Conklin BR**. (2009) Mining biological pathways using WikiPathways web services. *Plos One* 4:e6447. PMID: PMC2714472
12. 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: PMC2652391
13. Salomonis N, Nelson B, Vranizan K, Pico A, Hanspers K, Kuchinsky A, Ta L, Mercola M, and **Conklin BR**. Alternative splicing in the differentiation of human embryonic stem cells into cardiac precursors. *PLoS Computational Biology*. 2009;5(11):e1000553. PMID: PMC2764345
14. Nakamura K, Salominis N, Tomoda K, Yamanaka S, **Conklin BR**. G(i)-coupled CPCR signaling controls the formation and organization of human pluripotent colonies. *PLoS One*. 2009;4(11):e7780. PMID: PMC2777408
15. 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, and **Conklin BR** (2010)

Alternative splicing regulates mouse embryonic stem cell pluripotency and differentiation. *Proc Natl Acad Sci U S A* 107:10514-10519. PMC2764345

#### D. Research Support

##### ACTIVE

**CIRM, RL1-00639 Conklin (PI) 02/01/09–01/31/12**

##### **Induced Pluripotent Stem Cells for Cardiovascular Diagnostics**

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.

**Role: PI**

**NIH/NHLBI, 2R01 HL060664 Conklin (PI) 07/01/03–06/30/13**

##### **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.

**Role: PI**

**NIH, 5R01 GM080223 Conklin (PI) 08/01/07–07/31/11**

##### **GenMAPP-CS, a Dynamic Resource for 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.

**Role: PI**

**NIH/NHLBI, U01 HL098179, Bruneau-Yamanaka-Pollard-Srivastava-Conklin (PIs), 09/30/2009-08/31/2015, The Epigenetic Landscape of Heart Development**

This project as part of the NHLBI Heart Development consortium to provide an integrated epigenetic landscape for heart development, with a focus on CHD-related genes.

**Role: co-PI**

**NIH/NHLBI, U01 HL100406, Srivastava-Bruneau-Yamanaka- Conklin (PIs), 09/30/2009 – 06/30/2016**

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

The major goals of this project are: 1) to develop integration-free methods of human iPS cell generation for future cell-based therapies, 2) to develop efficient directed differentiation of human iPS cells and methods of direct reprogramming into cell types relevant for future cell-based therapies directed at cardiovascular disease, and 3) to use iPS technology for discovery of human cardiovascular disease mechanisms and for drug discovery approaches.

**Role: co-PI**

**UCSF/NIH, U01 GM094614 Fletterick (PI) 09/30/2010-06/30/2011**

##### **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.

**Role: Subcontract-PI**

**NIH/NHLBI, 1P01 HL089707 Srivastava (PI) 09/01/08–05/31/13**

##### **Signaling and Transcriptional Networks in Cardiac Patterning**

Program Director/Principal Investigator (Last, First, Middle): Pollard, Katherine S

The overall goal of this PPG is to decipher the signaling and transcriptional pathways that dictate early decisions of cardiac differentiation in different regions of the developing heart and the mechanisms that guide such patterning events during cardiogenesis. The projects are: (Project 1) Wnt regulation of heart field progenitors (Srivastava), and (Project 2) Patterning of the heart field by Tbx5 and its transcriptional partners (Bruneau); Core A: Advanced embryonic stem cell technology (Conklin), Core B: Histopathology and imaging (Bruneau), and Core C: Advanced genomics (Barker), Core D: Administrative (Srivastava).

Role: Director of Core A

**CIRM, T3-00003, Mahley (PI), 04/01/06–03/28/12**  
**The Gladstone-CIRM Stem Cell Training Program**

The goal of the training program is to use stem cell and related research to develop new therapies for disease.  
**Role: co-PI, Associate director of training program**

### **COMPLETED**

**NIH/NHLBI U01HL066621 Young (PI) 09/02/04–08/31/08**  
**The NHLBI Bay Area Functional Genomics Consortium**

The major goals of this program was to start the BayGenomics project. This project used custom gene-trap vectors to generate 2500 ES cell lines per year with well characterized insertional mutations. The BayGenomics project made over 15,000 gene trap mouse ES cell lines available to the research community. Portions of the BayGenomics project team, continue the same area of work in the Knockout Mouse Project (KOMP). Dr. Conklin advises the KOMP project periodically, but is no longer involved with day-to-day management of this resource.

**Role: Co-PI, and Associate Director of BayGenomics project**

**NIH/NHLBI, R03 HL096254, Srivastava (PI), 12/01/08–05/31/09**  
**Induced Pluripotent Stem Cells in the Understanding and Treatment of Heart Disease**

The major goals of this project are: 1) to develop integration-free methods of human iPS cell generation for future cell-based therapies, 2) to develop efficient directed differentiation of human iPS cells and methods of direct reprogramming into cell types relevant for future cell-based therapies directed at cardiovascular disease, and 3) to use iPS technology for discovery of human cardiovascular disease mechanisms and for drug discovery approaches. This grant was for the planning period of P01 HL089707 above.

**Role: co-PI**

**NIH/NEI, 5PN2 EY016546, Lim (PI), 09/30/08–09/29/09**  
**Cellular Control: Synthetic Signaling/Motility**

The major goals of this project are: 1) to express all the major classes of RASSLs in embryonic stem (ES) cells that can be differentiated into cell types useful for tissue engineering, such as neurons, and 2) to derive mice from RASSL-ES cells to provide adult tissues for transplantation studies.

Role: co-PI leading subcontract

**CIRM, CL1-00514-1 Srivastava (PI) 08/03/07-06/30/10**  
**The Gladstone CIRM Shared Human Embryonic Stem Cell Core Laboratory**

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. This laboratory will provide shared research facilities for use by California scientists and also help train students from a nearby college to become laboratory technicians.

**Role: Founder of Core Lab, currently advisor of Core Director (Kathy Ivey PhD)**