
BIOGRAPHICAL SKETCH

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| NAME Bruce R. Conklin | POSITION TITLE Gladstone, Senior Investigator | | |
| eRA COMMONS USER NAME BCONKLIN | UCSF, Professor of Medical Genetics, and Cellular and Molecular Pharmacology | | |
| EDUCATION/TRAINING | | | |
| INSTITUTION AND LOCATION | DEGREE (if applicable) | YEAR(s) | FIELD OF STUDY |
| University of California, Berkeley, CA | A.B. | 1982 | Public Health |
| Case Western Reserve Univ., Cleveland, OH | M.D. | 1988 | Medicine |

A. POSITIONS AND HONORS

Positions and Employment

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| 1986–1988 | Howard Hughes Medical Institute–NIH Research Scholar, Preceptor: <u>Julius Axelrod, Ph.D., Nobel Laureate</u> , Bethesda, MD |
| 1988–1990 | Internal Medicine Internship and Residency, Johns Hopkins Hospital, Baltimore, MD |
| 1990–1994 | Postdoctoral Fellow with <u>Henry R. Bourne, M.D.</u> , 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

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| 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; Izumi Inc, Scientific Advisory Board |

Selected Honors

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| 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 (top science 50 stories) |

B. PEER-REVIEWED PUBLICATIONS (SELECTED FROM OVER 50)⁽¹⁻³¹⁾

1. Conklin BR, Burch RM, Steranka LR, Axelrod J. (1988) Distinct bradykinin receptors mediate stimulation of prostaglandin synthesis by endothelial cells and fibroblasts. *J Pharmacol Exp Ther* 244:646-9.
 2. Conklin BR, Chabre O, Wong YH, Federman AD, Bourne HR. (1992) Recombinant Gq alpha. Mutational activation and coupling to receptors and phospholipase C. *J Biol Chem* 267:31-4.
 3. Federman AD, Conklin BR, Schrader KA, Reed RR, Bourne HR. (1992) Hormonal stimulation of adenylyl cyclase through Gi-protein beta gamma subunits. *Nature* 356:159-61.
 4. Wong YH, Conklin BR, Bourne HR. (1992) Gz-mediated hormonal inhibition of cyclic AMP accumulation. *Science* 255:339-42.
 5. Conklin BR, Bourne HR. (1993) Structural elements of G alpha subunits that interact with G beta gamma, receptors, and effectors. *Cell* 73:631-41.
 6. 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.
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7. Conklin BR, Bourne HR. (1994) Homeostatic signals. Marriage of the flytrap and the serpent. *Nature* 367:22.
 8. 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.
 9. Coward P, Chan SD, Wada HG, Humphries GM, Conklin BR. (1999) Chimeric G proteins allow a high-throughput signaling assay of Gi-coupled receptors. *Anal Biochem* 270:242-8.
 10. 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.
 11. Redfern CH, Degtyarev MY, Kwa AT, Salomonis N, Cotte N, Nanevicz T, Fidelman N, Desai K, Vranizan K, Lee EK, Coward P, Shah N, Warrington JA, Fishman GI, Bernstein D, Baker AJ, Conklin BR. (2000) Conditional expression of a Gi-coupled receptor causes ventricular conduction delay and a lethal cardiomyopathy. *Proc Natl Acad Sci U S A* 97:4826-31.
 12. 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.
 13. Doniger SW, Salomonis N, Dahlquist KD, Vranizan K, Lawlor SC, Conklin BR. (2003) MAPPFinder: using Gene Ontology and GenMAPP to create a global gene-expression profile from microarray data. *Genome Biol* 4:R7.
 14. Skarnes WC, von Melchner H, Wurst W, Hicks G, Nord AS, Cox T, Young SG, Ruiz P, Soriano P, Tessier-Lavigne M, Conklin BR, Stanford WL, Rossant J. (2004) A public gene trap resource for mouse functional genomics. *Nat Genet* 36:543-4.
 15. Conklin BR. (2007) New tools to build synthetic hormonal pathways. *Proc Natl Acad Sci U S A* 104:4777-8.
 16. Kim W, Ng JK, Kunitake ME, Conklin BR, Yang P. (2007) Interfacing silicon nanowires with mammalian cells. *J Am Chem Soc* 129:7228-9.
 17. Nord AS, Vranizan K, Tingley W, Zambon AC, Hanspers K, Fong LG, Hu Y, Bacchetti P, Ferrin TE, Babbitt PC, Doniger SW, Skarnes WC, Young SG, Conklin BR. (2007) Modeling insertional mutagenesis using gene length and expression in murine embryonic stem cells. *PLoS ONE* 2:e617.
 18. Salomonis N, Hanspers K, Zambon AC, Vranizan K, Lawlor SC, Dahlquist KD, Doniger SW, Stuart J, Conklin BR, Pico AR. (2007) GenMAPP 2: new features and resources for pathway analysis. *BMC Bioinformatics* 8:217.
 19. 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.
 20. 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
 21. 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
 22. Hsiao EC, Yoshinaga Y, Nguyen TD, Musone SL, Kim JE, Swinton P, Espineda I, Manalac C, deJong PJ, Conklin BR. (2008) Marking embryonic stem cells with a 2A self-cleaving peptide: a NKX2-5 emerald GFP BAC reporter. *PLoS ONE* 3:e2532. PMID: PMC2430532
 23. Fish JE, Santoro MM, Morton SU, Yu S, Yeh RF, Wythe JD, Ivey KN, Bruneau BG, Stainier DY, Srivastava D. (2008) miR-126 regulates angiogenic signaling and vascular integrity. *Dev Cell* 15:272-84. PMID: PMC2695512
 24. Peng J, Bencsik M, Louie A, Lu W, Millard S, Nguyen P, Burghardt A, Majumdar S, Wronski TJ, Halloran B, Conklin BR, Nissenson RA. (2008) Conditional expression of a Gi-coupled receptor in osteoblasts results in trabecular osteopenia. *Endocrinology* 149:1329-37. PMID: PMC2275363
 25. Pico AR, Kelder T, van Iersel MP, Hanspers K, Conklin BR, Evelo C. (2008) WikiPathways: pathway editing for the people. *PLoS Biol* 6:e184. PMID: PMC2475545
 26. 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
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27. Ivey KN, Muth A, Arnold J, King FW, Yeh R-F, Fish JE, Hsiao EC, Schwartz RJ, Conklin BR, Bernstein HS, Srivastava D. (2008) MicroRNA regulation of cell lineages in mouse and human embryonic stem cells. *Cell Stem Cell* 2:219-229. PMID: PMC 2293325
28. 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
29. Pico AR, Smirnov IV, Chang JS, Yeh RF, Wiemels JL, Wiencke JK, Tihan T, Conklin BR, Wrensch M. (2008) SNPLogic: An interactive single nucleotide polymorphism selection, annotation, and prioritization system. *Nucleic Acids Res* In press. PMID: PMC2686434
30. Kita-Matsuo H BM, Prigozhina N, Salomonis N, Wei K, Jacot JG, Nelson B, Spiering S, Haverslag R, Kim C, Talantova M, Bajpai R, Calzolari D, McCulloch AD, Price JH, Conklin BR, Chen HSV, Mercola M (2009) Lentiviral vectors and protocols for creation of stable hESC lines for fluorescent tracking and drug resistance selection of cardiomyocytes. *PLoS One (in press)* 4:e5046. PMID: PMC2662416
31. Neumann S, Tingley W, Conklin BR, Shrader C, Peet E, Muldoon M, Jennings R, Ferrell R, Mauck S. (2009) AKAP10 (I646V) functional polymorphism predicts heart rate and heart rate variability in apparently healthy, middle-aged European-Americans. *Psychophysiology* 46:466-472.

Open Source Software Contributions

GenMAPP Project Leader since 2000: >17,000 unique registrations from >40 countries to download program (www.GenMAPP.org). WikiPathways, Project Leader: First pathway database with Wiki functionality (www.WikiPathways.org). Launched in September 2007.

C. RESEARCH SUPPORT

ACTIVE

RL1-00639-1 (Conklin) 02/01/09–01/31/12
 California Institute for Regenerative Medicine
 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.

2R01 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.

1P01 HL089707 (Srivastava) 09/01/08–05/31/13
 NIH/NHLBI
 Signaling and Transcriptional Networks in
 Cardiac Patterning
 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).

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

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.

CL1-00514-1 (Srivastava)

08/03/07-06/30/10

California Institute for Regenerative Medicine
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

5PN2 EY016546 (Lim)

09/30/08-09/29/09

NIH/NEI

Cellular Control: Synthetic Signaling/Motility
(RMI)

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.

COMPLETED

Conklin (PI)

09/02/04-08/31/08

NIH

The NHLBI Bay Area Functional Genomics
Consortium

The major goals of this project are: 1) to use custom gene-trap vectors to generate 2500 ES cell lines per year with well characterized insertional mutations, 2) to improve the annotation of our web site and to provide relevant genomics education programs to our users, 3) to use in situ hybridization studies to define gene-expression patterns for a subset of the trapped genes, in order to help users make informed choices which genes are likely to be relevant to cardiopulmonary development, and 4) to generate a limited number of genetically modified mice, for the purpose of defining the relevance of specific genes to cardiopulmonary development and disease.

T2-00003 (Mahley)

04/01/06-03/28/09

CIRM

CIRM Training Grant

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

R03 HL096254 (Srivastava)

12/01/08-05/31/09

NIH/NHLBI

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.
