#### **BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. DO NOT EXCEED FOUR PAGES.

NAME	POSITION TITLE
Stuart, Joshua M	Associate Professor
eRA COMMONS USER NAME (credential, e.g., agency login)  Joshstuart	

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 Colorado, Boulder, CO	B.A.	12/96	Molecular Biology
University of Colorado, Boulder, CO	B.S.	12/96	Computer Science
University of Colorado, Boulder, CO	R.A.	08/98	Chaos Theory
Stanford University, Stanford, CA	Ph.D.	01/2004	Biomedical Informatics

### A. Personal Statement

Dr. Stuart has an expertise in developing computational models to integrate multiple sources of information and a background in machine-learning applied to high-throughput datasets. He has recently developed pathway-based models to integrate multiple sources of gene activity to predict alterations and clinical outcomes in tumor samples. He co-directs the UCSC-Buck institute genome data analysis center and is a colead on pan-cancer analysis for the Cancer Genome Atlas project.

## **B.** Positions and Honors

# Positions and Employment

	<u> </u>
1993-1996	Laboratory Research Assistant, Dept. of Molecular Biology (Dr. G. Stormo), University of
	Colorado, Boulder, Colorado.
1994	University of Colorado Health Science Cancer Fellowship, Boulder Colorado, Summer.
1996-1997	Research Assistant, Dept. of Computer Science (Dr. L. Bradley), UC, Boulder.
2000	Teaching Assistant in Biomedical Informatics, Stanford, University, Stanford, CA.
2003-2009	Assistant Professor, Dept. of Biomolecular Engineering, University of California, Santa Cruz.
2009-present	Associate Professor, Dept. of Biomolecular Engineering, University of California, Santa Cruz.

### Honors

2009-2014 NSF CAREER Award.

2006-present Alfred P. Sloan research fellowship.

University of Colorado Kalpana Chawla Outstanding Recent Graduate Award 2006

1996 magna cum laude, MCD Biology, University of Colorado.

1995-1996 Achievement Rewards for College Scientists (ARCS) scholarship recipient for research in Dr. G.

Stormo's laboratory.

## C. Selected Peer-reviewed Publications

- Ng S, Collisson EA, Sokolov A, Goldstein T, Gonzalez-Perez A, Lopez-Bigas N, Benz C, Haussler D, Stuart JM. "PARADIGM-SHIFT predicts the function of mutations in multiple cancers using pathway impact analysis." ECCB 2012. In review.
- 2. Perou C et al. and The Cancer Genome Atlas. "Comprehensive molecular portraits of human breast tumors." Nature. In press.
- 3. Hammerman PS et al. and The Cancer Genome Atlas. "Comprehensive genomic characterization of squamous cell lung cancers." Nature. In press.

- 4. Kucherlapati R and The Cancer Genome Atlas. "Comprehensive Molecular Characterization of Human Colon and Rectal tumors." *Nature. In press.*
- 5. Ellis MJ *et al.* "Whole-genome analysis informs breast cancer response to aromatase inhibition." *Nature. In press.*
- 6. Karchin R, Ochs MF, Stuart JM, Bader JS. "Identification of Aberrant Pathway and Network Activity from High-Throughput Data." Pac Symp Biocomput. 2012. 17:1-6.
- 7. Heiser LM, et al. "Subtype and pathway specific responses to anti-cancer compounds in breast cancer." *Proc. Natl. Acad. Sci.* 2011.
- 8. The Cancer Genome Atlas. "Integrated Genomic Analyses of Ovarian Carcinoma." *Nature. 2011.* Jun 29; 474. 609-15.
- 9. Tripp HJ, Hewson I, Boyarsky S, Stuart JM, Zehr JP. "Misannotations of rRNA can now generate 90% false-positive protein matches in metatranscriptomics studies." Nucleic Acids Res. 2011 Jul 19. PMID: 21771858.
- 10. Tamble CM, St. Onge RP, Giaever G, Nislow C, Williams AG, Stuart JM, Lokey RS. "The synthetic genetic interaction network reveals small molecules that target specific pathways in Sacchromyces cerevisiae." *Mol. Biosyst.* 2011. Jun; 7(6):2019-30. PMID: 21487606.
- 11. Koeva M, Forsberg EC, Stuart JM. "Computational Integration of Homolog and Pathway Gene Module Expression Reveals General Stemness Signatures." *PLoS ONE* 2011. Apr 29. 6(4): e18968. PMID: 21559491 PMCID: PMC3084730.
- 12. International Cancer Genome Consortium (author list suppressed). "International network of cancer genome projects." *Nature*. 2010 Apr 15;464(7291):993-8.
- 13. Sanborn JZ, Benz SC, Craft B, Szeto C, Kober KM, Meyer L, Vaske CJ, Goldman M, Smith KE, Kuhn RM, Karolchik D, Kent WJ, Stuart JM, Haussler D, Zhu J. "The UCSC Cancer Genomics Browser: update 2011." Nucleic Acids Res. 2011 Jan; 39: D951-9. PMID: 21059681. PMCID: PMC3013705.
- 14. House CD, Vaske CJ, Schwartz AM, Obias V, Frank B, Luu T, Sarvazyan N, Irby R, Strausberg RL, Hales TG, Stuart JM, Lee NH. "Voltage-Gated Na+ Channel SCN5A Is a Key Regulator of a Gene Transcriptional Network That Controls Colon Cancer Invasion." *Cancer Res.* 2010 Sep 1;70(17):6957-67. PMID: 20651255.
- 15. Vaske CJ, Benz SC, Sanborn JZ, Earl D, Szeto C, Zhu J, Haussler D, Stuart JM, "Inference of patient-specific pathway activities from multi-dimensional cancer genomics data using PARADIGM." *Bioinformatics*. 2010. *In press*.
- 16. Wang BD, Kline CL, Pastor DM, Olson TL, Frank B, Luu T, Sharma AK, Robertson G, Weirauch MT, Patierno SR, Stuart JM, Irby RB, Lee NH. "Prostate apoptosis response protein 4 sensitizes human colon cancer cells to chemotherapeutic 5-FU through mediation of an NFkappaB and microRNA network." *Mol Cancer*. 2010 Apr 30;9(1):98. No PMCID. PMID: 20433755.
- 17. Forsberg EC, Passegué E, Prohaska SS, Wagers AJ, Koeva M, Stuart JM, Weissman IL. "Molecular signatures of quiescent, mobilized and leukemia-initiating hematopoietic stem cells." *PLoS One.* 2010 Jan 20;5(1). PMCID: PMC2808351.
- 18. Woehrmann MH, Gassner NC, Bray WM, Stuart JM\*, and Lokey RS\*. "HALO384: A halo-based potency prediction algorithm for high-throughput detection of antimicrobial agents." *J. Biomolec. Screening*. 2010 Feb; 15(2) 196-204. No PMCID. PMID: 20086209.
- 19. Vaske CJ, House C, Luu T, Frank B, Yeang CH\*, Lee NH\*, Stuart JM\*. "A Factor Graph Nested Effects Model to Identify Networks from Genetic Perturbations." *Public Library of Science Computational Biology*. 2009. Jan 5. e1000274. PMCID: PMC2613752.
- 20. Kanabar PN, Vaske CJ, Yeang CH, Yildiz FH, Stuart JM. "Inferring Disease-Related Pathways Using a Probabilistic Epistasis Model." *Proceedings of the Pacific Symposium on Biocomputing* 2009. 480-491. PMCID. PMID:19209724.
- 21. Weirauch MT, Wong CK, Byrne AB, Stuart JM. "Information-based methods for predicting gene function from systematic gene knock-downs." *Biomed Central Bioinformatics* 2008. Oct 29;9:463. PMCID: PMC2596148.
- 22. Byrne AB, Weirauch MT, Wong V, Koeva M, Dixon SJ, Stuart JM\*, Roy PJ\*. "A global analysis of genetic interactions in Caenorhabditis elegans." *J Biol.* 2007 Sep 26;6(3):8. PMCID: PMC2373897.
- 23. Hu Z, Mellor J, Wu J, Kanehisa M, Stuart JM, Delisi C. "Towards zoomable multidimensional maps of the cell." *Nat Biotechnol.* 2007 May;25(5):547-54. No PMCID.

- 24. Chen C, Weirauch MT, Powell CC, Zambon AC, Stuart JM. "A search engine to identify pathway genes from expression data on multiple organisms." *BMC Syst Biol.* 2007 May 4;1(1):20. PMCID: PMC1878502.
- 25. Ng DM, Woehrmann MH, Stuart JM. "Recommending pathway genes using a compendium of clustering solutions." *Proceedings of the Pacific Symposium on Biocomputing*. 2007 January. No PMCID.
- 26. Stuart JM\*, Segal E\*, Koller D, Kim SK. A Gene Coexpression Network for Global Discovery of Conserved Genetic Modules *Science* 2003 302:249-55. No PMCID.
- 27. Owen AB, Stuart JM, Mach K, Villeneuve AM, Kim SK. A gene recommender algorithm to identify coexpressed genes in *C. elegans Genome Research* 2003 13:1828-37. PMCID: PMC403774.
- 28. Roy PJ, Stuart JM, Lund J, Kim SK. Chromosomal clustering of muscle-expressed genes in *C. elegans*. *Nature* 2002 418:975-9. No PMCID.
- 29. Kim SK, Lund J, Kiraly M, Duke K, Jiang M, Stuart JM, Eizinger A, Wylie BN, Davidson GS. A Gene Expression Map for *Caenorhabditis elegans*. *Science* 2001 293:2087-2092. No PMCID.

# D. Research Support

# **Ongoing Research Support**

AACR subaward (Small) 7/1/2012 – 6/30/2015 0.5 calendar American Academy of Cancer Research \$374,000

Stand Up To Cancer Dream Team Award. Project supports identifying pathways in prostate cancer underlying androgen inhibition resistant disease. Dr. Stuart's lab will develop novel algorithms and deploy a data structure called to link together findings across labs.

Monterey Bay Aquarium Res Inst Co-PI (Worden) 7/1/2010 – 6/30/2013 0.5 calendar Department of Energy \$90,000

Connecting genomes to physiology and response in marine photosynthetic eukaryotes: Systems biology of the green alga Micromonas

The goal is to apply pathway analysis to one of the most abundant marine algal communities. The work should uncover mechanisms underlying robustness and sensitivity of carbon cycling to changing environmental conditions in the open ocean.

Harvard LINCS Project (Mitchison, Sorger) 9/27/2010 – 7/31/2013 0.5 calendar National Institutes of Health / NHGRI \$99,000 Pharmacological Response Signatures in Disease

The aims are to connect drug response measurements with genome-wide characterizations of cancer cell lines using integrated pathway modeling.

NSF DBI 0845783 (Stuart) 8/16/2009 – 7/31/2013 0.5 calendar National Science Foundation \$294,870

CAREER: Development of the UCSC Interaction Browser for Integrative Genomics

The goal is to create new algorithms for discovering causal genetic interactions and the UCSC Interaction Browser, an online functional genomics resource for investigating networks of gene-associated relationships.

AACR (Haussler) 8/1/2009 – 7/31/2012 0.5 calendar American Academy of Cancer Research \$35,000

<sup>\*</sup> equal contributions

Stand Up To Cancer Dream Team Award: Personalizing treatment of triple negative, metastatic breast cancer. The goals of the project are to develop tools to detect pathway perturbations in triple-negative breast cancer metastatic tumor samples, develop the UCSC BioIntegrator for predicting clinical outcomes from multiple data sources on these large patient cohorts, and develop the UCSC Cancer Browser to visualize high-throughput results for these patients. This grant funds 0.5 graduate student researchers and 1 summer month salary for Dr. Stuart.

CIRM Co-PI (Forsberg)
California Institute of Regenerative Medicine
Mechanisms of Stem Cell Fate Decisions"

3/1/08-2/28/13

0.5 calendar \$25,000

The goal is to develop computational tools to identify genetic markers of stem cells from genome-wide expression data. The work pays for ½ of a graduate student researcher in the Stuart lab.

## **Completed Research Support**

National Institutes of Health. Norman Lee, GWUMC (PI) 5/1/07-4/30/11

Title: Mapping Gene Networks in Colon Cancer

Project Goals: Develop probabilistic models to infer causal networks that predict invasiveness from gene expression data collected under single- and multiple-gene siRNA knock-downs.

Role: Sub-contractor. Oversee development of computational epistasis analysis to interpret high-throughput knock-down datasets.

National Science Foundation. Stuart (PI)7/1/06-6/30/10

Title: MSGR: A Multiple Species Gene Recommender Search Engine for Pathway Discovery Project Goals: Develop computational search engines to identify gene functions from functional genomics data. Combine search results across organisms to identify conserved and lineage-specific pathway involvement. Role: Pl. Direct the project.

Alfred P. Sloan Foundation Stuart (PI) 7/1/06-6/30/10

Title: Computational Tools to Discover Gene Functions from High-Throughput Data

Project Goals: To support the development of a functional genomics browser to integrate information from multiple sources of information and organisms.

Role: PI. Direct the project.

## **Overlap of Funded Research with Current Project**

The TCGA grant, SU2C grants, and MBARI contract each support aspects of integrated pathway analysis. For TCGA, we are supported to develop the PARADIGM software, incorporate it into NCI's centralized pipeline run at the Broad Institute called Firehose, and to make the analysis available for each tumor type. For the SU2C grant, we were funded to develop methods to identify signatures based on these PARADIGM pathway inferences and to collect datasets from contributing centers for this analysis. The MBARI project supports work to translate our pathway analysis to other species for use in projects outside of cancer genomics, which involves mapping genes across species and pathway interactions through "interlog" predictions. The current grant will fund new algorithm development specific for identifying targets of resistance in prostate cancer cells. Algorithms are needed to identify "Achilles Heels" as master regulatory hubs in our pathways that may be good points of further attack. The project will also fund new methods to share the results of these pathway inferences by relating many clinical attributes and samples together based on extracted pathway signatures.