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BIOGRAPHICAL SKETCH

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NAME: Grant A. Hartzog

eRA COMMONS USER NAME (credential, e.g., agency login): hartzo

POSITION TITLE: Professor

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

| INSTITUTION AND LOCATION | DEGREE(if applicable) | Completion DateMM/YYYY | FIELD OF STUDY |
| --- | --- | --- | --- |
| University of California, Berkeley, CA | B.A. | 06/84 | Biophysics |
| University of California, San Francisco, CA | Ph.D. | 09/92 | Biochemistry/Biophysics |
| Harvard Medical School, Cambridge, MA | postdoc | 09/92-09/98 | Genetics |

# A. Personal Statement

My training in the mechanisms of eukaryotic gene expression began in graduate school, where I worked with Richard Myers on the biochemical mechanisms governing regulated expression of the mouse beta-globin gene. For my post-doctoral training, I worked with Fred Winston, where I learned sophisticated yeast genetics while studying transcription and chromatin. During that time, I showed that Spt4 and Spt5 formed a complex that associates with and regulates elongating RNA Polymerase II (1,2). I also cloned the human *SPT4* gene and showed that it functions in yeast. Since joining the faculty at UC Santa Cruz, I have continued my work on Spt4/5, chromatin and transcription, and also initiated projects examining connections between pre-mRNA processing and transcription elongation.

From 2008-14, I taught in an HHMI-sponsored course in which beginning students isolate, purify, characterize (by EM and DNA restriction digests) novel phage and then they work together to sequence and annotate the genomes of one of these phage. Students present their results in posters, at a national meeting and have published their work (2). Many of the student participants in this course have gone on to independent research projects with other faculty. Our first several cohorts of these students have graduated and are now populating graduate programs that include UCSF, MIT, UC Irvine, Dartmouth, Rutgers and the University of Illinois; a number of other former phage students are in the biotech industry. In addition, I have helped two minority students from the phage lab and a third from our MARC/IMSD summer institute secure HHMI ExROP summer internships.

Throughout my time at UCSC, I have supported minority students in my lab. These minority students have been drawn from our MARC, IMSD and ACCESS (bridges to the baccalaureate, focusing on potential community college transfer students) programs as well as students that I have recruited from my regular lab and lecture courses. Many of these students have gone on to graduate program and the biotech industry. At least 8 of these former students currently work in the biotechnology industry or academic research labs, 2 are in PhD programs (UCSF, UC Riverside) and another 2 have earned Master’s degrees. Another student, Cameron Bess, earned a PhD at the Rockefeller University, did a postdoctoral fellowship at the NIH and is currently a AAAS Science and Technology Fellow. In addition, because of my extensive involvement in our curriculum, I am frequently called upon to advise students, including minority and transfer students who may face extra hurdles to success.

# B. Positions and Honors

Positions and Employment

1992-1998 Postdoctoral Fellow in the Laboratory of Fred Winston, Department of Genetics, Harvard Medical School, Cambridge, MA

1998-2004 Assistant Professor, Biology Department, University of California, Santa Cruz, CA

2004-2008 Associate Professor, MCD Biology Department, University of California, Santa Cruz, CA

2007 Vice Chair, MCD Biology Department, University of California, Santa Cruz, CA

2008-present Professor, MCD Biology Department, University of California, Santa Cruz, CA

2018-present Associate Dean, Academic Planning, Division of Physical and Biological Sciences, University of California, Santa Cruz, CA

Honors and Professional Memberships

1983 Phi Beta Kappa

1983-84 President’s Undergraduate Scholarship, University of California, Berkeley

1984 Highest Honors in Biophysics and Highest University Honors

1984 ARCS Foundation Scholar

1992-95 NIH NRSA Postdoctoral Fellowship

1995-98 Medical Foundation/Charles A. King Trust Postdoctoral Fellowship

2001 Nominated for Committee on Teaching’s Excellence in Teaching Award

2002 Non-tenured Faculty Development Award, University of California, Santa Cruz

2002 Instructor of the Year in MCD Biology.

2002-present Ad hoc grant reviews for the NSF

2003 Ad hoc member, NIH ZRG1 CDF4 special study section

2002-2004 Ad hoc member, NIH ZRG1 F05 study section

2005 Ad hoc member, NIH MGA study section

2005 Ad hoc member, NCI Leukemogenesis P01 cluster review

2006-2010 Permanent member of NIH MGA study section

2007 Ad hoc member, NIH CB-J study section

# C. Contribution to Science

Full list of published work:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/1Zy1gups8FGAI/bibliography/48327777/public/?sort=date&direction=ascending>

I. While a postdoctoral fellow, I discovered that the Spt4, Spt5 and Spt6 proteins are transcription elongation factors. I also began a series of collaborations, which continue to this day, that have considerably advanced our understanding of the function of the Spt5-Spt4 complex (Spt5/4). Among these were the first description of human Spt4, and structural characterization of the yeast Spt5/4 complex. I also am occasionally asked to write reviews on the current state of knowledge on Spt5/4.

1. Hartzog, G.A., Wada, T., Handa, H., and Winston, F. Evidence that Spt4, Spt5, and Spt6 control transcription elongation by RNA polymerase II in Saccharomyces cerevisiae. *Genes and Development* 1998; 12: 357-369.
2. Wada, T., Takagai, T., Yamaguchi, Y., Ferdous, A., Imai, T., Hirose, S., Sugimoto, S., Yano, K., Hartzog, G.A., Winston, F., Buratowski, S., and Handa, H. DSIF, a novel transcription elongation factor that regulates RNA polymerase II processivity, is composed of human Spt4 and Spt5 homologs. *Genes and Development 1998*; 12: 343-356.
3. Min Guo, Fei Xu, Jena Yamada, Thea Egelhofer, Yongxiang Gao, Grant A. Hartzog, Maikun Teng, Liwen Niu1. Core Structure of the yeast Spt4-Spt5 Complex: A Conserved Module for Regulation of Transcription Elongation. *Structure*, 2008; 6(11):1649-58. PMCID: PMC274391
4. Myer PA, Li S, Zhang M, Yamada K, Takagi Y., Hartzog GA, Fu J. Structures and functions of the multiple KOW domains of transcription elongation factor Spt5, *Mol. Cell. Biol* *2015 Oct;35(19):3354-69.* PMCID:PMC4561723

II. Genetic analysis of *spt4* and *spt5* mutations has led my lab to identify an extensive set of connections between Spt4/Spt5, transcription elongation and chromatin dynamics. My lab performed some of the initial descriptions of the roles of the Paf1 complex and Chd1 in regulation of transcribed chromatin and we have recently shown that Chd1 controls histone dynamics over the 3’ ends of genes.

1. Rajna Simic, Derek L. Lindstrom, Hien G. Tran, Kelli L. Roinick, Patrick J. Costa, Alexander D. Johnson, Grant A. Hartzog, and Karen M. Arndt. Chromatin remodeling protein Chd1 interacts with transcription elongation factors and localizes to transcribed genes and interacts with transcription elongation factors. *EMBO J.* 2003 22: 1846-1856.
2. Squazzo S., Costa P.J., Lindstrom D.L., Kumer K.E., Simic R., Jennings J.L., Link A.J., Arndt K.M., Hartzog G.A.. The Paf1 complex physically and functionally associates with transcription elongation factors *in vivo*. *EMBO J.* 2002; 21(7): 1764-1774.
3. Quan TK ,Hartzog GA Histone H3K4 and K36 methylation, Chd1 and Rpd3S oppose the function of *Saccharomyces cerevisiae* Spt4-Spt5 in transcription *Genetics*, 2010;184: 321-334. PMCID: PMC2828714.
4. Radman-Livaja M, Quan TK, Valenzuela L, Armstrong JA, van Welsem T, Kim T, Lee LJ, Buratowski S, van Leeuwen F, Rando OJ, Hartzog GA. (2012) A key role for Chd1 in histone H3 dynamics at the 3' ends of long genes in yeast. *PLoS Genet*. 2012;8(7):e1002811. PMCID: PMC3395613

III. My lab has also shown that Spt4/Spt5 influences pre-mRNA processing. In an early set of experiments, we found that Spt5 co-purified with a large set of RNA binding proteins and processing factors. Subsequent work showed that *spt4* and *spt5* mutations lead to splicing and mRNA nuclear export defects.

1. Lindstrom D.L., Squazzo S., Mustser N., Burckin T., Wachter K., Emigh C., McCleery J., Yates J., Hartzog G.A. Dual roles for Spt5 in pre-mRNA processing and transcription elongation revealed by identification of Spt5-associated proteins. MCB 2003; 23(4):1368-78.
2. Todd Burckin,\*, Roland Nagel,\*, Yael Mandel-Gutfreund, Lily Shiue, Tyson A. Clark, Jean-Leon Chong Tien-Hsien Chang, Sharon Squazzo, Grant Hartzog and Manuel Ares, Jr. Exploring functional relationships between components of the transcription, splicing, and mRNA export machineries by gene expression phenotype analysis. Nature Structural and Molecular Biology, 2005; 12:175-182. PMID: 15702072
3. Yuanyuan Xiao, Yee H Yang, Todd A Burckin, Lily Shiue,Grant A Hartzog and Mark R Segal. Analysis of a Splice Array Experiment,PLOS Computational Biology,2005; 1(4):e39. PMCID: PMC1214541

IV. Chemical Genetics. We have worked with my colleague Scott Lokey to screen yeast for sensitivity to chemical compounds and to identify potential molecular targets of those compounds.

1. Dustin A. Wride, Nader Pourmand, Walter M. Bray, Jacob J. Kosarchuk, Sean C. Nisam,

Tiffani K. Quan, Ray F. Berkeley, Sol Katzman, Grant A. Hartzog, Carlos E. Dobkin, R. Scott

Lokey. Confirmation of the cellular targets of benomyl and rapamycin using

next-generation sequencing of resistant mutants in *S. cerevisiae*. *Molecular BioSystems*, 2014, DOI:10.1039/C4MB00146J PMCID: PMC4653042

14. Zuckerman NB, Myers AS, Quan TK, Bray WM, Lokey RS, Hartzog GA, Konopelski JP. Structural determination of NSC 670224, synthesis of analogues and biological evaluation. ChemMedChem. 2012 May;7(5):761-5. doi: 10.1002/cmdc.201200038. Epub 2012 Feb 29.

 PMCID: PMC3516922

V. Phage genomics. Through my involvement in the HHMI phage course, we have isolated, purified and bioinformatically analysed a large number of bacteriophages.

13. Pope W, *et al*., Whole genome comparison of a large group of mycobacteriophages reveals a continuum of phage genetic diversity. *Elife*. 2015 Apr 28;4:e06416. doi: 10.7554/eLife.06416.

14. Cresawn SG, *et al.,* Comparitive Genomics of Cluster O Mycobacteriophages. *PLoS One.* 2015 Mar 5;10(3):e0118725. doi: 10.1371/journal.pone.0118725. eCollection 2015.

15. Jordan TC, *et al*. A Broadly Implementable Research Course in Phage Discovery and Genomics for First-Year Undergraduate Students. *mBio*. 2014, 5(1):e01051-13.

16. Pope WH *et al.,* Cluster M mycobacteriophages Bongo, PegLeg, and Rey with unusually large repertoires of tRNA isotypes. *J Virol.* 2014, 88(5):2461-80.

17. Hanauer D., *et al*., An inclusive Research Education Community (iREC): Impact of the SEA-PHAGES program on research outcomes and student learning. Proc Natl Acad Sci U S A. 2017 Dec 19;114(51):13531-13536. doi: 10.1073/pnas.1718188115. Epub 2017 Dec 5. PubMed PMID: 29208718.

# D. Research Support

**Ongoing Research Support**

NSF Hartzog (Co-PI) 4/1/13-3/30/17

Title: Investigation of the causal relationship between chromatin structure fluctuations and gene expression noise by electron and fluorescence.

Project Goals: This proposal combines mathematical modeling with single molecule measurements of nucleosome occupancy on purified *PHO5* gene circles from yeast, including from a novel set of histone mutants isolated in my lab. *This grant is currently in a no cost extension.*

NSF

Co-PI with Gretchen Andreasen, Debra Lewis, Patricia Stoddart, David Belanger

Title: Recruiting and Preparing STEM Teachers for High-Need Schools: Community College-University of California, Santa Cruz Partnerships

Project Goals: To increase the pipeline for highly qualified K-12 STEM teachers to high-need schools.

**Completed Research Support (last 3 years)**