OMB No. 3145-0279 (Expiration Date 10/31/2026)

NIH BIOGRAPHICAL SKETCH COMMON FORM

Name: GILL, GRACE B

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0009-0007-2384-6016

Position Title: Associate Professor

Organization and Location: Division of Oncological Sciences, School of Medicine, Oregon Health & Science University, Portland, Oregon, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
University of California Berkeley, Berkeley, California, United States	Postdoctoral Fellow	09/1989	08/1994	Mechanisms of Gene Regulation
Harvard University, Cambridge, Massachusetts, United States	DOCTOR OF PHILOSOPHY	09/1983	06/1989	Biochemistry
University of California Berkeley, Berkeley, California, United States	BACHELOR OF ARTS	09/1979	06/1983	Molecular Biology

Appointments and Positions

2022 - present	Associate Professor, Division of Oncological Sciences, School of Medicine, Oregon Health & Science University, Portland, Oregon, United States
2025 - present	Co-Associate Director Cancer Research Training and Education, Knight Cancer Institute, Oregon Health & Science University, Portland, Oregon, United States
2024 - 2025	Associate Director of Cancer Research Training and Education, Knight Cancer Institute, Oregon Health & Science University, Portland, OR, United States
2023 - 2023	Co-Associate Director of Cancer Research Training and Education, Knight Cancer Institute, Oregon Health & Science University, Portland, OR, United States
2022 - present	Associate Professor, Dept. of Cell, Developmental and Cancer Biology, School of Medicine, Oregon Health & Science University, Portland, OR, United States
2020 - 2021	Director, Academic Programs, Harvard University Graduate School of Arts & Sciences, Cambridge, MA, United States
2017 - 2020	Director, Harvard Integrated Life Sciences, Harvard University Graduate School of Arts & Sciences, Cambridge, MA, United States
2016 - 2017	Senior Scientific Editor, Cell Reports, Cell Press, Elsevier, Cambridge, MA, United States
2014 - 2014	AdHoc Reviewer, Fellowships: Neurodevelopment, Synaptic Plasticity and Neurodegeneration, ZRG1 F03A, National Institutes of Health, Bethesda, Maryland, United States
2013 - 2016	Associate Professor, Dept. of Developmental, Molecular and Chemical Biology, Tufts University School of Medicine, Boston, Massachusetts, United States
2013 - 2013	AdHoc Reviewer, Special Emphasis Panel ZGM1, National Institutes of Health, Bethesda, Maryland, United States
2012 - 2016	Member, Program Steering Committee , U54 UMass Boston-Dana Farber/Harvard Cancer Center Partnership, Boston, Massachusetts, United States
2007 - 2013	Associate Professor, Dept. of Anatomy and Cellular Biology, Tufts University School of Medicine, Boston, Massachusetts, United States
2006 - 2010	Permanent Member, Molecular Genetics C Study Section, National Institutes of Health, Bethesda, Maryland, United States
2004 - 2004	Temporary Member, Biochemistry Study Section, National Institutes of Health, Bethesda, Maryland, United States
2003 - 2006	Associate Professor, Department of Pathology, Harvard Medical School, Boston, Massachusetts, United States
2000 - 2001	Visiting Scientist, Cell and Molecular Cell, Cell Press, Cambridge, Massachusetts, United States

1997 - 2000	Co-Director and Instructor, Eukaryotic Gene Expression Course, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, United States
1995 - 2000	Member, Board of Tutors, Biochemical Sciences, Harvard University, Cambridge, Massachusetts, United States
1994 - 2003	Assistant Professor, Department of Pathology, Harvard Medical School, Boston, Massachusetts, United States
1989 - 1994	Postdoctoral Research Fellow, advisor Dr. Robert Tjian, Department of Molecular and Cell Biology , University of California, Berkeley, Berkeley, California, United States
1983 - 1989	Graduate student Researcher, advisor Dr. Mark Ptashne, Department of Biochemistry and Molecular Biology, Harvard University, Cambridge, Massachusetts, United States
1982 - 1983	Undergraduate Researcher, advisor Dr. Stephen Beckendorf, Department of Molecular Biology, University of California, Berkeley, Berkeley, California, United States

Products

Products Closely Related to the Proposed Project

1. Mazumdar S, Arendt LM, Phillips S, Sedic M, Kuperwasser C, Gill G. CoREST1 promotes tumor formation and tumor stroma interactions in a mouse model of breast cancer. PLoS One. 2015;10(3):e0121281. PubMed Central PMCID: PMC4368644.
2. Phillips S, Prat A, Sedic M, Proia T, Wronski A, Mazumdar S, Skibinski A, Shirley SH, Perou CM, Gill G, Gupta PB, Kuperwasser C. Cell-state transitions regulated by SLUG are critical for tissue regeneration and tumor initiation. Stem Cell Reports. 2014 May 6;2(5):633-47. PubMed Central PMCID: PMC4050485.
3. Ouyang J, Shi Y, Valin A, Xuan Y, Gill G. Direct binding of CoREST1 to SUMO-2/3 contributes to gene-specific repression by the LSD1/CoREST1/HDAC complex. Mol Cell. 2009 Apr 24;34(2):145-54. PubMed Central PMCID: PMC2727917.
4. Ross S, Best JL, Zon LI, Gill G. SUMO-1 modification represses Sp3 transcriptional activation and modulates its subnuclear localization. Mol Cell. 2002 Oct;10(4):831-42. PubMed PMID: 12419227.
5. Keegan L, Gill G, Ptashne M. Separation of DNA binding from the transcription-activating function of a eukaryotic regulatory protein. Science. 1986 Feb 14;231(4739):699-704. PubMed PMID: 3080805.

Other Significant Products Highlighting Contributions to Science

1. Sun X, Pinacho R, Saia G, Punko D, Meana JJ, Ramos B, Gill G. Transcription factor Sp4 regulates expression of nervous wreck 2 to control NMDAR1 levels and dendrite patterning. Dev Neurobiol. 2015 Jan;75(1):93-108. PubMed Central PMCID: PMC4261064.
2. Lalonde J, Saia G, Gill G. Store-operated calcium entry promotes the degradation of the transcription factor Sp4 in resting neurons. Sci Signal. 2014 Jun 3;7(328):ra51. PubMed Central PMCID: PMC4445882.
3. Pinacho R, Villalmanzo N, Lalonde J, Haro JM, Meana JJ, Gill G, Ramos B. The transcription factor SP4 is reduced in postmortem cerebellum of bipolar disorder subjects: control by depolarization and lithium. Bipolar Disord. 2011 Aug-Sep;13(5-6):474-85. PubMed Central PMCID: PMC3202296.
4. Ramos B, Gaudillière B, Bonni A, Gill G. Transcription factor Sp4 regulates dendritic patterning during cerebellar maturation. Proc Natl Acad Sci U S A. 2007 Jun 5;104(23):9882-7. PubMed Central PMCID: PMC1887555.
5. Di Bacco A, Ouyang J, Lee HY, Catic A, Ploegh H, Gill G. The SUMO-specific protease SENP5 is required for cell division. Mol Cell Biol. 2006 Jun;26(12):4489-98. PubMed Central PMCID: PMC1489136.

Certification:

I certify that the information provided is current, accurate, and complete. This includes, but is not limited to, information related to current, pending, and other support (both foreign and domestic) as defined in 42 U.S.C. § 6605.

In accordance with Section 10632 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19232), each individual identified as a senior/key person must certify that they are not a party to a malign foreign talent recruitment program.

Research Security Training Requirement for Federal Award Personnel: In accordance with Section 10634 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19234), each individual identified as a senior/key person must certify that they have completed the requisite research security training that meets the requirements specified in Item 2 of Important Notice No. 149 within 12 months prior to proposal submission.

Misrepresentations and/or omissions may be subject to prosecution and liability pursuant to, but not limited to, 18 U.S.C. §§287, 1001, 1031 and 31 U.S.C. §§3729-3733 and 3802.

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NIH BIOGRAPHICAL SKETCH SUPPLEMENT

Name: GILL, GRACE B

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0009-0007-2384-6016

Position Title: Associate Professor

Organization and Location: Division of Oncological Sciences, School of Medicine, Oregon Health & Science University, Portland, Oregon, United States

Personal Statement

I bring a strong foundation in pre-clinical research, a record of implementing impactful training as a research mentor and educational leader, and a passion to support effective mentoring skills that foster self-efficacy to my role as co-Associate Director of Cancer Research Training and Education Coordination at the Knight Cancer Institute.

I am a recognized expert in the gene expression field, with a track record of research whose findings have been transformative to the approaches and understanding of molecular mechanisms of eukaryotic transcriptional regulation. Studies from my laboratory established that post-translational modification by the small ubiquitin related modifier, SUMO, promotes association with co-repressors that have chromatin modifying activities, such as CoREST1, a co-factor for the histone lysine demethylase LSD1. We leveraged our studies of basic mechanisms of chromatin structure and gene expression to investigate programs important in normal breast development and aggressive, basal-like, breast cancers. Research from my laboratory also advanced understanding of how post-translational modification of transcription factors contributes to programs of gene expression important for establishing and maintaining proper connections in the mammalian nervous system and how these pathways are disrupted in the neuropsychiatric disorders bipolar disorder and Schizophrenia.

In addition to my research accomplishments, I have a record of engaged and successful training and mentoring of young scientists. I have been the primary research advisor for post-doctoral fellows, PhD students, Masters' students, and undergraduates working in my lab. All 24 of the students and postdoctoral fellows who did extended training with me have continued in biomedical research careers, many as independent investigators. I have served on 40 PhD thesis advisory committees (11 as Chair) and I have advised and mentored numerous postdoctoral fellows, formally as part of the IRACDA program at Tufts, or informally, as fellows in other labs sought out my advice on research projects, presentations, and professional development.

I held leadership positions in the graduate school at Tufts University School of Medicine and, in my role as Director of Harvard Integrated Life Sciences, I implemented initiatives to improve graduate training for over 1200 life sciences PhD students at the Harvard Graduate School of Arts & Sciences. I am a CIMER Certified Facilitator of Entering Mentoring based on positive reviews from faculty participants in the 9-10-hour workshops that I co-facilitated. At the Knight Cancer Institute (KCI), I direct the Biomedical and Bioinformatics Research Internship and Training Experience (B-BRITE) that provides undergraduates an introduction to hands-on cancer research; I coach Ph.D. students, postdoctoral fellows and early career faculty to improve their grantsmanship skills through small group workshops and one-on-one sessions; I provide mentorship training for graduate students, postdoctoral fellows and staff who supervise summer interns in our pathway programs; and I implement professional development opportunities for cancer researchers at all career levels. My efforts support KCI's goal to prepare a skilled and knowledgeable workforce of cross-disciplinary scientists and clinical researchers to accelerate translation of discoveries that benefit people dealing with cancer.

Honors

2022	Certified Facilitator, Entering Mentoring, Center for the Improvement of Mentored Experiences in Research (CIMER)
2002	Fellow, Hellman Family Faculty Fund at Harvard Medical School
1997	Basil O'Connor Starter Scholar Research Award, The March of Dimes
1996	New Investigator Award, The Jesse B. Cox Charitable Trust, The Medical Foundation
1992	Senior Fellow , American Cancer Society, California Division
1989	Fellow, Jane Coffin Childs Memorial Fund for Medical Research
1987	Certificate of Distinction in Teaching, Harvard University
1982	Phi Beta Kappa, University of California, Berkeley

Contributions to Science

1. **SUMO-modification of transcription factors promotes association with co-repressors that have chromatin-modifying activity**
   Many transcription factors are post-translationally modified by the small ubiquitin related modifier, SUMO, but the functional consequences of this modification were poorly understood. We reported that SUMO modification of transcription factor Sp3 is required for Sp3-dependent repression of reporter genes. In this study, we generated fusions of SUMO to Sp3 or to the Gal4 DNA binding domain and found that localization of SUMO to the promoter was sufficient to repress transcription. Our studies established the method of using SUMO fusions to analyze the impact of substrate SUMOylation and were the first to show that SUMO has an intrinsic repression function (Ross et al., 2002). Our findings supported the view that a major mechanism by which SUMO alters transcription factor activity, and gene expression, is by promoting interactions with co-repressors that have SUMO interaction motifs (SIMs). We went on to identify many SUMO binding co-repressors with chromatin modifying activities. Our studies of CoREST1 revealed that non-covalent interaction of a previously undescribed type of SIM in CoREST1 with SUMO-2/3 is required for gene-specific localization and repression by the LSD1/CoREST1/HDAC histone modifying complex (Ouyang et al., 2009). Our mechanistic studies provided a foundational support for subsequent investigations of SUMO biology and SUMOylation pathway inhibition in cancer.

2. **The chromatin regulators LSD1 and CoREST1 regulate cell fate and tumorigenesis**
   Altered expression and/or activity of epigenetic regulators that post-translationally modify histones contributes to pathogenesis of many cancers. The first identified histone demethylase, LSD1, often functions in complex with CoREST1. CoREST1 is required for LSD1-mediated demethylase activity on nucleosomal substrates and also regulates recruitment to specific genes through interactions with transcription factors, and, as we have shown, via non-covalent interactions with SUMO-2 (Ouyang et al., 2009). In collaboration with the Kuperwasser group, we examined the function of the LSD1/CoREST1 complex in normal and tumor-derived breast cells (Phillips et al, 2014). These studies revealed that LSD1/CoREST1 complex activity contributes to the development of aggressive breast cancer by altering chromatin structure and repressing transcription of specific genes associated with the luminal epithelial differentiation program. Unexpectedly, we also found a role for CoREST1 in promoting growth of breast tumors via regulation of tumor/stroma interactions (Mazumdar et al., 2015). Inhibitors of LSD1/CoREST complex activity are currently in clinical trials for multiple cancers.

3. **Transcription factor Sp4 controls dendrite patterning and is actively regulated by Store-operated Ca2+ Entry (SOCE) in neurons**
   While large scale genetic analyses in humans implicated altered transcription factor Sp4 in Bipolar Disorder and Schizophrenia, the function and regulation of Sp4 in neurons was not known. Using an RNAi knockdown approach, we discovered that Sp4 is required for proper dendrite patterning in developing cerebellar granule neurons (Ramos et al., 2007). We reported that Sp4 is required for membrane depolarization-dependent dendrite patterning and Sp4 phosphorylation and activity are regulated downstream of NMDA receptor 1, a glutamate receptor with critical roles in synaptic plasticity, learning, and memory (Saia et al, 2014). We identified several direct Sp4 target genes including Nwk2 (Fchsd1), an F-BAR domain protein that we found to control surface levels of NMDA receptor 1 and dendrite patterning (Sun et al., 2014). While voltage gated channels (VGCCs), such as NMDAR, were well known to mediate neuronal activity-dependent processes, the regulation and function of Store-operated Ca2+ Entry (SOCE) in neurons had not been described. We discovered that SOCE is active in neurons at resting membrane potential, under conditions when VGCCs are not active (Lalonde et al., 2014). Further, our studies showed that Ca2+ signaling downstream of SOCE regulates Sp4 protein stability and levels. Our findings indicate that SOCE not only functions to replenish calcium stores but we were the first to show that SOCE actively signals to promote changes in transcription factor activity in neurons. Others have since described a broad range of key functions for SOCE in the nervous system with implications for pathogenesis and treatment of neurological disease.

4. **Transcription factor Sp4 protein levels and post-translational modification are altered in Bipolar Disorder and Schizophrenia**
Genetic studies revealed an association between variations at the Sp4 locus and both Bipolar Disorder and Schizophrenia in humans, but it was not known whether or how Sp4 was altered in patients. In collaboration with a former postdoctoral fellow, we examined Sp4 mRNA and protein levels in post-mortem brain samples. Strikingly, Sp4 protein, but not mRNA, was reduced in postmortem cerebellum of Bipolar Disorder and we observed a correlation with Sp4 protein levels and negative symptoms in cerebellum of Schizophrenia (Pinacho et al., 2011 and 2013). Extending on our finding that phosphorylation of Sp4 at S770 is regulated by NMDAR signaling (Saia et al., 2014), we observed a relative increase in Sp4pS770 in cerebellum of Bipolar Disorder and associated with negative symptoms in Schizophrenia (Pinacho, et al., 2015). Negative symptoms are the most stable cluster of symptoms in chronic patients and the most resilient to current available therapies. Our pilot studies pioneered the use of negative symptom dimension for association studies of these symptoms with molecular features. We also observed reduced Sp4 protein and increased Sp4pS770 in lymphocytes from first-episode psychosis subjects, suggesting these features may appear at the onset of disease (Fuste et al, 2013 and Pinacho et al., 2015). Further, we reported that lithium, a mood stabilizer commonly used for treatment of Bipolar Disorder, regulates Sp4 protein levels and S770 phosphorylation (Pinacho et al., 2011 and 2015). Taken together, these studies strongly suggest that alterations in the pathways that regulate Sp4 protein levels and stability contribute to neuropsychiatric disease and the response to some therapeutics.

5. **Modularity and function of eukaryotic activation domains**
I contributed to early work defining the functional domains of eukaryotic transcription factors. As a graduate student in Mark Ptashne's lab, I showed that in vivo binding to the promoter by the DNA binding domain of Gal4 was not sufficient for transcriptional activation, ruling out some early models for how activators worked (Keegan et al., 1986). Together with other studies, this helped establish the now well-accepted view that eukaryotic transcription factors have separable DNA binding and activation (or repression) domains. This fundamental insight laid the foundation for current models of transcriptional activation mechanisms and for development of yeast two-hybrid approaches for screening protein interaction libraries. I also characterized key features of acidic activation domains in yeast and described how overexpression of activation domains could inhibit transcription by a competitive mechanism, a phenomenon dubbed "squelching" (Gill and Ptashne, 1987 and 1988). Other groups leveraged this competition phenomenon to identify essential coactivators (the mediator and the histone acetyltransferase Gcn5). As a postdoctoral fellow with Robert Tjian, I helped establish that some activators stimulate transcription via interactions with components of the TFIID complex composed of TATA binding protein, TBP, and TBP associated factors, TAFs (Gill et al., 1994). Thus, my early graduate and postdoctoral work was foundational to our current understanding of transcription factor function and laid the foundation for powerful screening tools.

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