BIOGRAPHICAL SKETCH

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NAME: **Pruitt, Kevin**

eRA COMMONS USER NAME (credential, e.g., agency login): **kpruitt1**

POSITION TITLE: **Associate Professor of Pharmacology**

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 Date MM/YYYY	FIELD OF STUDY
University of Texas at Austin	B.S.	12/1995	Chemical Engineering
University of North Carolina at Chapel Hill	Ph.D.	12/2001	Pharmacology
Johns Hopkins School of Medicine	Postdoctoral Fellow	07/2006	Oncology

A. Personal Statement

Research in my lab addresses three critical questions. First, we seek to address how the Wnt pathway, an iconic regulator of development that is co-opted in cancer, regulates immune cell infiltration into the tumor microenvironment (TME). Second, we are defining how Dishevelled (DVL), a master regulator of multiple branches of Wnt signaling, shapes the cancer epigenome and how it may be targeted therapeutically. This is important because Wnt pathway regulators are mutated in greater than 80% of colorectal cancers (CRC) and are dysregulated in most triple-negative breast cancers (TNBC). Third, we are establishing how cancer-associated estrogen biosynthesis contributes to tumor progression of both colorectal and breast cancer.

My ultimate goal is to secure R01 funding for each of these three core projects. I'm pursuing this goal not only with the intent of securing extramural funding and making major discoveries, but also with the intent of providing a platform for training the next generation of researchers. For the last 18 years I have made investments in guiding and mentoring students who tend to have limited research experience and exposure to science but abundant drive and aspiration. This intentionality has led to many successes both scientifically and with respect to developing the next generation of researchers who will lead future breakthroughs.

For the first project, since arriving at UNC, we have established a major proof-of-concept which has been lacking in the Wnt field. Our pilot studies have, for the first time, identified a role for tumor-intrinsic DVL in regulating T cell (via DVL3) and macrophage (via DVL2) infiltration of tumors using syngeneic mammary carcinoma models. A landmark paper published in Nature suggested that β-catenin regulates tumor-infiltrating lymphocytes (TILs), but little is known about the mechanism. Our recent pilot study was inspired by our previous publication which found an inverse correlation between tumor-intrinsic DVL expression in primary breast tumors and CD8+ T-cell infiltration (*BMC Cancer 2023*). Our next experiments planned seek to build upon this exciting new finding and further validate and establish a role for DVL in CRC and TNBC.

The second area of investigation stemmed from postdoctoral discoveries at Johns Hopkins demonstrating that stress-responsive sirtuins regulate epigenetic silencing of tumor suppressor genes (PLoS Genetics 2006; Nat. Genetics 2007). This investigation continued during my initial faculty appointments at LSU and progress accelerated during my recruitment to Texas Tech in 2014. Since moving to UNC, I have begun to build collaborations with local pioneers in the epigenetics field and will continue to assess how DVL impacts the cancer epigenome based on clues provided from earlier studies from my lab (*PNAS 2010; Oncogene 2013; Sci. Rep. 2019; EMBO Rep 2021*). Our most recent advance received considerable attention at the Gordon

Conference in June 2025 and our manuscript describing an elusive role of nuclear DVL1 was just accepted for publication in Nature Communications.

Our third area of investigation seeks to define how estrogen-biosynthesis contributes to tumor progression in non-canonical ways including activation of GPCRs in CRC and via aromatase post-translational regulation in multiple cancer types. Our findings on novel regulation of aromatase could be applicable to not only cancer and endometriosis, but to multiple disorders wherein aromatase is dysregulated or is targeted therapeutically. We identified critical druggable targets that regulate estrogen biosynthesis (*Mol. Endo. 2013*), and we identified entirely new post-translational regulatory mechanisms that control aromatase catalytic activity and estrogen biosynthesis (*Mol. Can. Res 2018*). Our recent data suggest that aromatase PTMs render it insensitive to aromatase inhibitors broadly used to treat post-menopausal breast cancer. Addressing these major questions will not only help to advance the field but will lead to new extramural funding and serve as a foundation for postdoc and graduate student training.

1R01AG082880 (Pruitt, PI)
"The impact of aging on intestinal estrogen biosynthesis"
12/01/2025 – 11/30/2030
Submitted, p*ending council review*

1R03AG080356-01 (Pruitt, PI)
03/15/2023 – 03/14/2026
"Post-translational regulation of aromatase in aging"

1R21CA277140-01
Ganapathy (PI); Pruitt (co-I),
12/16/2022 – 10/30/2024
"AA transporter SLC38A5 as a drug target for TNBC: Evaluation with genetic and pharmacologic approaches"

Epigenetics and Infectious Disease Seed Grant
Pruitt, Nichols, Almodovar (MPI)
06/01/2020 - 5/31/2024
The research focus was on the molecular identification of how infectious agents modify the host epigenome.

W81XWH1910113
Barnes (PI), Role: Pruitt (PI), sub-award
04/15/19 - 04/14/24
"Factors that regulate breast tumor immunogenicity and metastasis: Targeting interferon regulatory factor 5 (IRF5)".

Garrison Institute on Aging Grant
Pruitt, Lawrence (MPI)
02/01/20 - 07/31/21
This intramural grant from the GIA explored epigenetic regulation and aberrant Wnt/Ca2+ signaling.

CPRIT-140008
Pruitt (PI)
06/01/14 - 11/30/20
CPRIT Rising Star Recruitment Award

1. Holloway, K.R., Calhoun, T., Saxena, M., Metoyer, C.M., Kandler, E.F., Rivera, C.A. and **Pruitt, K.** (2010) SIRT1 regulates Dishevelled proteins and promotes transient and constitutive Wnt signaling. ***Proc Natl Acad Sci U S A.*** *May 18;107(20):9216-21. doi: 10.1073/pnas.0911325107.*
2. Saxena, M., Dykes, S.S., Malyarchuk, S., Wang A.E., Cardelli J.A., and **Pruitt, K.** (2013) The sirtuins promote Dishevelled-1 scaffolding of TIAM1, Rac activation, and cell migration. ***Oncogene.*** *Jan 8;34(2):188-98. doi: 10.1038/onc.2013.549.*

3. Castro-Piedras, Sharma, M., Brelsford, J., Vartak, D., Martinez, E, Rivera, C., Molehin, D., Bright, RK, Fokar, J. Guindon, J., and **Pruitt, K.** (2021) Nuclear Dishevelled targets gene regulatory regions and promotes tumor growth. ***EMBO Reports.*** *Jun 4;22(6):e50600. doi:10.15252/embr.202050600.*
4. Martinez-Marin D., Sharma M., van Wunnik J., Sardela F., Boligala G., Jull E., Stroman G, Babcock R., and **Pruitt, K** (2025) Dishevelled-1 regulates global transcriptomic changes and associates with ETS1 transcription factor ***Nature Communications.*** *(in press)*

B. Positions, Scientific Appointments, and Honors:

Positions

2023 – Present	**Associate Professor**, Department of Pharmacology, Lineberger Comprehensive Cancer Center, The University of North Carolina at Chapel Hill
2016 – 2023	**Childers-Fralick Endowed Chair in Cancer Research,** Department of Immunology & Molecular Microbiology, Texas University Tech Health Sciences Center-Lubbock
2014 – 2023	**Associate Professor (tenured),** Department of Immunology & Molecular Microbiology, Texas University Tech Health Sciences Center-Lubbock
2014	**Carroll Feist Endowed Chair in Cancer Epigenetics,** Department of Molecular and Cellular Physiology, LSUHSC & Feist-Weiller Cancer Center
2012 – 2014	**Associate Professor (tenured),** Department of Molecular and Cellular Physiology LSU Health Science Center-Shreveport & Feist-Weiller Cancer Center
2006 – 2012	**Assistant Professor,** Department of Molecular and Cellular Physiology LSU Health Science Center-Shreveport & Feist-Weiller Cancer Center
2002 – 2006	**ACS Post-doctoral Fellow,** Department of Oncology Johns Hopkins School of Medicine & Sidney Kimmel Comprehensive Cancer Center (Advisor – Stephen B. Baylin)
1997 – 2001	**NSF Pre-doctoral Fellow,** Department of Pharmacology & Lineberger Comprehensive Cancer Center University of North Carolina at Chapel Hill (Ph.D. Advisor – Channing J. Der)
1996	**Graduate Research Assistant,** Los Alamos National Laboratory – Los Alamos, NM, LS-5 and Mass Spectrometry Divisions
1994 – 1995	**Research Assistant,** Center for Energy Studies, University of Texas at Austin
1995	**Research Assistant,** Los Alamos National Laboratory, Los Alamos, NM, LS-5 Division
1994	**Research Assistant,** Los Alamos National Laboratory, Los Alamos, NM, LS-1 Division
1993 – 1994	**Research Assistant,** Balcones Research Center, University of Texas at Austin
1990 – 1992	**Engineering Summer Internships**, Union Carbide Corp., Texas City, TX

Scientific Appointments

2021 – Present	Member, DOD Breast Cancer Research Program Programmatic Review Panel
2020 – Present	Guest Editor, *Molecular and Cellular Endocrinology*
2014 – 2020	Member, NIH Cancer Genetics (CG) Study Section
2015 – 2016	Volume Editor, Elsevier, Molecular Changes in the Cancer Cell
2010 – 2013	*Ad Hoc* Reviewer, NIH Cancer Genetics (CG) Study Section
2008 – 2020	*Ad Hoc* Reviewer, DOD Breast Cancer Research (BCRP) Programmatic Review
2011	*Ad Hoc* Reviewer, Clinical Integrative Molecular Gastroenterology Study Section
2008	Member, American Cancer Society Postdoctoral Symposium Organizing Committee

Honors

2023	Outstanding Faculty of the Year Award, TTUHSC, GSBS
2022	Outstanding Research and Student Mentor Award, GSBS
2016 – 2023	Childers-Fralick Basic Cancer Research Endowed Chair, TTUHSC
2014 – 2020	Cancer Prevention and Research Institute of Texas Rising Star Recruitment Award
2018	Immunology and Molecular Microbiology Unsung Hero Award
2018	University Distinguished Faculty Award, TTUHSC
2017	Pruitt lab research featured in Pulse Magazine, and Avalanche Journal Newspaper
2016	Immunology and Molecular Microbiology Unsung Hero Award
2014	Carroll Feist Endowed Chair in Cancer Epigenetics, LSUHSC
2006 – 2007	Eli Lilly AACR Scholar in Training Award; Aspen Health Forum Fellow

2003 – 2006	American Cancer Society (ACS) Postdoctoral Fellowship
2000 – 2001	Merck-UNCF Graduate Research Dissertation Fellowship
1999	Thomas Collum Butler Award, UNC Chapel Hill, Pharmacology Department
1997 – 2000	National Science Foundation (NSF) Pre-doctoral Fellowship
1996 – 1997	Graduate School Excellence Award
1994 – 1995	Dept. of Energy, Associated Western Universities Research Fellowship
1994 – 1996	Texas Research Experience Fellowship, School of Engineering
1996	Hoechst-Celanese Corporation/UNC Chapel Hill Research Scholarship
1990	Jesse H. Jones Scholarship (Houston Endowment, Inc.); Texas Achievement Award
1990	Scurlock Foundation Award; Ronald E. McNair Memorial Scholarship

C. Contributions to Science

1. Nuclear roles of DVL and genomic profiling: DVL mutations and dysregulated expression are found in disparate pathologies ranging from congenital conditions such as Robinow syndrome to aging-linked pathologies such as cancer. Mutations in DVL in humans that drive the skeletal dysplasias characteristic of Robinow syndrome were only recently discovered in 2015 while its link to other pathologies are even more recent. To define the recently discovered nuclear role of DVL paralogs, our studies were the first to establish roles of specific DVL paralogs in transcriptional regulation. No previous studies addressed a potential role of nuclear DVL in direct transcriptional regulation. We have discovered novel mechanisms whereby DVL1 and DVL3 serve as promoter scaffolds for epigenetic enzymes that regulate histone modifications and function in a divergent manner. Our reports are the first to elucidate previously unknown dimensions of DVL nuclear function. We also demonstrated intriguing connections between DVL proteins, enzymes that regulate estrogen biosynthesis, immune cell function and a host of biological processes identified via ChIP-seq for both DVL1 and DVL3. Finally, we demonstrated that specific DVL PTMs are linked with tumor growth *in vivo* and with nuclear translocation. Our lab was also the first to demonstrate that DVL proteins bind to epigenetic enzymes at gene promoters and enhancers and regulate epigenetic marks in collaboration with epigenetic enzymes at transcription regulatory elements.

a. Sharma, M., Molehin, D.M., Castro-Piedras, I., Martinez, E.M., and **Pruitt, K** (2019). Acetylation of conserved DVL-1 lysines regulates its nuclear translocation and binding to gene promoters in triple-negative breast cancer. ***Scientific Reports.*** *Nov 7;9(1):16257. doi:10.1038/s41598-019-52723-3.*
b. Castro-Piedras, Sharma, M., Brelsford, J., Vartak, D., Martinez, E, Rivera, C., Molehin, D., Bright, RK, Fokar, J. Guindon, J., and **Pruitt, K.** (2021) Nuclear Dishevelled targets gene regulatory regions and promotes tumor growth. ***EMBO Reports.*** *Jun 4;22(6):e50600. doi:10.15252/embr.202050600.*
c. Sharma, M., Castro-Piedras, I., Rasha, F., Ramachandran S., Sennoune S., Furr, K., Almodovar S., Ganapathy, B., Grisham, M.B., Layeequr-Rahman, R., and **Pruitt, K** (2021). Dishevelled-1 DIX and PDZ domain lysine residues regulate oncogenic Wnt signaling. ***Oncotarget.*** *Oct 26;12(22):2234-2251. doi: 10.18632/oncotarget.28089.*
d. Martinez-Marin D., Sharma M., van Wunnik J., Sardela F., Boligala G., Jull E., Stroman G, Babcock R., and **Pruitt, K** (2025) Dishevelled-1 regulates global transcriptomic changes and associates with ETS1 transcription factor ***Nature Communications.*** *(in press)*

2. Characterization of epigenetic regulation in diverse tumor models: A critical question that remained unaddressed for years was how do cellular responses to diverse physiological or environmental stresses become imprinted in a cell's memory? Whether the stress comes from endocrine or immunologic dysfunction, the epigenetic basis for establishing aberrant cellular memory was poorly understood. Our work was the first to demonstrate novel cross-talk in the regulation of both epigenetic "erasers" and "readers" in the control of tumor suppressor gene (TSG) silencing and the epigenetic activation of novel oncogenes. When my laboratory relocated from LSUHSC to TTUHSC, we continued to gain insight into the molecular basis for this paradox. We have begun to solve this molecular riddle and have now identified novel PTMs on key epigenetic readers of DNA methylation. Aberrant DNA methylation across the cancer genome directs gene expression & drives tumor progression, and the DNA methylation "readers" (such as MeCP2) transmit tumor-promoting instructions. MeCP2 reads DNA methylation and thereby connects this information with other epigenetic marks by recruiting histone modifying enzymes and lncRNAs.

a. **Pruitt, K.**, Zinn, R.L., Ohm, J.E, McGarvey, K.M., Kang, S.L., Watkins, D.N., Herman, J.G., and

Stephen B. Baylin, S.B. (2006) Inhibition of SIRT1 Reactivates Silenced Cancer Genes Without Loss of Promoter DNA Hypermethylation. ***PLoS Genetics.*** *2(3): e40*). *doi: 10.1371/journal.pgen.0020040. (selected as Faculty of 1000 Must Read)*

b. Ohm JE, McGarvey KM, Yu, X, Schuebel KE, Cope L, Mohammad HP, Chen W, Daniel VC, Yu W, Berman DM, Jenuwein T, **Pruitt, K.**, Sharkis SJ, Watkins DN, Herman JG, Baylin SB. (2007) A stem cell-like chromatin pattern may predispose tumor suppressor genes to DNA hypermethylation and heritable silencing. ***Nat. Genetics.*** *39(2):237-42. doi: 10.1038/ng1972.*
c. Pandey, S., Simmons, G.E., Malyarchuk, S. M., Calhoun, T.N., and **Pruitt, K.** (2015). A novel MeCP2 acetylation site regulates association with ATRX and HDAC1. ***Genes & Cancer.*** *Sep;6(9-10):408-21. doi: 10.18632/genesandcancer.84.*
d. Castro-Piedras, I., Vartak, D., Sharma, M., Pandey, S., Casas, L., Molehin, D., Rasha, F., Fokar, M., Nichols, J., Almodovar, S., Rahman, RL, and **Pruitt, K.** (2020) Identification of novel MeCP2 cancer-associated target genes and post-translational modifications. ***Frontiers in Oncology.*** *Dec 10; 10:576362. doi: 10.3389/fonc.2020.576362.*

3. Characterization of novel molecular mechanisms impacting the tumor immune microenvironment: Emerging data reveal that many of the novel gene targets we identified recently are linked with cancer-associated biological dysfunction. We have performed extensive LC-MS/MS analyses of PTMs across diseased tissue, primary tumors and cell lines. We have found that lysine acetylation is significantly altered between normal and cancer tissue. We have demonstrated that lysine deacetylases targeted by FDA-approved drugs administered to patients in the clinic regulate PTMs of novel proteins that control diverse processes such as leukocyte chemotaxis, intra-tumor estrogen synthesis and other oncogenic properties. We have begun to create the first of its kind a comprehensive map of the PTMs on key proteins and enzymes that may uncover novel markers that predict acquired or *de novo* resistance to cancer therapies. We have also identified critical post-translationally regulated lysines that control enzymes involved in steps early and late stages in the estrogen biosynthesis pathway. We for the first time show these novel PTMs modulate estrogen production. We are also investigating how post-translational regulation and oncogenic signaling differentially influences malignancy in breast cancer subtypes and immune cell infiltration.

a. Molehin, D.M., C Castro-Piedras, I., Sharma, M., Sennoune, S.R., Arena, D., Manna, P.R., **Pruitt, K** (2018) Aromatase Acetylation Patterns and Altered Activity in Response to Sirtuin Inhibition. ***Mol. Can. Res****. Oct;10(10)1530-1542. doi: 10.1158/1541-7786.MCR-18-0047.*
b. Khan SY, Melkus MW, Rasha F, Castro M, Chu V, Brandi L, Khan H, Gill HS, **Pruitt, K** and Layeequr Rahman R (2022). Tumor-Infiltrating Lymphocytes (TILs) as a Biomarker of Abscopal Effect of Cryoablation in Breast Cancer: A Pilot Study. ***Ann Surg Oncol.*** *May;29(5)2914-2925. doi: 10.1245/s10434-021-11157-w*
c. Rasha F, Boligala GP, Yang MV, Martinez-Marin M, Castro-Piedras I, Furr K, Snitman A, Khan SY, Luis B, Castro M, Khan H, Jahan N, Almodovar S, Melkus MW, ***Pruitt, K** and *Layeequr Rahman, R. (2023) Dishevelled 2 regulates cancer cell proliferation and T cell mediated immunity in HER2-positive breast cancer. ***BMC Cancer*** *2023 Feb 21;23(1):172. doi: 10.1186/s12885-023-10647-2.* *co-corresponding authors.
d. Sardela de Miranda F, Martinez-Marin D, Babcock RL, Castro M, Boligala GP, Khan SY, Furr KL, Castro-Piedras I, Wagner N, Robison DE, Daniele K, Singh SP, **Pruitt, K**, Melkus MW, Layeequr Rahman R. Cryoablation of primary breast cancer tumors induces a systemic abscopal effect altering TIME (Tumor Immune Microenvironment) in distant tumors. ***Front Immunol.*** *2024;15:1498942. doi: 10.3389/fimmu.2024.1498942. eCollection 2024. PubMed PMID: 39703517.*

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