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

# NIH Biographical Sketch Common Form

Name: Kridel, Steven

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0009-0003-8246-4940

Position Title: Chair, Department of Cancer Biology

Organization and Location:Wake Forest University School of Medicine, Winston-Salem, North Carolina, United States

PROFESSIONAL PREPARATION

| INSTITUTION AND LOCATION | DEGREE | Start Date | Completion Date | FIELD OF STUDY |
|---|---|---|---|---|
| The Burnham Institute, La Jolla, CA, United States | Postdoctoral Fellow | 06/1997 | 09/2002 | Cancer Biochemistry |
| University of Califiornia, Irvine, CA, USA | DOCTOR OF PHILOSOPHY | 09/1992 | 06/1997 | Developmental and Cell Biology |
| California State University, Los Angeles, CA, USA | BACHELOR OF SCIENCE | 09/1987 | 06/1992 | Biological Sciences |

**Appointments and Positions**

| | |
|---|---|
| 2002 - present | Chair, Department of Cancer Biology, Wake Forest University School of Medicine, Winston-Salem, North Carolina, United States |
| 2026 - present | Board of Directors, Cancer Biology Training Consortium, Hanover, New Mexico, United States |
| 2024 - present | Chair, Department of Cancer Biology, Wake Forest University School of Medicine, Winston-Salem, North Carolina, United States |
| 2023 - present | Assistant Director, CRTEC, Winston-Salem, North Carolina, United States |
| 2012 - present | Associate Professor with Tenure, Wake Forest School of Medicine, Winston-Salem, NC, USA |
| 2014 - 2024 | Vice Chair, Department of Cancer Biology, Wake Forest School of Medicine, Winston-Salem, North Carolina, United States |
| 2012 - 2021 | Cancer Biology PhD Program Director, Wake Forest School of Medicine, Winston-Salem, North Carolina, United States |
| 2012 - 2014 | Interim Chair, Department of Cancer Biology, Wake Forest School of Medicine, Winston-Salem , NC, USA |
| 2009 - 2012 | Associate Professor, Wake Forest School of Medicine, Winston-Salem, NC, USA |
| 2002 - 2009 | Assistant Professor, Wake Forest School of Medicine, Winston-Salem, NC, USA |
| 1997 - 2002 | Postdoctoral Fellow, The Burnham Institute, La Jolla, CA, USA |
| 1992 - 1997 | Graduate Student, University of California, Irvine, CA, USA |

**Products**

*Products Closely Related to the Proposed Project*

1. Chmielewski JP, Bowlby SC, Wheeler FB, Shi L, Sui G, Davis AL, Howard TD, D'Agostino RB Jr, Miller LD, Sirintrapun SJ, Cramer SD, Kridel SJ. CD38 Inhibits Prostate Cancer Metabolism and Proliferation by Reducing Cellular NAD(+) Pools. Mol Cancer Res. 2018 Nov;16(11):1687-1700. PubMed Central PMCID: PMC6214722.
2. Anderson R, Pladna KM, Schramm NJ, Wheeler FB, Kridel S, Pardee TS. Pyruvate Dehydrogenase Inhibition Leads to Decreased Glycolysis, Increased Reliance on Gluconeogenesis and Alternative Sources of Acetyl-CoA in Acute Myeloid Leukemia. Cancers (Basel). 2023 Jan 12;15(2) PubMed Central PMCID: PMC9857304.
3. Kumar A, Kumar P, Sharma M, Kim S, Singh S, Kridel SJ, Deep G. Role of extracellular vesicles secretion in paclitaxel resistance of prostate cancer cells. Cancer Drug Resist. 2022;5(3):612-624. PubMed Central PMCID: PMC9511801.
4. Hill TK, Davis AL, Wheeler FB, Kelkar SS, Freund EC, Lowther WT, Kridel SJ, Mohs AM. Development of a Self-Assembled Nanoparticle Formulation of Orlistat, Nano-ORL, with Increased Cytotoxicity against Human Tumor Cell Lines. Mol Pharm. 2016 Mar 7;13(3):720-8. PubMed Central PMCID: PMC4783219.

*Other Significant Products, Whether or Not Related to the Proposed Project*


1. Kridel SJ, Axelrod F, Rozenkrantz N, Smith JW. Orlistat is a novel inhibitor of fatty acid synthase with antitumor activity. Cancer Res. 2004 Mar 15;64(6):2070-5. PubMed PMID: 15026345.
2. Little JL, Wheeler FB, Fels DR, Koumenis C, Kridel SJ. Inhibition of fatty acid synthase induces endoplasmic reticulum stress in tumor cells. Cancer Res. 2007 Feb 1;67(3):1262-9. PubMed PMID: 17283163.
3. Pemble CW 4th, Johnson LC, Kridel SJ, Lowther WT. Crystal structure of the thioesterase domain of human fatty acid synthase inhibited by Orlistat. Nat Struct Mol Biol. 2007 Aug;14(8):704-9. PubMed PMID: 17618296.
4. Little JL, Wheeler FB, Koumenis C, Kridel SJ. Disruption of crosstalk between the fatty acid synthesis and proteasome pathways enhances unfolded protein response signaling and cell death. Mol Cancer Ther. 2008 Dec;7(12):3816-24. PubMed Central PMCID: PMC2641993.


**Certification:**

I certify that the information provided is current, accurate, and complete. This includes but is not limited to information related to domestic and foreign appointments and positions.

I also certify that, at the time of submission, I am not a party to a malign foreign talent recruitment program.

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: Kridel, Steven

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0009-0003-8246-4940

Position Title: Chair, Department of Cancer Biology

Organization and Location: Wake Forest University School of Medicine, Winston-Salem, North Carolina, United States

## Personal Statement

My laboratory is interested in intermediary metabolism with a particular focus on de novo fatty acid synthesis and the role of NAD+ in cellular bio-energetics. We are particularly interested in fatty acid synthase (FASN) and acetyl-CoA carboxylase (ACC1), the enzymes that synthesize fatty acid. My research focus is on the metabolic pathways that contribute to the development and progression of prostate cancer, as well as other cancers. In particular, we are interested in understanding how the fatty acid synthesis and NAD+-linked pathway drive cancer. We take an integrated approach by combining crystallography, drug discovery, imaging, and in vivo methodologies to understand these pathways in cancer and to develop novel therapeutics. I discovered Orlistat as novel fatty acid synthase inhibitor and determined the role of FASN in multiple pathways. Moreover, we have developed several assays to study FASN metabolism. We have a growing collaboration with Dr. Said and her group investigating metabolic pathways in bladder and ovarian cancer, which have already yielded a publication. Our labs are adjacent to one another and we are working as a team to define the role of FASN and FA synthesis in bladder cancer and the impact of targeting FASN with specific drugs. My labs expertise in cancer cell biology assays to understand survival and metabolism will be valuable to the successful completion of the proposed research. In addition, I am also Chair of the Department of Cancer Biology and Assistant Director for CRTEC in the Atrium Health Wake Forest Baptist Comprehensive Cancer Center. I have trained 7 PhD students and served on mentoring committees for more than 30 others. I lead or co-lead three different undergraduate and postbac training programs as well.

## Honors

2026 - 2028 Board of Directors, CABTRAC

## Contribution to Science

1. Metabolic perturbations in cancer. Consistent with my laboratory interest in FASN, we have also focused on the consequences of metabolic perturbations in cancer. We provided the first demonstration that blockade of lipid metabolism through FASN inhibition activated the unfolded protein response (UPR) and ER stress. Subsequent work demonstrated that combining proteasome inhibition with metabolic blockade provides synergistic activation of the UPR and subsequent cell death. We were also demonstrated for the first time that blockade of fatty acid synthesis can reduce tumor cell invasion by disrupting the formation and activity of invadopodia. This provides a functional connection between the expression of fatty acid synthesis enzymes and tumor progression. My laboratory also pioneered the concept that NAD+ synthesis is required for fatty acid and lipid synthesis in tumor cells and that blockade of NAD+ synthesis induces cell death in prostate cancer. Altogether, this body of work demonstrates a long and broad history of studying metabolic pathways in cancer and the impact of blocking these ubiquitous cancer-associated pathways.
2. NAD+ metabolism in prostate cancer. Cancer cells are known to require NAD+ to fuel metabolic demands and macromolecular synthesis. We have contributed to the field by providing the first demonstration of NAMPT being overexpressed in prostate cancer and that blockade of NAMPT activity impact lipid synthesis. Conversely, we also demonstrated that CD38, the primary NAD'ase in mammalian cells, is lost in prostate cancer. Subsequent expression of CD38 reduced cellular metabolism at many levels, including glycolysis, TCA, and lipid synthesis. This body provides an understanding of NAD metabolism in prostate cancer and identifies new potential therapeutic avenues.
3. Matrix Metalloprotease biology. My postdoctoral training consisted of protein biochemistry and enzymology training mixed with cancer biology. During my NIH NRSA-funded training I developed a novel substrate phage display screening methodology. In this system, random peptide were expressed on the surface of pahge which allowed for the negative selection of protease substrates following exposure to proteases. Using this system, I identified the substrate specificity for MMP 9, MMP-14 (MT-1-MMP, and MMP-2), three proteases involved in matrix remodeling and cell surface hydrolysis in cancer. Using this system, we employed a bioinformatics approach to understand substrate hydrolysis by MMP-9 is neuronal cell death, demonstrating the utility of the system in protein substrate identification.

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