BIOGRAPHICAL SKETCH

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NAME: **Burnstein, Kerry L.**

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POSITION TITLE: Professor of Medicine

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
Wesleyan University, Middletown, CT	BA	05/1981	Biology
University of North Carolina at Chapel Hill, Chapel Hill, NC	PhD	10/1986	Genetics
University of North Carolina at Chapel Hill, Chapel Hill, NC	Postdoctoral (T32 & NRSA Fellowships)	08/1990	Molecular Endocrinology

A. Personal Statement

I am Professor and Chair of the Department of Molecular and Cellular Pharmacology at the University of Miami Miller School of Medicine and member of the Tumor Biology Research Program at the NCI-designated Sylvester Comprehensive Cancer Center. Since 2015, I have served as the Associate Director (AD) for Education and Training at Sylvester. With the support of a Center-staffed Office, I coordinate and track education and training efforts targeted for learners from early-stage students to the levels of professional academic faculty. I also oversee the strategic development, coordination, and evaluation of these efforts as part of Sylvester's leadership. In addition, I work with Sylvester Research Program leaders to ensure that faculty (particularly at early career stage) receive optimal mentoring and career development and that program faculty participate fully in educational and training initiatives to optimize trainee engagement and success.

During the past 30 years, I have developed international recognition for expertise in the field of steroid hormone action and mechanisms of intracellular cross talk between steroid receptors and other signaling pathways. My current research is to identify and exploit therapeutic targets that are downstream of androgen receptor and constitutively active AR variant signaling in castration-resistant prostate cancer. I was the 2019 recipient of the Society for Women in Urology / Society for Basic Urologic Research Joint Award for Excellence in Urologic Research.

I have developed strong leadership, mentoring, and administrative skills through many years of directing both the Pharmacology Graduate Program and Sylvester's interdisciplinary Cancer Biology Graduate Program. I am also a previous President and current Board Member of the national Cancer Biology Training Consortium (CABTRAC). My service on the University of Miami's Academic Personnel Board (highest tenure and promotion committee) has also provided considerable insight and helped me to successfully mentor junior and mid-career faculty.

Highlighted ongoing projects:

1P30CA240139 Nimer (PI) 07/10/2019 - 06/30/2024
The Sylvester Cancer Center Support Grant
The goal of this project is to support the Sylvester Comprehensive Cancer Center's mission to reduce the human burden from cancer through research, education, prevention, and the delivery of quality patient care.
Role: Associate Director for Education and Training

1I01BX005466 Burnstein (PI) 04/01/2021 - 03/31/2024
Veteran Affairs
Covid-19: Fast-tracking treatment by exploiting the steroid hormone receptor/TMPRSS2 axis

Evaluate steroid hormone receptor (AR and GR) regulation of TMPRSS2 in human primary airway and lung epithelial cells and lung adenocarcinoma cell line models. Examine the capacity of FDA-approved AR and GR antagonists to block CoV-2 entry and infectivity in human primary airway and lung epithelial cells.

HT9425-23-1-0369 Burnstein (PI) 06/15/2023 - 06/14/2026
Department of Defense
Targeting KIF20A, a kinesin with a novel, non-canonical role in castration-resistant prostate cancer
Determine the mechanisms by which KIF20A confers castration resistance. Evaluate KIF20A as a therapeutic target in lethal PC.

HT9425-23-1-0389 Burnstein (PI) 05/01/2023 - 04/30/2026
Department of Defense
Proprietary arginine vasopressin receptor type 1a (AVPR1a) antagonists for treatment of lethal prostate cancer
Evaluate novel AVPR1A antagonist in robust CRPC pre-clinical models of established CRPC (including PDXs) and invasive disease. Evaluate the lead AVPR1A antagonist in late stage CPRC growth in the bone metastatic niche (including an immunocompetent model) and determine the importance of AVPR1A targeting in the context of autocrine/paracrine actions of AVP.

PC200118 Zhang (PI) 09/01/2021 - 08/31/2024
Department of Defense
Exploit Cellular Weakness Associated with ATE1 Downregulation in Advanced Prostate Cancer
Role: Collaborator

U01 CA244101 Lynch (PI, Moffitt Cancer Center) 06/11/2020 - 05/31/2025
NIH-NCI
Defining bone ecosystem effects on metastatic prostate cancer evolution and treatment response using an integrated mathematical modeling approach.
Role: Collaborator

2I01BX002773-05 (recommended for funding) Burnstein (PI) 01/1/2024-12/31/2027
Veteran Affairs
A Novel Drug Target for Aggressive Prostate Cancer
Elucidate mechanisms of BUB1B action in lethal CRPC and NEPC and develop drug-like potent selective small molecule BUB1B inhibitors through sophisticated deep neural network multi-task (DNNMT) predictors coupled with biochemical assays and test the most promising compounds in robust PC patient-derived models.

Citations:

1. Heidman LM, Peinetti N, Copello VA, **Burnstein KL** Exploiting dependence of castration-resistant prostate cancer on the arginine vasopressin signaling axis by repurposing vaptans 2022 *Mol Cancer Res* doi: 10.1158/1541-7786.
2. Copello VA, **Burnstein KL** The kinesin KIF20A promotes progression to castration-resistant prostate cancer through autocrine activation of the androgen receptor. *Oncogene* 2022 PMID 35418689
3. Zhao N, Peacock SO, Lo CH, Heidman LM, Rice MA, Fahrenholtz CD, Greene AM, Magani F, Copello VA, Martinez MJ, Zhang Y, Daaka Y, Lynch CC, **Burnstein KL**. Arginine vasopressin receptor 1a is a therapeutic target for castration-resistant prostate cancer. *Science Translational Medicine* 2019 Jun 26;11(498). pii: eaaw4636. doi:10.1126/scitranslmed.aaw4636. PubMed PMID: 31243151.
4. Magani F, Bray E, Martinez MJ, Zhao N, Ciopello VA, Heidman L, Peacock SO, Wiley DJ, D'Urso G **Burnstein KL**. Identification of an oncogenic network with prognostic and therapeutic value in prostate cancer. *Molecular Systems Biology*. 2018:14(8):e8202. doi: 10.15252/msb.20188202. PubMed PMID: 30108134.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2018-present Chair, Department of Molecular and Cellular Pharmacology, University of Miami Miller School of Medicine, Miami, FL
2015-present Associate Director for Education and Training, Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, FL
2014-present Veteran Affairs Intramural Program for Non-Clinician Scientists, Miami VA, Miami, FL
2003-present Professor, Department of Molecular and Cellular Pharmacology, University of Miami Miller School of Medicine, Miami, FL

2009-2016 Director, Sheila and David Fuente Graduate Program in Cancer Biology, Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, FL
2001-2009 Pharmacology Graduate Program Director, University of Miami Miller School of Medicine, Miami, FL
1997-2003 Associate Professor (with tenure), Department of Molecular and Cellular Pharmacology, University of Miami Miller School of Medicine, Miami, FL
1991-1997 Assistant Professor, Department of Molecular and Cellular Pharmacology, University of Miami Miller School of Medicine, Miami, FL
1990-1991 Research Instructor, Department of Physiology, University of North Carolina at Chapel Hill, Chapel Hill, NC

Other Experience and Professional Memberships

2023 Invited Speaker Coffey-Holden Prostate Cancer Academy Meeting, Los Angeles 6/22-6/25/2023
2021 Member, External Advisory Boards: Medical College of Wisconsin Cancer Center; Fred & Pamela Buffett Cancer Center at the University of Nebraska Medical Center; Penn State Cancer Institute
2020-2026 NIH, Mechanisms of Cancer Therapeutics-2 [MCT2] Study Section, **Standing Member**
2020 NCI Program Project III Panel, Ad Hoc Reviewer
2019 NIH, Mechanisms of Cancer Therapeutics-2 [MCT2] Study Section, Ad Hoc Reviewer
2019 NCI Clinical and Translational R21 & Omnibus R03 Review (SEP-4), **Co-Chair**
2019 NIH, Mechanisms of Cancer Therapeutics-2 [MCT2] Study Section, Ad Hoc Reviewer
2018 NIH Tumor Signaling and Biology - Special Emphasis Panel (SEP) – ZRG1 OBT-B (02)
2017-2018 **President**, Cancer Biology Training Consortium (CABTRAC)
2017 NIH, Molecular Targets and Cancer Intervention, Ad Hoc Reviewer
2017 NIH F09A Fellowships, Oncology 1, Ad Hoc Reviewer
2016- pres **Editorial Board**, Cancer Research
2015-2018 Editorial Board, Steroids
2015-2018 Annual Meeting Steering Committee Member and **Team Leader**, Endocrine Society
2014-pres Miami Veterans Administration Medical Center, Scientific Review Subcommittee
2013-2016 University of Miami Academic Personnel Board
2013-2016 Editorial Board, Molecular Endocrinology
2012-pres Board of Directors, Cancer Biology Training Consortium (CABTRAC)
2009-2015 NIH, Tumor Cell Biology Study Section, **Standing Member**
2009-2012 **Co-Chair**, Research Affairs Committee, Endocrine Society
2008-2009 NIH, Tumor Cell Biology Study Section, Ad Hoc Reviewer
2006-2008 NIH, Molecular and Cellular Endocrinology Study Section, Ad Hoc Reviewer
2004 NIH-NCI Subcommittee C PO1 Cluster Review Panel, Ad Hoc Reviewer
2004 NIH-NCI Subcommittee C (Parent Committee), Ad Hoc Reviewer
2003-2005 NIH, Molecular and Cellular Endocrinology Study Section, **Standing Member**
2002-2005 Editorial Board, Endocrinology
2001-2003 NIH, Biochemical Endocrinology Study Section, **Standing Member**

Honors

2021 University of Miami Women in Academic Medicine Excellence in Mentorship Award
2021 Sylvester Cancer Center Outstanding Mentor of the Year for Trainees
2019 Award for Excellence in Urologic Research, Society for Women in Urology / Society for Basic Urologic Research
2016 Researcher of the Year, Woman's Cancer Association of University of Miami
2011 Inaugural Year "Discovery Grand Rounds," Selected by Basic Science Chairs, University of Miami

Patent

US Patent 10, 231, 952 issued 3/19/19; Inventor: **Burnstein K.** Title: Use of Arginine Vasopressin Receptor Antagonists for the Treatment of Prostate Cancer.

Patent application

New International Patent Application No. PCT/US2018/026097. Inventors: **Burnstein K** and Magani F. Title: Biomarkers Indicative of Prostate Cancer and Treatment Thereof.

C. Contributions to Science

1. Vav3, a Key Androgen Receptor Coactivator that Drives Prostate Cancer Therapeutic Resistance

The mainstay therapy for advanced prostate cancer is androgen deprivation. While this treatment results in tumor regression, eventually prostate cancer growth resumes in virtually all patients. The androgen receptor (AR) and constitutively active AR variants continue to drive tumor growth in recurrent disease despite diminished circulating androgen levels. It was demonstrated that Vav3, a Rho GTPase guanine nucleotide exchange factor, is upregulated during prostate cancer progression following androgen withdrawal therapy and reinforces robust AR signaling in castration-resistant prostate cancer (CRPC) (a-d). Vav3 enhances AR and AR variant transcriptional activity and stimulates prostate cancer growth. Strikingly, Vav3 is sufficient to confer castration-resistant tumor growth in vivo. These studies support the therapeutic targeting of Vav3 signaling pathways that cross talk with AR and AR variants. This work led to the identification of a new therapeutic target in CRPC.

a. Lyons LS, **Burnstein KL**. Vav3, a Rho GTPase guanine nucleotide exchange factor increases during progression to androgen independence in prostate cancer cells and potentiates androgen receptor transcriptional activity. Mol Endocrinol. 2006 May;20(5):1061-72. PMID: 16384856.
b. Rao S, Lyons LS, Fahrenholtz CD, Wu F, Farooq A, Balkan W, **Burnstein KL**. A novel nuclear role for the Vav3 nucleotide exchange factor in androgen receptor coactivation in prostate cancer. Oncogene. 2012 Feb 9;31(6):716-27. PMCID: PMC3203328.
c. Wu F, Peacock SO, Rao S, Lemmon SK, **Burnstein KL.** Novel interaction between the co-chaperone Cdc37 and Rho GTPase exchange factor Vav3 promotes androgen receptor activity and prostate cancer growth. J Biol Chem. 2013 Feb 22;288(8):5463-74. PMCID: PMC3581368.
d. Magani F, Peacock SO, Rice MA, Martinez MJ, Greene AM, Magani PS, Lyles R, Weitz JR, **Burnstein KL**. Targeting AR variant-coactivator Interactions to exploit prostate cancer vulnerabilities. Mol Cancer Res. 2017 Nov 15(11):1469-1480. PMCID: PMC5770277.

2. Identification and Pre-clinical Evaluation of Novel Therapeutic Approaches for Aggressive Prostate Cancer

My laboratory published (in collaboration with Dr. Andrew Schally) work showing that a new growth hormone-releasing hormone (GHRH) antagonist is effective in CRPC (a). This collaboration and other studies (b-d) speak to my substantial experience in identifying and evaluating new therapeutic targets and elucidating mechanisms of drug resistance and metastasis using robust in vitro and in vivo pre-clinical models.

a. Fahrenholtz CD, Rick FG, Garcia MI, Zarandi M, Cai RZ, Block NL, Schally AV, **Burnstein KL**. Preclinical efficacy of growth hormone-releasing hormone antagonists for androgen-dependent and castration-resistant human prostate cancer. Proc Natl Acad Sci U S A. 2014 Jan 21;111(3):1084-9. PMCID: PMC3903215.
b. Fahrenholtz CD, Beltran PJ, **Burnstein KL**. Targeting IGF-IR with ganitumab inhibits tumorigenesis and increases durability of response to androgen-deprivation therapy in VCaP prostate cancer xenografts. Mol Cancer Ther. 2013 Apr;12(4):394-404. PMCID: PMC3644513.
c. Rice MA, Ishteiwy RA, Magani F, Udayakumar T, Reiner T, Yates TJ, Miller P, Perez-Stable C, Rai P, Verdun R, Dykxhoorn DM, **Burnstein KL**. The microRNA-23b/-27b cluster suppresses prostate cancer metastasis via Huntingtin-interacting protein 1-related. Oncogene. 2016 Sep 8;35(36):4752-61. PMCID: PMC5770234.
d. Samaranayake GJ, Troccoli CI, Huynh M, Lyles RDZ, Kage K, Win A, Lakshmanan V, Kwon D, Ban Y, Chen SX, Zarco ER, Jorda M, **Burnstein KL**, Rai P. Thioredoxin-1 protects against androgen receptor-induced redox vulnerability in castration-resistant prostate cancer. Nat Commun. 2017 Oct 31;8(1):1204. PMCID: PMC5663934

3. Hyperactive Rac1 as a Therapeutic Target in Prostate and Breast Cancers

In investigating the mechanisms underlying CRPC, it was found that monomeric Rho GTPase Rac1 is hyperactive but not overexpressed in advanced prostate cancer supporting the therapeutic targeting of Rac1 (a). Constitutively active Rac1 was demonstrated to stimulate the transcriptional activity of AR in a ligand-independent manner and is sufficient for in vivo recurrent growth of prostate tumors under conditions of androgen deprivation (b). That Rac is hyperactivated in advanced prostate tumors supports the existence of a therapeutic window to permit targeting of Rac in CRPC. In related work, Rac1 was discovered also as a compelling target in estrogen receptor-positive breast cancer (c).

a. Knight-Krajewski S, Welsh CF, Liu Y, Lyons LS, Faysal JM, Yang ES, **Burnstein KL**. Deregulation of the Rho GTPase, Rac1, suppresses cyclin-dependent kinase inhibitor p21(CIP1) levels in androgen-independent human prostate cancer cells. Oncogene. 2004 Jul 15;23(32):5513-22. PMID: 15077174.

b. Lyons LS, Rao S, Balkan W, Faysal J, Maiorino CA, **Burnstein KL.** Ligand-independent activation of androgen receptors by Rho GTPase signaling in prostate cancer. Mol Endocrinol**.** 2008 Mar;22(3):597-608. PMCID: PMC2262175.
c. Rosenblatt AE, Garcia MI, Lyons L, Xie Y, Maiorino C, Désiré L, Slingerland J, **Burnstein KL**. Inhibition of the Rho GTPase, Rac1, decreases estrogen receptor levels and is a novel therapeutic strategy in breast cancer. Endocr Relat Cancer**.** 2011 Feb 23;18(2):207-19. PMCID: PMC3644524.

4. Mechanisms Underlying the Anti-cancer Actions of Vitamin D

Having contributed substantially to elucidating the mechanisms underlying the tumor-suppressive and antiproliferative actions of vitamin D (1,25 dihydroxyvitamin D_3), which are mediated by the vitamin D receptor, vitamin D was shown to inhibit the growth of prostate cancer cells by blocking G1 to S phase cell cycle progression through inhibition of cyclin-dependent kinase 2 activity. My laboratory discovered a novel mechanism responsible for this vitamin D-mediated G1 arrest in which vitamin D/vitamin D receptors mediate the nuclear exclusion of cyclin-dependent kinase 2, thereby decreasing its access to nuclear substrates, and identified GADD45γ, a new vitamin D receptor target gene that participates in vitamin D-mediated growth inhibition. Failure of vitamin D to induce GADD45γ is a key mechanism for vitamin D resistance in prostate cancer cells.

a. Zhuang S-H, **Burnstein KL**. The antiproliferative effect of 1a,25-dihydroxyvitamin D_3 in the human prostate cancer cell line LNCaP involves reduction of cyclin dependent kinase 2 activity and persistent G1 accumulation. Endocrinology 1998;139:1197-1207. PMID: 9492054.
b. Yang ES, **Burnstein KL**. Vitamin D inhibits G1 to S progression in LNCaP prostate cancer cells through p27Kip1 stabilization and Cdk2 mislocalization to the cytoplasm. J Biol Chem. 2003 Nov 21;278(47):46862-8. PMID: 12954644.
c. Flores O, Wang Z, Knudsen KE, **Burnstein KL**. Nuclear targeting of cyclin-dependent kinase 2 reveals essential roles of cyclin-dependent kinase 2 localization and cyclin E in vitamin D-mediated growth inhibition. Endocrinology. 2010 Mar;151(3):896-908. PMCID: PMC2840684.
d. Flores O, **Burnstein KL**. GADD45gamma: a new vitamin D-regulated gene that is antiproliferative in prostate cancer cells. Endocrinology. 2010 Oct;151(10):4654-64. PMCID: PMC2946153.

5. Molecular Mechanisms of Androgen Receptor Regulation

My laboratory performed the early mechanistic analyses of AR autoregulation, was the first to show MYC-mediated induction of AR gene expression and identified the critical role of the AR amino-terminus in conferring selective gene regulation. In recent years, the clinical significance of this work has come into clearer focus, as it is now recognized that the expression of the AR gene and reactivation of AR transcriptional activity are essential for CRPC. Further, the important role of the AR amino terminus is clinically validated by discovery of AR variants containing the amino terminus but lacking the ligand-binding domain. These AR variants confer CRPC in preclinical models, and expression of the variant AR-V7 in circulating tumor cells is associated with resistance to the new generation AR antagonist enzalutamide and the androgen synthesis inhibitor abiraterone in men with prostate cancer.

a. Grad JM, Lyons LS, Robins DM, **Burnstein KL**. The androgen receptor (AR) amino-terminus imposes androgen-specific regulation of AR gene expression via an exonic enhancer. Endocrinology. 2001 Mar;142(3):1107-16. PMID: 11181525.
b. Grad JM, Dai JL, Wu S, **Burnstein KL**. Multiple androgen response elements and a Myc consensus site in the androgen receptor (AR) coding region are involved in androgen-mediated up-regulation of AR messenger RNA. Mol Endocrinol. 1999 Nov;13(11):1896-911. PMID: 10551783.
c. Dai JL, **Burnstein KL**. Two androgen response elements in the androgen receptor coding region are required for cell-specific up-regulation of receptor messenger RNA. Mol Endocrinol. 1996 Dec;10(12):1582-94. PMID: 8961268.
d. Luo J, Attard G, Balk SP, Bevan C, **Burnstein K**, Cato L, Cherkasov A, De Bono, JS, Dong Y, Gao AC, Gleave M, Heemers H, Kanayama M, Kittler R, Lang JM, Lee RJ, Logothetis CJ, Matusik R, Plymate S, Sawyers CL, Selth LA, Soule H, Tilley W, Weigel NL, Zoubeidi A, Dehm SM, Raj GV. Role of Androgen Receptor Variants in Prostate Cancer: Report from the 2017 Mission Androgen Receptor Variants Meeting. Eur Urol. 2017 Dec 16. Pii: s0302-2838 (17) 31030-8. PMID: 29258679.

Complete List of Published Work in MyBibliography:
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