Jennifer E. Koblinski, PhD



Associate Professor of Pathology Director of the Cancer Mouse Models Core Co-Director of the Tissue and Data Acquisition and Analysis Core Department of Pathology Virginia Commonwealth University Email: Jennifer.Koblinski@vcuhealth.org

Education

Graduate Education

1999 Ph.D., Cancer Biology, Wayne State University School of Medicine, Detroit, MI

VCU Service

2024 - present	Co-Leader, Women in Oncology, Massey Comprehensive Cancer Center
2023 - present	Member, Taskforce for Massey Comprehensive Cancer Center Vivarium, Massey Comprehensive Cancer Center
2023 - 24	Peer review committee for P&T
2023 - present	President, Women in Science, Medicine and Dentistry
2023	Member, Search Committee for Massey Barrier Vivarium Manger
2022 - 23	President-elect, Women in Science, Dentistry, and Medicine (WISDM)
2021 - 23	Member, Basic Health Science Realignment steering committee
2021 - present	Co-Director, Tissue and Data Acquisition and Analysis Core
2015 - present	Director, Cancer Mouse Models Core Laboratory, VCU, Massey Cancer Center, Richmond, VA
2019 - present	Treasurer, Women in Science, Dentistry, and Medicine (WISDM)

Professional Organizations

American Association for Cancer Research Women in Cancer Research Association of Biomolecular Resource Facilities

Professional Service

2023 - present	Member, Organizing committee for MidAtlantic directors and staff of scientific cores Association of Biomolecular Resource Facilities annual meeting
2024	Organized animal track sessions for the Association of Biomolecular Resource Facilities national annual meeting
2020 - 2022	Ad-hoc reviewer, American Cancer Society TheroyLab Collaborative Pilot Grant-F-20
Nov. 2020	NSF National I-Corps Customer Insight member for Rutgers University
2017 - 2019	Ad-hoc reviewer for Breast Cancer Now, London, England
Oct. 2020	Academic speaker, Women in STEM leadership series, Minnesota State University, Mankato, MN

Editorial Advisory Boards

2018 Co-Editor: Analytical Cellular Pathology special issue Molecular Regulation of Cancer Cell Migration, Invasion, and Metastasis

Recent Invited Presentations

August 2024	"Transforming Cancer Research with Patient-Derived Xenograft Models: A Core Approach" invited speaker, Greater Virginia Branch- American Association for Laboratory Animal Science, Annual Vendor Show and Educational Seminar, Glenn Allen, VA.
May 2024	"Cancer mouse models core approach to imaging." Invited Speaker, Preclinical Imaging Consortium "Imaging behind the barrier, and beyond- a lifer in a BSL facility", University of Colorado Anschutz Medical Campus, Aurora, CO
April 2024	"Collaboration, people skills & working as a team" Panelist, VCU career services, the office of graduate education in the school of medicine and women in science, VCU Richmond, VA
March 2024	"Cancer mouse models core approach to imaging." Invited Speaker, Revvity Imaging Symposium, Research Triangle Park, Durham, NC
June 2023	"VCU's Tissue and Data, Acquisition and Analysis Core and Cancer Mouse Models Core facilitate Preclinical/Translational Research" Speaker for Veteran Affairs Hospital, Richmond, VA
May 2023	Ott, A, Chitty, A, Koblinski, J.E., and Patil, S. Career Path for Core Leadership, Association for Biomedical Research Facilities 2023 Annual meeting, Boston, MA -Panelist
Jan. 2023	"Technologies in TDAAC" Speaker for MDTRP Research meeting, Department of Neurology, VCU
April 2021	"Updates to CMMC services and discussion of PDX/PDO models" Speaker for Cancer Biology Program meeting, Massey Cancer Center, VCU, Richmond, VA
March 2021	"Technologies and animal models that can enhance your research" Speaker for Pharmacology and Toxicology Seminar Series, VCU, Richmond, VA

Research Grants/Contracts

Title: Understanding and Targeting Nrf1 Pathway in Triple-negative Breast Cancer

The main goal of this research is to examine the role of Nrf in the proteasome pathway in triple-negative breast cancer and how targeting Nrf in combination with proteasome inhibitors may be more successful for treatment. Start and End Date: 7/1/2021 - 6/30/2025; Total Award Amount (including Indirect Costs): \$792,000

Title: Lifestyle associated reactive metabolites and their negative impact on breast cancer risk

The objective of this study is to examine if increases in AGE levels during puberty represents a critical event during mammary development that increases future breast cancer risk and promotes tumor growth.

Start and End Date: 5/21/2022 - 6/30/2025; Total Award Amount (including Indirect Costs): \$1,182,331

Title: Role of the DREAM complex in the lung tumor suppression

Will determine whether the loss of DREAM complex can promote lung carcinogenesis caused by genotoxic stress or by activation of Ras pathway Project/Proposal Start and End Date: 2/3/2023 - 1/31/2025; Total Award Amount (including Indirect Costs): \$390,114

Title: Massey Cancer Center - Cancer Center Support Grant

The CCSG supports efforts across the MCC senior and programmatic leadership, administration, community outreach and engagement, cancer research training and education coordination, promotion of center-wide diversity, equity, and inclusion, shared resource support and management, clinical research infrastructure, and developmental funding to supporting team-based, transdisciplinary research strategies focused on well-defined, catchment area priorities. Project/Proposal Start and End Date: 5/1/2023 - 4/30/2028; Total Award Amount (including Indirect Costs): \$12,546,270

Title: United for Health Equity - Living PDX Program (U4HELPP)

The United for Health Equity-Living PDX Program (U4HELPP) seeks to develop, characterize and test >500 new patient-derived xenograft (PDX) models from underrepresented patient populations such that our research studies can more adequately represent the diverse patient population that our cancer center serves._Project/Proposal Start and End Date: 7/1/2023 - 6/30/2028;_Total Award Amount (including Indirect Costs): \$4,980,221

Title: SUMOylation disruption is toxic for SS18-SSX-driven synovial sarcoma

Project aims include (1) Test a diverse set of synovial sarcoma mouse models for efficacy and safety of SUMOylation inhibition, and (2) Investigate the relationship between SS18-SSX and the SUMOylated proteome in synovial sarcoma. Project/Proposal Start and End Date: 8/2/2023 - 7/31/2028; Total Award Amount (including Indirect Costs): \$2,746,402

Title: Development of Mouse and Humanized Models to Study Sex Disparities in Tumor Progression and Treatment of NSCLC

This project is designed to address the problem of sex disparities in NSCLC progression and treatment. Studies in both cell culture and tumor bearing animals will identify the contribution(s) of bioactive molecules, and differences in the immune system between males and females that can affect NSCLC growth and their response to therapies. Project/Proposal Start and End Date: 7/1/2023 - 6/30/2025; Total Award Amount (including Indirect Costs): \$399,186

Title: MYCN drives a ferroptotic vulnerability in neuroblastoma

Provide evidence that amplified MYCN orchestrates a complex and intricate rewiring of the neuroblastoma cell to 1) increase iron metabolism and 2) increase cysteine and selenocysteine biosynthesis to counteract reactive oxygen species created from iron metabolism- related Fenton reactions; the result of which is the creation of a synthetic lethality and therapeutic vulnerability to ferroptosis induction which we aim to explore, clarify and translate to new therapeutic Project/Proposal Start and End Date: 9/1/2023 - 8/31/2028; Total Award Amount (including Indirect Costs): \$3,318,908

Title: Sabasumstat as a sensitizer to radiation therapy in synovial sarcoma

Project aims include (1) Test a diverse set of synovial sarcoma mouse models for efficacy and safety of SUMOylation inhibition, and (2) Investigate the relationship between SS18-SSX and the SUMOylated proteome in synovial sarcoma. Project/Proposal Start and End Date: 9/15/2023 - 9/14/2026; Total Award Amount (including Indirect Costs): \$519,403

Title: Targeting cancer cachexia drivers using antibody-based approaches

Pancreatic cancer-mediated muscle cachexia is a severe wasting syndrome that occurs in virtually every patient and strongly predicts poor outcome. How pancreatic cancer drives muscle cachexia is still unfolding. Upon completion, this study will shed new insights into mechanistic paradigms of muscle cachexia, perhaps thereby paving the way for therapeutic breakthroughs to curb this life-threatening condition. Project/Proposal Start and End Date: 9/1/2023 - 8/31/2028; Total Award Amount (including Indirect Costs): \$2,094,703

Title: Enhancing Tumor Cell Immunogenicity using Improved Molecules Targeting Chromatin Remodeling

This project is designed to address the problem of low cancer immunogenicity by evaluating the capacity of a combination of epigenetic inhibitory agents to eliminate breast tumor cells by enhancing the antitumor immune response. Studies will include the optimization of novel inhibitors to epigenetic remodeling complexes to achieve improved effectiveness in animals. Project/Proposal Start and End Date: 12/1/2023 - 11/30/2025; Total Award Amount (including Indirect Costs): \$411,855

Title: MYCN drives a druggable SUMOylation program in neuroblastoma

Provide insights into an exciting new area of research in MYCN-amplified neuroblastoma, with the ultimate goal to bring TAK-981 into clinical testing in NB patients with our clinical collaborator at the National Cancer Institute. Project/Proposal Start and End Date: 1/1/2024 – 12/31/2028; Total Award Amount (including Indirect Costs): \$2,125,542

Title: Early detection of cancer disparity and treatment resistance in TNBC

The major aims of this proposal are: (1) Validate and quantify the prognostic value of SIAH to stratify patients with TNBC at high risk of recurrence in a retrospective study, forecasting early tumor relapse and predicting patient survival to overcome TNBC disparity, (2) Validate and quantify the prognostic value of SIAH to stratify patients with TNBC at high risk of recurrence in a prospective study, forecasting early tumor relapse and predicting patient survival to overcome TNBC disparity, and (3) Demonstrate the curative potency of SIAH^{PD} to eradicate incurable TNBC using PDX models, and the RPPA kinomic analysis and cancer signaling mapping of TNBC malignancy to identify actionable targets and druggable tumor vulnerability to overcome TNBC racial disparity. Project/Proposal Start and End Date: 12/1/2023 - 11/30/2026; Total Award Amount (including Indirect Costs): \$961,900

Title: ABT-199 based therapies to treat neuroblastoma

In this grant renewal, we reveal two clinically-relevant rational drug partners with venetoclax, SHP2 allosteric inhibitors, which have entered clinical trials at a blistering pace, and ABBV-155, a first in-class, in-human antibody drug conjugate BCL-xL inhibitor; in both cases, SHP2 inhibitor + venetoclax, and ABBV-155 + venetoclax, complimentarily modulate BCL-2 family proteins and induce toxicity and marked tumor responses in MYCN-amplified neuroblastoma. Overall, this grant aims to methodically test these two novel combination therapies to gather the preclinical evidence of an effective treatment regimen to put forward in a

pediatric cancer with a high unmet need. Project/Proposal Start and End Date: 6/1/2024 - 5/31/2029; Total Award Amount (including Indirect Costs): \$2,474,242

Title: Modeling Marginal Zone Lymphomagenesis

Marginal zone lymphomas are the second most common subtype of indolent non-Hodgkin's lymphomas, that are strongly dependent on the tumor microenvironment in order to grow and lack adequate preclinical models. Recently, the impressive clinical activity of inhibitors of the phosphoinositide-3kinase (PI3K), protein kinase B (Akt), mammalian target of rapamycin (mTOR) pathway has brought to the spotlight the role of this pathway in the pathogenesis of this disease. We propose to characterize novel mouse models and study the effect of the PI3K/AKT/mTOR alone and in combination with the anti-apoptotic protein B-cell lymphoma 2 (Bcl-2) in the pathogenesis of this incurable lymphoma. Project/Proposal Start and End Date: 7/5/2024 - 6/30/2026; Total Award Amount (including Indirect Costs): \$399,187

Recent Publications

Peer Reviewed Publications

Katner, S., Ginsburg, E., Hampton, J., Peterson, E., **Koblinski, J.E.**, and Farrell, N. A comparison of Di- and Trinuclear Platinum complexes interacting with glycosaminoglycans for targeted chemotherapy. (2023) ACS Med Chem Lett. 14:1224-1230. PMCID:PMC10510529.

Bryan, A., Pingali, P., Joslyn, M., Li, H., Berans, T., **Koblinski, J.E.,** Landry, J., Lee, W., Patel, B. and Neuwelt, A. High dose acetaminophen with n-acetylcysteine rescue inhibits M2 polarization of tumor associated macrophages. (2023) Cancers 15:4770. PMCID:PMC10571846.

Neely, V., Manchikalapudi, A., Nguyen, K., Dalton, K., Hu, B., **Koblinski, J.E.**, Faber, A.C., Deb, S., and Harada, H. Targeting oncogenic mutant p53 and BCL-2 for small cell lung cancer treatment. (2023) Int. J. Mol. Sci. 24:13082. PMCID: PMC107506.

Menon, V., Katner, S.J., Lee, D.E., Peterson, E.J., **Koblinski, J.E.,** and Farrell, N.P. Antitumor active trans-platinum complexes through metabolic stability and enhanced cellular accumulation. (2024) J. Inorg. Biochem. 252:112475. PMID: 36112089.

Wu, P.Y., Van Scoyk, M., McHale, S.A., Chou, C.F., Kamran, F., Hu, B., Kraskauskiene, V., **Koblinski, J.,** Vudatha, V., Zhang, D., Trevion, J.G., Huang, Y., Ma, S.F., North, I., Hughes-Halbert, C., Seewaldt, V.L., Chen, C.Y., and Winn, R.A. Cooperation between PRMT1 and PRMT6 drives lung cancer health disparities among Black/African American men. (2024) iScience 27:108858. PMCID:PMC10830871.

Floros, K.V., Fairchild, C.K., Li, J., Zhang, K., Roberts, J.L., Kurupi, R., Hu, B., Kraskauskiene, V., Hosseini, N., Shen, S., Inge, M.M., Smith-Fry, K., Li, L., Sotiriou, A., Dalton, K.M., Jose, A., Abdelfadiel, E., Xing, Y., Hill, R.D., Slaughter, J.M., Shende, M., Lorenz, M.R., Hinojosa, M.R., Blevin, B.R., Lai, Z., Boikos, S.A., Stamatouli, A.M., Lewis, J.P., Manjili, M.H., Valerie, K., Li, R., Banito, A., Poklepovic, A., **Koblinski, J.E.**, Sigger, T., Dozmorov, M.G., Jones, K.B., Radhakrishnan, S.K., and Faber, A.C. Targeting of SUMOylation leads to cBAF complex stabilization and disruption of the SS18::SSX transcriptome in synovial sarcoma. (2024) *Res Sq. rs.3.rs-4362092*. PMCID:PMC11177989.

Shen, S., Radhakrishnan, S.K., Harrell, J.C., Puchalapalli,M., **Koblinski, J.***, Clevenger, C. The human intermediate prolactin receptor I-tail contributes breast oncogenesis by targeting Ras/MAPK Pathway. (2024) Endocrinology. 165:bqae039. PMID: 38713636.

May, L. Hu, B., Jerajani, P., Jagdessh, A., Alhawiti, O., Cai, L., Semenova, N., Guo, C., Isbell, M., Deng, X., Faber, A., Pillappa, R., Bandyopadhyay, D., Want, XY., **Koblinski, J.,** Bos, P., Li, H., Martin, R., and Landry, J. A sex-bias in Trail-Bcl-XL induced apoptosis could represent a new target for women with lung cancer. *(2024) Cancer Res. in press*

Chougoni, K.K., Neely, V., Ding, B., Oduah, E., Lam, V., Hu, B., **Koblinski, J.**, Windle, B., Deb, S.P., Deb, S., Radhakrishnan, S., Harada, H., Nieva, J., and Grossman, S. Oncogenic Mutant p53 Sensitizes Non-Small Cell Lung Cancer Cells to Proteasome Inhibition via Oxidative Stress-Dependent Induction of Mitochondrial Apoptosis. *(2024) Cancer Res. Commun. in press*

Altman, J.E., Olex, A.L. Zboril, E.K., Walker, C.J., Boyd, D.C., Myrick, R.K., Hairr, N.S., **Koblinski, J.E.,** Puchalapalli, M., Hu, B., Dozmorov, M.G., Chen, X.S., Chen, Y., Pero, C.M., Lehmann, B.D., Visvader, J.E., and Harrell, J.C. Single-cell transcriptional atlas of human breast cancers and model systems. *(2024) CTM in press*

Jacob, S., Tuner, T.H., Cai, J., Floros, K.V., Yu, A.K., Coon, C., Kharti, R., Alzubi, M.A., Jakubik, C.T., Bouck, Y.M., Puchalapalli, M., Shende, M., Boikos, S., Dozmorov, M.G., Hu, B., Harrell, J.C., Benes, C., **Koblinski, J.E***., Costa, C.*, and Faber, A*. Genomic screen reveals UBA1 as a potent and druggable target in c-MYC-high TNBC models. (2022) PNAS Nexus 1: 1-13. PMCID: PMC9802478. *Co-Corresponding author

Manna, D., Reghupaty, S.C., Camarena, M.D.C., Mendoza, R.G., Subler, M.A., **Koblinski, J.E.**, Martin, R., Dozmorov, M.G., Mukhopadhyay, N.D., Liu, J., Qu, X., Das, S.K., Lai, Z., Windle, J.J., Fisher, P.B., and Sarkar, D. Melanoma Differentiation Associated Gene-9/Syndecan Binding Protein (MDA-9/SDCBP) Promotes Hepatocellular Carcinoma (HCC). (2022) Hepatology PMID:36120720

Kurupi, R., Floros, K.V., Jacob, S., Chawla, A.T., Cai, J., Hu, B., Puchalapalli, M., Coon, C.M., Kharit, R., Crowther, G.S., Egan, R.K., Murchie, E., Greninger, P., Dalton, K.M., Ghotra, M.S., Boikos, S.A., **Koblinski, J.E.,** Harada, H., Sun, Y., Morgan, I.M., Basu, D., Dozmorov, M.G., Benes, C.H., and Faber, A. Pharmacological inhibition of SHP2 blocks both PI3K and MEK signaling in lowepiregulin HNSCC via GAB1. (2022) Cancer Res Commun. 2:1061-1074. PMCID: PMC9728803.

Hampton, J.D, Peterson, E.J., Katner, S.J., Turner, T.H., Alzubi, M.A., Harrell, J.C., Dozmorov, M.G., Gigliotti, P.J., Kraskauskiene, V., Shende, M., Idowu, M.O., Puchalapalli, M., Hu, B., Litovchick. L., Katsuta, E., Takabe, K., and *Farrell, N.P. and ***Koblinski, J.E.** Exploitation of sulfated glycosaminoglycan status for precision medicine of platinums in triple-negative breast cancer. In press Mol. Cancer Ther. *These authors are both corresponding authors. Research Highlight in the issue. (2022) Mol. Cancer Ther. 21:243.

Ahmadinejad, F., Bos, T., Hu, B., Britt, E., **Koblinski, J.**, Souers, A.J., Leverson, J.D., Faber, A.C., Gewirtz, D., and Harada, H. Senolytic-mediated elimination of head and neck tumor cells induced into senescence by cisplatin. (2022) Mol Pharmacol. 101:168-180. PMID:34907000.

Editorials, Reviews, Book Chapters (Peer and Non-Peer Reviewed):

Bear, H., Landry, J., Rozeboom, A., Muralidaran, V., Peran, I., Byers, S.W., Kraskauskiene, V., Berry, D.L., and **Koblinski, J.E.** "Multiplex immunofluorescence for Murine Tissue Models" In: M. Surace, H. Abdulsater, and J. Rodriguez Canales (Ed)., Methods in Molecular Biology, Springer Nature *to be published in Fall 2024*. Neff, E. P. **Koblinski, J.E.**, Covid-19 Q&A: Keeping a cancer core going. (2020) Lab Animal 49:163.

Naydenov, N., Wang, D, Dozmorov, D., **Koblinski, JE**, and Ivanov, A. "Anillin regulates breast cancer cell migration, growth and metastasis by noncanonical mechanisms involving control stemness and differentiation." Experimental Biology 2020, April 4-7, 2020, San Diego, CA.

Lay Press Interview or Publications:

October 2022: <u>https://www.masseycancercenter.org/news/massey-scientists-pinpoint-druggable-target-in-aggressive-breast-cancer</u>

August 2022: <u>https://www.mcvfoundation.org/news/stories/platinum-precision</u>

February 2022: <u>https://pathology.vcu.edu/news/2022/with-personalized-</u> medicine-a-shelved-cancer-drug-could-get-another-shot/