BIOGRAPHICAL SKETCH

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NAME: **Kathleen L. O'Connor, PhD**

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

POSITION TITLE: Professor of Molecular and Cellular Biochemistry
Associate Director for Cancer Education and Mentoring, Markey Cancer Center

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
James Madison University, Harrisonburg, VA	BS	05/1988	Biology
Case Western Reserve University, Cleveland, OH	PhD	09/1996	Molecular Biology
Harvard Medical School, Beth Israel Deaconess Medical Center, Boston, MA	Postdoctoral	12/2001	Cancer Cell Biology

A. Personal Statement

My research focuses on how integrin signaling promotes carcinoma invasion and metastasis with special emphasis on the integrin α6β4. Integrin α6β4 confers an invasive and metastatic phenotype in many types of carcinomas, including triple-receptor negative breast cancer (TNBC). Dissecting the pathways altered by integrin α6β4 has given and will continue to contribute great insight into the processes that perpetuate invasion and metastasis. I originally discovered links between integrin signaling and the cAMP pathway. I also determined that integrin α6β4 could stimulate the small GTPase RhoA leading to lamellae formation. These studies continue to be actively cited. We have further expanded our work to include investigations on how integrin α6β4 modifies the transcriptome toward an invasive signature. Through these studies, we have identified the first transcriptional targets for NFAT1 and NFAT5 in cancer and found that integrin α6β4 can stimulate select demethylation of the promoters of pro-metastatic genes, including S100A4, amphiregulin, and epiregulin. Our work on how integrin α6β4 mediates promoter DNA demethylation uncovered a novel function for the integrin in regulating DNA repair. We find that integrin stimulates and utilizes base excision repair in active DNA demethylation. We are currently investigating how the integrin α6β4 signals to DNA repair and how this impacts therapeutic response, including cisplatin and the standard-of-care combination of doxorubicin and cyclophosphamide. Our long-term goal is to determine how integrin α6β4 drives the aggressive properties of TNBC so that this information can be used to guide precision medicine for TNBC.

In my role as Associate Director for Cancer Education and Mentoring at the Markey Cancer Center, I am charged with 1) improving the educational environment for undergraduates, graduate students, post-docs and medical residents/fellows performing cancer-related research; and 2) promoting faculty development through structured mentorship programs. In 2021, I created The Markey Science Training in Research, Oncology, Networking, and professional Growth (STRONG) Scholars Program, funded in part by the American Cancer Society, to develop mentored research opportunities for undergraduate science majors. Over my career, I have mentored or co-mentored 33 junior and senior faculty members and 40 students and postdoctoral fellows; served on 37 PhD dissertation and 6 master's thesis supervisory committees; and trained 10 undergraduate and 4 medical students in research. In addition, I have successfully mentored 6 students in attaining F31/F30 National Research Service Award fellowships and 3 PhD students in obtaining F99/K00 awards, developed and run a fellowship boot camp, and directed our Breast Translational Group. I currently serve President-Elect of the Cancer Biology Training Consortium, which provides national networking opportunities and leadership for Markey. These educational and research experiences position me well as the AD of CRTEC.

Ongoing projects I would like to highlight include:

P30 CA177558 (NCI)
Evers (PI); Role: Associate Director of Cancer Education and Mentoring
07/01/2013 – 06/30/2028
University of Kentucky Markey Cancer Center – Cancer Center Support Grant

Principal Investigator: O'Connor, Kathleen

DICR POST-BACC-22-1042000-01-DPBACC, American Cancer Society
O'Connor (PI)
01/01/2023 – 12/31/2025
Markey STRONG Post-baccalaureate Program

IRG-22-152-34, American Cancer Society
O'Connor (PI)
01/01/2023 – 12/31/2026
Institutional Research Grant

T32 CA160003 (NCI)
Evers/Hull/O'Connor (MPI)
07/01/2011 – 06/30/2028
Oncology Research Training for Surgeon-Scientists

T32 CA165990 (NCI)
O'Connor/Evers (MPI)
04/01/2013 – 06/30/2027
Interdisciplinary Research Training in Cancer Biology

B. Positions, Scientific Appointments, and Honors

Positions (including Scientific Employment, Honorary and Volunteer):

2023-present	Director, Markey STRONG Post-baccalaureate Fellows Diversity in Cancer Research Program, University of Kentucky, Lexington, KY
2021-present	Director, Markey STRONG Scholars Diversity in Cancer Research Program, University of Kentucky, Lexington, KY
2014-2021	Director, Breast Translational Group, Markey Cancer Center, University of Kentucky
2013-present	**Professor, Department of Molecular and Cellular Biochemistry**, University of Kentucky, Lexington, KY (tenured)
2012-2014	Co-director, Breast Translational Group, Markey Cancer Center, University of Kentucky, Lexington, KY
2010-present	**Associate Director for Cancer Education and Mentoring**, Markey Cancer Center, University of Kentucky, Lexington, KY
2009-2013	Associate Professor, Department of Molecular and Cellular Biochemistry, University of Kentucky (tenured), Lexington, KY
2006-2009	Associate Professor, Departments of Surgery and Biochemistry & Molecular Biology and Sealy Center for Cancer Cell Biology, University of Texas Medical Branch, Galveston, TX
2005-2009	Director, Cancer Cell Biology Track within Biochemistry & Molecular Biology, Cell Biology and Pharmacology/Toxicology Graduate Programs, University of Texas Medical Branch, Galveston, TX
2002-2006	Assistant Professor, Departments of Surgery and Biochemistry & Molecular Biology and Sealy Center for Cancer Cell Biology, University of Texas Medical Branch, Galveston, TX
1996-2001	Research Fellow, Department of Pathology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA
1990-1996	Graduate Student Research Assistant, Case Western Reserve University, Cleveland, OH
1988-1990	Research Assistant, Department of Pathology, University of Texas Health Sciences Center, Houston, TX

Service-Oriented Appointments:

2026	President-Elect, Cancer Biology Training Consortium
2025-present	External Advisory Board for the University of Kansas Cancer Center
2025-present	External Advisory Board for University of Texas Health San Antonio Mays Cancer Center
2024-present	External Advisory Board for Thomas Jefferson University Sidney Kimmel Comprehensive Cancer Center
2024-present	External Advisory Committee for the GW Cancer Biology Training Program
2024	DoD Breast Cancer Research Program, Panel Chair (December)
2023	DoD Breast Cancer Research Program, Panel Chair (June)
2022	Advisor to University of Arizona Cancer Center's Office of Cancer Research Training and Education Coordination (CRTEC)
2022	DoD Breast Cancer Research Program, Panel Chair (July)

2021	DoD Breast Cancer Research Program, Panel Chair (June)
2021	DoD Breast Cancer Research Program, Panel Member (August)
2021-present	External Advisory Committee for The Ohio State University James Comprehensive Cancer Center CCSG
2021-2026	Board Member of the Cancer Biology Training Consortium
2020-present	External Advisory Board for University of Oklahoma Stephenson Cancer Center CCSG
2020	DoD Breast Cancer Research Program, Panel Chair (November)
2020	NIH F09A Fellowships: Oncology Study Section (March)
2020	NCI Subcommittee F, T32/R25 program review (February)
2019	The NCI Predoctoral to Postdoctoral Fellow Transition Award (F99/K00) Review
2018-2021	Editorial Board Member, Scientific Reports
2018, 2019	NCI-A RTRB-L R1 Workgroup 005 NCI Cancer Center Support Grant (P30) cancer center review and site visit
2016	Ad Hoc member of the NIH BMCT-C Study Section
2015, 2016	DoD Breast Cancer Research Program, Panel Member
2015	ZCA1 SRLB-1 NCI Omnibus Biology Study Section (March)
2015	NCI-A RTRB-R (P1) NCI Cancer Center Support Grant (P30) cancer center review and site visit (February)
2015	NIH Special Emphasis Panel F09A-D Fellowships: Oncology (November)
2014	Temporary Members NCI Initial Review Group (IRG) Subcommittee A Parent Committee
2014	NCI-A RTRB-L R1 Workgroup 005 NCI Cancer Center Support Grant (P30) cancer center review and site visit
2014	ZCA1 SRLB-1 NCI Omnibus Biology Study Section (March and November)
2013	ZCA1 SRLB-1 National Cancer Institute (NCI) Omnibus Biology Study Section (July, November)
2013	Department of Defense (DoD) 2013 Breast Cancer Research Program, Panel Member
2013	NCI-A RTRB-L R1 Workgroup 005 NCI Cancer Center Support Grant (P30) cancer center review and site visit
2012	Ad Hoc member of NIH Tumor Progression and Metastasis Study Section (June)
2012	Ad Hoc, NIH Special Emphasis panel ZRG1 FO9-P(20) (F32 review)
2012	Ad Hoc member of NIH Tumor Progression and Metastasis Study Section (June)
2010	Ad Hoc member of NIH Tumor Progression and Metastasis Study Section (Feb, Nov)
2009-2015	Regular Member of the American Cancer Society Cell Structure and Metastasis Peer Review Committee; Vice Chair, 2011; Chair 2012-2015
2002-present	Ad hoc manuscript reviewer for: American Journal of Physiology-Cell Physiology; Angiogenesis; Biochemistry and Cell Biology; Biology Open; BMC Cancer; Cancer Research; Carcinogenesis; Cell Motility and the Cytoskeleton; Clinical and Experimental Metastasis; Experimental Cell Research; Expert Review of Anti-Cancer Therapy; European Journal of Cancer; International Journal of Cancer; Journal of Cell Biology; Journal of Cell Physiology; Journal of Cell Science; Journal of the National Cancer Institute; Modern Pathology; Molecular and Cellular Biology; Molecular Pharmacology; PLoS One; Science; Trends in Endocrinology and Metabolism

Honors:

2026	Mission, Values, and Pillar (MVP) Award in Area of Mission, University of Kentucky College of Medicine
2025	Wethington Award for Research Excellence, University of Kentucky
2024	University of Kentucky College of Medicine Academy of Medical Educators' Excellence in Medical Education Award in the area of Leadership
2024	Markey Women Strong Distinguished Researcher Award
2024	Wethington Award for Research Excellence, University of Kentucky
2023	Power of Women Honoree
2021	University of Kentucky College of Medicine Academy of Medical Educators' Excellence in Medical Education Award in the area of Mentorship
2019	Wethington Award for Research Excellence, University of Kentucky
2018	Markey Women Strong Distinguished Researcher Award
2017	Markey Women Strong Distinguished Researcher Award
2016-2018	Finalist, University of Kentucky Women in Medicine and Science Mentorship Award (yearly nomination)
2013-2017	Wethington Award for Research Excellence, University of Kentucky (Annual award)

2013	Distinguished Achievement Award in Pancreatic Cancer Research, Shanghai International Conference on Pancreatic Cancer
2010	Wethington Award for Research Excellence, University of Kentucky
2007	University of Texas Medical Branch Graduate Student Organization Student Advocacy Award
2006	Nominated for University of Texas Medical Branch Graduate Student Organization's Distinguished Faculty Teaching Award
2005	Representative, University of Texas Medical Branch at the Association of American Medical Colleges Early Career Women Faculty Professional Development Seminar, Santa Fe, NM
1997-2001	Department of Defense Breast Cancer Research Program Postdoctoral Fellowship (DAMD17-98-1-8033)
1991-1995	National Research Service Award, Predoctoral Fellowship under NIH Aging Training Grant (AG00105)

C. Contributions to Science

1. The microenvironment influences cancer epigenetics, but mechanisms governing this phenomenon are not well understood. We were the first to determine that integrins can dramatically alter the transcriptome by activating specific transcription factors and promoting DNA demethylation of select promoters. Through these studies, we identified the first transcriptional targets for NFAT1 and NFAT5 in cancer and provided evidence that integrin α6β4 can stimulate select demethylation of the promoters of pro-metastatic genes, including PTPRZ1, S100A4/metastasin, amphiregulin, and epiregulin. Our laboratory continues to follow up on these findings and is funded to elucidate the mechanisms by which integrin α6β4 alters the epigenome.
   a. Chen M, Karimpour PA, Elliot A, He D, Knifley T, Liu J, Wang C, **O'Connor KL**. Integrin α6β4 Upregulates PTPRZ1 Through UCHL1-Mediated Hif-1α Nuclear Accumulation to Promote Triple-Negative Breast Cancer Cell Invasive Properties. Cancers 16(21), 3683, 2024. PMCID: PMC11545476.
   b. Carpenter BL, Liu J, Wang C, **O'Connor KL**. Integrin α6β4 upregulates amphiregulin and epiregulin through base excision repair-mediated DNA demethylation and promotes genome-wide DNA hypomethylation. Sci Rep 7:6174, 2017. PMCID: PMC5522472.
   c. Carpenter BL, Chen M, Knifley T, Davis KA, Harrison SMW, Stewart RL, **O'Connor KL**. Integrin α6β4 promotes autocrine EGFR signaling to stimulate migration and invasion toward hepatocyte growth factor (HGF). J Biol Chem 290:27228-27238, 2015. PMCID: PMC4646402.
   d. Chen M, Sinha M, Luxon BA, Bresnick AR, **O'Connor KL**. Integrin α6β4 controls the expression of genes associated with cell motility, invasion and metastasis including S100A4/metastasin. J Biol Chem 284:1484-1494, 2009. PMCID: PMC2615501.

2. First identified as a tumor progression antigen, integrin α6β4 has subsequently been shown to associate with some of the most aggressive properties of carcinomas including enhancing invasion and metastasis, proliferation, tumor cell survival and therapeutic resistance/sensitivity. We have contributed to the understanding of integrin α6β4 in the pathology of human cancers.
   a. Chen M, Marrs B, Qi L, Knifley T, Weiss HL, D'Orazio JA, **O'Connor KL**. Integrin α6β4 signals through DNA damage response pathway to sensitize breast cancer cells to cisplatin. Front Oncol 12:1043538, 2022. PMCID: PMC9686853.
   b. Qi L, Chen M, Knifley T, **O'Connor KL**. Integrin α6β4 requires plectin binding and vimentin to drive adhesion complex distribution and invasive growth. J Cell Sci 135:jcs258471, 2022. PMCID: PMC8917354.
   c. Stewart RL, West DS, Wang C, Weiss HL, Gal TS, Durbin EB, Chen M, **O'Connor KL**. Elevated integrin α6β4 expression is associated with venous invasion and decreased overall survival in non-small cell lung cancer. Hum Pathol 54:174-183*,* 2016. PMCID: PMC4938774.
   d. Cruz-Monserrate Z, Qiu S, Evers BM, **O'Connor KL**. Upregulation and redistribution of integrin α6β4 expression occurs at an early stage in pancreatic adenocarcinoma progression. Mod Pathol 20:656-667, 2007. PMCID: PMC4697742.

3. S100A4 is a metastasis-associated protein and has been implicated in the progression of several types of cancer. Toward the understanding of how S100A4 contributes to breast cancer invasion and metastasis, we demonstrated that S100A4 is epigenetically regulated by integrin α6β4 signaling in conjunction with NFAT5, linking a metastasis protein to a receptor that senses the microenvironment. Our most recent work on lung cancer further highlights the importance of S100A4 in altering cellular metabolism and promoting lung cancer invasion and metastasis. We further demonstrate that niclosamide, a U.S. Food and Drug

Administration-approved drug can inhibit S100A4-mediated function, thus providing a rationale for targeting S100A4 to combat lung cancer.

a. Liu L, Qi L, Knifley T, Piecoro DW, Rychahou P, Liu J, Mitov MI, Martin J, Wang C, Wu J, Weiss HL, Butterfield DA, Evers BM, **O'Connor KL***, Chen M*. S100A4 alters metabolism and promotes invasion of lung cancer cells by up-regulating mitochondrial complex I protein NDUFS2. J Biol Chem 294:7516-7527, 2019. PMCID: PMC6509482.
b. Stewart RL, Carpenter BL, West DS, Knifley T, Liu L, Wang C, Weiss HL, Gal TS, Durbin EB, Arnold SM, **O'Connor KL***, Chen M*. S100A4 drives non-small cell lung cancer invasion, associates with poor prognosis, and is effectively targeted by the FDA-approved anti-helminthic agent niclosamide. Oncotarget 7:34630-34642, 2016. PMCID: PMC5085181.
c. Chen M, Bresnick AR, **O'Connor KL**. Coupling S100A4 to Rhotekin alters Rho signaling output in breast cancer cells. Oncogene 32:3754-3764, 2013. PMCID: PMC3525797.
d. Chen M, Sastry SK, **O'Connor KL**. Src kinase pathway is involved in NFAT5-mediated S100A4 induction by hyperosmotic stress in colon cancer cells. Am J Physiol Cell Physiol 300:C1155-1163, 2011.

4. Though our interests in breast cancer and development of important resources for translational breast cancer research, we have collaborated with our colleagues in breast cancer research to extend our knowledge in clinically important areas of cancer biology.
   a. Walker B, Pollard E, Howard SP, Jones VM, **O'Connor KL**, Durbin EB, Hull PC, Jones SR, Adegboyega A, Wang X, Owen WAB, Szabunio MW, Williams LB and More JX. Investigating the Role of Race/Ethnicity on the Association between Neighborhood Deprivation and Breast Cancer Outcomes in Kentucky Breast Cancer Patients, 2010-2022. Cancer Epidemiol Biomarkers Prev 3:474-492, 2025. PMCID: PMC11966108.
   b. Harper NK, Hodges KD, Stewart RL, Wu J, Huang B, **O'Connor KL**, Romond EH. Adjuvant treatment of triple-negative metaplastic breast cancer with weekly paclitaxel and platinum chemotherapy: Retrospective case review from a single institution. Clin Breast Cancer 19:e495-e500, 2019. PMCID: PMC6693323.
   c. Huang X, Ye Q, Chen M, Li A, Mi W, Fang Y, Zaytseva YY, **O'Connor KL**, Vander Kooi CW, Liu S, She Q-B. N-glycosylation-defective splice variants of neuropilin-1 promote metastasis by activating endosomal signals. Nat Commun 10:3708, 2019. PMCID: PMC6697747.
   d. Xiong G, Stewart RL, Chen J, Gao T, Scott TL, Samayoa LM, **O'Connor KL**, Lane AN, Xu R. Collagen proly-hydroxylase 1 is essential for HIF-1α stabilization and TNBC chemoresistance. Nat Commun 9:4456, 2018. PMCID: PMC6203834.

5. I originally discovered links between integrin signaling and the cAMP pathway, and I also determined that integrin α6β4 could stimulate the small GTPase RhoA leading to lamellae formation. The dogma says that RhoA drives stress fiber formation; however, stress fibers are not generally seen in carcinomas despite the fact that RhoA contributes actively to tumor progression and invasion. We have shown that integrin α6β4 stimulates and changes the function of RhoA to promote lamellae. Furthermore, we have elucidated the switch that regulates the functional change in RhoA function by showing that the metastatic protein S100A4 binds to the Rho effector Rhotekin that inhibits the contractility mediated by RhoA which in turn results in lamellae formation and enhanced cell migration and invasion. We further defined how RhoA and Rac1 cooperate in tumor invasion and found a novel way to target small GTPase function through isoprenylation.
   a. Chen M, Knifley T, Subramanian T, Spielmann HP, **O'Connor KL**. Use of synthetic isoprenoids to target protein prenylation and Rho GTPases in breast cancer invasion. PLOS One 9:e89892, 2014. PMCID: PMC3935959.
   b. **O'Connor KL**, Chen M. Dynamic functions of RhoA in tumor cell migration and invasion. Small GTPases 4:141-147, 2013. PMCID: PMC3976970.
   c. Chen M, Bresnick AR, **O'Connor KL**. Coupling S100A4 to Rhotekin alters Rho signaling output in breast cancer cells. Oncogene 32:3754-3764, 2013. PMCID: PMC3525797.
   d. **O'Connor KL**, Chen M, Towers LN. Integrin α6β4 cooperates with LPA signaling to stimulate Rac through AKAP-Lbc-mediated RhoA activation. Am J Physiol Cell Physiol 302:C605-614, 2012. PMCID: PMC3287157.

Complete List of Published Work in PubMed:
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