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

NIH BIOGRAPHICAL SKETCH COMMON FORM

Name: Johnson, Rachelle

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0003-2755-9851

Position Title: Associate Professor of Medicine

Organization and Location: Vanderbilt University Medical Center, Nashville, Tennessee, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
Stanford University, Palo Alto, California, United States	Postdoctoral Fellow	01/2014	08/2015	Tumor Dormancy
St. Vincent's Institute of Medical Research, Fitzroy, Not Applicable, N/A, Australia	Postdoctoral Fellow	08/2011	11/2013	Bone Cell Biology
Vanderbilt University, Nashville, Tennessee, United States	Doctor of Philosophy (PHD)	08/2007	08/2011	Cancer Biology
University of Georgia, Athens, Georgia, United States	Bachelor of Science (BS)	08/2003	05/2007	Biochemistry and Molecular Biology

Appointments and Positions

2022 - present	Associate Professor of Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, United States
2026 - present	Research Program Fellow, Vanderbilt-Ingram Cancer Center, Nashville, Tennessee, United States
2025 - present	Adjunct Associate Professor, Meharry Medical College, Nashville, Tennessee, United States
2024 - present	Program Director, Graduate Program in Cancer Biology, Vanderbilt University School of Medicine, Nashville, Tennessee, United States
2023 - 2025	Adjunct Assistant Professor, Meharry Medical College, Nashville, Tennessee, United States
2022 - present	Director of Graduate Studies, Graduate Program in Cancer Biology, Vanderbilt University School of Medicine, Nashville, Tennessee, United States
2016 - present	Member, Vanderbilt-Ingram Cancer Center, Nashville, Tennessee, United States
2016 - 2022	Assistant Professor of Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, United States
2015 - 2016	Basic Life Science Research Associate, Stanford University, Palo Alto, California, United States

Products

Products Closely Related to the Proposed Project

1. Joseph GJ, Vecchi Iii LA, Uppuganti S, Kane JF, Durdan M, Hill P, McAdoo AG, Tanaka H, Kell D, Searcy MB, Chen W, Rosenthal EL, Harrison DG, Nyman JS, Weivoda MM, Johnson RW. Programmed cell death protein 1 (PD-1) blockade regulates skeletal remodeling in a sex- and age-dependent manner. J Bone Miner Res. 2025 Jul 28;40(8):950-964. PubMed Central PMCID: PMC12340981.
2. Kane J, Joseph G, Vecchi L, Miller J, Ludington B, Gibson-Corley K, Johnson R. Abaloparatide increases bone mass without affecting growth of bone-disseminated cancer cells. JBMR Plus. 2025 July; 9(7):-. Available from: https://academic.oup.com/jbmrplus/article/doi/10.1093/jbmrpl/ziaf080/8123870 DOI: 10.1093/jbmrpl/ziaf080
3. Edwards CM, Kane JF, Smith JA, Grant DM, Johnson JA, Diaz MAH, Vecchi LA 3rd, Bracey KM, Omokehinde TN, Fontana JR, Karno BA, Scott HT, Vogel CJ, Lowery JW, Martin TJ, Johnson RW. PTHrP intracrine actions divergently influence breast cancer growth through p27 and LIFR. Breast Cancer Res. 2024 Feb 26;26(1):34. PubMed Central PMCID: PMC10897994.
4. Clements ME, Holtslander L, Edwards C, Todd V, Dooyema SDR, Bullock K, Bergdorf K, Zahnow CA, Connolly RM, Johnson RW. HDAC inhibitors induce LIFR expression and promote a dormancy phenotype in breast cancer. Oncogene. 2021 Aug;40(34):5314-5326. PubMed Central PMCID: PMC8403155.

5. Clements ME, Holtslander L, Johnson JR, Johnson RW. Select HDAC Inhibitors Enhance Osteolysis and Bone Metastasis Outgrowth but Can Be Mitigated With Bisphosphonate Therapy. JBMR Plus. 2023 Mar;7(3):e10694. PubMed Central PMCID: PMC10020917.

Other Significant Products Highlighting Contributions to Science

1. Todd V, Vecchi L, Clements M, Snow K, Ontko C, Himmel L, Pinelli C, Rafat M, Johnson R. Hypoxia inducible factor signaling in breast tumors controls spontaneous tumor dissemination in a site-specific manner. Communications Biology. 2021 September 23; 4(1):-. Available from: https://www.nature.com/articles/s42003-021-02648-3 DOI: 10.1038/s42003-021-02648-3
2. Omokehinde T, Jotte A, Johnson RW. gp130 Cytokines Activate Novel Signaling Pathways and Alter Bone Dissemination in ER+ Breast Cancer Cells. J Bone Miner Res. 2022 Feb;37(2):185-201. PubMed Central PMCID: PMC8828687.
3. Sowder ME, Johnson RW. Enrichment and detection of bone disseminated tumor cells in models of low tumor burden. Sci Rep. 2018 Sep 24;8(1):14299. PubMed Central PMCID: PMC6155169.
4. Clements ME, Johnson RW. PREX1 drives spontaneous bone dissemination of ER+ breast cancer cells. Oncogene. 2020 Feb;39(6):1318-1334. PubMed Central PMCID: PMC7007387.
5. Johnson RW, Finger EC, Olcina MM, Vilalta M, Aguilera T, Miao Y, Merkel AR, Johnson JR, Sterling JA, Wu JY, Giaccia AJ. Induction of LIFR confers a dormancy phenotype in breast cancer cells disseminated to the bone marrow. Nat Cell Biol. 2016 Oct;18(10):1078-1089. PubMed Central PMCID: PMC5357601.

Certification:

I certify that the information provided is current, accurate, and complete. This includes, but is not limited to, information related to current, pending, and other support (both foreign and domestic) as defined in 42 U.S.C. § 6605.

In accordance with Section 10632 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19232), each individual identified as a senior/key person must certify that they are not a party to a malign foreign talent recruitment program.

Research Security Training Requirement for Federal Award Personnel: In accordance with Section 10634 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19234), each individual identified as a senior/key person must certify that they have completed the requisite research security training that meets the requirements specified in Item 2 of Important Notice No. 149 within 12 months prior to proposal submission.

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: Johnson, Rachelle

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0003-2755-9851

Position Title: Associate Professor of Medicine

Organization and Location: Vanderbilt University Medical Center, Nashville, Tennessee, United States

Personal Statement

I am an Associate Professor of Medicine with tenure at Vanderbilt University Medical Center with expertise in mechanisms of breast cancer bone metastasis. My research program focuses on mechanisms of breast cancer bone metastasis and the impact of tumor-targeted therapies and immune cells on skeletal health and metastatic disease. For the last ten years we have investigated cytokine signaling, oxygen tensions, and osteoimmunology mechanisms that control cancer metastasis to bone, which have been primarily funded by the DoD and NIH. These studies have led us to identify unexpected roles for hypoxia and parathyroid hormone-related protein (PTHrP) in breast cancer dormancy and bone metastatic progression using xenograft, syngeneic, and genetically engineered autochthonous mouse models that spontaneously develop tumors and disseminate to distant sites. We recently discovered that therapies targeted to our proteins of interest profoundly impact skeletal remodeling, causing bone metastatic progression of cancers that are otherwise slowed down by these drugs when tumors are localized to the primary tumor site. This has led us to look closer at how tumor-targeted therapies impact bone metastases by disrupting bone homeostasis and investigate novel ways to improve skeletal outcomes, including bone anabolic agents like PTH and PTHrP analogs. We have capitalized on our expertise in mouse models of bone metastasis, ultra-sensitive methods to detect cancer cells, and knowledge of both cancer and bone cell signaling to identify critical roles for immune checkpoint proteins in skeletal remodeling and cancer progression. Our most recent publications on tumor-immune interactions in bone and breast cancer bone metastasis and dormancy report on our most recent DoD Level 2 award and NIH-funded projects, which are highlighted below. Institutionally, I am the Program Director and Director of Graduate Studies for Cancer Biology at Vanderbilt University. At the national level, I am Past-President of the Cancer and Bone Society (CABS) and Chair the Innovation Committee for the American Society for Bone and Mineral Research (ASBMR). In these national leadership roles, I helped create and implement leadership training and mentoring programs, which continue to provide training to students, postdocs, and junior faculty around the globe.

My lab was established in 2016 and since that time I have mentored dozens of trainees, including two postdocs and eight PhD and MD/PhD students in my lab who have gone on to postdocs, faculty, and industry positions. I am committed to providing training for students in ethical data interpretation, rigor and reproducibility, and help students find their path forward in biomedical research careers. As a former K99/R00 awardee and preceptor on numerous training grants, I am aware of the benefit of career development awards and mentored training programs. I am delighted to serve as a mentor for the Vanderbilt MSTP R25 training mechanism.

Honors

2025	ZCA1 RTRB-R Grants Review Panel, NIH/NCI
2025	ZRG1 BTC-K Grants Review Panel, NIH/NCI
2025	TEHM Study Section Review Panel, NIH/NCI
2024	Shirley Hohl Service Award, American Society for Bone and Mineral Research (ASBMR)
2023	CDMRP BCRP PB-2 Panel, DOD
2023	F09C Review Panel, NIH/NCI
2023 - 2026	Innovation Committee Chair, American Society for Bone and Mineral Research (ASBMR)
2023 - 2025	President, Cancer and Bone Society
2022	Medical Research Future Fund (MRFF) Early to Mid-Career Researcher Assessment Review Panel, National Health and Medical Research Council (NHMRC), Australia
2021	Presidential Challenge Coin Recipient for Extraordinary Achievement and Dedication, American Society for Bone and Mineral Research (ASBMR)

2021	e-ASIA 2021 Joint Research Program Review Panel, National Health and Medical Research Council (NHMRC), Australia
2020 - 2023	Secretary/Treasurer, Cancer and Bone Society
2015	Kaye Ibbertson Award for Bone and Mineral Medicine, Australian and New Zealand Bone and Mineral Society (ANZBMS)
2015 - 2020	K99/R00 Pathway to Independence Award, NIH/NCI

Contributions to Science

1. **Therapy-induced skeletal toxicities and osteoimmunologic interactions:** My lab has explored how hypoxia regulates the tumor suppressor LIFR and discovered that this is achieved through hypoxia-induced chromatin remodeling of the LIFR promoter, with loss of histone H3 lysine 9 acetylation in hypoxia. We subsequently discovered that histone deacetylase (HDAC) inhibitors potently induce LIFR expression, offering a potential therapeutic avenue to induce chronic tumor dormancy. This study was one of the first to demonstrate that promoting long-term tumor dormancy rather than eliminating every tumor cell may be a viable therapeutic approach to manage tumor recurrence and was a paradigm shift for the tumor dormancy field. We also made the surprising discovery that HDAC inhibitors fuel tumor growth in the bone marrow by disrupting bone homeostasis, but that this can be reversed by FDA-approved anti-resorptives. This led to more recent studies in my lab to investigate how cancer therapies like immune checkpoint inhibitors that target PD-1/PD-L1 signaling disrupt bone remodeling and alter the tumor-immune microenvironment. We have found that inhibiting the immune checkpoint protein PD-1 profoundly disrupts reduces bone mass, increases bone resorption, and makes bone more prone to fracture. These studies are ongoing, with multiple manuscripts out for review.

   a. Clements, M.E., et al., …Johnson, R.W. HDAC inhibitors induce LIFR expression and promote a dormancy phenotype in breast cancer. Oncogene. 2021.
   b. Clements, M.E., et al., …Johnson, R.W. Select HDAC inhibitors enhance osteolysis and bone metastasis outgrowth but can be mitigated with bisphosphonate therapy. JBMR Plus. 2023.
   c. Joseph, G.J., et al., …Johnson, R.W. PD-1 blockade regulates skeletal remodeling in a sex- and age-dependent manner. J Bone Miner Res. 2025.

2. **Bone anabolic PTHrP analogs and intracrine signaling in breast cancer:** The parathyroid hormone-related protein (PTHrP) molecule is essential for tumor-induced bone destruction. My lab discovered unique intracrine actions of PTHrP; we found that PTHrP regulates the breast tumor suppressor LIFR through the LIFR promoter, rather than canonical cAMP, in breast cancer. This was surprising, since no transcriptional target for PTHrP has been identified. Since my lab discovered the importance of PTHrP intracellular actions in regulating LIFR and tumor dormancy, we determined that PTHrP functions as both a tumor suppressor and oncogene through its nuclear localization signal and C-terminal region, respectively. This is a pivotal finding since there are decades of conflicting published data on the role of PTHrP in breast cancer. Since PTHrP fuels tumor growth in bone, there has been considerable interest in whether bone anabolic PTHrP analogs, which are used to improve bone mass in osteoporosis, would be detrimental to use in patients with cancer. We confirmed that the FDA-approved PTHrP analog abaloparatide is safe and effective in models of early breast cancer bone metastasis alone and in combination with chemotherapy or immunotherapy, clearing the way for follow-up studies in more advanced disease.

   a. Edwards, C.E., et al., …Johnson, R.W. PTHrP intracrine actions divergently influence breast cancer growth through p27 and LIFR. Breast Cancer Res. 2024.
   b. Kane, J.F., et al., …Johnson, R.W. Abaloparatide increases bone formation without affecting growth of bone-disseminated cancer cells. JBMR Plus. 2025.

3. **Breast cancer dormancy and hypoxia:** As a postdoc, I discovered that leukemia inhibitory factor receptor (LIFR) is a pro-dormancy factor in breast cancer bone metastasis. This finding formed the basis of my independent research program. I found that LIFR and STAT3 maintain breast cancer cell quiescence in the bone marrow, which were the first pro-dormancy factors reported in bone-disseminated tumor cells, through JAK/STAT signaling. Since those foundational studies, my lab has discovered dozens of tumor-promoting and tumor-suppressive signaling pathways that are paracrine-activated by LIFR, highlighting its signaling complexity. My lab also identified two key negative regulators of LIFR: hypoxia and parathyroid hormone-related protein (PTHrP). We confirmed that hypoxia regulates LIFR independent of HIF1α and HIF2α. Using the MMTV-PyMT tumor model, my lab discovered that both HIF1α and HIF2α support tumor seeding to bone, but HIF1α paradoxically limits spontaneous dissemination of breast cancer cells to the lung. This discovery has strong clinical implications since it suggests that targeting HIF1α may prevent or worsen metastasis at opposing sites.

   a. Johnson R.W., et al. Induction of LIFR confers a dormancy phenotype in breast cancer cells disseminated to the bone

marrow. Nat Cell Biol. 2016. Cover article. (cited >170 times)
b. Omokehinde, T., et al, ...Johnson, R.W. gp130 cytokines activate novel signaling pathways and alter bone dissemination in ER+ breast cancer cells. J Bone Miner Res. 2022.
c. Todd V.M., et al, ...Johnson, R.W. Hypoxia inducible factor signaling in breast tumors controls spontaneous tumor dissemination in a site-specific manner. Commun Biol. 2021.

4. **Advanced imaging and detection of bone-disseminated tumor cells in breast cancer bone metastasis:** My lab has developed multiple models of bone metastasis and flow cytometric/genomic methodologies to facilitate detection of rare, bone-disseminated tumor cells in the marrow. These techniques have been widely adopted in the cancer and bone field. My lab also developed a bone-metastatic variant of an estrogen receptor-positive breast cancer cell line (MCF7b), the first of its kind, which has been requested by numerous laboratories worldwide. Using this cell line, my lab discovered that upregulation of the molecule PREX1 is the underlying molecular driver for increased bone metastasis of MCF7b cells in mice. This was the first time the molecule has been implicated in bone metastasis. We have also used magnetic resonance imaging (MRI) and Matrix-Assisted Laser Desorption/Ionization Imaging Mass Spectrometry (MALDI IMS) techniques, co-registered with histology, to longitudinally map tumor-induced bone destruction and create a protein atlas of the tumor-bone interface. This was the first report of this combination of technologies to image tumor cells in bone and holds great promise for uncovering molecular changes in the bone during tumor progression and in response to treatment.

   a. Clements, M.E. and Johnson, R.W. PREX1 drives spontaneous bone dissemination of ER+ breast cancer cells. Oncogene. 2020.
   b. Sowder, M.E., Johnson, R.W. Enrichment and detection of bone disseminated tumor cells in models of low tumor burden. Sci Rep. 2018.

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