San Antonio Breast Cancer Symposium® - December 9-12, 2025

PS3-08-22

DO NOT TAKE PICTURES

Uncovering mechanisms of ILC glucocorticoid receptor activity in cell cycle regulation and bone metastasis using *in vivo* models and human samples.

Baylee A. Porter-Hansen[1,2], Amanda Briceno [1,2],Muriel Laine[5], Jessica Finlay-Schultz[4], Sunati Sahoo[1,3],Geoffrey Greene[5], Carol Sartorius[4] , Andrew Devilbiss[1,2], Lynda Bennett[1,2], Suzanne D. Conzen[1,2]

[1]University of Texas Southwestern Medical Center, Dallas, TX, 75390, USA. [2]Division of Hematology Oncology, Department of Internal Medicine. [3]Department of Pathology, [4]Univeristy of Colorado, [5]Ben May Department of Cancer Research, The University of Chicago, Chicago, IL 60637, USA

UT Southwestern Medical Center

0000-0002-9503-6537

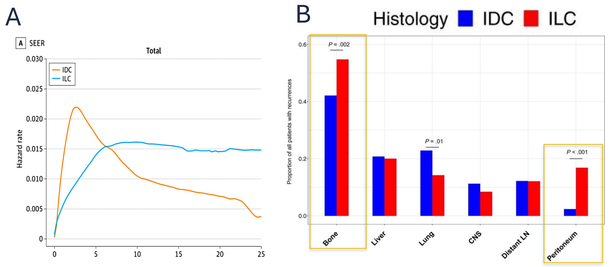
Abstract

Background: Estrogen receptor (ER+) positive invasive lobular carcinoma comprises 15% of all breast cancer. Lacks e-cadherin expression, highly metastatic to **bone** and compared to triple-negative breast cancer, invasive ductal carcinoma, and luminal B ER+ BC and has a low proliferative rate >15%.

Results: *In vivo* models show that high GR (versus low GR) expression in ILC is associated with markedly reduced ILC cell proliferation without reducing metastatic colonization ability. We observed decreased tumor cell proliferation and tumor burden 150 days post-mammary gland injection of GR+ expressing ILC cells compared to GR null or GR low cells in the MDA-MBIV-134, and BCK4 cell lines. GR +pos ILC had equivalent metastatic burden to GR-negative ILC with much larger primary tumors.

Conclusions: This suggests that reduced proliferation in the mammary gland tumor does not affect metastatic efficiency in distant organs. *We hypothesize that tumor intrinsic GR may increase bone metastatic colonization* and metastatic latency through activation of "bone mineralization" gene expression signaling pathways, "IL-6 signaling pathways" and dormancy associated pathways.

Introduction



The lifetime risk of metastatic recurrence remains high for early-stage pre-menopausal ILC patients.

Figure 1. A) SEER data was used to compare ILC to IDC recurrences over 25 years. Unlike IDC, a high risk of ILC relapse continues after year 5. B) Preferential metastatic sites for IDC versus ILC[1].

Objective: Determine how GR affects ILC tumor biology and metastatic disease

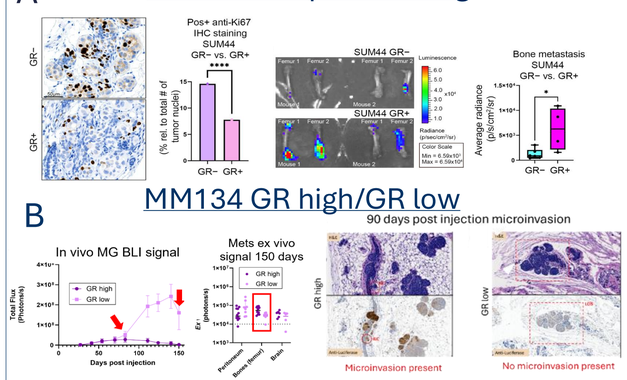


Figure 2. A) GR+ SUM44 ILC cells injected via MIND model show decreased tumor burden and incr ased bone mets compared to GR-. B) MM134 GR high ILC cells injected via MIND show decreased tumor growth over time and increased bone mets with more invasion in MG compared to GR low.[2]

Methods

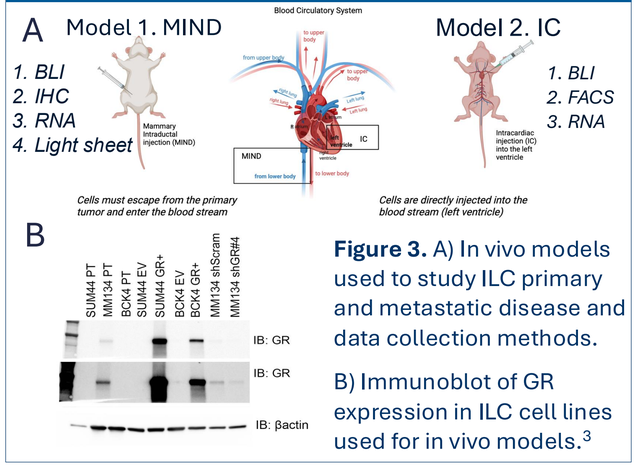


Figure 3. A) In vivo models used to study ILC primary and metastatic disease and data collection methods.

B) Immunoblot of GR expression in ILC cell lines used for in vivo models.[3]

BCK4 GR+ ILC tumors have decreased tumor growth

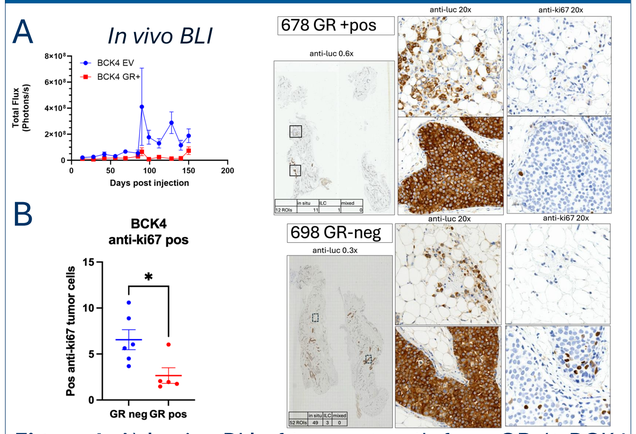


Figure 4. A) In vivo BLI of tumor growth from GR-/+ BCK4 cells 150 days post MIND model B) anti-ki67 antibody stain of MG harvested from mice engrafted with BCK4 isogenic cell line. C) IHC of MG tumors stained using anti-luciferase antibody and anti-ki67 antibody stains.[4].

BCK4 GR+ ILC tumors have more bone metastasis

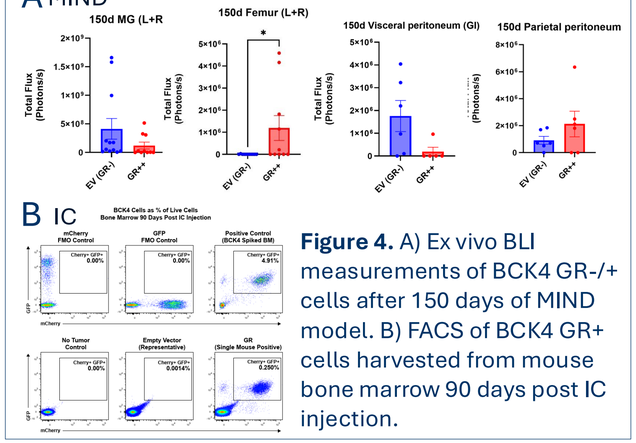
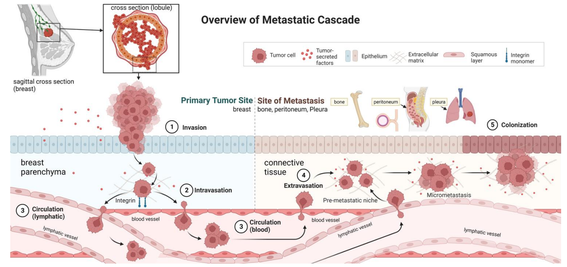


Figure 4. A) Ex vivo BLI measurements of BCK4 GR-/+ cells after 150 days of MIND model. B) FACS of BCK4 GR+ cells harvested from mouse bone marrow 90 days post IC injection.

Working model



GR positive BCK4 ILC may have more bone metastasis via GR transcriptional program shown in Porter et al. 2023. GR may act both anti-proliferative and pro-metastatic as previously shown in SUM44 and MM134 cells.[2]

Conclusions

- GR +pos BCK4 mammary gland tumors have reduced proliferation compared to GR –neg
- GR expression in ILC BCK4 cell line has increased bone metastasis captured via MIND and intracardiac injection.
- Lack of GR expression led to increased visceral peritoneum metastasis in BCK4 tumors
- Future experiments include matched gene expression of primary and bone mets to identify targetable pathways relating to bone metastasis

Funding sources & Acknowledgments

Supported by R01238519, CPRIT RR190037 Scholar Award, Charles Pak Family Cancer & Bone Initiative (CBI) Research Grant CBI-2024-01, Translational Cancer Biology (TCB) T32 Training Program, NCI T32 CA291654.

References

1) Oesterreich S., et al. *JNCI 2022. 2). Porter et al. Cancers. 2023. 3) Jambal P. et al Breast Cancer Res Treat. 2013. 4) Tonsing-Carteret al. 2019. Lobularbreastcancer.org. SEER database.*

This presentation is the intellectual property of the author/presenter and UT southwestern medical center. Contact them at baylee.hansen@utsouthwestern.edu for permission to reprint and/or distribute.