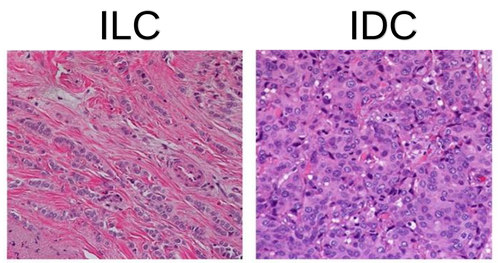
University of Colorado Anschutz Medical Campus

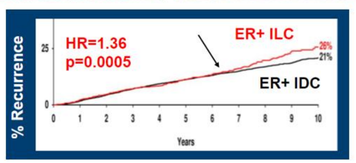
Understanding Radiation Therapy Sensitivity in Invasive Lobular Carcinoma of the Breast

Michael Boysen, Madeleine Shackleford, Joseph Sottnik, Matthew J. Sikora
Dept of Pathology, University of Colorado Anschutz Medical Campus

Background on ILC – Why is it an Issue?

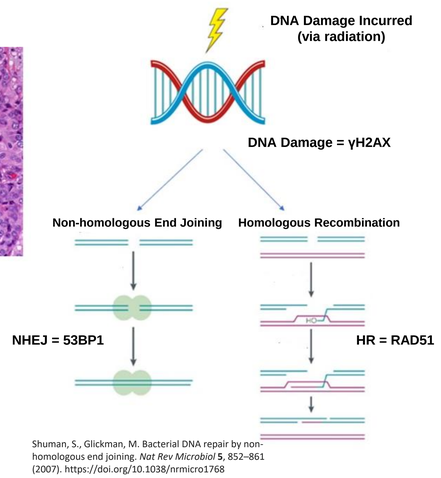
- Invasive Lobular Carcinoma (ILC) of the breast is a top ten most common cancer affecting women
- Despite biomarkers of good long-term prognosis, ILC associated with anti-estrogen resistance and is typically unresponsive to chemotherapy
- **Anecdotally ILC is more responsive to radiation therapy**



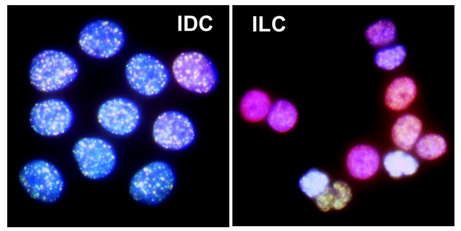


PD14-08: Effectiveness of aromatase inhibitors versus tamoxifen in lobular compared to ductal carcinoma: Individual patient data meta-analysis of 9328 women with central histopathology, and 7654 women with e-Cadherin status

ILC May Not Initiate HR-Mediated DNA Repair

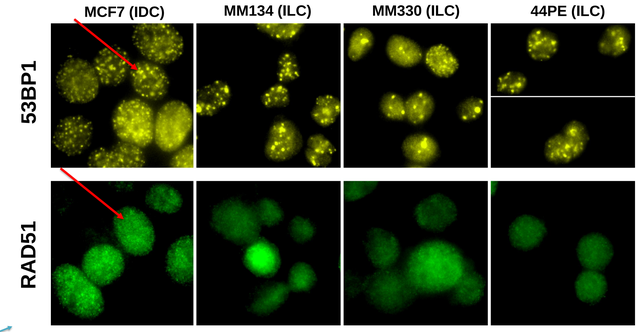


Shuman, S., Glickman, M. Bacterial DNA repair by non-homologous end joining. *Nat Rev Microbiol* **5**, 852–861 (2007). https://doi.org/10.1038/nrmicro1768



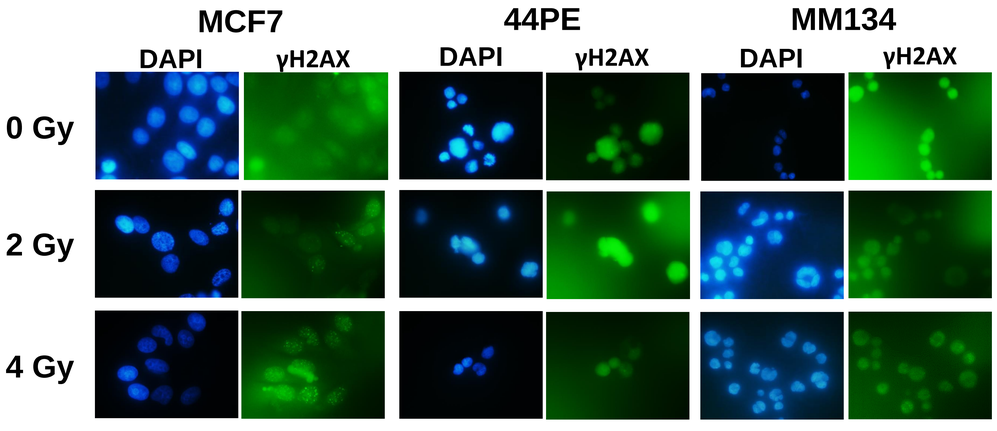
Sottnik and Bordeaux et al, Molecular Cancer, Research 2021; PMID 33947745

- ILC cells demonstrate sustained pan-nuclear γH2AX indicating inefficient or incomplete DDR initiation.
- DNA damage does not induce RAD51 foci in ILC cell lines



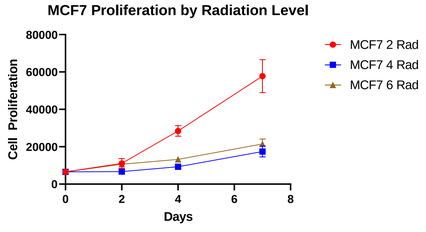
Unpublished, Sikora Lab

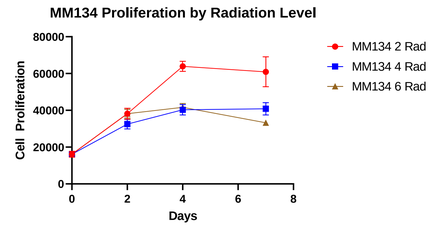
ILC Cells Are Deficient in γH2AX Foci Formation

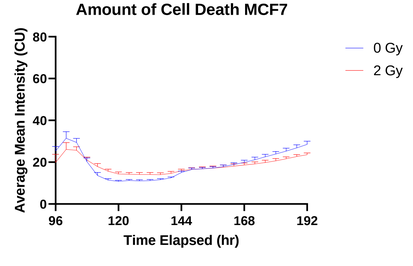


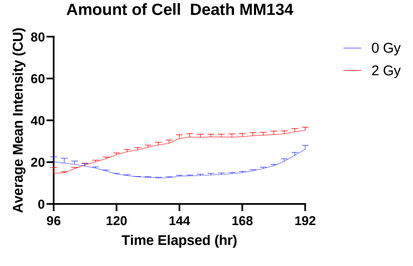
- MCF7 cells (IDC): XRT induces γH2AX foci formation
- 44 PE cells (ILC): No apparent foci formation with XRT
- MM134 Cells (ILC): No apparent foci formation with XRT

ILC Cells Are More Sensitive to Radiation









- ILC cells demonstrate more difficulty in recovering from XRT post-day 4
- DDR dysfunction may be present in ILC cells when undergoing XRT

Conclusions and Future Directions

- ILC deficiency in γH2AX formation may explain early cell arrest and poor DNA damage repair when exposed to XRT
- ILC cells appear to be more sensitive to XRT than IDC Cells
- XRT may provide a more efficacious route for treating ILC
- Explore efficacy and interaction between XRT and endocrine therapy

Sikora Lab
Joe Sottnik, PhD
Maddy Shackleford
Maggie Musick, PhD

Bitler Lab
Momie Yamamoto, PhD

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