



Highlights from Research Supported by the IBC Network Foundation

Biomarkers-related Research:

Description: Devi Laboratory is focused on understanding the role of the programmed cell death pathway in progression and treatment resistant phenotype of aggressive breast cancers including triple negative, basal-like and inflammatory breast cancer. Of particular interest is X-linked inhibitor of apoptosis protein (XIAP) considered the most potent inhibitor of cell death. Recently, we undertook a study to evaluate the correlations between XIAP expression and clinicopathological features, including disease-free survival (DFS) and pathological complete response (pCR) to chemotherapy, in more than 2,300 invasive primary breast cancer samples. We found a significant association of XIAP expression with younger patients' age (≤ 50 years), pathological ductal type, lower tumor grade, node-positive status, and PAM50 luminal B subtype. Analysis of molecular subtypes revealed a stronger prognostic value in HR+/HER2- tumors. Higher XIAP expression was associated with shorter DFS and lower pCR rate to chemotherapy in both uni- and multivariate analyses. All of these correlations were observed at both the RNA and protein level and indicates the potential of XIAP as a promising therapeutic target in primary invasive breast cancer.

Publication:

Devi GR, Finetti P, Morse MA, Lee S, de Nonneville A, Van Laere S, Troy J, Geradts J, McCall S, Bertucci F. Expression of X-Linked Inhibitor of Apoptosis Protein (XIAP) in Breast Cancer Is Associated with Shorter Survival and Resistance to Chemotherapy. *Cancers (Basel)*, 2021 Jun 4;13(11):2807. doi: 10.3390/cancers13112807 PMID: 34199946 PMCID: PMC8200223

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Honors for Trainees:

2020	Duke Undergraduate Research Award, Ulises Jair-Espino
2021	Duke Summer Undergraduate Research Award, Seayoung Lee
2021	American Association of Cancer Research Undergraduate Research Award: Seayoung Lee

Relevant Presentations by Dr. Devi

12/2020	MD Anderson IBC International virtual Education day; Session: Ongoing Clinical Studies
4/2021	Dana-Farber IBC program 10 th anniversary virtual education meeting April 24; Biography of Inflammatory Breast Cancer: From Rare to Care

Ongoing work:

Based on the aforementioned results revealing the role of XIAP in conferring shorter survival and resistance to chemotherapy in advanced breast cancers, we have initiated a detailed molecular profiling of a drug resistance-reversal preclinical models of inflammatory breast cancer wherein XIAP overexpression has been shown to play a dominant role in development of drug resistance.

IBC Preclinical Models Related Study:

Lymphovascular invasion (LVI), a critical feature of advanced cancers, is a major route of metastatic dissemination. Of the clinically-distinct types of breast cancer, the most lethal variant is inflammatory breast cancer (IBC) where LVI is a histopathological hallmark. Majority of IBC patients lack a distinct, solid tumor and instead present with diffuse tumor cell clusters cells, *also termed as tumor emboli*, in the breast and dermal lymphatics, which contributes to the clinical breast-skin symptoms and postulated to provide an efficient path to metastatic spread. The steps in lymphatic dissemination are challenging to study *in vitro*, and *in vivo* models are limited. Our goal is to develop new *in vivo* models that would enable direct visualization and quantitation of local tumor cell growth and tumor-lymphatic vessel interactions for improved understanding of the unique IBC tumor biology and for drug discovery. In order to allow direct study of tumor cell-lymphatic vessel interaction, we generated transgenic nude mice with fluorescent lymphatics [*tdTomato fluorophore* under control of a *Prox1* promoter, encodes a transcription factor (prospero-related homeobox 1) necessary for the formation and maintenance of lymphatic vessels]. Multichannel microscopy is being employed to serially quantify tumor growth, tumor spread and lymph-tumor interactions. These *in vivo* models provide in-depth imaging and quantitative measurements of locoregional invasion, tumor cell-lymphatic or endothelial vessel interactions of implanted tumor cells or tumor emboli. This model has the potential to be extended to study other cancer cell types exhibiting LVI as well as a screening metric for IBC therapies.

Presentations related to this work

Abstract P1-03-03- A. Rickard, P. Patel, S. J. Sauer, M. W. Dewhirst, G. M. Palmer, G. R. Devi. Multichannel serial imaging of transgenic, preclinical murine models provides the first quantitative analysis of the unusual growth kinetics and lymph-vascular invasion of patient-derived inflammatory breast cancer cells and tumor emboli. **San Antonio Breast Cancer Society** 2019 San Antonio, TX, USA.

Gayathri Devi, Plenary Symposium speaker- Dana-Farber IBC program 10th anniversary virtual education meeting April 24; Biography of Inflammatory Breast Cancer: From Rare to Care

Funding acknowledgement in abstract: Supported by DOD-Breakthrough-W81XWH-17-1-029, IBC Research Foundation, DCI pilot funds, [IBC Network Foundation](#), Duke Surgery Gardner Award.

Trainee Honors:

Samantha Bouchal, a Duke University student pursuing a Neuroscience Major is conducting her honors thesis in this project. Based on this, she received the prestigious Goldwater Scholarship and the Thomas Bardos AACR scholarship. Samantha has been accepted to the Mayo Clinic MD program (Fall 2021).

Ongoing work:

We are testing various strategies to study IBC metastasis in particular to the brain vs lung and evaluate if the anti-apoptotic signaling increases brain metastatic propensity and colonization of treatment-resistant IBC.

IBC Research Education and Community Engagement:

Dr. Devi discussed the collaboration with The IBC Network Foundation during the following talks

10/2020 Breast Cancer Awareness day; Union Baptist Church, Durham, NC, Oct 27

4/2021 Duke IBC Consortium Trainee Day Symposium April 9

Videos and presentations on the Duke IBC Consortium web page

<https://sites.duke.edu/consortium4ibc/>

Ongoing activities: Planning Spring 2022 Duke IBC Meeting to mark International Rare Disease Day