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The Ohio State University
College of Medicine

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PhD Candidate

“The Roles Of Metabolic Proteins, Fatty Acid Binding Protein 5 And S100A7, In Breast Cancer And Obesity”

February 25, 2015
BRT 105
2:30 pm
VITA

April 29, 1987. . . . . . . . . . . . Born – Elkton, MD

May 2009 . . . . . . . . . . . . . . . . . . . . . . B.S., University of Maryland

July 2009-present . . . . . . . . . . . . . . . . . . Graduate Research Associate
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Dr. Ramesh K. Ganju

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ABSTRACT

Fatty acid binding protein 5 (FABP5), an intracellular lipid binding protein, has been shown to play a role in various cancers, including breast cancer. However, FABP5 and its role in triple negative breast cancer (TNBC) have not been studied. We show FABP5 protein expression correlates with TNBC, high-grade tumors, and worse disease free survival in a tissue microarray containing 423 breast cancer patient samples. High FABP5 expression significantly correlates with epidermal growth factor receptor (EGFR) expression in these samples. FABP5 expression in a panel of breast cancer cell lines shows differential expression of FABP5 in TNBC and ER-positive cell lines. However, FABP4 does not associate with clinicopathological features of breast cancer.

Decreased tumor growth and lung metastasis were observed in FABP5−/− mice othotopically injected with murine breast cancer cells. FABP5 loss in TNBC tumor cells inhibited migration and invasion. Mechanistic studies revealed that FABP5 knockdown in TNBC cells results in decreased EGFR expression and FABP5 is important for EGF-induced metastatic signaling. Loss of FABP5 leads to proteasomal targeting of EGFR. Our studies show that FABP5 has a role in both host and tumor cell during breast cancer progression. These findings suggest that FABP5 mediates its enhanced effect on TNBC metastasis, in part, through EGFR, by inhibiting EGFR proteasomal degradation. These studies show, for the first time, a correlation between FABP5 and EGFR in enhancing TNBC metastasis through a novel mechanism.

Though a link between obesity and breast cancer exists, a clear mechanism has not been elucidated. S100A7 (Psoriasin) has been shown to promote breast cancer tumorigenesis and has been linked epidemiologically to obesity. However, there are no studies into the role of S100A7 in obesity. Bi-transgenic mice, MMTV-rtTA;TetO-mS100a7a15, that overexpress the mS100a7a15, the mouse homolog of S100A7, in the mammary gland upon treatment
for 3 months with doxycycline (1 g/kg) were found to be obese compared to their normal chow controls. MMTV-mS100a7a15 mice had increased body weight, white adipose tissue, liver weight, retro-peritoneal fat, and mesenchymal fat. No difference in brown adipose tissue was observed. Further studies showed that the increased body weight is not due to artifacts of the doxycycline diet as bi-transgenic mice had increased body weight and weight gain compared to single transgene control on doxycycline diet.

It is hypothesized that soluble mS100a7a15 is acting in a paracrine and endocrine manner to enhance obesity. To study the effect of S100A7/mS100a7a15 on adipogenesis, the differentiation of adipocytes, 3T3-L1, a preadipocyte fibroblast cell line was used. Pretreatment of 3T3-L1 with mS100a7a15 prior to induction of differentiation led to enhanced adipogenesis. mS100a7a15 mediates its affect, in part, through receptor for advanced glycation endproducts (RAGE). Neutralizing RAGE antibody treatment prior to mS100a7a15 led to dose dependent decrease in mS100a7a15 enhanced adipogenesis. Conditioned media from MDA-MB-231 overexpression S100A7 cells increased adipogenesis in human mesenchymal stem cells compared to vector control. An increase in PPARγ, a necessary early gene in adipogenesis, was found in S100A7 CM compared to vector. Taken together, these data suggest a role for S100A7 in adipogenesis and obesity.

RECENT PUBLICATIONS


AWARDS AND HONORS

- Systems in Integrative Biology Fellowship, College of Medicine 2010-2011

FUTURE PLANS

I am planning to pursue a postdoctoral fellowships focusing on clinical research in breast cancer.