SPRING 2021

Biochemistry and Molecular Biology Brown Bag Series

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"Stabilization of ERα by the F-box protein FBXL16 promotes ER$^+$ breast cancer cell growth and diminishes responsiveness to endocrine therapeutic drugs"

Tuesday, February 23, 2021

11:00 AM

Please contact x3249 if you would like to attend but did not receive an emailed link.

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https://science-math.wright.edu/biochemistry-and-molecular-biology

Abstract

Stabilization of ERα by the F-box protein FBXL16 promotes ER$^+$ breast cancer cell growth and diminishes responsiveness to endocrine therapeutic drugs

Breast cancer is the most prevalent cancer in women. One in every eight women in the U.S. is estimated to get diagnosed with invasive breast cancer during their lifetime. Approximately 75% of breast cancers are estrogen receptor alpha positive (ER$^+$) and are treatable with endocrine therapies and/or CDK inhibitors, but many patients eventually develop treatment resistance and metastasis. Mutations in ERα, dysregulation of ERα co-regulators and/or epigenetic and post-translational modifications on ERα protein are thought to stimulate ligand-independent ERα signaling and lead to disease progression and treatment resistance. Identifying regulators of estrogen receptor expression and transcriptional activity will help in designing better therapeutics for advanced ER$^+$ breast cancer. In our lab, we have identified F-Box and Leucine-Rich Repeat Protein 16 (FBXL16) as a positive regulator of ERα signaling. Preliminary data from our lab shows that FBXL16 increases protein expression and stability of many oncoproteins like c-myc, β-catenin and, Steroid Receptor Coactivator-3 (SRC-3) in lung and breast cancer cell lines. FBXL16 is highly upregulated in invasive ductal and lobular breast tumors, and its upregulation indicates poor patient survival in many cancer types. Through data mining from cancer databases, we observed overexpression of FBXL16 in ER$^+$ breast tumors and a positive correlation between FBXL16 expression and ERα status, implying that FBXL16 may play an important role in ERα-signaling mediated breast cancer growth. We show that silencing FBXL16 greatly reduced protein expression and stability of ERα resulting in decreased transcription of its target genes and breast cancer cell proliferation. FBXL16 is a poorly studied F-box protein whose activity and functions are largely unknown; for that, we also investigate if FBXL16 stabilizes ERα by antagonizing FBXO45, an SCF-E3 ligase that mediates ERα degradation, and thus decreases ERα ubiquitination and proteasomal degradation. Further investigation is being carried out to identify the roles of FBXL16 in endocrine therapy resistance and metastatic progression of breast cancer.