Fall 2025

Biochemistry and Molecular Biology Brown Bag Series

Rangarirai Makuku
Graduate Student

"The E3 Ligase FBXO45 Modulates ERα Stability and Fulvestrant-Induced Degradation in ER+ Breast Cancer"

Tuesday, October 14, 2025

11:00 AM

Location 135 Oelman Hall

Lab: Weiwen Long, Ph.D.

Boonshoft School of Medicine
WRIGHT STATE UNIVERSITY

WRIGHT STATE UNIVERSITY

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

Abstract

Estrogen receptor alpha (ERα) is a key driver of proliferation and survival in estrogen receptor–positive (ER+) breast cancer. Its stability is tightly regulated by the ubiquitin–proteasome system, which governs estrogen signaling and therapeutic response. Fulvestrant, a selective estrogen receptor degrader (SERD), binds the ligand-binding domain (LBD) of ERα, inducing conformational changes that promote ubiquitination and proteasomal degradation. However, ERα LBD mutations such as Y537S and D538G, common in endocrine-resistant breast cancers, stabilize ERα and reduce its susceptibility to Fulvestrant-induced degradation. Recent evidence suggests that FBXO45, an F-box protein component of the SCF E3 ubiquitin ligase complex, may regulate ERα stability through ubiquitin-mediated mechanisms. This project investigates the molecular role and biological significance of FBXO45 in ER+ breast cancer. Aim 1 examines how FBXO45 knockdown or overexpression affects ERα stability, Fulvestrant-induced degradation, and ERα–FBXO45 interactions in wild-type and mutant (Y537S, D538G) contexts. Aim 2 assesses the impact of FBXO45 silencing on cell growth and proliferation. Collectively, these studies clarify the role of FBXO45 in regulating ERα degradation and its potential contribution to endocrine resistance in ER+ breast cancer.

Key words: FBXO45, ER-Positive Breast Cancer, Fulvestrant, Ligand-Binding Domain Mutants (D538G, Y537S)