New dual-targeting approach for combating hormone receptor-positive breast cancer

Shaymaa Bahnassy
Hariprasad Thangavel
Maram Quttina
Ashfia Khan
Dhanya Dhanyalayam
Joan Ritho
Samaneh Karami
Jing Ren
Tasneem Bawa-Khalfe

Video Byte

Keywords: Cell Communication and Signaling, hormone receptor-positive breast cancer, HR+ BCa, endocrine resistance, androgen receptor, SUMO, enzalutamide, endocrine therapy, post-translational modification, PTM, small ubiquitin-like modifier, SUMO, SUMOylation, TamR-7, GI101A, GILM2, metastasis, tamoxifen, combination therapy, chromatin

Posted Date: November 12th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-106695/v1>

License: This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Hormone receptor-positive breast cancer (HR+ BCa) is the most frequently diagnosed subtype of breast cancer. Among those diagnosed with this form of cancer, acquired or intrinsic resistance to endocrine therapy represents one of the biggest challenges to treatment. While the androgen receptor has emerged as a promising therapeutic target, studies report conflicting results. Now, new research suggests that blocking certain forms of the androgen receptor prevents the metastatic progression of HR+ BCa. Experiments showed that HR+ BCa cells had elevated amounts of androgen receptors appended with small ubiquitin-like modifiers, or SUMOs. This "SUMOylation" upregulated androgen-receptor- dependent transcriptional activity and gene expression in breast cancer cell lines. Treating these receptors with both the receptor- blocking drug enzalutamide (Enz) and a SUMO inhibitor (GA) decreased the migration and metastasis of breast cancer cells. While more work is needed to understand how these dynamics might play out inside the human body, this dual-targeting approach offers a promising way to attack one of the most pernicious forms of breast cancer.