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Decreased cell proliferation with 2, 3- Dichloro-5, 8-Dimethoxy-1, 4-Naphthoquinone and 4-Hydroxy Tamoxifen in triple negative breast cancer cell lines

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Triple negative breast cancer (TNBC) is a subtype of breast cancer (BC) that makes up 10-15% of BC diagnosis. This form of the disease disproportionately affects African American (AA) women as compared to women of other ethnicities. TNBC is classified by lack of expression of three receptors: As specific targets are not present, surgery, radiation, and chemotherapy have been the mainstay of therapy for TNBC. A novel compound, 2, 3-dichloro-5, 8-dimethoxy-1, 4-naphthoquinone (Z285) belongs to the class of naphthoquinones that demonstrate activities as anticancer compounds. These compounds have been shown to cause an increase in reactive oxygen species (ROS) production as well as effects signaling pathways associated with epidermal growth factor receptor (EGFR). Moreover, it has been reported that treatment with tamoxifen can cause cell death. This is based on the accumulation of the drug and its active metabolites within cells that may cause an increase in the ROS production ultimately leading to cellular death, even in ERα negative cell lines.

In the current study, three triple negative cell lines, HCC1806, MDA MB 231, and HS578T were used. These cells were treated with Z285 and 4-hydroxy tamoxifen (4OH-Tam) for 24 or 72hrs with 1, 2, 4, 8, 16µM, and 3, 6, 12, 24, 48µM respectively. Synergestic activity was demonstrated using SynergyFinder. In other experiments, cells were treated with the IC50 of Z285 which was established in prior experiments. mRNA and protein were isolated between 6 and 24hrs. Results showed alterations of several mRNAs in response to these treatments. In addition, there were modifications to Nrf2 protein concentration, a transcription factor associated with oxidative stress. Therefore, these results indicate that combination treatment of Z285 and 4OH-Tam induces cell death at lower concentrations. Thus, this novel compound which causes an increase in ROS in these TNBC cells may render them more susceptible to tamoxifen therapy.

Recent Publications

1. Robert L Copeland, et.al, (2021): A panel of miRNAs as prognostic markers for African-American patients with triple negative breast cancer. BMC Cancer. 21(1):861.

2. Robert L Copeland, et.al, (2021): New targets in triple-negative breast cancer. Nature Reviews Cancer. 21(12).

3. Robert L Copeland, et.al, (2021): Sodium Butyrate Protects Against Ethanol-Induced Toxicity in SH-SY5Y Cell Line. Neurotoxicity Research. 39(2).

Biography

Robert Copeland has completed his PhD from Howard University, USA. He is the Associate Professor and Chair of the Dept of Pharmacology, Coll of Medicine. He has over 80 publications that have been cited over 700 times, and his publication H-index is 13 and has been serving as an editorial board member of reputed Journals. His research efforts are in directions that will delineate molecular differences in breast cancers amongst the two ethnic groups (African Americans and European Americans) which will help identify ethnic-specific markers for breast cancer progression. The major focus is on the development of novel pharmacological approaches for the prevention and treatment of breast cancers thus developing a more tailored treatment approach leading to better management of breast cancer.

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