Background According to the American Cancer Society there is a 1 in 8 chance that a woman in the United States will develop breast cancer. Additionally, 43,700 women are predicted to die from breast cancer in 2023. Current breast cancer treatments, including anti-cancer drugs such as daunorubicin, cause harmful side effects such as hair loss, difficulty breathing, severe decrease in red blood cell count in bone marrow, and life-threatening heart problems. Therefore, there is an urgent need for identifying novel targets for intervention with reduced toxicity. In breast cancer cells the protein Mitochondria Nuclear Retrograde Regulator 1 (MNRR1) is highly expressed compared to healthy cells. MNRR1 is a biorganellar protein that controls cellular function by acting in two compartments. In the mitochondria, it enhances energy production and inhibits apoptosis, whereas in the nucleus, it controls the transcription of genes involved in stress-responsive pathways. Since MNRR1 controls two key features of cancers—energy production which may affect cellular growth; and apoptosis, we hypothesized that MNRR1 may play a role in carcinogenesis and that inhibition of MNRR1 could reduce the dose of anti-cancer drugs such as daunorubicin and thereby minimize the toxic side effects of anti-cancer drugs.

Methods We treated triple negative breast cancer cells (MDA-MB-231) with an MNRR1 inhibitor and analyzed the effects on cellular apoptosis using a Phosphatidylserine Apoptosis Assay. We then assessed the viability of cells that were treated with both daunorubicin and the MNRR1 inhibitor using a RealTime-Glo MT Cell Viability Assay. Further, we evaluated the changes in expression levels of MNRR1 and PARP in the cells after treatment with the drugs via Western blotting.

Results Our results indicated that treatment of breast cancer cells with MNRR1 inhibitor alone reduced cell count (figure 1) even though it did not significantly increase apoptosis (figure 2). However, when co-treated with daunorubicin it increased the expression of cleaved PARP (figure 3), an indicator of apoptosis, and increased cell death (figure 4). These results suggest that MNRR1 inhibitor has a potentiating effect in inducing apoptosis in triple-negative breast cancer cells treated with daunorubicin.

Conclusions Overall, these findings suggest that MNRR1 is a potential drug target, and its inhibition may improve cancer treatment paradigms, such as the use of daunorubicin, by reducing the dose and therefore toxicity of drugs that are currently used in the treatment of breast cancer.

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REFERENCES
Abstract 470 Figure 4  MNRR1 inhibition enhances daunorubicin-mediated cell death. The RealTime-Glo MT Cell Viability Assay indicated that the amount of breast cancer cell death is significantly increased after co-treatment with MNRR1 inhibitor compared to treatment with daunorubicin alone. The results are expressed as mean ± standard deviation, n = 7, *** indicates p<0.001

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