

Investigating the Effects of Doxorubicin on Mesenchymal Versus Basal Triple Negative Breast Cancer Survival in 3D Culture

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Introduction. Breast cancer is the most diagnosed cancer in women in the United States, and the second leading cause of cancer-related mortality behind only lung cancer. Triple negative breast cancers (TNBC) present unique treatment challenges in that they are resistant to endocrine therapy, leaving chemotherapeutic and surgical interventions as the standard of care. Mesenchymal TNBC displays stem-like characteristics with a higher potential to metastasize, necessitating investigation of novel treatment modalities for this phenotype specifically. Our lab and others have previously shown that breast cancer cells cultured in a biologically relevant extracellular matrix respond differently to treatment. The current study aimed to determine whether doxorubicin chemotherapy has different effects on cell survival of the TNBC mesenchymal cell line MDA-MB-157 grown in 3D, compared to less aggressive basal TNBC cell line MDA-MB-468.

Methods. Cells were plated in Matrigel and serum-starved overnight prior to treatment with doxorubicin (10^{-12} - 10^{-6} M). Cells were fixed and imaged on a confocal microscope after six days of treatment.

Results. Treatment of MDA-MB-157 with doxorubicin yielded an EC_{50} of 110.3 nM, a more than 3-fold increase when compared to MDA-MB-468 (EC_{50} = 30.3 nM). Interestingly, this is more than 10-fold the reported EC_{50} for 2D culture of MDA-MB-157.

Conclusions. 3D cell culture displays significant differences in treatment response between mesenchymal and basal TNBC. These findings highlight the role of 3D models in the *in vitro* investigation of breast cancer treatment, as cell line-specific treatment response may be altered in the presence of a 3D extracellular matrix.

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