An in vitro Model for Studying Breast Cancer
Invasiveness in Response to Chemotherapy

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BACKGROUND

Triple-negative breast cancer (TNBC) is the most aggressive subtype of breast cancer, characterized by its high metastatic potential and lack of targeted therapies [1]. Novel therapeutic strategies for managing TNBC are urgently needed, especially those aimed at prevention during the early stages of metastasis. However, current in vitro models struggle to replicate the complex metastatic cascade, primarily due to the challenge of accurately establishing a tumor microenvironment (TME) [2].

This study aims to evaluate the influence of the TME on TNBC treatment response. Specifically, the effects of the chemotherapeutic agents doxorubicin (DXR) and paclitaxel (PTX) were assessed on three TNBC cell lines (MDA-MB-231, MDA-MB-468, and HCC1806) across different conditions: 2D traditional cell culture, spheroids, and matrix embedded spheroids. Additionally, the impact of these drugs on invasion was analyzed on a 3D invasive model, consisting of MDA-MB-231 spheroids embedded in a collagen I hydrogel simulating the extracellular matrix of cancerous breast tissue.

METHODS

RESULTS

Different response to DXR and PTX in 3D versus 2D culture

All the TNBC cell lines studied were less responsive to both DXR and PTX when cultured in three dimensions (spheroids) versus two dimensions.

Effect of DXR and PTX on early and late invasion models

Both drugs reduced the invasion and viability of the collagen hydrogel-embedded invasive MDA-MB-231 spheroids (early tumor model). However, in the case of DXR, the drug effect was less pronounced when it was applied after the cells had invaded the extracellular matrix in the so-called late tumor model (day 4 after invasion).

CONCLUSIONS

The fact that all three TNBC cell lines evaluated showed greater resistance to DXR and PTX when cultured on 3D rather than on traditional 2D culture highlights the importance of the TME in determining treatment response. Furthermore, both drugs might reduce the risk of metastasis on TNBC, but once cancer cells have invaded the extracellular matrix, their effect might be compromised.

REFERENCES