New tetraamine compounds targeting BCSCs from chemoresistant basal-like TNBC subtypes

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Introduction

Triple negative breast cancer (TNBC) is a highly aggressive breast cancer subtype that lacks prognostic markers, preventing the use of widespread targeted therapies. Lehmann classified TNBC into six subtypes, dividing basal subtypes into groups named Basal-Like 1 (BL1) and 2 (BL2)1.

The lack of therapeutic alternatives targeting cells displaying stem-like properties allow for relapse. Thus, there is an urgent need for the development of breast cancer stem cell (BCSC) specific drugs2.

The main objective of this study was to test the capability of new tetraamine-based compounds to target BCSCs from BL TNBC cell models and their potential to overcome chemoresistance.

Methods

MDA-MB-468 (BL1) and HCC1806 (BL2) TNBC cell lines resistant to doxorubicin (DXR) and paclitaxel (PTR) were developed. Differences in gene expression related to stemness and resistance were studied by means of qRT-PCR.

MTT assays were performed to confirm chemoresistance and determine the effect of the compounds. Mammosphere-forming efficiency (MFE) assays were carried out to assess the ability of the compounds to target the BCSC population.

Results

- SLUG, Twist, SOX2 and Hedgehog pathway’s influence in chemoresistance acquisition was identified in BL1 and BL2 TNBC resistant models, with Notch pathway changes in BL2.
- All the compounds showed cytotoxicity in BL TNBC models with no significant differences between sensitive and chemoresistant models for ssPDP.
- MFE inhibition caused by the tetraamine compounds provides the rationale to further study their anti-BCSCs potential, significantly reducing the stem-like cell population.

Conclusions

References


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