Effect of ErbB4 on Triple-Negative Breast Cancer Cell Growth & Migration

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Abstract

One of the primary functions of ErbB4 in vivo is in the terminal differentiation of mammary glands during late-pregnancy and lactation induction. Parity and prolonged lactation are known factors that reduce breast cancer risk. ErbB4 expression has been associated with cell growth inhibition, a relatively well-differentiated histopathological grade, in addition to estrogen and progesterone receptor positivity. All of these findings indicate a favorable prognosis, supporting the protein's tumor suppressive role. However, overexpression of ErbB4 was shown to transform rodent mammary epithelial cells and induce tumorigenesis. A precise explanation of ErbB4 activities and mechanisms of action remains elusive to this day.

Methods

Plasmid transfection

Results: Experiment 1

Figure 2: a. GFP fluorescence demonstrating successful ErbB4 and empty vector construct transfection; b. Western blot confirming ErbB4 expression in TNBC cell lines. The expression of ErbB4 was examined at each assay's endpoint.

Results: Experiment 2

Figure 3: Graph of TNBC cell growth using SRB assay. These results depict normalized data for cell growth on day 5 post-seeding across the 3 TNBC cell lines tested. In the BT-20 and BT-549 cell lines, ErbB4 exhibited a growth inhibitory character, while in the MDA-MB-468 cell line, ErbB4 had no significant effect on cell growth.

Discussion and Conclusions

- The loss of ErbB4 is a frequent event in TNBC which occurs through various genomic mechanisms.
- The TNBC cell lines were transfected with either ErbB4 or empty vector expression constructs. GFP fluorescent microscopy as well as western blot confirmed the expression of ErbB4 in TNBC cell lines.
- Our study demonstrated that overexpression of ErbB4 enhanced migration of BT-20 cells, but yielded no significant difference in the migration of BT-549 or MDA-MB-468 cells compared to the empty vector control.
- Furthermore, ErbB4 overexpression inhibited growth of BT-20 and BT-549 cells, while causing no significant change in growth of MDA-MB-468 cells.
- Our study adds to the scarce amount of literature on the role of ErbB4 and triple-negative breast cancer and sets a foundation for additional functional and mechanistic studies.
- Weaknesses of the study include both limitations of the assays used, e.g. the SRB growth assay lacks sensitivity to distinguish cell death from cell proliferation, as well as limitations in scope, e.g. subcellular localization of ErbB4 and the influences of the other ErbB2 receptors were not investigated during our experiment.
- The next steps include performing additional functional and mechanistic studies to further elucidate the role of ErbB4 in TNBC. These studies are intended to lead to clinically meaningful findings.

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