Frequency of TLE3 over-expression in breast carcinoma subtypes including a large cohort of triple negative patients.

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Abstract

Introduction

The TLE family of proteins is composed of transcriptional co-regulators that play multiple roles in development and tumorigenic pathways. TLE3 is periodically expressed during the M phase of the cell cycle. Since TLE3 was found to be over-expressed in the majority of HER2 positive breast cancer patients, we aimed to determine the hormonal status, expressivity and amplification of TLE3 positive versus negative breast cancer patients. TLE3 was found to be over-expressed in the majority of HER2 positive breast cancer patients, and triple negative breast cancer patients. HER2. Samples were considered positive if HER2 was over-expressed and/or amplified. The percentages of triple negative, hormone receptor positive, HER2 positive with and without ER/PR positivity is depicted in the pie chart (A).

Conclusions

• TLE3 is expressed in majority of HER2 positive and hormone receptor positive breast cancer patients. Among the three subtypes tested, the frequency of TLE3 expression was lowest in the triple negative subtype.

• The expression of drug resistance protein, MRP1 was above 95% and the expression of Pgp was below 10% in all three breast cancer subtypes profiled, highlighting the fact that MRP1 is the predominant multi-drug resistance protein in breast cancer patients.

• We identified a new biomarker, TLE3 positive that can be used as a tool to predict response to taxanes warrants further study. Even though it is not entirely clear as to how TLE3 predicts taxane response, but it is possible that it acts as an indicator of lipid pathway activity which impacts cytotoxic sensitivity and ultimately tumor sensitivity.

• Our results show that TLE3 is over-expressed in the majority of HER2 positive and hormone receptor positive breast cancer patients. Interestingly, the frequency of over-expression of TLE3 was lowest in the triple negative subtype thereby making it more important to identify those patients in this group who are most likely to respond to taxanes therapy. To sub-classify the 978 breast cancer patients, we utilized hormone receptors (ER and PR) and HER2 expression/amplification. Overall, 95% of the total breast cancer patients were hormone receptor positive, 15% were HER2 positive and 49% were triple negative. The percentage of triple negative breast cancer patients was higher in our cohort, given the fact that molecular subtyping is not standardized.

• A total of 447 patients were triple negative of which 95% stained positive for TLE3 expression. Of the 102 HER2 positive patients, 73% stained positive for TLE3 as compared with 67% TLE3 positivity in the 931 hormone receptor positive patients. By pairwise comparison, the hormone receptor positive vs triple-negative subtype showed the highest statistical significance in ratios of TLE3 positivity (p<0.01-0.001).

• Conclusions: Our results show that TLE3 is over-expressed in the majority of HER2 positive and hormone receptor positive breast cancer patients. Interestingly, the frequency of over-expression of TLE3 was lowest in the triple negative subtype thereby making it more important to identify those patients in this group who are most likely to respond to taxanes therapy. To sub-classify the 978 breast cancer patients, we utilized hormone receptors (ER and PR) and HER2 expression/amplification. Overall, 95% of the total breast cancer patients were hormone receptor positive, 15% were HER2 positive and 49% were triple negative. The percentage of triple negative breast cancer patients was higher in our cohort, given the fact that molecular subtyping is not standardized.

Results

Distribution of molecular subtypes of breast cancer

Figure 1: A total of 978 cases were stained with ER/PR, HER2, Pgp and MRP1 antibodies to determine the hormonal status. When ER and PR stained positively, the sample was considered ER/PR positive. Further, HER2 (IHC, IHC, IHC, IHC) and FISH was done to determine over-expression and amplification of HER2. Samples were considered HER2 positive if HER2 was over-expressed and/or amplified. The percentages of triple negative, hormone receptor positive, HER2 positive with and without ER/PR positivity is depicted in the pie chart (A).

References


