Co-expression of MELK and DEL1 as a prognostic marker for Triple negative breast cancer

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Purpose: We previously identified developmental endothelial locus-1 (Del-1) as a promising prognostic marker for breast cancer and maternal embryonic leucine zipper kinase (MELK) as a potential downstream molecule in transcriptome analysis using RNA-seq. Therefore, we examined tumoral MELK expression and analyzed its prognostic impact among patients with early breast cancer (EBC).

Methods : MELK expression was assessed in breast epithelial and cancer cells. Meanwhile, the tumoral expression of MELK was determined by immunohistochemistry based on tissue microarrays from 354 EBC patients and scored based on stain intensity and the percentage of cancer tissue that is stained. Result: MELK was highly expressed MCF7, SK-BR3, MDA-MB-231, and HS578T but down-regulated in MDA-MB-468 and BT20 cell lines. Tumoral MELK expression was associated with ER/PR expression, and low Ki 67 but not with DEL1 expression. Based on molecular subtype, high MELK expression was observed in 74.5, 55.0, and 57.6% for luminal, HER2 enriched, and triple negative breast cancer (TNBC), respectively. MELK expression was marginally associated with survival in patients with TNBC. However, co-expression of MELK and DEL1 was significantly associated with poor survival in TNBC cohort (DFS: HR=7.1 and P=0.045; DDFS: HR=14.5 and P=0.035; DSS: HR=15.1 and P=0.008) adjusted with age, tumor size and node involvement.

Conclusion: MELK expression was higher in luminal subtype but MELK and DEL1 co-expression was a prognostic marker for TNBC among early breast cancer cohort. Therefore, MELK/DEL1 could act as a druggable target in TNBC patients.

Fig 1. MELK expression in breast cancer cell lines

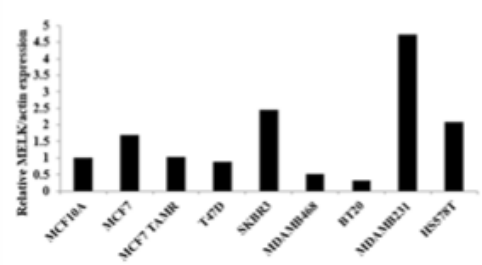

Fig 2. Survival curves according to MELK expression