Weill Cornell Medicine

Improved Epigenetic Signatures for Breast Cancer Prognosis and Treatment Selection

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Background & Unmet Need

- Breast cancer is the second leading cause of cancer deaths in women, with more than 40,000 deaths annually
- Immunohistochemically defined markers, including estrogen (ER) and progesterone receptors (PR), human epidermal growth factor receptor 2 (HER2), and the proliferation marker Ki67, play a major role in therapy recommendations
- There are currently several commercially-available prognostic molecular signatures (e.g., Oncotype, Endopredict, Prosigna, BCI) that are used for predicting breast cancer recurrence
- However, these tests are only recommended by ASCO for use in lymph node negative, early stage, ER-positive and HER-negative breast cancers
- **Unmet Need:** Need for molecular signatures that are applicable to all types of breast cancer, such as triple-negative breast cancer (TNBC) and HER2+

Technology Overview

- **The Technology:** Epigenetic signature ET-9 was identified as prognostic markers for breast cancer that function independent of patient characteristics
- **The Discovery:** ZNF92 overexpression is strongly associated with breast cancer and can predict patient outcomes
- **PoC Data:** The ET-9 signature successfully identified patients with 8.7 years shorter overall survival (p=1.56e-5) and 6.3 years shorter relapse free survival (p=1.63e-4)
- High ET-9 expression was associated with greater hazard ratios compared to the commercially available signatures
- ZNF92 over-expression appears to be even more specific for breast cancer compared to common benchmarks such as estrogen receptor (ER) and HER2

Inventor:
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Patents:
PCT Application Filed

Publications:
Battacharya et al. *Cancers (Basel)*. 2023
Kamran et al. *npj Breast Cancer*. 2022.

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Technology Applications

- Assay to identify breast cancer patients at high risk of relapse and shorter survival
- Assay to identify patients who are most likely to benefit from HDAC inhibitor therapy
- Identifies ZNF92 as a novel target for breast cancer drug development

Technology Advantages

- Outperforms existing commercial tests (Oncotype, Endopredict, Prosignia, BCI, and Mammaprint)
- Prognostic value of assay functions independently of patient demographics and tumor characteristics
- Accurately identifies breast cancer patients with 6-8 years shorter relapse-free and overall median survival that may benefit from additional or alternative therapies

Supporting Data / Figures

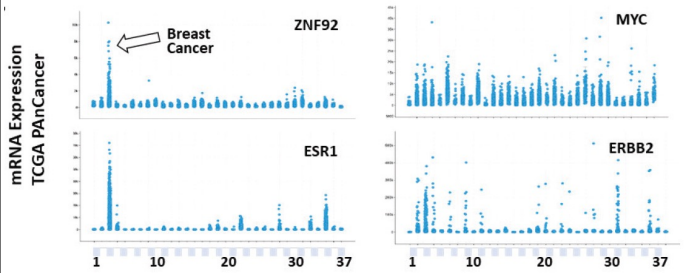

Figure 1: ZNF92 expression in human tumors. The relative mRNA expression of ZNF92, Estrogen receptor (ERSR1), HER2 (ERBB2) and MYC in the cBioportal TCGA PanCancer dataset that includes 37 tumor types with 10,967 samples. Breast cancer is the third tumor type from the left.

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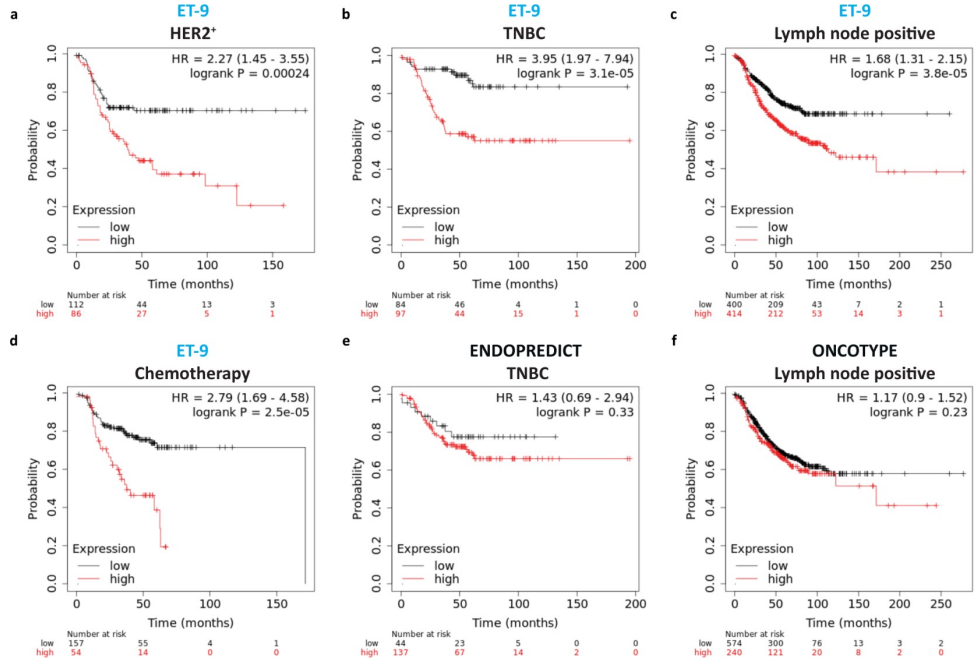

Figure 2: ET-9 in breast cancer subgroups. Kaplan-Meier (KM) charts of relapse free survival of human breast cancer are shown that were generated using Kaplan-Meier plotter [Breast] where high risk is shown as red lines, and low risk is shown as black lines.

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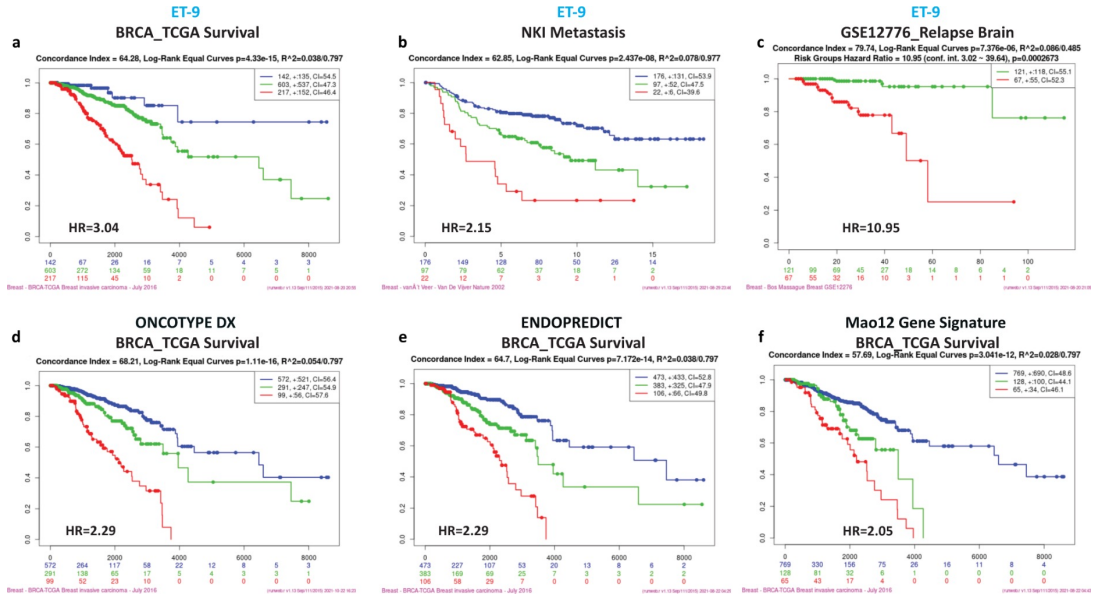

Figure 3: The Kaplan-Meier survival plots were generated using SurvExpress. The graphs illustrate ET-9 overall survival high risk (red), medium risk (green), low risk (blue) tumors.

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