Biomarkers in breast cancer

LOW EXPRESSION OF FGD3, A PUTATIVE GUANINE NUCLEOTIDE EXCHANGE FACTOR FOR CDC42, IS PROGNOSTIC OF POOR OUTCOME IN BREAST CANCER

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Identification of single gene biomarkers that are prognostic of outcome can gain insight into the molecular mechanisms that drive breast cancer. Exploratory analysis of single gene biomarkers in Metabric discovery and validation cohort indicates that low expression of FGD3 mRNA is prognostic of poor outcome. FGD3 has been shown to induce morphological changes in HeLa Tet-Off cells where high expression induces sheet-like protrusions and inhibits cell migration (Hayakawa et al. 2008). FGD3 is found to have high expression in immune response cells using curated data in 79 human and 61 mouse tissues from the GeneAtlas (Wu et al. 2013). Tumors with high expression of FGD3 and favorable outcome could indicate an immune response. The z-score mRNA expression of FGD3 as a continuous variable in a cox regression model results in a hazard ratio (HR) = 0.684 (CI 0.61-0.77) p = 6.4x10^-7 in Metabric Discovery (n = 980) and HR = 0.71 (CI 0.63-0.79) p = 3.4x10^-7 in Metabric Validation (n = 991) for OS. The potential of FGD3 as a prognostic biomarker was verified in SuperCohort (n = 741) HR = 0.76 (CI 0.65-0.89) p = 8.05x10^-4 for DMFS. In TCGA breast cancer cohort, FGD3 mRNA expression (n = 544) when less than the mean are compared to samples with expression greater than the mean (n = 197) the Kaplan-Meier analysis shows low expression denotes poor outcome for OS with a logrank p-value = 0.008. In the TCGA breast cancer cohort FGD3 has a gain in 96 of 749 samples and a heterozygous deletion in 210 of 749 samples indicating a high percentage of chromosomal aberrations. With clear evidence that low expression of FGD3 mRNA indicates poor outcome, in four distinct cohorts encompassing 3,256 tumors and the role of FDG3 regulating cell migration suggests an important biomarker.

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