Imperial College London - Cancer & Surgery

SPIB - A potential biomarker in breast cancer?

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1 Introduction

Breast cancer is the most common cancer in women. One in every seven women in the UK will be diagnosed with breast cancer in their lifetime. Due to the high incidence, breast cancer is also accountable for the most cancer/associated deaths. To predict patient outcomes and to find new actionable targets for cancer therapy new biomarkers are required. There is already a multitude of established clinical markers like the tumour size, lymphatic node invasion status, distant metastasis status (as in the TNM classification) and molecular characterization (mainly oestrogen, progesterone and HER2 receptor status). High throughput data is becoming more readily available, allowing for in silico analysis of multiomics (e.g., genomics, proteomics, ...) of large cohorts. This essay tries to demonstrate the utility of Spi-B as a possible breast cancer biomarker. The transcription factor Spi-B is encoded by the gene SPIB and is a member of the Erythroblast Transformation Specific (ETS) group, which is defined by a common highly conserved DNA/binding domain. In the literature Spi-B is described as both a tumor suppresor and an oncogenic protein. Studies in lung cancer cells found Spi-B to be involved in recruitment of tumor associate macrophages (TAM) [1], further Spi-B was found to promotes anoikis resistance [2].
(Introduction word count: 210)

2 Methods

2.1 Data Sources

The Cancer Genome Atlas (TCGA) dataset for breast cancer (BRCA)[3] was acquired from the Xena platform [4] and from cBioPortal [5].

2.2 Identification of a possible novel prognostic marker

A multivariate Cox proportional hazards regression model was created with data from 1218 breast cancer patients. Over all survival was defined as the dependent variable and mRNA z-scores (as determined by RNA sequencing from the primary tumour) together with age and tumour stage (I/II as low; III/IV as high) as the independent variables. The calculated p-values were corrected with the false discovery rate (FDR) method and are shown as q-values.

2.3 Survival Analysis

The patient population was divided into SPIB-high and SPIB-low divided by the median of the SPIB mRNA expression. A logrank test and an associated Kaplan-Meier plot were generated for the two subpopulations.

2.4 Methylation and mRNA Expression Correlation

Methylation beta-values from the Illumina HumanMethylation450 BeadChip were correlated against the mRNA z-scores utilizing the spearman's rank correlation.

2.5 Copy Number and mRNA Expression

Putative copy-number alteration data (GISTIC2) were obtained in an already transformed format ordering the data in five levels from deep deletion (-2) to high-level amplification (+2). The data was then correlated (spearman's rank correlation) against the mRNA z-scores.
(Methods word count: 213)

3 Results

3.1 Identification of a possible novel prognostic marker

In a multivariate Cox analysis in 1218 breast cancer patients I could identify 2078 significantly (q-value ¡ 0.05) associated genes with the overall survival. SPIB was associated with a beneficial harzard ratio (HR: 0.91; q-value: 2.82%).
(Results word count: 39)

4 Conclusion

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(Conclusion word count: 0)

5 Figures and Tables

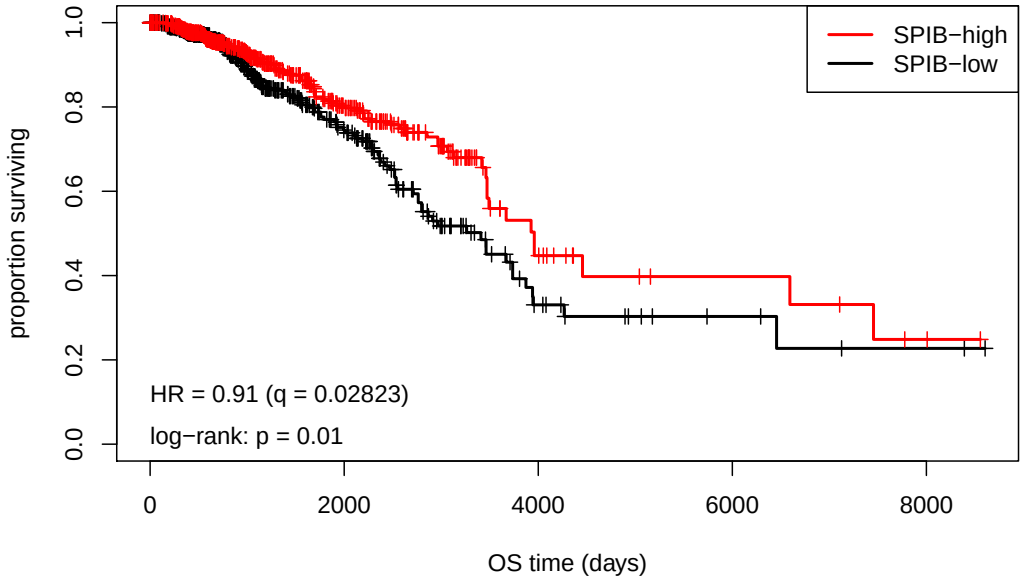

Figure 1: Survival of SPIB-high and SPIB-low breast cancer patients. Data from the TCGA dataset [3, 4]

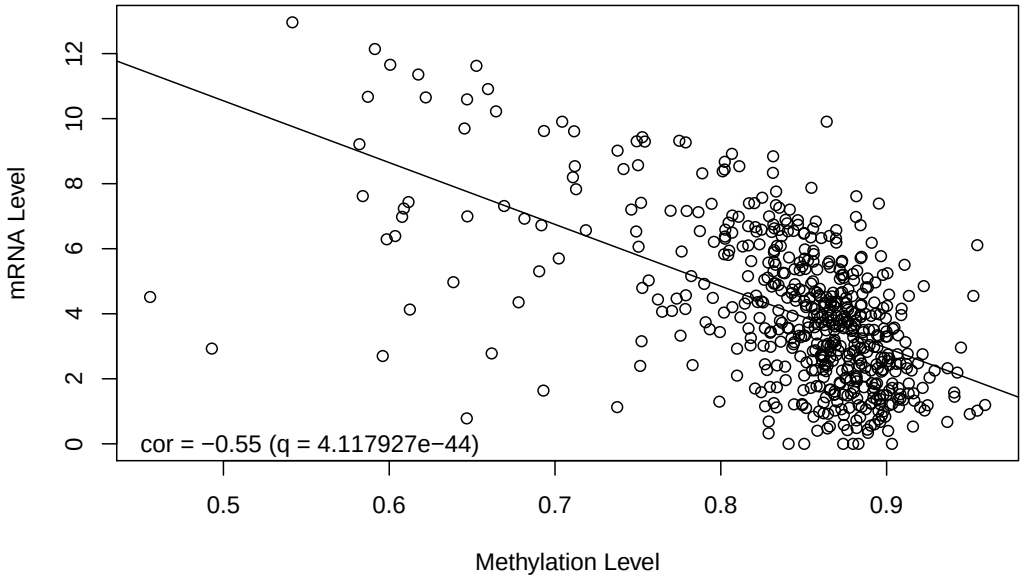

Figure 2: methylation [3, 4]

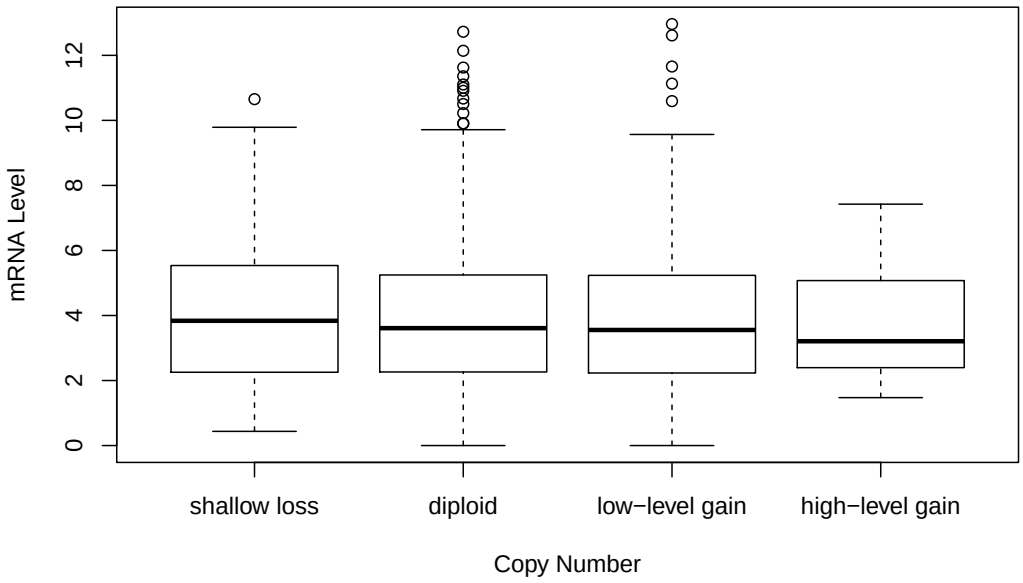

Figure 3: Copy number alteration [3, 4]

References

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