

A prognostic signature based on three-genes expression in triple-negative breast tumours with residual disease

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BACKGROUND: Residual disease after neoadjuvant chemotherapy (NAC) in triple-negative breast cancer (TNBC) is related with poor prognosis; however, the risk of recurrence after 3 years from surgery, becomes similar to other breast cancer subtypes indicating that TNBC is composed of tumours of different prognosis. **HYPOTHESIS:** We can develop a gene signature predictor of prognostic from the analysis of genes associated with the aggressiveness of TNBC. **METHODS:** We profiled 82 samples of residual tumours whose expression for 449 genes was quantified with NanoString. The validation set (GSE25066) consisted of 113 TNBC cases with residual disease. The stepwise multivariate survival analysis performed by the Cox proportional hazards mode selected CCL5, DDIT4 and POLR1C as independent prognostic factors for distant recurrence-free survival (DRFS). We developed a three-genes signature using the regression coefficients for each gene. **RESULTS:** The signature was: $-0.393 \times \text{CCL5} + 0.443 \times \text{DDIT4} + 0.490 \times \text{POLR1C}$. The median score in the discovery set (0.1494) identified two subgroups with different DRFS ($P < 0.001$). The median score in the validation set was 0.0024 and was able to discriminate patients with different DRFS ($P = 0.002$). In addition, the three-genes signature was a prognostic factor in TNBC patients regardless their response to NAC (data set SE58812; $P = 0.001$) and in patients with oestrogen-receptor-negative tumours (data set GSE16446; $P = 0.041$).