Nuclear localisation of LASP-1 correlates with poor long-term survival in female breast cancer.

Abstract: LIM and SH3 protein 1 (LASP-1) is a nucleo-cytoplasmatic signalling protein involved in cell proliferation and migration and is upregulated in breast cancer in vitro studies have shown that LASP-1 might be regulated by prostate-derived ETS factor (PDEF), p53 and/or LASP1 gene amplification. This current study analysed the prognostic significance of LASP-1 on overall survival (OS) in 177 breast cancer patients and addressed the suggested mechanisms of LASP-1-regulation. Nucleo-cytoplasmatic LASP-1-positivity of breast carcinoma samples was correlated with long-term survival, clinicopathological parameters, Ki67-positivity and PDEF expression. Rate of LASP1 amplification was determined in micro-dissected primary breast cancer cells using quantitative RT-PCR. Cell-phase dependency of nuclear LASP-1-localisation was studied in synchronised cells. In addition, LASP-1, PDEF and p53 expression was compared in cell lines of different tumour entities to define principles for LASP-1-regulation. We showed that LASP-1 overexpression is not due to LASP1 gene amplification. Moreover, no correlation between p53-mutations or PDEF-expression and LASP-1-status was observed. However, nuclear LASP-1-localisation in breast carcinomas is increased during proliferation with peak in G2/M-phase and correlated significantly with Ki67-positivity and poor OS. Our results provide evidence...
that nuclear LASP-1-positivity may serve as a negative prognostic indicator for long-term survival of breast cancer patients.