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Titel des Beitrags:
Urokinase receptor splice variant uPAR-del4/5-associated gene expression in breast cancer: identification of rab31 as an independent prognostic factor.

Abstract:
PURPOSE: To evaluate the pure prognostic impact of the uPA-receptor splice variant uPAR-del4/5 for lymph node-negative breast cancer patients, and to identify differentially expressed genes associated with high or low uPAR-del4/5 mRNA levels.

PATIENTS AND METHODS: mRNA transcript levels were measured by real-time PCR in tumor samples from 280 node-negative breast cancer patients who had not received adjuvant systemic therapy. Endpoints were distant metastasis-free survival (DMFS) and overall survival (OS). Gene expression analysis was performed with RNA isolated from breast cancer tissue and breast cancer cell lines using Affymetrix U133a GeneChips. RESULTS: In multivariate analysis, uPAR-del4/5 significantly contributed to the base model of traditional prognostic factors for DMFS (HR = 3.29, P< 0.001) and OS (HR = 2.87, P = 0.002). Using microarrays, seven genes were found to be up-regulated in tumor samples and cancer cell lines with high uPAR-del4/5 mRNA expression. The gene encoding rab31, a member of the Ras oncogene family, was selected for quantitative analysis of mRNA expression in the set of 280 patients. High rab31 values were significantly associated with worse outcome of patients for DMFS (HR =
2.27, P< 0.001) and OS (HR = 2.01, P = 0.008) in multivariate analysis, independent from uPAR-del4/5. The patient subgroup with high uPAR-del4/5 and rab31 levels showed the worst DMFS and OS (P< 0.001, both) compared with tumors with low values of both factors. CONCLUSIONS: Our results suggest that uPAR-del4/5 and rab31 mRNA represent independent prognostic markers in breast cancer and may be components of different, but possibly associated, tumor-relevant signaling pathways.

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