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学位論文の題名	FOXA1 expression after neoadjuvant chemotherapy is a prognostic marker in estrogen receptor-positive breast cancer （エストロゲンレセプター陽性乳癌における術前化学療法後の FOXA1 の発現は予後因子である） Breast Cancer, Published online before print June 16, 2013.
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Background Neoadjuvant chemotherapy has been established as a standard treatment strategy for patients with operable breast cancer as well as locally advanced breast cancer. The main expected benefit from neoadjuvant chemotherapy is a reduction in the extent of surgery. Recent studies have indicated that the response to chemotherapy and the prognostic impact of a pathological complete response (pCR) after neoadjuvant chemotherapy differ among breast cancer subtypes [1, 2]. Predictors of response to chemotherapy and prognostic factors for survival might be different in estrogen receptor (ER)-positive breast cancer.

Methods A total of 42 women with Stage II to III ER-positive HER2-negative breast cancer treated with anthracycline and taxane-containing neoadjuvant chemotherapy between 2003 and 2011 were retrospectively analyzed. Previous studies revealed that expression of forkheadbox A1 (FOXA1), B-cell lymphoma 2 (BCL2) and microtubule-associated protein tau (MAPT) was associated with survival in breast cancer [3-12]. Expression of FOXA1, BCL2 and MAPT as well as ER, progesterone receptor, HER2 and Ki67 was examined by immunohistochemistry in pre- and post-treatment specimens. Factors predictive of response to neoadjuvant chemotherapy and distant disease-free survival were analyzed.

Results Tumor grade was positively correlated with Ki67 expression. A positive association was found between expression levels of FOXA1 and MAPT. Expression levels of ER were positively correlated with expression levels of HER2, BCL2, FOXA1 and MAPT in pre-treatment tumors. The Ki67 labeling index was the only factor that was significantly associated with clinical response and pCR. Expression levels of BCL2, as well as those of ER, PgR and Ki67, were significantly lower in post-treatment tumors compared with those in pretreatment samples. Although expression levels of FOXA1 were also reduced in post-treatment tumors compared to pretreatment specimens, these changes were not significant. Lymph node status, expression of ER before neoadjuvant chemotherapy and expression of FOXA1 after neoadjuvant chemotherapy were significantly associated with distant disease-free survival, both by univariate and multivariate analyses. When the cut-off point for FOXA1 expression was set at 53 %, a Kaplan–Meier analysis showed that high FOXA1 expression after neoadjuvant chemotherapy was strongly associated with increased distant disease-free survival.

Conclusions High FOXA1 expression in post-treatment tumors correlates strongly with superior distant disease-free survival. Patients with ER-positive HER2-negative breast cancer should be selected for neoadjuvant chemotherapy. FOXA1 expression could be a prognostic marker in ER-positive breast cancer.

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