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**Gene Expression Profiles in Formalin-Fixed, Paraffin- Embedded (FFPE) Core Biopsies Predict Docetaxel Chemosensitivity.**

**Background:** Docetaxel has one of the highest response rates as a single agent in breast cancer, but de novo resistance is frequent. Previously, we had identified a 92-gene expression pattern that predicted response to neoadjuvant docetaxel. Other studies have validated that a high Recurrence Score (RS) by the 21-gene RT-PCR assay is predictive of worse prognosis (Paik, NEJM 2004) but better response to chemotherapy (Gianni, JCO 2005). We investigated whether tumor gene expression of these 21 genes and other candidate genes can predict response to docetaxel.

**Methods:** Core biopsies from 97 patients were obtained before treatment with neoadjuvant docetaxel (4 cycles, 100 mg/m<sup>2</sup> q3 weeks). Baseline and posttreatment measurements of the primary breast cancers were recorded. Three 10-micron FFPE sections were submitted for quantitative RT-PCR assays of 192 genes that were selected from our previous work and the literature.

**Results:** Of the 97 patients, 81 (84%) had sufficient invasive breast cancer, 80 (82%) had sufficient RNA for assay of 192 genes, and 72 (74%) had clinical response data. Mean age was 48.5 years, and the median tumor size was 6 cm. Clinical complete responses (CR) by RECIST were observed in 12 (17%), partial responses in 41 (57%), stable disease in 17 (24%), and progressive disease in 2 patients (3%). The concordance of IHC and RT-PCR results was >80% for ER, PgR, and HER2. By univariate logistic regression, a significant correlation ( $p < 0.05$ ) between gene expression and CR was observed for 14 genes. Notably, CYBA-1 involved in mitochondrial metabolism, identified by gene expression profiling, significantly predicted CR ( $p = 0.006$ ). CR was associated with lower expression of the ER gene group and higher expression of the proliferation gene group. Multivariate analysis indicated that panels of genes better predictors of docetaxel response. Of note, CR was more likely with high RS and less likely with a low RS ( $p = 0.008$ ).

**Conclusion:** We have established molecular profiles for breast cancers either responding or not responding to neoadjuvant docetaxel. This technology is a potential predictive test for docetaxel sensitivity by using small amounts of FFPE material, and may reduce unnecessary treatment, toxicity, and cost for breast cancer patients.