

## ASCO 2004 Abstract Submission

### Gene expression profiles of paraffin-embedded core biopsy tissue predict response to chemotherapy in patients with locally advanced breast cancer

**Short Title:**

GEP and breast cancer response

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**Background:** Previous studies validated a 21 gene RT-PCR Recurrence Score assay to quantify the likelihood of distant recurrence in node -, ER+, tamoxifen treated patients (pts). Tumor gene expression quantified using these 21 genes and/or other candidate genes may predict the likelihood of chemotherapy response.

**Methods:** Pts with locally advanced breast cancer were treated with doxorubicin (60 mg/m<sup>2</sup>) and paclitaxel 200 (mg/m<sup>2</sup>) q 3wk x 3, followed by weekly paclitaxel (80 mg/m<sup>2</sup>) x 12 before surgery, and adjuvant intravenous CMF q 4wk x 4 thereafter. A high-throughput RT-PCR assay quantified fixed tumor tissue expression of 384 genes selected from literature and previous gene expression studies.

**Results:** Of 93 pts with available biopsy enrolled between 1998 and 2002, 89 pts (97%) had sufficient RNA extracted for analysis. Mean age was 50 yr and median tumor size was 6 cm. Pathologic complete response (pCR) was observed in 11 pts (12.4%).

Quantitative gene expression results were obtained for 383 genes. Using univariate analysis, a significant correlation between gene expression and pCR was observed for 87 genes (p<0.05), including 5 with p<0.001 and 30 with p<0.01. 30 of the 87 genes that correlated with pCR clustered by both expression and function into 3 groups—an ER group (e.g., ER, PR, SCUBE2), a proliferation group (e.g. MYBL2, E2F1, MCM6), and an immune group (e.g., CD3z, CD18, FASL). pCR was more likely with lower expression for the ER group and higher expression for the proliferation and immune groups. Multivariate analysis indicates that combinations of genes are more powerful predictors of response than single genes. Notably, pCR was more likely with high Recurrence Score as calculated from a previously defined 21-gene panel, and less likely with low Recurrence Score (p<0.01).

**Conclusions:** RT-PCR analysis of an ER gene cluster predicts pCR to primary chemotherapy, and addition of other genes increases predictive power. These results will be used to define a multi-gene panel for validation in a larger independent study.

**Keyword (Complete):** Breast cancer ; Preoperative chemotherapy ; gene expression profiles