S32. Hormone Replacement Therapy Influences Gene Expression Profiles and Is Associated With Breast Cancer Prognosis

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Introduction: Postmenopausal hormone replacement therapy (HRT) increases breast cancer risk. The influence of HRT on the biology of the primary tumor is, however, not well understood.

Methods: We obtained breast cancer gene expression profiles using the Affymetrix human genome U133A arrays and examined their relationship with HRT use, tumor characteristics, and recurrence free survival in 88 postmenopausal women.

Results: HRT use in patients with estrogen receptor (ER) protein positive tumors (n=72) was associated with an altered regulation of 276 genes. Expression profiles based on these genes clustered ER positive tumors into two molecular subclasses, one of which was associated with HRT use and had a significantly better recurrence free survival despite lower ER levels. A comparison with external data obtained from MCF-7 cell lines on 33 of the 276 genes revealed that gene regulation in tumors associated with HRT use was negatively correlated with gene regulation induced by short term estrogen exposure (R=-0.55). In contrast, HRT associated gene regulation was positively correlated with the effect of tamoxifen (R=0.76).

Conclusions: Our findings suggest that post-menopausal HRT use is associated with a distinct gene expression profile associated with a better recurrence free survival. HRT use is also linked to lower ER protein expression, a finding not confounded by age. HRT exposed tumors show a gene expression pattern mimicking the effect of tamoxifen exposure of MCF-7 cells.