

Abstract #3049

Title: Associations between estrogen receptor (ER) Alpha expression levels and ER genotypes.

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Background: Estrogen receptors (ER) and associated factors, including progesterone receptors (PgR), modulate estrogenic effects both in normal tissue and in hormone receptor (HR)-positive breast cancers. ER α expression occurs in the majority of breast cancers, although the level of overexpression varies between tumors. Multiple single nucleotide polymorphisms (SNPs) in the genes that encode ER, termed ESR1 (ER α) and ESR2 (ER β), have been shown to affect phenotypic outcomes, including breast cancer risk, bone mineral density, hot flashes, and lipid levels. We hypothesized that SNPs in genes that encode ER may affect level of ER overexpression.

Methods: DNA was extracted from white blood cells from 100 subjects with HR-positive breast cancer enrolled in a tamoxifen observational study. SNPs in ESR1 (*XbaI*: rs#9340799, *PvuII*: rs#2234693) and ESR2 (01: rs#1256049; 02: rs#4986938) were determined from germline DNA using TaqMan. ER overexpression in paraffin-embedded formalin-fixed tumor specimens was quantified with immunohistochemistry (IHC) of tumor specimens on slides (Ventana Image Analysis System) and with RT-PCR using the Oncotype DX breast cancer assay (Genomic Health, Inc). Gene expression of other ER-associated genes (PgR, BCL2, and SCUBE2) was determined using RT-PCR (Oncotype DX). Expression of ER and associated genes across ER genotype was performed using the Kruskal-Wallis test. For all analyses, a p value of <0.05 was considered statistically significant.

Results: ER expression assessed using IHC and RT-PCR was statistically significantly correlated, with a Pearson correlation coefficient of 0.43 (p=0.0006). However, there was no association between the ESR1 or ESR2 genotypes and ER expression assessed by either method. A trend between ESR1 *XbaI* genotype and PgR expression by RT-PCR was noted (p=0.08 for gene-dose effect). No other associations between ER polymorphisms and expression of ER-related genes were identified.

Conclusions: SNPs in genes encoding for ER do not appear to be associated with level of ER expression in breast cancer. Differences in ER expression between individual tumors are likely due to mechanisms other than these inherited mutations in the ER genes.