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The Effects of Soy Supplementation on Gene Expression in Breast Cancer: A Randomized Placebo-Controlled Study

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Abstract

Background

There are conflicting reports on the impact of soy on breast carcinogenesis. This study examines the effects of soy supplementation on breast cancer-related genes and pathways.

Methods

Women (n = 140) with early-stage breast cancer were randomly assigned to soy protein supplementation (n = 70) or placebo (n = 70) for 7 to 30 days, from diagnosis until surgery. Adherence was determined by plasma isoflavones: genistein and daidzein. Gene expression changes were evaluated by NanoString in pre- and posttreatment tumor tissue. Genome-wide expression analysis was performed on posttreatment tissue. Proliferation (Ki67) and apoptosis (Cas3) were assessed by immunohistochemistry.

Results

Plasma isoflavones rose in the soy group (two-sided Wilcoxon rank-sum test, $P < .001$) and did not change in the placebo group. In paired analysis of pre- and posttreatment samples, 21 genes (out of 202) showed altered expression (two-sided Student's t-test, $P < .05$). Several genes including *FANCC* and *UGT2A1* revealed different magnitude and direction of expression changes between the two groups (two-sided Student's t-test, $P < .05$). A high-genistein signature consisting of 126 differentially expressed genes was identified from microarray analysis of tumors. This signature was characterized by overexpression (>2-fold) of cell cycle transcripts, including those that promote cell proliferation, such as FGFR2, E2F5, BUB1, CCNB2, MYBL2, CDK1, and CDC20 ($P < .01$). Soy intake did not result in statistically significant changes in Ki67 or Cas3.

Conclusions

Gene expression associated with soy intake and high plasma genistein defines a signature characterized by overexpression of *FGFR2* and genes that drive cell cycle and proliferation pathways. These findings raise the concerns that in a subset of women soy could adversely affect gene expression in breast cancer.