

**Contributions toward Scientific Advances:
NCI’s “Living Scientific Presentations” Book**

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“FGFR1-Transformed Mammary Epithelial Cells are Dependent on RSK Activity for Growth and Survival.”

These studies provide further support that FGFR1 is involved in lobular carcinoma and identify two potential targets for therapeutic intervention, FGFR1 and its downstream target, Rsk. Small molecule or siRNA inhibition of ribosomal S6 kinase (RSK) activity was found to induce death of the FGFR1-transformed cells in three distinct mouse and human models, without affecting normal breast epithelial cells.

<http://www.ncbi.nlm.nih.gov/pubmed/19258500>

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“Cell-type selective chromatin remodeling defines the active subset of FOXA1-bound enhancers.”

In previous work supported by the SPORE, we found that the pioneer factor FOXA1 plays a critical role in mediating the action of the estrogen receptor in breast cancer. In this paper, we monitored the chromatin structure at FOXA1 binding sites across the genome and compared breast cancer cells to other cancer types. We find that a significant proportion of the inactive FOXA1-bound regulatory sites in one cell type are actually functional in another cellular context suggesting that mechanisms that restrict the activity of shared FOXA1-bound enhancers likely play a significant role in defining the cell-type-specific functions of FOXA1.

<http://www.ncbi.nlm.nih.gov/pubmed/19129543>

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“Altered proliferation and differentiation properties of primary mammary epithelial cells from BRCA1 mutation carriers.”

The data show that primary mammary epithelial cells in BRCA1 mutation carriers have altered proliferation and differentiation properties before they transform into cancer cells. These altered cellular features are associated with heterozygosity for BRCA1, and they do not require loss of heterozygosity. BRCA1 mutant primary mammary epithelial cells show an increase in EGFR pathway activation which could potentially serve as a target for chemoprevention.

<http://www.ncbi.nlm.nih.gov/pubmed/19190334>

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“Trends in Racial and Age Disparities in Definitive Local Therapy of Early-Stage Breast Cancer.”

SEER data was used to assess local therapy for early stage breast cancer by race/ethnicity and age and examined trends over time. In 375,547 diagnosed from 1988 through 2004, we

determined that 85.8 percent of women had definitive local therapy. As breast conservation has increasingly substituted mastectomy, our findings suggest few women are receiving definitive local breast cancer therapy, with persistent disparities for black and Hispanic women as well as women age ≤ 60 and older than 70 years.

<http://www.ncbi.nlm.nih.gov/pubmed/19103731>

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“Tolerability of and Adherence to Combination Oral Therapy with Gefitinib and Capecitabine in Metastatic Breast Cancer.”

This phase I study explored gefitinib and capecitabine in metastatic breast cancer. In this phase I study of gefitinib and capecitabine in metastatic breast cancer a capecitabine maximum tolerated dose was identified and significant toxicity was observed.

<http://www.ncbi.nlm.nih.gov/pubmed/19294501>