## Re-programming the Epigenome: Molecular Mechanisms for Responding to Environmental Exposures

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It has been hypothesized that exposures to environmental agents during the development of the mammary gland can influence breast cancer risk in adult women. Insights into the molecular mechanisms that underlie these influences would aid in developing methods to reverse or prevent their effects.

Recently, studies of human epithelial cells and fibroblasts from healthy individuals have been providing novel insights into how early epigenetic and genetic events affect genomic integrity and influence breast cancer risk. Key epigenetic changes in breast epithelial cells, such as the hypermethylation of the p16 promoter sequence, create a previously unappreciated pre-clonal phase of tumorigenesis in which a subpopulation of epithelial cells is positioned for progression to malignancy (Nature 409:636, 2001). These key changes generate epigenetic and genetic mosaicism, precede the clonal outgrowth of pre-malignant lesions and occur frequently in healthy, disease-free individuals (Cancer Cell 5:263, 2004; JBC 281: 24790-24802, 2006). These cells have activated programs that allow epigenetic re-programming of the genome. Ongoing work from our laboratory has identified biomarkers that may be useful for risk assessment as well as provide targets for the elimination of these cells. Understanding more about these early events should provide novel molecular targets for reducing breast cancer risk and prevention of the disease.

**References**

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