

# Research Sheds Light On How DES Exposure Causes Breast Cancer

“In Utero Exposure to Diethylstilbestrol (DES) or Bisphenol-A (BPA) Increases EZH2 Expression in the Mammary Gland: An Epigenetic Mechanism Linking Endocrine Disruptors to Breast Cancer,” Taylor, HS, et al, *Hormones & Cancer*, June 2010, a Journal of The Endocrine Society.

## Reviewed by Fran Howell

We have come to understand that DES exposure before birth can set up DES Daughters for an increased risk of breast cancer more than forty years later. Now we have a clearer understanding of the mechanism for why that can happen.

This research confirms, with scientific/biologic results, the epidemiologic findings of the DES Follow-up Study, which shows that DES Daughters over age 40 develop breast cancer at a higher rate than unexposed women.

A team led by Hugh S. Taylor, M.D., professor in the Yale Department of Obstetrics, Gynecology and Reproductive Science, gave DES to pregnant mice and studied their female offspring.

He suspected the drug of interfering with a specific gene-regulating protein and his findings bear that out. DES Daughter mice produced higher than normal levels of EZH2, which plays a part in regulating the functioning

of genes. Scientists recognize that increased EZH2 levels are associated with a greater breast cancer risk in humans.

What Taylor did was identify DES as an endocrine disruptor that alters EZH2 production before birth. He says the alteration continues into adulthood leading to the possibility of increased breast cancer development. He adds, “elevated EZH2 levels caused by DES exposure were found only in breast tissue, not in other parts of the body, and were associated with aggressive forms of disease.”

Taylor makes it clear that DES does not mutate the DNA sequence itself, but rather, changes the regulating system that influences how genes operate,

or turn on and off. His work shows that DES may cause changes in tumor suppressing genes that can lead to breast cancer formation.

The Yale researcher notes that his research confirms, with scientific/biologic results, the epidemiologic findings of the National Cancer Institute DES Follow-up Study, which shows that DES Daughters over age forty develop breast cancer at a higher rate than unexposed women.

## BPA Also Implicated in Breast Cancer Risk

In this study, Taylor also exposed a separate group of pregnant mice

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**Research Sheds Light** from page 1 to bisphenol-A (BPA), another endocrine-disrupting chemical often found in plastics. BPA has estrogenic properties like DES, and in this study also caused increased levels of EZH2 in prenatally exposed adult mice — therefore raising their breast cancer risk.

According to Taylor this study serves to warn that all estrogen exposures before birth, from strong ones like DES to weak ones like BPA, can alter fetal development with dangerous repercussions in adulthood.

He says, “We have demonstrated a novel mechanism by which endocrine-disrupting chemicals regulate developmental programming in the breast,” and adds that DES Daughters should have the annual health screenings they need, “to monitor for the development of breast lesions as adults.”