DES Action VOICE

A FOCUS ON DIETHYLSTILBESTROL

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No Specific Tumor or Gene Mutation Associated with Increased Risk for Breast Cancer in DES Daughters

"In Utero Exposure to Diethylstilbestrol (DES) Does Not Increase Genomic Instability in Normal or Neoplastic Breast Epithelium," Pamela S. Larson, et al., *Cancer*, Volume 107, Issue 9, 1 November 2006.

Reviewed by Kari Christianson

Since the publication last year of research confirming an increased risk for DES Daughters over the age of 40 developing breast cancer (reported in Voice 110), DES Action has received a number of questions about whether there is a specific breast cancer tumor linked with this increased risk. This is a very good question for DES Daughters, considering a specific type of cancer, clear cell adenocarcinoma (CCA), is associated with the lifelong need for gynecologic screening for this vaginal or cervical cancer. We now have an answer.

A first report concerning genetic characteristics of breast tissue from DES Daughters has been released. Researchers, using the medical records and tissue samples of breast cancer from some of the participants of the NCI DES Follow-up Study, reviewed the pathology reports. **They investigated whether or not breast tissue from these DES Daughters exhibited any of the genetic abnormalities that characterize other DES-associated tumors, like clear cell adenocarcinoma of the vagina or cervix.**

Headed by Pamela S. Larson, Ph.D., Department of Pathology and Laboratory Medicine at Boston University Medical Center, the team of researchers ". . . investigated DNA from normal, hyperplastic and malignant breast epithelium in DES-exposed and unexposed women. We expected that the breast tumors, and even the premalignant or normal-appearing tissue, arising in DES daughters might exhibit global or chromosome-specific increases in genotoxicities reported in other DES-associated tumors, specifically MI (micro-satellite instability) and AI (allele imbalance, also known as loss of heterozygosity [LOH])."

These researchers found no genetic differences between the breast cancer tumors of DES Daughters and unexposed women. There was an absence of the micro-satellite instability (MI) that is found in vaginal clear cell adenocarcinoma. This finding confirms "that MI is unusual in human breast cancers" and suggests "that **prenatal DES exposure does not affect DNA mismatch repair mechanisms in the breast.** Similarly, the equivalent amounts of AI (allele imbalance or LOH) seen in the breast tissue,

"...prenatal DES exposure may increase the growth of any cells which develop into breast cancer."

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regardless of exposure, differs from findings in animal models and in vitro systems. Therefore, in utero DES exposure effects, if any, may be tissue, timing and/or species specific. . . ."

The authors conclude that, ". . . combined with the absence of genetic differences detected between groups, younger age of diagnosis (in the exposed group) is also consistent with potential effects of DES on human breast carcinogenesis being mediated by enhanced proliferation."

In consumer-friendlier language this means that there is no specific malignant tumor type associated with the increased risk for breast cancer among DES Daughters over the age of 40. Rather, prenatal DES exposure may increase the growth of any cells which develop into breast cancer. It is this potential for a more rapid growth rate that results in the increased risk for and incidence of breast cancer at an earlier age for DES Daughters. DES VOICE