

Common, estrogen-mimicking chemicals found in plastics affect genomic composition of rat mammary gland tissue

Compounds such as bisphenol A (BPA) and butyl benzyl phthalate (BBP) that have xenoestrogenic effect are found in the plastic packaging used for most foods, in dental sealants, in products like compact disks, and in many cosmetics.

As part of studies funded by the NIEHS, Jose Russo, M.D., F.A.C.P., of the Fox Chase Cancer Center and Coral Lamartiniere, Ph.D, of the University of Alabama at Birmingham, investigated these two compounds to determine their influence on mammary gland development in an experimental system. Dr. Russo presented the results of research into the two compounds at the 2005 conference on Emerging Topics in Breast Cancer and the Environment Research.

Russo and Lamartiniere tested the effects of BPA and BBP on mammary gland development in laboratory rats by exposing pre-pubertal animals through their mothers' milk. The results were striking.

By the time the rats had attained puberty at the age of 21 days, the genetic signatures — the patterns of active and inactive genes — in their mammary glands had changed, Dr. Russo said. The genetic signature is a snapshot of those genes that are upregulated, or turned on, and those that are downregulated, or switched off and inactive. Researchers seek genetic signatures for a variety of disease entities, including cancer, to better understand the mechanisms of disease progression and genetic susceptibility. "Among the BPA-treated rats, the mammary glands at 21 days showed upregulated genes related to proliferation and differentiation, whereas at 50 days, the upregulated genes were involved in metabolism, signal transduction and immune surveillance," he said. In other words, from the ages of 21-100 days, the activity of these genes changed, especially in areas that may promote or regulate growth and differentiation.

The 21-day picture of BBP-treated rats also showed an upregulation of genes involved in proliferation, differentiation and cell adhesion (the ability of cells to stick together), but also in tumor suppression, he said.

Besides these differences in upregulated genes, the research group also identified one gene that was downregulated in both the BPA- and BBP-treated rats, regardless of their age. It was a gene called GAD1 that ultimately produces an enzyme known as glutamate decarboxylase 1. This enzyme is important for another compound, known as a neurotransmitter, which helps nerves communicate with one another. Research has shown that the GAD1 gene is often overexpressed, or much more active, in primary breast cancer, and that it could play a part in tumor development.

The research clearly shows that BPA and BBP are having an impact on the genomic composition of the mammary gland, Dr. Russo said. He added that the critical question surrounds the significance of these changes in relation to the susceptibility or refractoriness of this organ to carcinogenesis. Studies are in progress in Dr. Lamartiniere's laboratory to test this issue.

Dr. Russo is a senior member of the Fox Chase Cancer Center, where he serves as director of the Breast Cancer Research Laboratory, and the Breast Cancer and the Environment Research Center. Details of his research appear in "The Proceeding of the American Association for Cancer Research 2005."