

# **Prenatal Exposure to Bisphenol A increases Dimethylbenzanthracene-induced mammary cancer in adult rats**

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## **Abstract**

Mammary gland development is influenced by many hormones including estrogen. Although with less potency, some chemicals found in the environment have the ability to elicit similar responses as those caused by hormones. These chemicals are known as endocrine disruptors. One such a chemical is the plasticizer Bisphenol-A (BPA) which posses estrogenic properties. Since exposure to estrogenic chemicals during critical periods of mammary gland development has been suggested to have the potential to influence the susceptibility to develop breast cancer, we investigated the ability of *in utero* exposure to BPA to alter the susceptibility of the mammary gland to carcinogenesis.

**Methods:** Pregnant Sprague-Dawley CD rats were fed phytoestrogen-free AIN-76A diet and gavaged from post-conception day 10 until birth with 1) sesame oil (control), 2) 25 µg/kg BW BPA (low BPA), or 3) 250 µg/kg BW BPA (high BPA). For tumorigenesis studies, female offspring were exposed to 30 mg dimethylbenzanthracene (DMBA)/kg body weight at 50 or 100 days of age.

**Results:** In rats exposed prenatally to BPA and at day 100 with DMBA as compared to DMBA at day 50, mammary tumor multiplicity was increased and latency (time to develop first tumor) was significantly decreased. Western blot analysis showed different effects of prenatal BPA exposure on estrogen receptor- $\alpha$  (ER- $\alpha$ ), steroid receptor co-activators (SRCs) 1–3, phospho-IGF receptor beta, EGF-receptor, phospho c-Raf, and 14-3-3 eta and sigma protein expressions between 50 and 100 day old rats that can account for differential mammary cancer susceptibility.

**Conclusions:** Prenatal exposure to BPA alters expression of steroid receptor and co-activator proteins, growth factor signaling proteins and susceptibility to chemically-induced mammary cancer in a rodent model.

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