**AP-137**

**Title:** Antiproliferative effect of genistein on the growth of estrogen-dependant BG-1 ovarian cancer cells induced by 17beta-estradiol or bisphenol a via down-regulation of the cell cycle progression

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Xenoestrogens are chemical compounds that imitate estrogen in living organisms and classified as a type of endocrine disrupting chemicals (EDCs). Bisphenol A (BPA) is a widely used industrial compound, and also known as one of EDCs and especially a xenoestrogen. One of estrogens in the body, 17β-estradiol (E2), is a pleiotropic hormone that regulates the growth and differentiation of many tissues and also acts as a mitogen that promotes the development and proliferation of hormone-responsive cancers. In this study, we examined the effect of a phytoestrogen, genistein, on the cell growth of BG-1 ovarian cancer cells induced by the treatment of E2 or BPA. In the cell proliferation test *in vitro*, E2 or BPA increased the growth of the BG-1 ovarian cancer cells expressing estrogen receptors (ERs). Their proliferation activity was reversed by the treatment of ICI 182,780, a well-known antagonist of ERs, which demonstrates that the cell proliferation by E2 or BPA is mediated by ERs and BPA certainly acts as a xenoestrogen in the BG-1 ovarian cancer cells. Genistein, an isoflavone, is one of phytoestrogens that are plant-derived, naturally occurring, and dietary xenoestrogens and influences multiple biochemical functions. In this study, genistein effectively suppressed the BG-1 cell proliferation induced by E2 or BPA by adversely downregulating the cell cycle progression that was upregulated by E2 or BPA. Concretely, E2 or BPA decreased the gene expression of p21, which is a potent cyclin-dependent kinase (Cdk) inhibitor and responsible for the cell cycle arrest at G1 phase, to proliferate the BG-1 cells. On the other hand, genistein upregulated the expression of p21 gene cultured in the presence of E2 or BPA, leading to the growth inhibition of the BG-1 cells. Also, the alteration of p21 gene expression by E2, BPA, or genistein affected the expression of its downstream genes of cell cycle, cyclin D1 and Cdk-4. Taken together from these results, we may suggest an anticancer effect of genistein, a dietary phytoestrogen, on the estrogen-dependant cancers like ovarian cancer prompted by E2 or BPA. [This work was supported by a National Research Foundation of Korea (NRF) grant funded by the Ministry of Education, Science and Technology (MEST) of Korea government (no. 2011-0015385)]

**Keywords:** Endocrine disrupting chemicals (EDCs), estrogen (E2), genistein, bisphenol A (BPA), ovarian cancer, p21

**AP-138**

**Title:** Bisphenol A and phthalate caused the stimulation of cell growth and the alteration of TGF-beta signaling pathway in human prostate cancer cells

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Endocrine disrupting chemicals (EDCs) can bind to the hormone receptor and induce the unexpected hormone response to activate estrogen receptor (ER) and androgen receptor (AR) mediated signaling pathways, which have potential to effect on the hormone-dependent carcinogenesis. As prostate cancer progression, steroid hormones, specifically androgen, is important factor in cancer growth and diagnosis. Among EDCs, Bisphenol A (BPA) has the detrimental effect on the endocrine system and is suspected to promote human breast and ovarian cancer. Recent studies have reported that phthalate can disrupt endocrine system and has weak estrogenic activity with binding to ERs. Thus, we demonstrated in this study whether BPA and dibutyl phthalate (DBP) stimulate the proliferation of prostate cancer cells, LNCaP cells having both ERs and ARs. We evaluated proliferation rate of LNCaP cells following BPA and DBP treatment using a cell viability assay compared to EtOH. Both BPA and DBP increased LNCaP cells proliferation over two-fold at 10^{-7} M to 10^{-5} M. Moreover, these EDCs altered translational expression of cell cycle related genes, cyclin D1 and p21 at 6 h in LNCaP after exposure of BPA and DBP. Overexpression of Cyclin D1 and downexpression of p21 can rapidly transit G1/S phase during the cell cycle. Further, we examined the alteration of gene expression of c-myc and c-fos by using the semi-quantitative RT-PCR. Like 17β-estradiol (E2) and dihydrotestosterone (DHP), treatments of BPA and DBP lead to increase the transcriptional levels of c-myc and c-fos in LNCaP cells from 30 min to 6 h. In addition, BPA and DBP decrease the protein level of not only p-smad but also total smad. These facts show effects of EDCs on TGF-β signaling in cancer. Taken together, these results suggest that BPA and phthalate can alter various gene expressions in TGF-β signaling and stimulate cell growth in prostate cancer cells *in vitro*. A further study warranties to determine the potential of EDCs in the carcinogenesis of prostate cancer *in vivo*. [This work was supported by a National Research Foundation of Korea (NRF) grant funded by the Ministry of Education, Science and Technology (MEST) of Korea government (no. 2011-0015385).]