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Bisphenol A and its derivatives decrease expression of chemerin, which reverses its stimulatory action in ovarian cancer cells

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Highlights

- Chemerin and its receptor CLKMR1 are expressed in various ovarian non-cancer and cancer cell lines.
- Expression of chemerin and its receptor varies among different ovarian epithelial and granulosa tumors.
- BPA, TBBPA, and TCBPA down-regulate chemerin expression only in granulosa cell tumors.
- Both PPARγ and ERs are involved in the BPA-induced decrease in chemerin expression and secretion in COV434 cells.
- Chemerin reverses the mitogenic properties of BPA and TBBPA in granulosa cell tumors.

Abstract

Chemerin is an adipocyte-secreted protein that associates with obesity, inflammation, metabolic dysfunction, and carcinogenesis. Previous studies have shown human granulosa cells to produce bioactive chemerin and its receptor CMKLR1. In the present study, we demonstrated that the mRNA level of chemerin receptor is higher in a granulosa cell tumor cell line than in epithelial cancer cells, whereas chemerin expression and secretion were lower. Various exogenous factors, such as bisphenol A and its halogenated derivatives tetrabromobisphenol A and tetrachlorobisphenol A, can affect adipokine expression. For this reason, we investigated the effects of bisphenol A and its derivatives on the expression of chemerin and its receptor. At low nanomolar concentrations, BPA, TBBPA, and TCBPA decreased chemerin expression and secretion only in granulosa cell tumor COV434 cells by both peroxisome proliferator-activated receptor γ and estrogen receptor signaling pathways. Chemerin treatment had no effect on proliferation of ovarian non-cancer and cancer cell lines. However, we also found evidence to support the inhibition of BPA- and TBBPA-induced cell proliferation by chemerin. Taken together,