Endocrine Disruptor Bisphenol A Increases Cell Migration via an Estrogen Receptor Independent Pathway in Triple Negative Breast Cancer

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Various endocrine disruptors are suggested to contribute to the development of breast cancer. Bisphenol A (BPA) is one of the endocrine disruptors that is known to be an estrogen receptor (ER) agonist due to structural similarities to the estrogen molecule. BPA has also been reported to bind to receptors other than the estrogen receptor such as estrogen-related receptor γ (ERR γ) and G protein-coupled estrogen receptor (GPER), and activate the estrogen receptor independent pathways in breast cancer cell lines that lack the estrogen receptor. Our goal of this study was to examine whether BPA acts independently from the estrogen receptor, and whether it increases the migration via an estrogen receptor independent pathway. MDA-MB-231 is a triple negative breast cancer cell line lacking ERα, Progesterone Receptor, and HER2, and it is known to have mesenchymal characteristics, including rapid migration in culture. MCF-7 is a cell line that expresses ERα; it has epithelial characteristics, including a slower rate of migration in culture. These cell lines were treated with estrogen (100 pM) and BPA (100 nM and 1 µM) for 1 day. Cell proliferation marker C-MYC was determined by Western blot. The protein level of C-MYC increased in both estrogen and BPA treatments in MCF-7 but not in MDA-MB-231. Cell migration was determined by scratch-wound assays. MCF-7 and MDA-MB-231 were treated with estrogen (100 pM) and BPA (100 nM and 1 µM), and observed for 6 hours to measure the rate of migration. The rate of migration was faster in MCF-7 cells in the presence of estrogen than in its absence. The rate of migration was faster in MDA-MB-231 treated with BPA than in cells treated with estrogen or vehicle control. Our findings suggest that BPA increases the proliferation through ER-mediated action, and that an ER-independent mechanism contributes to the increase in the rate of migration by BPA. Further research is necessary to better understand the estrogen receptor independent actions of BPA involving specific receptors like GPER or ERR γ. Supported by NIH R01 AT007036, R03 CA259650, Busch Biomedical Grant, School of Graduate Studies, the Rutgers Office for Research and Economic Development. and New Jersey Health Foundation.