The Effect of Acute and Chronic Bisphenol A (BPA) Exposure on Benign and Malignant Human Thyroid Cells

ABSTRACT

The global incidence of the most prevalent endocrine cancer, thyroid, has been increasing at a rate of 3-5% per year. Lifestyle and environmental factors are now considered to be the primary effectors. Environmental endocrine disruptors such as BPA have been shown to directly affect hormone regulated cancers including prostate and breast. Their effect on thyroid cells is largely unknown although BPA has been shown to disrupt estrogen and thyroid hormone cellular processes. Thus, the effects of acute (A-BPA) and chronic (C-BPA) BPA treatment on cell proliferation and migration of benign (ORI, THJ) and malignant (FRO, SW1736) thyroid cells were determined. MicroRNAs (miR), noncoding RNA, have recently been shown to play a critical role in tumorigenesis. MiR profiles (MiRp) were determined to reveal cellular processes that might by affected by BPA treatment. The effects of BPA removal after chronic exposure (R-BPA) on miRp were also determined. BPA caused concentration dependent changes in cell proliferation in both benign and malignant cells. In contrast, BPA significantly stimulated cell migration in benign but not malignant cells. Further, A-BPA & C-BPA exposure at 10^{-6} and 10^{-8} M differentially altered the miRp of benign and malignant cells. Benign cell miRp was significantly altered by 10^{-8} M BPA whereas in malignant cells, the miRp was significantly altered by the larger 10^{-6} M BPA concentration. Benign cells were found to have distinct miRps with minimal to no overlap in miR for C-BPA and R-BPA whereas in malignant cells extensive overlap existed. BPA treatment altered miRs that have been previously identified as tumorigenic including tumor suppressors (miR-15a, miR-622) and proto-oncogenes (miR-155). Of particular interest, BPA increased miR-146a which inhibits thyroid hormone receptor β, a proposed tumor suppressor. In conclusion, these studies provide the first evidence that BPA alters cellular processes in thyroid cells. Future studies and pending western analysis will identify corresponding genes and proteins regulated by the altered miRs, respectively.