CALIFORNIA SCIENCE & ENGINEERING FAIR
2018 PROJECT SUMMARY

Name(s)

Amy X. Zhong

Project Number

38591

Project Title

Plastics Destroying Your DNA: An Inquiry into the R-Loop Inducing Behaviors of Bisphenol A and Its Implications

Abstract

Objectives/Goals

Bisphenol A (BPA) is a plastic monomer used in nearly every form of plastic packaging. BPA is known to be an estrogen disruptor and imitator, which has massive potential implications for our public health and safety. Estrogen can cause R-loops, a three-stranded nucleic acid structure composed of a single-stranded DNA and a DNA:RNA hybrid, which often causes DNA double-strand breaks (DSBs). I wanted to know whether BPA also poses similar threats to our genomes by causing R-loops in our DNA. Specifically, I wanted to investigate the effects of BPA on ER-positive breast cancer cells, particularly focusing on R-loop formation and cell viability to therapeutics.

Methods/Materials

Cells were treated with BPA and/or 4-hydroxytamoxifen, and cell survival was determined using XTT assays. Growth inhibitory properties were analyzed using GraphPad software to determine the EC50. Cell lysate was prepared from treated cells and run on SDS-polyacrylamide gel electrophoresis for western blot analysis. Nucleic acid from treated cells was spotted onto Nylon membrane using a slot blot apparatus and probed with antibodies. The treated cells were also fixed and probed with antibodies following immunostaining procedures.

Results

MCF7 cells treated with BPA have higher proliferation rates, exhibit a 4-10 fold increase in R-loop formation, elevated levels of DNA double-strand breaks, and high percentages of cells containing micronuclei. I also found that MCF7 cells are more resistant to 4-hydroxytamoxifen agents when cultured in BPA containing medium. The 4-hydroxytamoxifen treatment follows the typical Hormetic dose-response curve, where low doses of 4-hydroxy Tamoxifen promote MCF7 cell growth and at higher doses of 4-hydroxy Tamoxifen inhibit cell growth.

Conclusions/Discussion

My results show that BPA, in concentrations relevant to average consumers and plastics workers around the world, causes R-loop formation, DNA double-strand breaks, and checkpoint activation, and therefore, could be a mutagen. This is particularly important for those who would be more susceptible to these acute responses to BPA, such as children and the elderly. These results call for a more responsible use of plastics, not just for environmental reasons, but also for the potential health risks to our population. Constant DNA damage, especially from double-strand breaks caused by R-loops, is a crucial component in the development of cancer.

Summary Statement

My study analyzes and reveals the effects of Bisphenol A on the formation of R-loops and thus DNA damage, which leads to weakened genomic integrity and a higher risk of cancer.

Help Received

Used lab facility for my own individual project at UC Irvine under the supervision of Dr. Phang-Lang Chen.