CLASTOGENIC POTENTIAL OF XENOBIOTICS ON NORMAL BREAST CANCER CELLS

Nadia Abou-Zeid¹, Ali Ishaque¹, Kelly Mack¹ and Katherine Squibb²

¹University of Maryland Eastern Shore, Department of Natural Sciences, Princess Anne, MD 21853, USA
²University of Maryland School of Medicine, Department of Epidemiology, Baltimore, MD 21201, USA

Abstract: The etiology of breast cancer has been the subject of hundreds of studies. Risk factors belong to different domains: reproductive life, hormonal factors, diet, genetics and exposure to xenobiotics. Environmental data documented widespread exposure to atrazine, arsenic, cadmium and nitrate in Eastern Shore populations. Evidence indicates that the herbicide atrazine may be a direct carcinogen based on its clastogenic effects. Arsenic and Cadmium have both been classified as human carcinogens by IARC. Arsenic has been implicated in the etiology of skin, lung, bladder and liver cancers and Cadmium has been associated with lung and prostate cancers. Nitrate exposure through drinking water has been associated with an increased risk of bladder cancer. This study involves exposing MCF-10A cells to ATZ, Cd, As and NO₃ at environmentally relevant concentrations either individually or in different mixtures to study their clastogenic potential by flow karyotyping. Actively growing cells were exposed for 96 hours, seven days to 75 ppt estrogen, 3, 5, 10 and 10,000 ppb of atrazine, Cd, As and NO₃ respectively, and to 10%, 100%, and 1000% MCL mixtures of afore mentioned chemicals. The mitotic spindle was extracted after 96hrs and one week. After one week exposure, cells were continuously grown in growth media without chemical exposure. The mitotic spindle was extracted after 15, 30 and 45 days to study recovery after chemical exposure. Mitotic cells were selected by the addition of colemid. Flowkaryotyping analysis was conducted with a FACSCalibur at an excitation wavelength of 488nm provided by 5W argon ion laser. The coefficients of variation (CV) of the largest chromosome were analyzed manually. Analysis of variance was determined on the CVs of the various treatments and a least significant difference (LSD) analysis was performed. Level of significance were designated at p <0.05. Results indicated that after 96 hours of exposure, all chemicals including estrogen have clastogenic potential towards MCF10A chromosomes. While after one week of exposure, atrazine, arsenic, cadmium, nitrate, 10% and 1000% mixture have significant chromosomal damage compared to control. The chemical mixture at a concentration as low as 10% MCL did cause chromosomal damage indicating synergistic effect among these chemicals at low concentrations. When chemicals were removed the results showed that in all treated cells, CVs of largest chromosome was significantly different from control after 15 days. After 30 and 45 days, cells treated with 10%, 100% and 1000% mixtures were able to recover. On the other hand, the chromosomal damage persisted after 30 and 45 days exposure to 3 ppb atrazine, 5ppb cadmium, 10 ppb arsenic and 10ppm nitrate. These findings stress on the importance of studying acute and chronic exposures to chemical mixtures in comparison to individual chemicals.

Keywords: Xenobiotics, clastogeneity, flowkaryotyping, largest chromosome.