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MUTATION SPECTRUM OF 1,2-DIBROMO-3-CHLOROPROPANE, AN ENDOCRINE DISRUPTOR, IN THE *lacI* TRANSGENIC BIG BLUE® RAT2 FIBROBLAST CELL LINE

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1,2-Dibromo-3-chloropropane (DBCP), a soil fumigant against nematodes, is a genotoxic carcinogen and also is classified by World Wildlife Fund as endocrine disruptors. DBCP has been extensively studied on genotoxicity, carcinogenicity, and damage in male reproductive-related organs. However, information on precise mechanism of mutagenesis and carcinogenesis of DBCP is yet unknown. Thus the mutation spectrum and mechanism of DBCP was determined in *lacI* transgenic Big Blue® Rat2 fibroblast cell lines. As exposure concentrations, 0.21, 0.39, and 0.75 mM DBCP were adopted, which are approximately correspond to 80, 70, and 50% relative cell survival, respectively. The mean mutant frequencies (MFs, $\times 10^{-5} \pm$ SEM) of medium and 1% DMSO solvent control revealed as 6.43 $\pm$ 0.616 and 5.28 $\pm$ 1.086, respectively. The MFs ($\times 10^{-5} \pm$ SEM) of cells exposed to 0.21, 0.39, and 0.75 mM DBCP revealed as 8.09 $\pm$ 1.02, 10.86 $\pm$ 2.17, and 12.26 $\pm$ 0.79, respectively, with dose-dependent manner. Moreover, MFs in 0.75 and 0.39 mM DBCP-treated groups were increased with statistical significance (ANOVA, $P < 0.05$). The majority of recovered mutations (31/40, 77.5%) after DBCP treatment was single base pair substitutions. Among 31 single base pair substitutions, 25 mutations (62.5%) occurred at G:C base pairs while 6 (15%) at A:T base pairs. The predominant mutation was G:C → A:T transition (40%, 16/40), followed by G:C → T:A transversion (22.5%, 9/40). These results suggest that DBCP is a potent base substitution mutagen, especially, in guanine base. The mechanism of carcinogenic effect of DBCP was assumed by mutations in endogenous genes such as proto-oncogenes, tumor suppressor genes and repair related genes, which will be involved in the initiation stage of carcinogenesis.