THE STUDY OF MUTATION SPECTRUM IN *lac 1* GENE OF TRANSGENIC BIG BLUE[®] CELL LINE FOLLOWING SHORT-TERM EXPOSURE TO 4-NITROQUINOLINE N-OXIDE

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4-Nitroquinoline N-Oxide(4-NQO) is potent mutagen and carcinogen which widely used as positive control in many mutagenic and carcinogenic studies.

To investigate the mutational spectrum of 4-NQO in mammalian system, we used the transgenic Big Blue cell line, derived from a Rat2 embryonic fibroblast. Transgenic Big Blue cell line used in this study harbor very useful lambda shuttle vector containing *lac I* gene as a mutational target. This assay using transgenic cell line is performed by treatment with 0, 0.03125, 0.0625, 0.125ug/ml of 4-NQO, isolation of genomic DNA from cells, exposure the DNA to *in vitro* packaging extract, plating and sequencing.

Our results indicated that 4-NQO induced mutant frequencies increased with dose-dependency about 3 - 7 folds. DNA sequence analysis of *lac I* mutants from the control and 4-NQO treatment group demonstrated that 4-NQO is a base substitution mutagen(93.9% out of entire mutations) and induces increase of transversion(68.8%) of G:C -> T:A(43.8%) compared to control(5% of 35% transversion). From these results, we could assume mutagenic effect of 4-NQO in cancer related genes and confirm that this assay system is very powerful to understand the mechanisms of specific chemical carcinogenesis involved.

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