[BIO42]

Application of comparative genomic hybridization and fluorescence *in situ* hybridization on human glioma cell lines treated with bis[*s*-methyl-β-*n*-(2-furylmethylketone) dithiocarbazato] cadmium(II).

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Comparative genomic hybridization (CGH) and fluorescence *in situ* hybridization (FISH) have become invaluable tools for the diagnosis and identification of the numerous chromosomal aberrations either in haematological malignancies or solid tumors. CGH is a modified *in situ* hybridization technique that allows detection and mapping of DNA sequence copy differences between two genomes in a single experiment whereas FISH is a quantitative analysis of specific chromosomes and genes. In this study, both techniques were used in three gliomas cell lines; A 172 (glioblastoma), U87 MG (astrocytoma grade III) and T98G (glioblastoma multiforme) to investigate the genomic imbalance and to detect cancer-related genes before and after treatment with a new synthetic cadmium compound. Bis[*S*-methyl-β-*N*-(2-furylmethylketone) dithiocarbazato] cadmium(II) (SMDB-Cd) was synthesized at Chemistry Department, Universiti Putra Malaysia and has been shown to have the potential as an anticancer agent. The EC_{50} values for SMDB-Cd on A172, U87MG, T98G and HCN-2 were at 0.7, 0.3, 0.4 and 1.5 µg/ml respectively, compared to tamoxifen which is commonly used to treat brain cancer were at 7.0, 5.0, 4.0 and 6.0 µg/ml. CGH data indicated that these three cell lines have various DNA copy number changes, the most frequent gains of DNA found were at 7p and 13q, and losses of chromosome 9p, 17p and 19q indicate that these regions contain candidate tumor suppressor genes involved in gliomas. Upon treatment with SMDB-Cd at those EC_{50} concentrations, U87 MG was shown to be more sensitive to the compound compared to A172 and T98G. Chromosome 7p was neither shown any changes amplified nor deleted based on the line movement in the entire cell lines. Involvement of one of the important tumor suppressor genes in many human cancers, p53, which is mapped to the short arm of chromosome 17, was then examined. The amplification status of this region was evaluated by using FISH through the locus specific p53 (17p13.1) probe. About 60% of cells were detected to have deletion on one or both of p53 gene in A172 and U87MG however two copy of p53 gene was detected in T98G which means no deletion of p53. After treatment with the SMDB-Cd, p53 level was observed to be amplified in T98G. Increasing of p53 level may have been induced by the action of SMDB-Cd on the cells that inhibit cell growth and lead to cell damage. Thus, the combined use of CGH and FISH provided an efficient method for resolving the origin of aberrant chromosomal material unidentified by conventional cytogenetic analysis.