【S-15】

Enhanced Prediction of Potential Rodent Carcinogenicity by Utilizing Comet Assay and Apoptotic Assay in Combination

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The comet assay has been recently validated as a sensitive and specific test system for the quantification of DNA damage. with 11 substances that demonstrated positive results in at least one test among 4 standard short-term genotoxicity tests, and to evaluate its ability to predict rodent carcinogenicity. Out of The objectives of this study are to investigate the utility of comet assay for detecting mutagens 11 test substances, positive comet results were obtained for colchicine, hydroxyurea and actinomycin D. No effect on DNA migration, determined as the tail moment, was found with theophylline or 2,4-dinitrophenol. Bisphenol A, vinblastine, paclitaxel and p-anisidine appeared cytotoxic clastogens because these induced tail moment at concentrations showing 60% or less cell survival. In addition, among 3 test substances showing the bimodal distribution of DNA damage, which is a characteristic of apoptosis, true apoptosis result was obtained for camptothecin and dexamethasone with the Annexin V affinity assay. With this limited data-set, an investigation into the predictive value of these short-term genotoxicity tests for determining the carcinogenicity showed that comet assay has relatively high sensitivity and superior specificity to other 4 short-term genotoxicity assay. Therefore, our data suggest that comet assay, especially in combination with apoptotic assay, would be a good predictive test to minimize false positives in evaluation of the potential rodent carcinogenicity.