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(BHA) is a suspected human carcinogen. The present study was conducted to determine the role of p16INK4a and cyclin D1 in BHA-induced mouse kidney cell carcinogenesis. BHA was administered by feeding to rats or mice for 16 weeks. Nephrocarcinogenesis was induced in male F344 rats by BHA feeding. In the mouse kidney cell tumor model, BHA was administered by gavage to female ICR mice and the tumors developed in the BHA-treated group. When the expression of p16INK4a and cyclin D1 was evaluated by immunohistochemistry, the expression of p16INK4a was positive in the hyperplastic and dysplastic lesions but negative in the tumor and in a kidney cell line (MCT). In the MCT, up-regulation of p16INK4a expression was also observed in a dose-dependent manner. The expression level of p16INK4a was correlated with the presence of neoplastic lesions or cancer cells in the kidney. The

data indicated that the suppression of cyclin D1 expression due to the up-regulation of p16INK4a may be an early molecular event in BHA nephrocarcinogenesis. The Biblical Submission of Men is a book which attempts to show that there are indeed specific c6a93da74d

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