

The mode of action of tumors induced in the mouse forestomach by oral exposure to benzo[*a*]pyrene (BaP) is likely multifactorial. Clearly hyperplasia of the squamous epithelial cell plays a role (Culp et al., *Carcinogenesis* 21:1433-1449, 2000), but one cannot discount additional strong evidence of mutagenicity. Culp and Beland (*Carcinogenesis* 15:247-252, 1994) showed linearity for formation of r7,t8 ,t9-trihydroxy-c-10-(*N*²-deoxyguanosyl)-7,8,9,10-tetrahydrobenzo[*a*]pyrene (dG-N²-BPDE), the major stable DNA adduct induced by BaP, in forestomachs of mice fed BaP for 21 days at 5 different BP dose levels. Furthermore, there was a dose-response relationship between BaP concentration and forestomach tumors in a 2 year feeding study, in which mice were fed three different levels of BaP in the diet (Culp et al., *Carcinogenesis* 19:117-124, 1998). Lastly, 78% of the forestomach tumors induced by lifetime feeding of BaP had combined *H-ras* and *K-ras* mutations, further indicating that mutation-driven oncogene activation played a role in the etiology of these tumors (Culp et al., *Carcinogenesis* 21:1433-1449, 2000). Taken together these studies reveal that both cell proliferation and a mutagenic mode of action contributed to the induction of forestomach tumors in mice fed BaP in the diet for 21 days to 24 months.