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Gene Expression Profiles in the Fetal Mouse Brain after Etoposide (VP-16) Administration

Chunja NAM, Hirofumi YAMAUCHI, Xi Jun HE, Gye-Hyeong WOO, Byeongwoo AHN, Sang-Yoon NAM, Kunio DOI, Hiroyuki NAKAYAMA

Department of Veterinary Pathology, Graduate School of Agricultural and Life Sciences,The University of Tokyo, 1–1–1 Yayoi, Bunkyo-ku, Tokyo 113-8657, Japan

Abstarc :

The aim of this study was to analyze the response of gene expression caused by etoposide (VP-16) in the fetal mouse brain. Four miligrams/kilogram of VP-16 was intraperitoneally injected into pregnant mice on day 12 of gestation (GD 12). Gene expression profiling of the VP-16-treated fetal mouse brain by DNA microarray was performed. The expression changes of the target genes of p53 were also examined by real-time RT-PCR. VP-16 induced S-phase accumulation, G2/M arrest, and eventually apoptosis of neuroepithelial cells in the fetal brain. DNA microarray analysis revealed that 8 of cell cycle control- and apoptosis-related genes were upregulated and that 5 of DNA damage, repair, replication, and transcription genes were also upregulated in the fetal telencephalons at 4 h after VP-16 treatment (HAT). The results of real-time RT-PCR demonstrated that the expression of *topoisomerase II?* was increased at 4 and 8 HAT. The expression of pro-apoptotic factors such as *puma*, *noxa*, *bax*, and *cyclin G* was also increased from 4 to 12 HAT. These results suggest that VP-16 induces DNA damage, DNA repair, cell cycle alternation, and apoptosis in the fetal mouse brain. In addition, VP-16-induced apoptosis is mediated through the mitochondrial pathway in a p53-related manner. The present study will provide a better understanding of the mechanisms of VP-16-induced fetal brain injury.

Key Word :
apoptosis, cell cycle arrest, etoposide (VP-16), neuroepithelial cell, p53

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