

ZR-75-1 human breast cancer cells to study the mechanism of action of PAHs

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Recent industrial society has human widely exposed to PAHs that are coming from the incomplete combustion of organic material as widespread environmental contaminants.

Biological activities of PAHs are not known although PAHs are considered as carcinogens. PAHs in the mammalian cells affect CYP1A1 gene expression as well as other phase II drug metabolizing enzymes as UDPGT, NMOR etc. The mechanism of action of PAHs has been studied extensively, however it is not clear how PAHs turn on CYP1A1 in human breast cancer.

Our laboratory have been studied the effect of PAHs in the human breast cancer cell line MCF7. In this study, we examined the ZR-75-1 human breast cancer cells as a new system to evaluate bioactivity of PAHs.

ZR-75-1 human breast cancer cell line has been established from the breast cancer patient, has estrogen receptors and progesterone receptors. We have been able to establish long term culture system of this cells then used for the study to observe the effect of PAHs.

We demonstrate that PAHs induced the transcription of an aryl hydrocarbon-responsive reporter vector containing the CYP1A1 promoter and 7-ethoxyresolufin O-deethylase (EROD) activity of CYP1A1 enzyme in a concentration-dependant manner. RT-PCR analyses indicated that PAHs significantly up-regulate the constitutive level of CYP1A1 mRNA.

Apparently, ZR-75-1 cells have Aryl hydrocarbon receptors, therefore it would be good experimental tool to study the cross-talk between PAHs and steroid actions.

[PA4-5] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

The Screening of Hepatic Functional Improvement, Liver Protection and Antifibrotic Effect from Dried Extracts of *Concha Cipangopaludinae*

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Oxidative stress and its consequent lipid peroxidation exert harmful effects, which have been currently involved in the generation of carbon tetrachloride (CCl₄)-induced fibrosis (cirrhosis). In this study, it was investigated whether dried extract of *田螺* (*Concha Cipangopaludinae*; CC) is liver functional improvement, antioxidative and antifibrotic effect under the liver fibrotic (cirrhotic) condition by CCl₄ administration. The female Sprague-Dawley rats were divided into 3 groups (Normal, AC, AC-CC), and were observed for 3 weeks. Except for normal group, the rats rendered fibrotic (cirrhotic) by CCl₄ administration (0.8 ml/rat/week) for 3 weeks. And the prepared CC was treated p. o. 2 ml/day/rats in 3 weeks for AC-CC groups. At the time of sacrifice, the liver, kidney, spleen were weighted and the ratio of organ weight/body weight was calculated. The MDA, the hyp and biochemical parameters (AST, ALT, ALP, t-bili) were measured in sera and liver tissue of rats. In the result, the strong yellow color of urine was observed in all CCl₄-treated group compared with in normal group but jaundice didn't appeared in CCl₄-treated group. Also, mortality of CCl₄-treated group during 3 weeks of observation time is very low (<13%). The ratio of liver/body as well as the weight of liver in CCl₄-treated rats significantly increased compared with that in normal group (p<0.001). The level of clinical parameters in sera of all liver fibrosis (cirrhosis) developed rats were significantly higher than in normal group (p<0.001 ~ 0.05). Especially the value of BUN, ALP, t-bilirubin in AC-CC group showed 20.9%, 19.6%, 47.9% lower than that in AC group. The content of hyp in CCl₄-treated rats was significantly higher than in normal group (p<0.001 ~ <0.05), and showed 12.2% lower value in the AC-CC group than in AC group (p<0.05). The product of lipid peroxidation (MDA) in sera and liver tissue significantly increased under the fibrotic (cirrhotic) condition (p<0.001 ~ <0.05). Especially the MDA value of AC-CC group in sera significantly 46.5% decreased compared with that of AC group (p<0.05), and the MDA value of AC-CC in liver tissue showed 21.4% lower than that of AC group. In the histological change, the excessive lipid droplet, septum formation, lysis of cytoplasm and crashed down of nucleus were observed in CCl₄-treated group compared with in normal group. In conclusion, *Concha Cipangopaludinae* can be improved hepatic function, and may have effect of liver protection and antifibrosis.

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