Dimethylnitrosamine-induced Experimental Liver Cirrhosis in Rats

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The effect of DA-9601, an Artemisia asiatica extract, on hepatic fibrogenesis or fibrosis was evaluated using experimental liver cirrhosis induced in rats by the administration of dimethylnitrosamine (DMN) intraperitoneally three times a week for 2 weeks. DA-9601 at a dose of 30 or 100 mg was orally administered to DMN treated rats daily for 3 weeks from 1 week before the DMN. Seven days after last DMN treatment, the animals were sacrificed in order to assess the degree of hepatic fibrogenesis and damage using serum biochemical, hepatic biochemical and histopathological examination. Treatment of DA-9601 significantly reduced the elevation of serum ALT, AST and total histological score on the damaged liver ($p<0.05$). The hepatic levels of collagen and malondialdehyde (MDA), an indicative of lipid peroxidation, in DA-9601 treated rats were decreased significantly when compared to DMN-treated control ($p<0.05$). In addition, immunohistochemical examination showed that DA-9601 reduced the disposition of type I collagen in the liver than DMN-treated control. These results suggest that DA-9601 may be useful to prevent the aggravation of liver cirrhosis through the inhibition of lipid peroxidation and disposition of collagen.

[OC-1] [04/21/2000 (Fri) 10:40 - 10:55 / Rm B113, Bldg 26]

Bacterial injection induced syntheses of N-b-alanyldopamine and DOPA decarboxylase in the hemolymph of coleopteran insect, Tenebrio molitor larvae

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Injection of *Escherichia coli* into larvae of the coleopteran *Tenebrio molitor* resulted in the appearance of a dopamine-like substance on the electrochemical detector. To characterize this dopamine-like substance, we purified it to homogeneity from the immunized hemolymph and determined its molecular structure to be N-b-alanyldopamine (NBAD) by the liquid chromatographic/tandem mass spectrometric (LC/MS) method. Chemically synthesized NBAD showed the same retention time on HPLC as the purified NBAD from immunized larvae. To elucidate the molecular mechanism of NBAD synthesis in vivo, we examined the enzyme activity of DOPA decarboxylase (DDC) against *E. coli* injected hemolymph of *T. molitor* larvae. The enzyme activity of DDC dramatically increased about 8 h after injection; DDC activity of injected larvae being 10-times higher than naive larvae after 24 h. To evaluate the extent of quantitative changes of DDC in *Tenebrio* response to bacterial challenge, *Tenebrio* DDC was purified to homogeneity from the whole larvae and a cDNA clone for *Tenebrio* DDC was isolated. RNA blot hybridization revealed that expression of the DDC gene was transiently activated from 3 to 8 h after *E. coli* challenge. Immunoprecipitation experiments showed that *Tenebrio* DDC was detected from 8 to 24 h in *E. coli*-injected larval extract. Thus, bacterial injection into *T. molitor* larvae might induce transcriptional activation of a DDC gene, and then synthesis of NBAD. The synthesized NBAD might be used as a substrate by phenoloxidase during melanin synthesis in the humoral defense response or the melanotic encapsulation reaction of the cellular defense response. (*Eur.J.Biochem.*in press, 2000)

[OC-2] [04/21/2000 (Fri) 10:55 - 11:10 / Rm B113, Bldg 26]

BCL-2 ATTENUATES HYDROGEN PEROXIDE- AND BETA-AMYLOID-INDUCED OXIDATIVE PC12 CELL DEATH VIA NF-KAPPA B ACTIVATION

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