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Meeting abstract

iNOS expression and levels of nitric oxide in a hepatocarcinogenesis model of p47-NADPH knockout mice

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Background

Nitrosamines occur in traces in food or may be generated endogenously. They are one chemical factor involved in hepatocarcinogenesis, a process mediated by genotoxic and cytotoxic events. Ethanol is a widely consumed hepatotoxic agent and has been shown to increase hepatocarcinogenesis in humans. Both compounds can activate Kupffer cells to produce cytotoxic reactive oxygen species (ROS) and growth promoting cytokines. Therefore, p47-NADPH oxidase knockout (phox$^{-/-}$) mice were thought to be protected from hepatocarcinogenesis. We found that tumor formation in phox$^{-/-}$ took place, although to a lower extent than in wild type mice.

Objectives and methods

To examine whether reactive nitrogen species alternatively could be responsible for carcinogenesis in these livers. Experimental model: diethylnitrosamine (DEN) [1]; quantitative RT-PCR of iNOS mRNA; sum of nitric oxides by Griess reaction.

Results

iNOS expression was increased in phox$^{-/-}$ as compared to wt mice. This is in agreement with a higher level of iNOS protein 24 hrs after DEN-treatment in phox$^{-/-}$ mice. However, total nitric oxide levels did not differ significantly between both strains. Correlation analysis of iNOS mRNA and NO levels on a per liver basis did not reveal significant associations.

Discussion

We conclude that although iNOS appears to be induced in phox$^{-/-}$ mice the resulting nitric oxides may no longer be accessible for biochemical measurements at later times after treatment.

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References

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