[PA4-7] [ 04/17/2003 (Thr) 14:00 - 17:00 / Hall P ]

## Effects of 17b-Estradiol on the Inducible Nitric Oxide Synthase Expression in macrophages

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In some tissues 17b-estradiol (E2) is known to increase endothelial NOS expression. In the present study we examined the effects of E2 on estrogen receptors (ERa and b) and inducible nitric oxide synthase (iNOS) expression and analyzed the mechanisms in rat peritoneal macrophages. Reverse-transcription polymerase chain (RT-PCR) and transient transfection experiments using a reporter plasmid that contained a luciferase gene under the transcriptional control of an estrogen responsive elements revealed that peritoneal macrophages are responsive to E2 and express both ERa and ERb mRNAs. Incubation with E2 leads to an increased ERb mRNA expression. When rat peritoneal macrophages were incubated with physiological concentrations of E2, E2 induced a dose-dependent increase in NO production. E2 significantly affected secretion at concentrations levels of more than 10-11 M, and its maximum effect was at a concentration of 10-8 M. RT-PCR reactions showed that increases in NO secretion were due to an increase in iNOS mRNA. Coincubation with ICI 182.780, an estrogen-receptor antagonist, inhibited the influence of E2 on NO production and iNOS expression. Thus E2 stimulated iNOS expression by a classic receptor?mediated pathway. We here prove that E2 increases the iNOS expression in macrophages and this effect appears to be the consequence of ER activation.

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## Chemopreventive Effect of Retinoids on Cellular NF-kappaB Activity Induced by Alkylating Carcinogens in Human Epidermal Keratinocytes

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Retinoids have been shown to be effective in suppressing tumor development in chemical carcinogens such as *N*-nitroso-*N*-methylurea (NMU) and *N*-nitroso-*N*-ethylurea (NEU) induced mammary tumors in various animals. However, retinoids-mediated chemopreventive process, linked to transcription factor NF-kappaB activation on chemoprevention has yet to be studied. To elucidate the implication of NF-kappaB activation in chemopreventive role of retinoids, their effect on cellular NF-kappaB activity induced by known alkylating chemical carcinogens, i.e., NMU and NEU in human transfectant SCC-13 cells was investigated. In a cell-based assay system for the quantitative measurement of the level of NF-kappaB activity, all-*trans* retinoic acid and 13-*cis* retinoic acid showed remarkable downregulation of the cellular NF-kappaB activities upregulated by NMU (5 μM) and NEU (5 μM) in a dose-responsive manner (1, 5, 10 mM). Both retinoids had equivalent downregulatory effects on NF-kappaB activation. These results led to suggest the hypothesis that the chemopreventive effect of retinoids may be mediated by down-regulated activation of the NF-kappaB and implicated by the activation of NF-kappaB in human skin cells.