PC12/PS2w cells. These findings indicate the PC12/PS2m is more sensitive than PC12/PS2w cells in response to apoptotic stimuli, L-glutamate and Aβ stimuli.

[PA1-53] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Btg-1 Induction by Oxidative Stress

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B cell translocation gene-1 (Btg-1), originally discovered from chromosomal translocation in chronic B-cell lymphocytic leukemia, belongs to the APRO family. Btg-1 exhibit antiproliferative function, being expressed during the G_0/G_1 transition phase of cell cycle. Btg-1 is fully expressed in quiescent and differentiated cells, while the protein expression decreases as the cell progresses through the cell cycle. Previous studies from this laboratory have shown that Btg-1 is induced by protein calorie malnutrition, a condition of *in vivo* oxidative stress. In the present study, we investigated the effects of oxidative stress on the activation of Btg-1, the role of Btg-1 in the expression of inflammatory mediators and the responsible signaling pathway(s) in Raw264.7 cells. Btg-1 was induced by sulfur amino acid deprivation and other oxidative stress (i.e. *t*-BHQ, SIN-1 and BSO) in the cells. Btg-1 induction was controlled by the signaling pathways involving PI3-kinase and p70S6 kinase, but not MAP kinases. Confocal microscopic analysis using pEGFP-Btg1, which encodes GFP-Btg-1, revealed that oxidative stress caused cytoplasmic Btg-1 to translocate into the nucleus. Oxidative stress reduced the expression of iNOS in macrophages, Overexpression of Btg-1 also inhibited iNOS induction, suggesting that the induction of Btg-1 by oxidative stress may affect expression of the gene. These results provide evidence that oxidative stress induces Btg-1 in macrophages and leads to the inhibition of iNOS expression. The approaches to the modulation of cell function in association with Btg-1 may allow us to identify the pharmacological targets for immune modulation or therapeutic advantages. (Supported by the fund of Ministry of Welfare and Public Health, 02-PJ1-PG3-21403-0003)

[PA1-54] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Preventive effect of whole bee venom on arthritis and its mechanism: inhibition of COX-2 and iNOS expression through inactivation of $NF-_kB$

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Bee venom (BV) has been utilized to relieve pain and to treat inflammatory diseases such as rheumatoid arthritis (RA). BV contains a variety of different peptides including melittin, apamin, adolapin and mast cell degranulating (MCD) peptide. In addition, it also contains enzyme (i.e. phospholipase A2), biologically active amines and non-peptide components. However, it is likely that a complex stimulation effect of individual components of BV may be responsible for anti-inflammatory effect. Although the treatment of bee venom (BV) has been reported to show an anti-arthritis effect in vivo, the mechanism by which BV-induced anti-arthritis effect has been

not reported yet. Therefore, in the present study we investigated anti-inflammatory effect of whole BV extract in the arthritis animal model, and further investigated the mechanism of BV-induced anti-inflammatory effect in a murine marcrophage cell line Raw 264.7 cells. The present data showed that whole BV extract has a preventive effect on the mycobacterium butyricum-induced arthritis, and blocks lipopolysaccharide (LPS)-induced induction of COX-2, PLA2 and iNOS expression, and the production of NO and PGD2 through inactivation of $NF-_kB$.

[PA1-55] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Effects of glycine on the development of tolerance to and physical dependence on morphine in mice

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This study was performed to investigate the effects of glycine on the development of tolerance to and physical dependence on morphine. Repeated adminstration of morphine developed tolerance and physical dependence. Glycine (100, 200 and 400 mg kg^{-1} i.p.) was administered intraperitoneally to mice for 7 days once a day 30 minutes prior to the morphine (10 mg kg^{-1} s.c.). Analgesic resposes were estimated at 0. 30. 60. 90, 120 minutes by the tail flick methods 24 hours after the final injection of morphine. The inhibitory degree of morphine tolerance development of the test morphine (10 mg kg^{-1} s.c.) by i.p. administration of glycine was evidenced by the increase in analgesic response to morphine (5 mg kg^{-1} s.c.). Glycine inhibited the development of tolerance to morphine.

In addition, we separately measured the naloxone (5 mg kg^{-1} i.p.)-precipitated withdrawal sign (jump) in mice that had received the same morphine (10 mg kg^{-1} s.c.) for 7 days. Glycine (100, 200 and 400 mg kg^{-1} i.p.) inhibited naloxone-precipitated withdrawal in morphine dependent mice.

These results sugest that glycine might be useful the prevention or treatment of morphine tolerance and physical dependence.

[PA1-56] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Inhibition of glycine on morphine-induced hyperactivity, reverse tolerance and postsynaptic dopamine receptor supersensitivity in mice

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We examined the effects of glycine on the morphine-induced hyperactivity, reverse tolerance and postsynaptic dopamine receptor supersensitivity in mice. A single administration of morphine (10 mg kg^{-1} s.c.) induced hyperactivity as measured in mice. The morphine-induced hyperactivity was inhibited dose-dependently by the pretreatment with glycine (100, 200 and 400 mg kg^{-1} i.p.). In addition, repeated administration of morphine (10 mg kg^{-1} s.c.) to mice once a day for 7 days causes an increase in motor stimulation induced by a subsequent morphine dose, an effect known as reverse tolerance or sensitization. Glycine (100, 200 and 400 mg kg^{-1} i.p.) also inhibited morphine-induced reverse tolerance, in a dose dependent manner. Mice that had received 7 days-repeated administration of morphine also developed postsynaptic dopamine