Relationship between activation of transcription factors and neurite outgrowth of embryonic midbrain cells exposed by ochratoxin A

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Ochratoxin A has been known to produce microcephaly in animals and cultured whole embryos. Alteration of apoptosis and/or differentiation of the embryonic brain were proposed as an underlying mechanism responsible for the induction of microcephaly. In previous our study, inhibition of differentiation of cultured embryonic cells was found. In this study, we extended our previous study to examine possible mechanism of the inhibitory effect of ochratoxin A. In the view of the emerging important role of peroxisome proliferator activated receptor-gamma (PPAR-γ) and transcription factors in cell differentiation, we investigate (a) possible mechanism(s) for the ochratoxin A's inhibition of cell differentiation may be through inactivation of transcription factors and/or PPAR-γ expression. Twelve-day embryo midbrain were cultured in Dulcecco's modified Eagle's medium and Ham's F-12 (1:1) mixture in the presence of various doses of ochratoxin A and PPAR-γ agoinst, 15-deoxy-Δ 12,14-prostaglandin J2. Cell differentiation was assessed by the neurite outgrowth. Activation of AP-1 and NF-κB was increased by the extension of cell culture, which resulted in increase of neurite formation. Ochratoxin A induced cytotoxicity and inhibited neurite outgrowth dose dependently. The concomitant decrease of neurite outgrowth and transcription factors in addition to PPAR-γ expression by ochratoxin A exposure suggest that AP-1 and NF-κB signals may be important in the neurite formation, and neurotoxic mechanism of ochratoxin A.

[PB3-7] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

The effects of Hwang-Ryun-Hae-Dok-Tang (Huang-Lian-Jie-Du-Tang) on a focal model of transient cerebral ischemia in rats

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Hwang-Ryun-Hae-Dok-Tang (HRHDT), a tradtional Chinese medicine against ischemic insults induced by transient cerebral ischemia was investigated in rats. There have been many reports on the pharmacological effects of HRHDT with respect to gastrointestinal disorders, inflammation, acute liver injury, and other cardiovascular disease. This study was designed to determine whether HRHDT treatment after ischemia exerts neuroprotective effects after ischemic insults and, if so, which kind of medicinal herbs is the main contributing ingradients. Rats were subjected to 120 min of focal cerebral ischemia by means of the filament method of middle cerebral artery occlusion (MCAo). After 120 min transient MCAo, reperfusion was achieved by pulling the filament out of the ICA under the anesthetic conditions. After 22 hours of reperfusion, infarct size was measured and neurological function was quantified. The functional significances of the protecting effects of HRHDT on ischemic brain insults are under study.[Supported by MOHW grant HMP-00-CO-04-0004]

[PB3-8] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Activation of transcription factors in peroxisome proliferator-gamma agonist - induced neurite outgrowth in cultured PC-12 cells

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The peroxisome proliferator-activated recetor-γ(PPAR-γ), a member of the nuclear hormone receptor superfamily, is activated by structually distinct ligands, including anti-diabetic thiazolidinediones, several non-steroidal anti-inflammatory drugs (NSAIDs), and 15-deoxy-Δ12,14-prostaglandin J2 (15 d-PGJ2). Activation of PPAR-γ has been found to promote neurite outgrowth of differentiating PC 12 cells. However, it is not clear yet as to what signaling pathway is required for the promotion of neurite outgrowth. Since transcription factors AP-1 and NF-κB are known to play a predominant role in the cell differentiation, this study was designed to investigate the activation of AP-1 and NF-κB during the neurite outgrowth in cultured PC-12 cells, a useful system for the study of differentiation function. Activation of AP-1 and NF-κB was concomitantly increased by the increase of neurite formation by nerve growth factor with/without 15-deoxy PGJ2. In addition, ochratoxin A, which blocked neurite formation, inhibited activation of AP-1 and NF-κB. These data show that AP-1 and NF-κB signals may be important in the neurite formation. Apoptosis during neurite outgrowth, role of PPAR-γ, and crosstalk between PPAR-γ expression and activation of transcription factors are being investigated.

[PB3-9] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

NO modulates the anxiolytic effects of acute morphine in the plus-maze

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This experiment was performed to investigate whether NO precursor (L-arginine), NO donor (S-nitroso-N-acetlypenicillamine, SNAP) and NO synthase inhibitors [L-NG-nitro-arginine methyl ester (NAME) and NG-nitro-L-arginine (NOARG)] modulate morphine-induced anxiolytic effect in the plus maze. L-arginine (200 and 300 mg/kg, i.p) and SNAP (4, 8 and 10 mg/kg, i.p) reduced the anxiolytic effect of morphine (20 mg/kg, s.c). NAME (10, 20 and 40 mg/kg, i.p) and NOARG (10, 15 and 20 mg/kg, i.p) enhanced the anxiolytic effect of morphine (20 mg/kg, s.c). L-arginine and SNAP increased the morphine-induced locomotor activity. NAME decreased the mophine-induced locomotor activity but NOARG did not modify the morphine-induced locomotor activity. Therefore, the results suggest that the anxiolytic effects of morphine can be modulated by NO system in independent manner of locomotor.

Poster Presentations - Field B4. Immunology

[PB4-1] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Effect of B30-MDP, a MDP derivative, as an adjuvant for tumor vaccine

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The effect of B30-MDP, a derivative of muramyl dipeptide (MDP), on enhancement of antitumor