## 5-Fluorouracil stabilizes the IκBα in stomach cancer cells

Jung IDo, Yang SY, Lee KB1, Lee HY

Department of Pharmacology, Department of Biochemistry<sup>1</sup>, College of Medicine, Konyang University, Nonsan 320-711

The antimetabolite 5-fluorouracil (5-FU) is one of the more prominent clinical antitumor agents for stomach and colorectal cancers. In the present study, we characterized the effects of 5-FU on nitric oxide (NO) production by stomach cancer cells, NCI-N87. IFN- $\gamma$  increased the production of NO and pretreatment of 5-FU inhibited the production of NO in response to IFN- $\gamma$  in a dose dependent manner. The increased expressions of iNOS mRNA and protein by IFN- $\gamma$  were completely blocked by 5-FU through the inactivation of NF- $\kappa$ B and the stabilization of I $\kappa$ B $\alpha$  in stomach cancer cells. These data suggest that the efficacy of 5-FU may include the inhibition of NO production.

[PA1-12] [ 04/20/2001 (Fri) 10:30 - 11:30 / Hall 4 ]

## INFLUENCE OF BROMOCRIPTINE ON THE BLLOD PRESSURE AND VASCULAR SMOOTH MUSCLE IN RATS

DONG-YOON LIMO, OK-MIN KIM

Department of Pharmacology, College of Medicine, Chosun University, Gwangju501-759, Korea

INFLUENCE OF BROMOCRIPTINE ON THE BLLOD PRESSURE AND VASCULAR SMOOTH MUSCLE IN RATS

DONG-YON LIM, OK-MIN KIM, Department of Pharmacology, College of Medicine, Chosun University, Gwangju 501-759, Korea

Bromociptine, a dopamine D2 receptor agonist, causes hypotensive effects through stimulation of dopaminergic D2 receptors (Roquebert et al., 1990; Lahou & Demenge, 1991; Luchsinger et al., 1995; Blanco et al., 1997; Luchsinger et al., 1998; Lahlou, 1998; Lahlou & Duarte, 1998). However, bromocriptine is also known to block postsynaptic α-adrenoceptors (Simonic et al., 1978; Gibson & Samni, 1979; Montastruc & Montastruc, 1982). Therefore, the present study was attempted to examine the effects of bromocriptine on contractile responses evoked by stimulation of adrenergic α1receptors and membrane depolarization in the isolated aortic strips as ell as on arterial blood pressure of the rat and to clarify the mechanism of its action. Phenylephrine (an adrenergiα1-receptor agoc nist) and high potassium (a membrane-depolarizing agent) caused greatly contractile responses in the isolated aortic strips, respectively. This phenylephrine (1~10 μM)-induced contractile responses were greatly inhibited in the presence of bromocriptine (2.5 µM) while high potassium (35~56 mM)-induced contractile responses not affected. Also, under the presence of apomorphine (1.6 µM), an agonist of dopamine D2 receptors, phenylephrine (10 µM)-induced contractile response was attenuated but high potassium (56 mM)-induced contractile response not affected. Bromocriptine (5-50 μg/kg) given into a femoral vein of the normotensive rat produced a dose-dependent depressor response. This hypotension induced by intravenous bromocriptine was greatly inhibited by the pretreatment with phentolamine (2 mg/kg, i.v.). Interestingly, the infusion of a moderate dose of bromocriptine (15 цд/kg/30min) made a significant reduction in pressor responses induced by intravenous norepinephrine.

Taken together, these experimental results demonstrate that intravenous bromocriptine causes a dose-dependent depressor action in the anesthetized rat at least partly through the blockade of adrenergic  $\alpha1$ -receptors, and that bromocriptine also causes vascular relaxation in the isolated aortic strips of the rat via the blockade of adrenergic  $\alpha1$ -receptors, in addition to the activation of dopaminergic D2 receptors.