5-Fluorouracil stabilizes the IκBα in stomach cancer cells

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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-γ increased the production of NO and pretreatment of 5-FU inhibited the production of NO in response to IFN-γ in a dose dependent manner. The increased expressions of iNOS mRNA and protein by IFN-γ were completely blocked by 5-FU through the inactivation of NF-κB and the stabilization of IκBα in stomach cancer cells. These data suggest that the efficacy of 5-FU may include the inhibition of NO production.

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

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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 α1-receptors 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 μg/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 α1-receptors, and that bromocriptine also causes vascular relaxation in the isolated aortic strips of the rat via the blockade of adrenergic α1-receptors, in addition to the activation of dopaminergic D2 receptors.