5-Fluorouracil Stabilizes the IκBα in Stomach Cancer Cells

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Background The antimitabolite 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.

Methods 1. We examined the effects of 5-FU on nitric oxide production by NCI-N87 cells stimulated with IFN-γ.
2. We tested whether the inhibition of NO production by 5-FU in response to IFN-γ is caused by its effect on iNOS mRNA and protein expression.
3. We treated NCI-N87 cells with 40μM 5-FU to investigate whether 5-FU inhibits the activation of NF-κB by IFN-γ in stomach cancer cells.
4. We investigated whether 5-FU caused the stabilization of IκBα and prevented the translocation of p65 to the nucleus by preparing cytoplasmic extracts from 5-FU treated cells and analyzing the extract using gel electrophoresis followed by Western blot with IκBα and p65-specific polyclonal antibodies.

Results 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.

Conclusion Treatment of stomach adenocarcinoma cells with 5-FU strongly inhibited the production of nitric oxide in response to IFN-γ through stabilization of IκBα and inactivation of IKK.