Abstract: 
Trefoil factor 1 (TFF1) is expressed in the normal superficial epithelium of the stomach and is implicated in the maintenance of gastric epithelial structure and function. During gastric carcinogenesis, in which pro-inflammatory cytokines play a crucial role, its expression level decreases suggesting a role as tumor suppressor factor. We have compared expression of TFF1 in gastric mucosa from cancer patients, in which several degrees of inflammatory infiltrate are present, with that in normal mucosa from non-cancer patients without infiltrating inflammatory cells. TFF1 is less expressed in the superficial gastric epithelium from cancer patients than in that from normal individuals in which the nuclear factor (NF)-κB pathway is not activated. We analyzed TFF1 expression in ex vivo samples of gastric mucosa from cancer patients, and in MKN45 gastric cancer cell line after exposure to proinflammatory cytokines interleukin (IL)-1? or tumor necrosis factor (TNF)-?, that activate the NF-κB pathway. We found that IL-1? and TNF-? activate the NF-κB pathway, as reflected in the nuclear expression of p65 and the activation of p-IκB?, and downregulate TFF1 expression after 1 or 2 h of exposure. Moreover, cells in the superficial gastric epithelium in ex vivo samples co-expressed TFF1/p65 at cellular level, whereas tumor cells did not. In summary, downregulation of TFF1 expression during gastric neoplastic transformation is associated with...
activation of the NF-κB pathway through IL-1β or TNF-α, but other regulatory mechanisms might also be involved.