Tumor Necrosis Factor-Alpha Effects on Rat Gastric Enterochromaffin-Like Cells

Abstract:
Gastric enterochromaffin-like (ECL) cells are histamine-producing cells in the gastric epithelium which are responsible for the peripheral regulation of acid secretion. The gastric mucosa is frequently infected with Helicobacter pylori, leading to increased levels of the pro-inflammatory cytokine tumor necrosis factor-α (TNF-α). The aim of our current study was to identify the effect of TNF-α on programmed cell death. ECL cells were isolated from the rat corpus mucosa to a purity >90%. TNF receptor and adapter protein presence were determined using RT-PCR, Western blot and immunocytochemistry. Apoptosis was measured by Tdt-mediated dUTP nick end labeling reaction and by DNA fragmentation based ELISA. Isolated ECL cells were found to express the TNF receptor p55 and IFN-γ receptor, but not the TNF receptor p75 or CD95. TNF-α (25 ng/ml) increased apoptosis in ECL cells approximately 4-fold, IFN-γ had no effect. Western blot analysis revealed that TNF-α caused degradation of IκBα within 10 min. EMSA demonstrated that TNF-α led to increased DNA-binding activity of NFκB and that proteasome inhibitors counteracted NFκB activation. Proteasome inhibitors, specific antisense oligodeoxynucleotides against the p65 subunit of the NFκB complex and the NO synthase inhibitor NG-monomethyl-L-arginine completely prevented TNF-α-induced apoptosis. Our data suggest that TNF-α induces apoptosis of isolated gastric ECL cells via activation of...
NFκB and the generation of NO.

Stichworte:
Apoptosis; Electrophoretic mobility shift assay; Interferon-γ; Nuclear factor κB; Inducible nitric oxide synthase; N\(^{G}\)-Monomethyl-L\(\text{arginine aceta}

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