Adenocarcinoma esofageal de Barrett A inibição do MAPK e do PI3K inibem a proliferação de células do adenocarcinoma esofageal

MAPK and PI3K inhibition reduces proliferation of Barrett’s adenocarcinoma in vitro.

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Abstract

BACKGROUND: Esophageal adenocarcinoma often arises from Barrett's esophagus. Mitogen-activated protein kinase (MAPK) and phosphatidylinositol 3-kinase (PI3K) play critical roles in cell survival. We hypothesized that inhibition of these pathways in Barrett’s adenocarcinoma would decrease cell proliferation and alter apoptosis in vitro.

MATERIALS AND METHODS: Two Barrett’s-associated adenocarcinoma cell lines, SEG-1 (wild-type p53) and BIC-1 (mutant p53), were treated with MAPK (U0126) and PI3K (LY294002) inhibitors at 20 microm concentrations. After 24 and 72 h, cell viability was measured by MTT assay. Apoptosis and necrosis were evaluated by the Annexin V-FITC assay. Statistical analysis was performed by ANOVA.

RESULTS: LY294002 and U0126 treatment produced significant reductions (range 15.7 to 62.0%, P < 0.05) in cellular proliferation at both 24 and 72 h in the SEG-1 cells. BIC-1 cell viability was reduced (39.3 to 56.4%, P < 0.05) at 72 h. Both early and late apoptotic activity were significantly increased (P < 0.05) in the SEG-1 cells using both inhibitors. Necrosis was significantly reduced (P < 0.05) using both inhibitors. No changes in either early or late apoptosis or necrosis were observed in the BIC-1 cells.

CONCLUSIONS: Herein, we report significant antiproliferative effects against Barrett’s adenocarcinoma by MAPK and PI3K inhibition in vitro. Pro-apoptotic mechanisms prevail in the wild-type p53 cells. Further investigation is warranted to advance the clinical treatment of this devastating disease.

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