Abstract:

Pancreatic cancer patients have an abysmal prognosis because of late diagnosis and lack of therapeutic options. Pancreatic intraepithelial neoplasias (PanINs), the precursor lesions, are a potential target for chemoprevention. Targeting eicosanoid pathways is an obvious choice because 5-lipoxygenase (5-LOX) has been suggested as a tumor promoter in pancreatic carcinogenesis. Here we provide evidence that 15-lipoxygenase-1 (15-LOX-1) expression and activity may exert antitumorigenic effects in pancreatic cancer. Reverse transcription-polymerase chain reaction (RT-PCR) and Western blot analysis showed absence or very weak expression of 15-LOX-1 in all pancreatic cancer cell lines tested. 15-LOX-1 was strongly stained in normal ductal cells, tubular complexes, and centroacinar cells, but no staining was seen in islets, cancer cells, PanIN lesions, or in tumor cells in lymph node metastases, indicating that 15-LOX-1 expression is lost during tumor development in human pancreas. Overexpression of 15-LOX-1 in pancreatic tumor cells or treatment with its arachidonic acid-derived metabolite resulted in decreased cell growth. These findings provide evidence that loss of 15-LOX-1 may play an important role in pancreatic carcinogenesis, possibly as a tumor suppressor gene. Thus, induction of 15-LOX-1 expression may
be an attractive option for the prevention and treatment of pancreatic cancer.