Expression pattern and functional relevance of epidermal growth factor receptor and cyclooxygenase-2: novel chemotherapeutic targets in pancreatic endocrine tumors?

OBJECTIVES: Pancreatic endocrine tumors represent morphologically and biologically heterogeneous neoplasms. Well-differentiated endocrine tumors (benign or of uncertain behavior) can be distinguished from well-differentiated and poorly differentiated endocrine carcinomas. Although many well-differentiated endocrine carcinomas show rather low rates of tumor growth, more than two-thirds of pancreatic endocrine carcinomas display distant metastases at the time of diagnosis. As the currently applied therapies beyond surgery only achieve partial or complete response rates of approximately 15%, additional chemotherapeutic targets are needed, especially in the therapy of inoperable and progressive pancreatic endocrine carcinomas. METHODS: The expression of epidermal growth factor receptor (EGFR) and cyclooxygenase (COX)-2 were investigated in 110 clinically and pathomorphologically well-characterized pancreatic endocrine tumors, using immunohistochemistry and immunoblot analyses. Functional tests were performed using the human pancreas carcinoid cell line BON and the mouse insulinoma cell line beta-TC-3. RESULTS: The expression of EGFR correlated significantly with the grade of malignancy, increasing
from low rates of expression in benign tumors and tumors of uncertain behavior to high rates of expression in well- and poorly differentiated endocrine carcinomas. The expression of COX-2 was independent of the malignant potential, but was more frequently expressed in primary tumors than in metastases. The treatment of the human pancreas carcinoid cell line BON and the mouse insulinoma cell line beta-TC-3 with EGFR and COX-2 inhibitors (monotherapy and combined therapy) resulted in a significant, dose-dependent reduction of cell viability coupled with increased apoptosis.

CONCLUSIONS: Our results suggest that EGFR and COX-2 may represent useful additional chemotherapeutic targets in pancreatic endocrine tumors.