Ex vivo chemosensitivity testing and gene expression profiling predict response towards adjuvant gemcitabine treatment in pancreatic cancer.

Abstract:
Efficacy of chemotherapy for pancreatic cancer may be improved by tailoring it to individual chemosensitivity profiles. Identification of nonresponders before initiation of treatment may help to avoid side effects. In this study, primary pancreatic cancer cells were isolated from 18 patients undergoing pancreaticoduodenectomy for pancreatic cancer. Eight commonly used pancreatic cancer cell lines were used as controls. Ex vivo chemosensitivity for gemcitabine, 5-fluorouracil, mitomycin-C, cisplatinum, oxaliplatinum, paclitaxel and a combination of gemcitabine with oxaliplatinum or mitomycin-C was determined using a cellular ATP-based tumour chemosensitivity assay (ATP-TCA). Quantitative real-time-polymerase chain reaction was performed to determine RNA expression levels of genes implicated in chemoresistance. Chemosensitivity towards cytotoxic agents was highly variable in primary pancreatic cancer cells and pancreatic cancer cell lines. ATP-TCA results for gemcitabine correlated to the tissue expression of human equilibrative nucleoside transporter-1 (hENT1). Time to relapse in patients with gemcitabine-sensitive tumours was significantly higher than in patients with chemoresistant pancreatic cancers (P=0.01; 71 vs 269 days). Furthermore, time to relapse in
gemcitabine-treated patients was related to hENT1 expression (P=0.0067). Thus, chemosensitivity testing using ATP-TCA in pancreatic cancer is feasible and correlated with time to relapse in gemcitabine-treated patients. This suggests that ATP-TCA testing could be used as a decision-making tool in the adjuvant treatment of pancreatic cancer.