Expression of the Coxsackie and Adenovirus Receptor (CAR) in Pancreatic Cancer and Normal Pancreatic Tissue

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Background: Pancreatic cancer has a poor prognosis. Because the response to existing therapies is limited, gene therapy may offer a new approach to treatment. Efficient adenovirus infection of target cells depends upon the presence of the Coxackie and adenovirus surface receptor CAR.

Aim: To evaluate the potential efficacy of adenoviral therapy in pancreatic cancer, we evaluated expression of CAR in human pancreatic cancer cell lines and archival tissues of pancreatic cancer and normal pancreas.

Method: Surface CAR expression in 10 human pancreatic cancer cell lines was analysed by flow cytometry following treatment with a polyclonal rabbit anti-CAR antibody. CAR expression was correlated with the efficiency of transduction of these cell lines with recombinant Ad5CMVEGFP virus. Using the same antibody, immunostaining was performed on tissue microarrays containing 188 pancreatic ductal adenocarcinomas and 68 matched controls.

Results: The level of surface CAR expression varied amongst the pancreatic cancer cell lines, and correlated with their susceptibility to adenoviral transduction. Immunostaining for CAR was absent in 103 (55%) of adenocarcinomas, while moderate and strong staining was observed in 59 (31%) and 26 (14%) cases, respectively. Absence of CAR immunolabeling correlated with poor histological differentiation and clear cell morphology of pancreatic cancer. In normal tissue, strong immunolabeling was seen in the majority of islet cells as well as in peripheral and interlobular pancreatic ducts.

Conclusion: Absence of CAR expression in a considerable proportion of pancreatic cancers and constitutive CAR expression in normal pancreatic tissue may reduce the suitability of adenoviral gene therapy in pancreatic cancer patients.