

## **EXPRESSION PROFILING IDENTIFIES microRNA SIGNATURE IN PANCREATIC CANCER**

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microRNAs are functional, 22 nt, noncoding RNAs that negatively regulate gene expression. Disturbance of microRNA expression may play a role in the initiation and progression of certain diseases. A microRNA expression signature has been identified that is associated with pancreatic cancer. This has been accomplished with the application of real-time PCR profiling of over 200 microRNA precursors on specimens of human pancreatic adenocarcinoma, paired benign tissue, normal pancreas, chronic pancreatitis and nine pancreatic cancer cell lines. Hierarchical clustering produced complete separation of the tumor, normal, pancreatitis and cell lines into unique clusters demonstrating that expression profiling of ~200 microRNA genes sufficiently distinguishes these tissue types. The PAM algorithm correctly classified 28 of 28 tumors, 6 of 6 normal pancreas and 11 of 15 adjacent benign tissues. One hundred microRNA precursors were aberrantly expressed in pancreatic cancer or desmoplasia ( $P < 0.01$ ) including microRNAs previously reported as differentially expressed in other human cancers (miR-155, miR-21, miR-221 and miR-222) as well as those not previously reported in cancer (miR-376a, miR-301, miR-345, miR-142-3P, miR-100, miR-125b and miR-181a). Expression of the active, mature microRNA was validated using a real-time PCR assay to quantify the mature microRNA and Northern blotting. Reverse transcription in situ PCR showed that three of the top differentially expressed miRNAs were localized to tumor cells and not to stroma or normal acini or ducts. Aberrant microRNA expression may offer new clues to pancreatic tumorigenesis and may provide diagnostic biomarkers for pancreatic adenocarcinoma.

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