



MicroRNAs Linked to Pancreatic Cancer

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INVESTIGATORS AT OHIO STATE UNIVERSITY, in Columbus, and the University of Oklahoma Health Sciences Center, in Oklahoma City, have found an association between pancreatic cancer—which carries the worst prognosis of all cancer types—and the expression of certain small regulatory molecules called microRNAs. The findings may offer clues to pancreatic tumorigenesis and provide new diagnostic markers (Lee EJ et al. *Int J Cancer*. 2007;120:1046-1054).

LARGE EFFECTS OF SMALL RNA

Revelations that microRNAs influence both normal development and disease progression have put them in the spotlight of late. The importance of microRNAs, short segments of RNAs that selectively silence gene expression, was driven home last year when the Nobel Prize in physiology or medicine was awarded to 2 scientists—Andrew Fire, PhD, and Craig Mello, PhD—whose studies laid much of the groundwork for microRNA and other RNA interference research (Kuehn BM. *JAMA*. 2006;296:2189-2190). Normal functions for RNA interference include protecting cells against viruses whose genetic codes include double-stranded RNA and directing gene expression.

A variety of studies have linked aberrant microRNA expression to cancer. In one study, for example, the expression pattern of 217 microRNAs identified cancer type better than did expression data from 16 000 messenger RNA molecules (Lu J et al. *Nature*. 2005;435:834-838). While microRNAs' connection to cancer has been indisputably made, many mysteries remain concerning the molecules' roles in normal and malignant states and whether they play any role in cancer development and progression.

In this latest study, the researchers used a technology called real-time polymerase chain reaction to profile microRNA expression in specimens of human pancreatic adenocarcinoma, adjacent benign tissue, normal pancreas (from individuals without pancreatic cancer), and 9 pancreatic cancer cell lines. They identified approximately 100 different microRNAs that were present at much higher levels—some more than 50-fold—in cancer cells compared with other samples. In addition, a few microRNAs were expressed in tumor tissues at levels 8- to 15-fold less than in control tissues. The aberrantly expressed microRNAs included ones previously reported as differentially expressed in other human cancers, as well as some not previously linked to cancer.

“This study looked at pancreatic cancer, and it appears that different types of cancers have different expression profiles,” said principal investigator Thomas Schmittgen, PhD, of Ohio State University's Comprehensive Cancer Center.

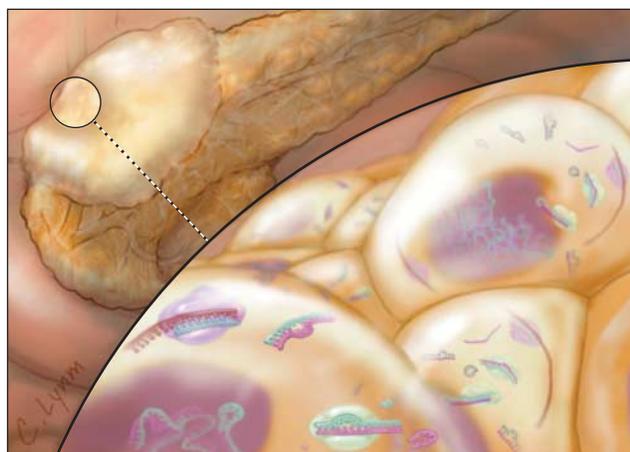
PANCREATIC PATTERN

The researchers also found that particular microRNAs were overexpressed in

pancreatic tumor tissue and discovered a microRNA gene-expression pattern unique to pancreatic tumors. Schmittgen and colleagues used this pattern in a computer analysis that correctly identified 28 out of 28 pancreatic tumors, 11 of 15 adjacent benign tissues, and 6 of 6 normal pancreatic tissues. Most of the benign samples fell between the normal pancreas and tumor samples on the microRNA expression map.

As increased expression of microRNAs was associated with pancreatic tumors in this study, drugs designed to inhibit these microRNAs might offer a promising treatment strategy and tests based on microRNA expression levels might help to diagnose the disease, the researchers said. “One of the directions we'd like to proceed in is to see if we can detect microRNAs in the circulating blood as a blood-based diagnostic,” said Schmittgen.

To achieve these goals, it will also be important to get more precise information on the microRNAs involved. “This study has given us a very large list,” said Schmittgen. “We're now trying to narrow down the list to the most important microRNAs in pancreatic cancer.” □



Cancer cells from a pancreatic tumor show increased expression of small regulatory molecules called microRNAs (inset).