

Tiny samples could yield big predictive markers for pancreatic cancer

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A handful of proteins, detected in incredibly tiny amounts, may one day help doctors distinguish between a harmless lesion in the pancreas and a potentially deadly one, say researchers at Fox Chase Cancer Center.

The researchers believe that these <u>protein biomarkers</u>, if confirmed in subsequent studies, could represent reliable indicators of <u>pancreatic</u> <u>cancer</u> or precancerous pancreatic lesions, which would allow for earlier, perhaps more successful, treatment. Their findings appear in the March issue of the journal *Pancreas*, available online now.

"New technologies have become very good at identifying <u>pancreatic</u> <u>cysts</u> when they appear, but we know very little about how to categorize these cysts," says the study's senior author Anthony Yeung, Ph.D., molecular biologist and member of Fox Chase's faculty. "We can detect, in as little as 40 <u>microliters</u> of cyst fluids a group of proteins that might collectively be used as indicators of a potentially cancerous cyst."

The difficulty of detecting pancreatic cancer early is one of the reasons that the disease remains one of the deadliest forms of cancer. In some cases, pancreatic cancer develops within small pancreatic cysts that are originally benign, but become cancerous over time. As high-resolution imaging techniques, such as <u>magnetic resonance imaging</u> (MRI), are used more often in clinical medicine, doctors are finding many more small, fluid-filled cystic lesions of the pancreas.

"Many of these cysts are completely benign and have little or no risk of



becoming cancerous. However, a subset of pancreatic cysts carry a real risk of becoming malignant over time," says co-author Jeffrey Tokar, M.D., Fox Chase gastroenterologist. "Many patients with pancreatic cysts are referred to us for endoscopic <u>needle aspiration</u> of fluid within the cyst, which is then sent to the laboratory and a variety of tests are commonly performed. However, while these tests can be useful, it often remains impossible to tell a patient their absolute risk of progression to cancer."

According to Tokar, there are currently two main options for doctors once they find a pancreatic cyst, and neither is ideal. One option is to advise the patient to have major surgery to remove the portion of the pancreas that contains the cyst, in hopes of eliminating the chance that it will develop into cancer. Unfortunately, with this approach, some patients will be subjected to the risks of surgery for a cyst that was never going to cause them any problems. The other option is to take a "watchand-wait" approach, which can become costly, expose patients to additional radiation (i.e., if computerized tomography, or CT scans, are used), and may not always detect cancers within cysts at its earliest stages. "What we need are methods to identify benign cysts that do not have significant cancer risk, so that we can concentrate on the cysts that have the greatest risk of malignancy," Tokar says.

Using an endoscopic ultrasound-guided technique, Tokar and his colleagues collected fluid from the cysts of 20 research participants with a small needle. Yeung and his laboratory team then assayed the fluid to determine the number and type of proteins it contained. Identifying the proteins took more than eight months of continuous time with a mass spectrometer, an instrument that can determine the makeup of - and thereby identify - individual molecules. Among the proteins they found were members of three families of proteins previously proposed to be biomarkers for pancreatic cancer, called mucins, CEACAMs, and S100s.



"From these samples we've identified a panel of these proteins that could all be considered harbingers of cancer in some way," Yeung says. "Now that we know what we are looking for, we can use even more powerful spectrometry techniques to find this pattern of proteins fast enough that it could be used as part of a clinical service."

The researchers are looking to expand their study and to follow patients over a longer period of time to see how well this biomarker profile predicts the likelihood that a pancreatic lesion already contains or may develop into pancreatic cancer, but they will need to recruit more patients. Fortunately, it helps that they can do more with less, as their technique can find biomarkers amid very small amounts of fluid obtained from small pancreatic lesions that are less than one centimeter (0.39 inches) in size.

"We are in great need for powerful tests, such as the ones that Dr. Yeung performs, which require only a tiny volume of fluid but can provide a tremendous amount of useful information," says Tokar. "We will need to work with colleagues at multiple medical centers to continue studying this promising technique for evaluating pancreatic cyst fluid, in hopes of building enough evidence to make it a routine part of patient care."

Source: Fox Chase Cancer Center

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