New discovery could help diagnose precursor to pancreatic cancer

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A recent Van Andel Institute study could lead to the development of tools to improve the diagnosis of precancerous cysts in the pancreas, one type of which leads to the invasive and hard-to-detect cancer.

Pancreatic cancer is the fourth leading cause of cancer death in the United States. The National Cancer Institute projects more than 45,000 new cases of the disease in 2013 and more than 38,000 deaths. Pancreatic cancer often spreads rapidly and is seldom detected in its early stages. Symptoms may not appear until the cancer is advanced and surgical removal is no longer an option.

"Cysts in the pancreas can be a clinical challenge to patients and physicians since some are precancerous and may progress to invasive cancer, while others remain indolent," said Brian Haab, Ph.D., Associate Professor in Van Andel Institute's Center for Translational Medicine, Head of the Laboratory of Cancer Immunodiagnostics and lead author of the study.

Two types of pancreatic cysts—intraductal papillary mucinous neoplasms (IPMNs) and mucinous cystic neoplasms (MCNs), together termed mucinous cysts—have malignant potential, while other non-mucinous types of cysts, such as serous cystadenomas (SCs) and pseudocysts (PCs), are essentially benign.

Results

In the study, published in July in the journal *Molecular & Cellular Proteomics*, researchers identified a three-marker panel that performed well in distinguishing mucinous from non-mucinous cysts in two independent sets of samples: 93% accuracy in a pre-validation sample set and 91% accuracy in independent, blinded samples.

"If the results hold up in larger studies, the new biomarker will have the potential to positively affect clinical practice," Haab said.

The study, "Specific glycoforms of MUC5AC and endorepellin accurately distinguish mucinous from non-mucinous pancreatic cysts," carried out in conjunction with researchers from the University of Oklahoma Health Sciences Center, University of Pittsburgh Medical Center, Ospedale Sacro Cuore Don Calabria, Negrar, Italy, Memorial Sloan-Kettering Cancer Center, University of Michigan, University of Arizona Health Sciences Center and the Fred Hutchinson Cancer Research Center, can be viewed here.

Current commonly-used methods to assess pancreatic cysts are endoscopic ultrasound and cyst fluid aspiration followed by the carcinoembryonic antigen (CEA) assay and cytology. Cytology (microscopic analysis of the cells in the fluid) has limited value due to lack of consistency in obtaining reliable cellular material. Other biomarkers, including DNA analysis, have yet to gain widespread use.

"The most accurate current method is CEA, which distinguishes mucinous cysts from non-mucinous cysts with 70-80% accuracy," Haab said. "However, since these tests are not conclusive for many patients, new, more effective molecular markers are needed to provide more accurate diagnoses and to help guide management."

Methods

The study's methods build upon previous efforts to identify carbohydrate biomarkers found exclusively in the fluid from mucinous cysts – with a particular emphasis on basic molecular building blocks known as glycans and lectins.

Glycans are carbohydrates that interact with glycan-binding proteins. These interactions are involved in many biological processes including the immune recognition of pathogens, pathogen infection, immune cell migration, protein processing, regulation of cell-surface receptors and sperm and egg binding. The abnormal production of certain glycans or glycan-binding proteins can have damaging consequences.

Lectins are carbohydrate-binding proteins that serve many different biological functions in animals, from the regulation of cell adhesion to glycoprotein synthesis and the control of protein levels in the blood. Lectins are also known to play important roles in the immune system by recognizing carbohydrates that are found exclusively on pathogens, or that are inaccessible on host cells.

An earlier 2013 Van Andel Institute study advances the field of glycomics, or carbohydrate biology, and has implications for the future of cancer diagnosis.

The research, carried out with the Palo Alto Research Center and published in *Molecular & Cellular Proteomics*, for the first time incorporates large amounts of data from the Consortium for Functional Glycomics, and may aid in the development of biomarkers to help determine the stages of many types of cancers upon diagnosis. Determining disease progression at the earliest possible stage is a crucial factor in long-term survival.

The study, "Global Comparisons of Lectin–Glycan Interactions Using a Database of Analyzed Glycan Array Data," can be viewed here.

"The study of carbohydrate biology has shown it to be complex and highly involved in many disease states," said Sudhir Singh, Ph.D., Van Andel Institute Postdoctoral Research Fellow and lead author of the study along with Doron Kletter, Ph.D., of the Palo Alto Research Center. "The contribution of a typical glycan-lectin interaction to disease pathology has been established for several diseases, but is unknown for others that display abnormal glycans or glycan-binding proteins."

"A difficulty in making that link often is a lack of information about the proteins that bind certain glycans, and about the glycans that are recognized by certain glycan-binding proteins," Singh added.

Obtaining more complete knowledge about the interaction between glycans and glycan-binding proteins is an important aspect of glycomic research.

"Glycan arrays can provide the experimental information for such analyses, and the thousands of glycan array datasets available through the Consortium for Functional Glycomics provide the opportunity to extend the analyses to a broad scale," Haab said.

Provided by Van Andel Institute