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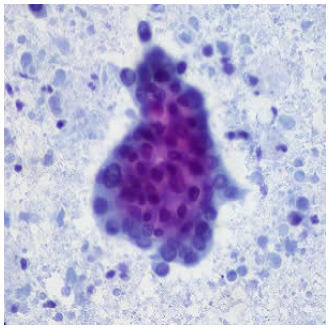
Simple test for detecting invasive pancreatic cancer



Johns Hopkins researchers have developed a new simple molecular test to detect chromosomal abnormalities — biomarkers known as telomere fusions — in pancreatic tumour specimens and cyst fluids. The detection of telomere fusions will help physicians determine which pancreatic lesions are likely to develop into cancer requiring surgical resection, according to a study published in The Journal of Molecular Diagnostics.

More sophisticated imaging of the pancreas has led to increased detection of presymptomatic lesions. However, "pancreatic imaging does not provide sufficient information about the neoplastic nature of a pancreatic cyst. Better characterisation of pancreatic cysts could allow more patients with worrisome cysts to continue with surveillance, avoiding the morbidity and risks related to pancreatic surgery," explained Michael Goggins, MD, Sol Goldman Professor of Pancreatic Cancer Research, Departments of Pathology, Surgery, and Oncology, Sol Goldman Pancreatic Cancer Research Center, Johns Hopkins University School of Medicine (Baltimore).

Telomeres are regions of repetitive nucleotide sequences found at the ends of chromosomes that, under normal circumstances, keep the chromosome intact. When telomeres lose most or all of their telomere repeat sequences, the ends can fuse, leading to cell death or chromosomal instability. “This is a major mechanism that contributes to the progression of many precancerous neoplasms to invasive cancers,” said Dr. Goggins.

Telomere fusions can serve as a marker for predicting the presence of high-grade dysplasia and/or invasive cancer, according to Dr. Goggins, and the new assay test developed by his team "is a cheaper method for evaluating pancreatic cyst fluid than many next-generation sequencing approaches that are being evaluated for this purpose.” The assay incorporates two rounds of PCR with the second round using a telomere repeat probe to detect the fusions in samples of pancreatic tumour or cyst fluid.

The researchers analysed tissues from intraductal papillary mucinous neoplasm (IPMN) tumour samples taken from patients undergoing resection, surgical cyst fluid samples, and normal pancreas. IPMNs are the most common type of pancreatic neoplastic cysts. They are characterised by the papillary proliferation of mucin-producing epithelial cells and cystic dilatation of the main or branch pancreatic duct.

This telomere fusion assay was able to identify telomere fusions in more than half of the pancreatic cell lines. Telomere fusions were often detected in tumours with high-grade dysplasia (containing more abnormal cells). Telomere fusions were not found in normal pancreas or samples with low-grade dysplasia.

Similar findings were seen in analyses of cyst fluid, in which the presence of telomere fusions raised the likelihood of high-grade dysplasia or invasive cancer sixfold. The telomere fusion events were found to be associated with high telomerase activity (an enzyme that lengthens telomeres) and shortened telomere length.

“The authors succeed in showing the presence of shortened telomeres, sporadic telomeric fusions, and increased telomerase activity in a modest proportion of pancreatic lesions,” commented Loren Joseph, MD, of the Department of Pathology at Beth Israel Deaconess Medical Center, Harvard Medical School (Boston), in an accompanying editorial. He added that the techniques used to detect fusions from cyst DNA and to measure telomere length and telomerase activity are within the scope of many molecular diagnostic laboratories.

Source: Elsevier
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