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PANCREATIC CANCER

Biomarkers for the early detection of PDAC

> Lack of diagnostic tests for the early detection of PDAC contributes to its poor prognosis…

A new study reports a novel biomarker panel for the detection of early-stage pancreatic ductal adenocarcinoma (PDAC). Measured using conventional ELISAs, the test combines the detection of two blood-based biomarkers, thrombospondin-2 (THBS2) and carbohydrate antigen 19-9 (CA19-9).

Lack of diagnostic tests for the early detection of PDAC contributes to its poor prognosis as patients are often diagnosed at an advanced stage of disease. "PDAC is especially lethal because it is usually detected too late for effective intervention. In assessing the field of biomarkers to detect pancreatic cancer, it appeared that most of the discovery work was done with late-stage tumours or human tumour cell lines," explains author Kenneth Zaret. "There was a lack of early-stage human cell models from which early-stage biomarkers could be found."

In the initial discovery phase, Zaret and colleagues looked for candidate PDAC markers by examining secreted proteins first identified in a human PDAC cell reprogramming model that mimics the progression of human PDAC, focusing on proteins released from precursor lesions such as pancreatic intraepithelial neoplasia. This approach identified THBS2 as a candidate biomarker for further analysis using patient samples.

A series of validation studies (phase I, $n = 20$; phase IIa, $n = 189$; phase IIb, $n = 537$) confirmed that plasma concentrations of THBS2 discriminated between all stages of PDAC with receiver operating characteristic c-statistics of 0.76–0.87. When combining THBS2 with CA19-9, an existing PDAC biomarker, the two biomarker panel yielded c-statistics of 0.96 and 0.97 in phase IIa and IIb studies, respectively. Finally, the THBS2–CA19-9 panel was able to distinguish PDAC from intraductal papillary mucinous neoplasms and from pancreatitis, improving the discriminatory power of CA19-9 alone.

Further tests of the biomarker panel on a wider range of samples are planned. "In addition, we are going to test our biomarker panel on prospectively collected blood samples, to determine if we can detect pancreatic cancer prior to when it would be presented in the clinic," Zaret adds.

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ORIGINAL ARTICLE Kim, J. *et al.* Detection of early pancreatic ductal adenocarcinoma with thrombospondin-2 and CA 19-9 blood markers. *Sci. Transl. Med.* **9**, eaah5583 (2017)

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In the version of this Research Highlight initially published online, the article should have referred to a human PDAC cell reprogramming model. The error has been corrected for the HTML, PDF and print versions of the article.