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IMAGING

Probing the pancreas

> this *in vivo* imaging technique … could improve detection and therefore potentially the survival of patients with pancreatic tumours

Patients with pancreatic ductal adenocarcinoma (PDAC) have a 5-year survival rate of less than 5%, often because patients are not diagnosed until they have late-stage disease. Indeed, evidence suggests that the detection of earlier stages — pancreatic intraepithelial neoplasia (PanIN) — is likely to increase the number of patients diagnosed with surgically resectable tumours and therefore increase survival rates. Saur and colleagues report the use of an *in vivo* imaging technique that could improve diagnosis of PanIN.

Pancreas-specific transcription factor 1a (*Ptf1a*)$^{Cre/+}$ *LSL-Kras*$^{G12D/+}$ mice have been reported to develop PanIN and then PDAC in a manner that is reminiscent of disease development in humans. So, Eser, Messer and colleagues analysed gene expression profiles of lesions from these mice and found that several cathepsin proteases — cathepsin B (CTSB), CTSH, CTSL and CTSS — were overexpressed in PanINs and early PDAC lesions, which was confirmed by immunohistochemistry of human samples. Importantly, these proteases were not overexpressed in inflamed pancreatic tissue (pancreatitis). Near infrared fluorescence (NIRF) imaging using a cathepsin-activatable probe showed that this probe was strongly activated in PanIN and PDAC lesions following injection into *Ptf1a*$^{Cre/+}$ *LSL-Kras*$^{G12D/+}$ mice, compared with wild-type mice and those with pancreatitis. The signal intensity correlated with the grade of PanIN and PDAC, and further analyses suggested that the probe is specific for pancreatic tumour tissue. Next, the authors showed that activation of the NIRF probe could be detected *in vivo* using confocal fluorescence laser microscopy (CFL) via a fibre optic miniprobe that was placed in contact with the pancreas. This technique allows single-cell resolution and the authors found that they could accurately discriminate between low-grade PanIN, high-grade PanIN and early-stage PDAC lesions in *Ptf1a*$^{Cre/+}$ *LSL-Kras*$^{G12D/+}$ mice in a double-blinded study.

There are problems with accessing the pancreas in humans, but strategies to overcome this issue are undergoing clinical testing and could allow this *in vivo* imaging technique to be translated to the clinic, which could improve detection and therefore potentially the survival of patients with pancreatic tumours.

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ORIGINAL RESEARCH PAPER Eser, S. *et al.* *In vivo* diagnosis of murine pancreatic intraepithelial neoplasia and early-stage pancreatic cancer by molecular imaging. *Proc. Natl Acad. Sci. USA* 31 May 2011 (doi:10.1073/pnas.1100890108)