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PANCREATIC CANCER

Early events in pancreatic cancer

Plasma levels of branched-chain amino acids (BCAA) are increased in early pancreatic ductal adenocarcinoma (PDAC), according to a study published in *Nature Medicine*. This finding might suggest that whole-body protein breakdown is an early event in PDAC.

PDAC is associated with metabolic changes, such as obesity and insulin resistance, but no studies had previously investigated circulating metabolites in early disease. "The origins of the project stemmed from Brian Wolpin's group, and his work using materials from prospective cohort studies to study risk factors for pancreatic cancer," explains Matthew Vander Heiden, corresponding author. "We had a discussion with Clary Clish about whether doing a metabolomics study on plasma from the cohorts might help predict risk or find a biomarker." Interestingly, this study used plasma samples from individuals before they were even diagnosed with cancer, enabling important insights into early disease progression.

The researchers profiled plasma metabolites in individuals from four prospective cohort studies—both patients who went on to develop PDAC and matched controls. Increased plasma levels of BCAA were found to be associated with an increased risk of a future diagnosis of PDAC. In fact, the team hypothesized that elevated BCAA levels might be a marker of early disease (rather than simply predicting risk). The investigators thus used mouse models of *Kras*-driven tumours to show that plasma BCAA levels were increased in mice with pancreatic cancers, but not tumours in other tissues.

"We are interested in what benefits protein turnover and BCAA elevation has for the tumour," says Vander Heiden. The team would also like to find the factors regulating whole-body protein breakdown.

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Original article Mayers, J. R. *et al.* Elevation of circulating branched-chain amino acids is an early event in human pancreatic adenocarcinoma development. *Nat. Med.* doi:10.1038/nm.3686