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PANCREATIC CANCER

Novel pathway identified for glutamine metabolism in PDAC

A new study published in *Nature* reports that pancreatic ductal adenocarcinoma (PDAC) cells utilise a novel glutamine metabolism pathway that is essential for tumour growth.

Previous work showing that oncogenic Kras reprogrammed anabolic glucose metabolism in PDAC led Alec Kimmelman, Lew Cantley and colleagues to ask whether glucose metabolism was critical for redox balance in PDAC cells and if the cells use an alternative carbon source. "We therefore began investigating the role of glutamine in pancreatic cancer growth," says Kimmelman.

The researchers used several different cell-based and *in vivo* assays to assess the glutamine metabolism pathway in PDAC. They found that glutamine was metabolised via a novel pathway that was regulated by oncogenic Kras, which is a characteristic genetic alteration in PDAC. The pathway was also shown to be essential for redox balance. Inhibiting the pathway by knockdown of component enzymes at any stage resulted in attenuated tumour growth. "Importantly, this pathway seems to be dispensable in normal cells and therefore might provide a novel therapeutic entry point for future initiatives," explains Kimmelman.

The authors of this paper are already expanding on these findings, with investigations underway to improve understanding of the relationship between this pathway and other metabolic pathways. "We are also working to develop small molecule inhibitors to essential enzymes of this pathway and to test their efficacy in pancreatic cancer models," says Kimmelman. They also note that determining whether these findings apply to other cancer types is important.

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Original article Son, J. *et al.* Glutamine supports pancreatic cancer growth through a Kras-regulated metabolic pathway. *Nature* doi:10.1038/nature12040