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Protein could offer therapeutic target for pancreatic cancer

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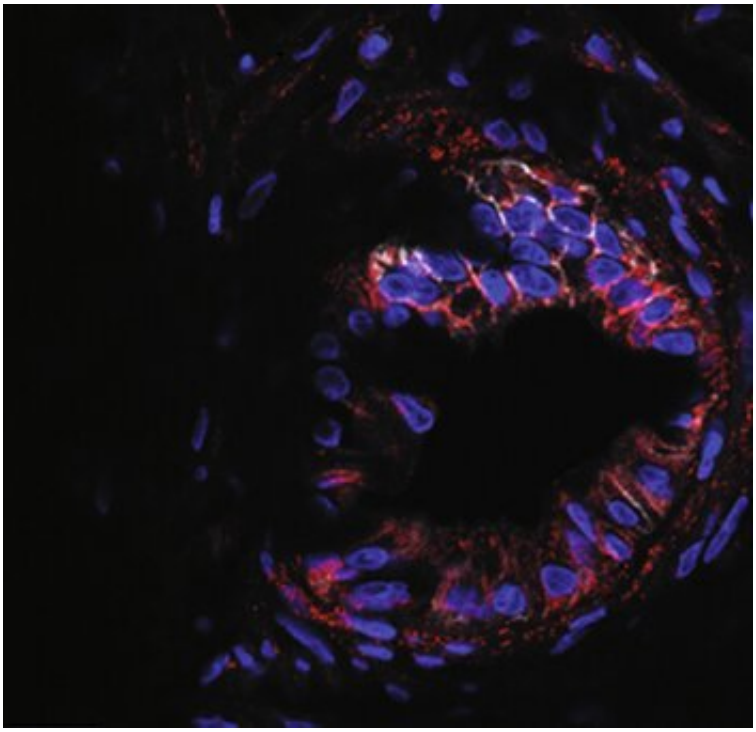

Human pancreatic ductal adenocarcinoma showing high levels of CD9 (red). Credit: Francis Crick Institute

A protein that drives growth of pancreatic cancer, and which could be a target for new treatments, has been identified by researchers at the Crick.

The study, published in *Nature Cell Biology*, looked into the most

common type of pancreatic cancer, pancreatic ductal adenocarcinoma. This is an aggressive cancer that develops from secretory and tubular cells of the pancreas.

There are no effective therapies to treat this cancer and only 8% of patients survive beyond five years after diagnosis.

The researchers analysed a specific group of tumour cells, called cancer stem cells. Similar to how healthy human stem cells repair tissues and organs, these cells have the ability to start new tumours and they can also differentiate into different types of tumour cells.

As these cells are a driving force behind cancer growth, being able to identify if they are present is an important step towards the development of new treatments. By analysing the gene expression of these cancer stem cells, the team found that a protein, called CD9, is present on their surface both when the tumour is developing and when it is more established. This protein could therefore be used as a marker to help locate these cells.

The study further established that this protein is not just a marker of cancer stem cells, but also promotes their malignant behaviour. The researchers altered the amount of CD9 in tumour cells in mice and found that when the levels of this protein were reduced, smaller tumours formed. Conversely, increasing levels of CD9 made cancer cells more aggressive and able to form large tumours quickly.

These findings were supported by existing clinical data showing that patients whose tumour cells have more CD9 have a poorer clinical prognosis. About 10% of people with this type of cancer have amplified levels of CD9.

"These cells are vital to pancreatic cancer and if even just a few of them

survive chemotherapy, the cancer is able to bounce back. We need to find effective ways to remove these cells, and so stop them from fuelling cancer growth. However, we need more experiments to validate the importance of CD9 in human pancreatic cancer," says Victoria Wang, lead author and member of the Adult Stem Cell Laboratory at the Crick.

To understand the mechanism behind how CD9 bolsters cancer, the team looked into the cancer stem cells' metabolism. Their findings showed that CD9 increases the rate cells take up glutamine, an amino acid which helps provide energy for the cancer to grow.

"Now we know this protein is both linked to cancer stem cells and helps cancer growth, this could guide the development of new treatments that are targeted at the protein and so cut off the supply of glutamine to cancer stem cells, effectively starving the cancer," says Axel Behrens, corresponding author and group leader in the Adult Stem Cell Laboratory at the Crick.

More information: Victoria M.-Y. Wang et al, CD9 identifies pancreatic cancer stem cells and modulates glutamine metabolism to fuel tumour growth, *Nature Cell Biology* (2019). DOI: 10.1038/s41556-019-0407-1

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