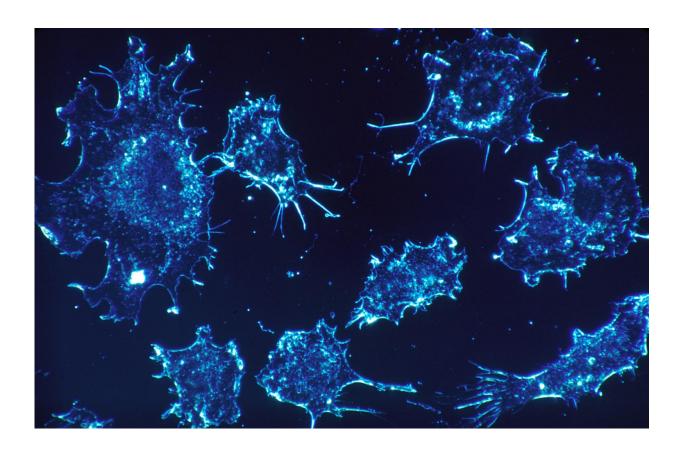


## Clues to the link between obesity and liver cancer—and identification of a new risk group

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New research from Monash University and the Peter MacCallum Cancer Centre has found a previously overlooked group of obese people may be



at risk of developing deadly liver cancer. The research, published today in *Cell*, has also explained how obesity is linked to liver cancer, both of which are increasing rapidly in the developing world.

In the last decade, <u>obesity</u> has become one of the biggest causes of cancer worldwide, and is expected to eclipse smoking. In women, obesity is a major driver of endometrial and breast cancer, whereas one of the main cancers caused by obesity in men is hepatocellular carcinoma (HCC), or <u>liver</u> cancer.

Liver cancer is the fifth most common cancer worldwide and the third most common cause of cancer death. Over the last 20 years, the incidence of liver cancer has doubled in the United States (US) and tripled in Australia. The obesity epidemic accounts for 30-40 per cent of this increase in liver cancer.

Most obese individuals who develop liver cancer first develop <u>non-alcoholic fatty liver</u> disease (NALFD), and then the more severe non-alcoholic steatohepatitis (NASH). This can lead to cirrhosis and <u>liver failure</u>, and in some cases to liver cancer.

However, research by a team led by Professor Tony Tiganis, from the Monash Biomedicine Discovery Institute and Peter Mac, reveals that there are pathways to the <u>development</u> of liver cancer in obese people that are not reliant on the development of NASH or cirrhosis.

Current guidelines in Europe and the US restrict the testing for liver cancer in obesity to patients with cirrhosis only.

This discovery means that there is potentially a group of people who may be at risk of liver cancer who are not being screened for the disease.

"What this research has shown is that the current screening for liver



cancer in obese patients is potentially missing a group of at-risk people. Until now, we have believed that the lack of development of serious <u>liver disease</u> has meant certain groups are unlikely to develop the deadly cancer," Professor Tiganis said.

According to Professor Tiganis, more research is needed to better understand the link between obesity and liver cancer, now that the existing assumptions have been overturned.

"If having NASH or cirrhosis are not the only pathways for the development of liver cancer in <u>obese people</u>, we urgently need to develop biomarkers to help identify those NAFLD patients that may be at risk of developing HCC," Professor Tiganis said.

The research used animal models and human tissue biopsies, which were provided by Professor Wendy Brown and her team from the Monash University Department of Surgery.

The research defined two separate molecular pathways for the development of NASH-cirrhosis versus liver cancer in obese mice, potentially opening the way for interventions to prevent the progression to cirrhosis or liver cancers in people with obesity.

The research reveals that the obesity-NASH-cirrhosis pathway is driven by the triggering of a protein called STAT-1. However those mice who developed liver cancer without developing NASH had their cancers triggered by a different protein, called STAT-3.

There are currently drugs available that are approved for use in other diseases that target the STAT-1 and STAT-3 pathways, however Professor Tiganis cautions that it is too early to assume that these drugs can have a beneficial impact on preventing the development of liver cancer in people who are obese.



Standard chemotherapy responses for <u>liver cancer</u> are poor, in most cases there is no impact on overall survival rates. Professor Tiganis believes there is an urgent need for the development of targeted therapeutics.

A 2017 report by the Centers for Disease Control and Prevention in the US revealed that in the previous decade 40 per cent of cancers were associated with obesity, overtaking smoking as the leading cause of <u>cancer</u>.

**More information:** Obesity drives STAT-1-dependent NASH and STAT-3-dependent HCC, *Cell* (2018). DOI: 10.1016/j.cell.2018.09.053

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