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Immune cells localized near pancreatic cancer cells have altered metabolism, could promote cancer

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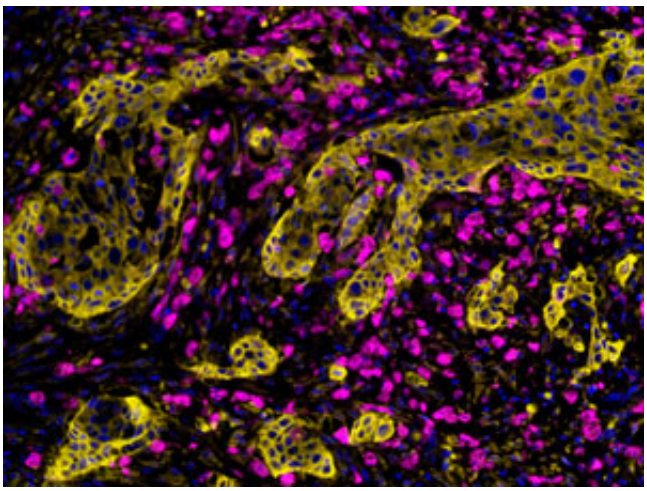

Large numbers of macrophages (stained pink) are found in pancreatic tumors (stained yellow). Credit: A*STAR Singapore Immunology Network

A diagnosis of pancreatic cancer is a virtual death sentence, with only 3 to 5 per cent of patients surviving beyond five years. A key reason that it has the lowest survival rate of all major cancers is that it readily spreads from the pancreas to other parts of the body. However, its extreme mobility has remained a mystery.

Now, A*STAR researchers have uncovered compelling evidence that tumors in the pancreas change the metabolism of white blood cells

known as macrophages (see image)1, which are described as the vacuum cleaners of the body because they gobble up microbes and cell debris. The team also found that these macrophages with altered metabolism may be involved in promoting the spread of cancer. These findings suggest that employing therapies that modify the metabolism of macrophages could help stem pancreatic cancer migration.

Tumor cells are known to exhibit a different metabolism from healthy cells. In particular, they preferentially generate energy from glucose by a process called glycolysis even under oxygen-rich conditions. But, Siew Cheng Wong at the Singapore Immunology Network and her co-workers suspected that tumors also alter the metabolism of macrophages in their vicinity.

To test this idea, the researchers generated human macrophages from blood monocytes cultured in media derived from either normal pancreatic cells or cancerous ones. They found that the macrophages grown using media from cancer cells showed an altered metabolism from those grown using media from normal cells—like cancer cells, the macrophages utilized glycolysis. Furthermore, the macrophages grown using cancer cell media promoted blood vessel growth, as well as the migration and establishment of cancer cells in distant organs, which are hallmarks of cancer spreading.

"Our study is the first to report a perturbation in the glucose metabolism pathway for macrophages in cancer," says Wong.

As well as providing clues about how pancreatic cancer spreads to other organs, this finding could help doctors to contain the cancer by resetting the metabolism of macrophages to their original state. "Macrophages are highly plastic cells," says Wong. "We have demonstrated that reprogramming the macrophages by switching their metabolic profile could reverse their propensity to promote cancer spreading.

Furthermore, targeting immune cells is a good strategy since they are less likely to mutate and develop resistance to drugs than cancer cells."

More information: Hweixian Leong Penny et al. Warburg metabolism in tumor-conditioned macrophages promotes metastasis in human pancreatic ductal adenocarcinoma, *OncoImmunology* (2016). DOI: 10.1080/2162402X.2016.1191731

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