Studies show that pancreatic cancer can run but not always hide from the immune system

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A pair of recent studies describes how pancreatic cancer cells produce a protein that attracts the body's immune cells and tricks them into helping cancer cells grow. The research, published by Cell Press in the June 12th issue of the journal *Cancer Cell*, also reveals that blocking the protein may be an effective way to treat pancreatic cancer.

"We found that simply disabling the ability of tumors to make this molecule leads to a house-of-cards effect that resulted in massive tumor death in experimental models," says Dr. Robert Vonderheide of the Perelman School of Medicine and Abramson Family Cancer Research Institute at the University of Pennsylvania, who is the senior author on the first paper.

Pancreatic cancer is one of the most deadly types of cancer, mostly because of its aggressiveness and its ability to suppress the cancer fighting properties of the immune system. Essentially, all pancreatic cancer cells harbor a mutation in the KRAS gene. Two teams of researchers looked to see how mutated KRAS gives pancreatic cancer its distinguishing properties.

Using mouse models of pancreatic cancer, the two groups each found that mutated KRAS triggers pancreatic tumors to express a protein called GM-CSF. They also discovered that tumor-derived GM-CSF recruits immature immune cells to the areas surrounding the tumor and then coaxes those cells to mature into so-called myeloid-derived suppressor cells, which suppress the surveillance function of other immune cells

that normally seek out and destroy foreign and malignant cells. In this way, pancreatic cells escape being seen by the body's immune system and are free to grow and divide. Blocking GM-CSF production, however, inhibited myeloid-derived suppressor cells and enabled the immune system to halt tumor development.

The researchers also showed that human pancreatic cancer cells prominently express GM-CSF, indicating that the findings could lead to new treatments for patients. "Our studies suggest a therapeutic strategy by which the antitumor properties of a patient's immune system can be restored," says Dr. Dafna Bar-Sagi of the NYU School of Medicine, who is the senior author of the second paper.

More information: Bayne et al.: "Tumor-derived granulocyte-macrophage colony stimulating factor regulates myeloid inflammation and T cell immunity in pancreatic cancer." DOI:10.1016/j.ccr.2012.04.025

Pylayeva-Gupta et al.: "Oncogenic Kras-induced GM-CSF production promotes the development of pancreatic neoplasia." DOI: 10.1016/j.ccr.2012.04.024

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