Nature Reviews Gastroenterology & Hepatology **9**, 426 (2012); published online 26 June 2012; doi:10.1038/nrgastro.2012.127

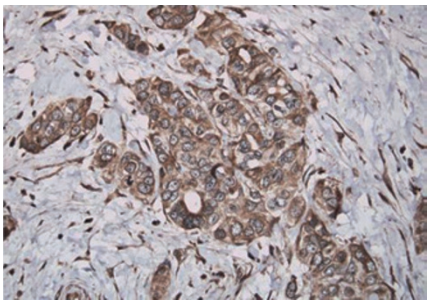
PANCREATIC CANCER

The role of GM-CSF in pancreatic cancer unveiled

Two recent papers have found that the cytokine granulocyte-macrophage colony-stimulating factor (GM-CSF), which is upregulated in many human pancreatic cancers, effectively 'masks' the tumour from the immune system. In two different mouse models, suppression of GM-CSF enabled the immune system to target the tumour.

In the first paper, the researchers used a mouse model of pancreatic adenocarcinoma to show that GM-CSF was key to the development of Gr-1$^+$CD11b$^+$ cells that suppressed antigen-specific T cells. "These cells suppress the surveillance function of other immune cells that normally seek out and destroy tumour cells," explains corresponding author Robert Vonderheide from the Abramson Family Cancer Research Institute at the University of Pennsylvania, USA.

When the researchers blocked GM-CSF, the Gr-1$^+$CD11b$^+$ cells were inhibited and the immune system was able to prevent tumour development. "Our findings suggest new possibilities for treating patients with pancreatic cancer," says Vonderheide. "Rather than going after the tumour cell directly, we hypothesize that new drugs that neutralize the immune suppressive features of the tumour might be able to unleash the immune system to benefit patients."



Human pancreatic adenocarcinoma stained by immunohistochemistry (brown) for granulocyte-macrophage colony-stimulating factor. Courtesy of N. Jhala and R. H. Vonderheide.

In the second paper, Dafna Bar-Sagi and colleagues found similar results in mouse pancreatic ductal epithelial cells. Most human pancreatic cancer cells have a mutation in the *KRAS* gene. The researchers showed that in mice, mutations in *Kras* upregulated the production of GM-CSF, which results in immunosuppressive cells being recruited to the tumour.

By suppressing the production of GM-CSF, the researchers demonstrated a reduction in the growth of cells containing mutated *Kras*, which was mediated by cytotoxic T cells. The authors note that these findings could help in the design of effective immunotherapeutic strategies against pancreatic cancer.

Claire Greenhill

Original articles Bayne, L. J. *et al.* Tumor-derived granulocyte-macrophage colony-stimulating factor regulates myeloid inflammation and T cell immunity in pancreatic cancer. *Cancer Cell* **21**, 822–835 (2012) | Pylayeva-Gupta, Y. *et al.* Oncogenic Kras-induced GM-CSF production promotes the development of pancreatic neoplasia. *Cancer Cell* **21**, 836–847 (2012)