

# Team discovers potential drug targets to reduce pain in pancreatic cancer patients

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Axial CT image with i.v. contrast. Macrocystic adenocarcinoma of the pancreatic head. Credit: public domain

The Translational Genomics Research Institute (TGen) has discovered potential drug targets to reduce pain in pancreatic cancer patients.

TGen researchers have found that [nerve growth factor](#) (NGF), a neurotrophic factor, and its receptor TRKA are associated with perineural invasion (PNI), which is the ability of pancreatic cancer cells to invade surrounding nerves.

Blocking the NGF signaling through inhibitors of NGF and TRKA reduces the potential of pancreatic cancer cells to migrate towards the surrounding nerves, according to a TGen study published in the scientific journal *PLOS ONE*.

"We have demonstrated that NGF signaling via the protein TRKA, between pancreatic cancer cells and surrounding nerves, is one of the molecular mechanisms involved in PNI," said Dr. Haiyong Han, Associate Professor of TGen's Clinical Translational Research Division and the senior author of the study.

Pancreatic cancer is one of the most aggressive types of malignancies, responsible for the deaths of nearly 42,000 Americans this year, and for the first time surpassing breast cancer as the third-leading cause of cancer related death in the U.S.

Many patients diagnosed with pancreatic cancer can succumb to the disease in less than a year, and the majority of these patients suffer from severe pain associated with their disease.

One of the reasons for this disease's dismal prognosis is due to the high rate at which the tumor recurs despite surgical removal. "A potential reason for the high rate of relapse has been postulated to be the ability of the pancreatic cancer cells to invade the surrounding nerves," the study said.

This invasion is a highly coordinated process, involving signaling molecules secreted by both the nerves and the pancreatic cancer cells.

The [nerve](#) ends are damaged and exposed by the pancreatic cancer cell invasion, resulting in pain.

The study found that this process also is associated with the growth and survival of pancreatic cancer cells. And, knocking down NGF or its receptors, TRKA and p75NTR, or treating TRKA with an inhibitor called GW441756, reduces the proliferation and migration of pancreatic cancer cells into the surrounding nerves.

The study concludes that additional research is needed, and that a clinical trial should be designed, using TRKA antagonists, to decrease the onset or worsening of pain for patients with advanced [pancreatic cancer](#).

"We are trying to convince groups that have the TRKA inhibitor to allow us to test them in our systems and in the clinic as soon as possible," said Dr. Daniel Von Hoff, TGen's Distinguished Professor, Physician-In-Chief and a co-author of the study, who is one of the world's leading authorities on this disease.

The study—Blocking Nerve Growth Factor Signaling Reduces the Neural Invasion Potential of Pancreatic Cancer Cells—was published Oct. 28 by *PLOS ONE*.

**More information:** Aditi A. Bapat et al, Blocking Nerve Growth Factor Signaling Reduces the Neural Invasion Potential of Pancreatic Cancer Cells, *PLOS ONE* (2016). [DOI: 10.1371/journal.pone.0165586](https://doi.org/10.1371/journal.pone.0165586)

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