Targeting CAFs: New Treatment for Pancreatic Cancer by Blocking Fibrotic Pathways

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BACKGROUND

Pancreatic ductal adenocarcinoma (PDAC), the most common type of pancreatic cancer, is currently the third- leading cause of cancer death in the United States, and is predicted to be the second such cause by 2020. The current 5-year survival rate of PDAC is ~8%. Factors that contribute to this high death rate include the early, asymptomatic phase of the disease, such that at the time of diagnosis, many patients have locally advanced or metastatic disease. Surgical resection, the only curative treatment, is feasible in <20% of patients. Chemotherapy of PDAC has had limited impact. The EGFR inhibitor erlotinib is the only approved targeted therapy and produces minimal clinical benefit. New, effective treatments of pancreatic cancer are thus a major, unmet medical need.

G protein-coupled receptors (GPCRs), the largest family of cell signaling receptors (~3% of the human genome), are seven transmembrane receptors that respond to numerous types of extracellular signals and regulate many physiological processes. Emerging evidence implicates GPCRs in cancer: certain GPCRs have increased expression in tumors and are involved in cancer initiation and/or progression. GPCRs can contribute to fibroblast myofibroblast conversion and increases in cellular cAMP (a second messenger for certain GPCRs) can blunt the myofibroblastic phenotype. Little is known regarding the role of GPCRs in pancreatic cancer-associated fibroblasts (CAFs).

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have studied the role of GPCRs that are expressed in pancreatic CAFs and PDAC cells. To this end, the researchers have identified a novel pH-sensing GPCR, GPR68, as a regulator of pancreatic CAFs and CAF-PDAC cell interaction. CAFs can alter the PDAC microenvironment by increasing the dense fibrotic stroma in parallel with an increase of GPR68 that increases IL-6 which promotes PDAC proliferation. Moreover, by downregulating GPR68, it may serve as a potential therapeutic target to mitigate the activity of CAFs and thus alter the features of pancreatic cancer. It may also favorably alter the microenvironment so that potential new drugs may be better able to target the tumor because of a reduction in expression of fibrotic stoma.

APPLICATIONS

GPR68 may serve as a potential therapeutic target to mitigate the activity of CAFs and thus alter the features of pancreatic cancer. It may also serve as a potential biomarker for pancreatic cancer.

STATE OF DEVELOPMENT

A research model to study pancreatic ductal adenocarcinoma.

INTELLECTUAL PROPERTY INFO

This technology is patent pending and available for licensing and/or research sponsorship.

RELATED MATERIALS

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OTHER INFORMATION

KEYWORDS

Pancreatic ductal adenocarcinoma (PDAC), G protein-coupled receptors, cancer-associated fibroblasts (CAF), pancreatic cancer, GPR68, tumor microenvironment, biomarker

CATEGORIZED AS

- Medical
  - Disease: Cancer
  - Therapeutics

RELATED CASES

2014-142-0

▶ Wiley SZ, Sriram K, Liang W, Chang SE, French R, McCann T,Sicklick J, Nishihara H, Lowy AM, Insel PA. GPR68, a proton-sensing GPCR, mediates interaction of cancer-associated fibroblasts and cancer cells. FASEB J. 2018 Mar;32(3):1170-1183. doi: 10.1096/fj.201700834R. Epub 2018 Jan 3. - 01/03/2018

PATENT STATUS

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Additional Patent Pending

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