

## Micro-Environment of Pancreatic Cancer and Its Clinicopathological Significance

Shintaro Goto\*

\*Department of Pathology and Bioscience, Graduate School of Medicine, Hirosaki University, Japan.

Published November 01, 2019

### ABSTRACT

Pancreatic cancer is one of the most aggressive human cancers. The most common histological type is invasive ductal adenocarcinoma, characterized by infiltrative growth and fibrous cancer stroma. The fibrous cancer stroma contains a lot of active fibroblasts called cancer-associated fibroblasts (CAFs) and is thought to promote the aggressive cancer growth and invasion. Histologically, the cancer cells/stroma ratio is various depending on the cases. This morphological diversity of pancreatic cancer is one of our pathophysiological issues. On the other hand, contrast-enhanced computed tomography (CECT) is useful clinical modality because it enables to observe the internal properties of tumors without invasive procedures. In this study, we examined whether the preoperative clinical image correlates with the histological diversity of pancreatic cancer. We reviewed pancreatic cancer cases without preoperative chemotherapy which were histologically diagnosed as invasive ductal adenocarcinoma. All cases were performed with dynamic CECT in Hirosaki University Hospital. We evaluated the density of cancer cells and the positive rate of immunoreactive  $\alpha$ -smooth muscle actin ( $\alpha$ SMA), a marker of the cancer stroma. Then, we analyzed dynamic CECT images, and draw out the time intensity curve of pancreatic cancer. Dynamic CECT images consist of non-contrast phase, arterial phase, portal phase and equilibrium phase. Time intensity curve represented the changes of CECT image value. We also examined the correlations between the histopathological findings and the dynamic CECT images. There were significant correlations between the CT value at arterial phase and the  $\alpha$ SMA positivity which indicating the cancer stroma. In contrast, there were no correlations between the cancer cells and CT values at any phases. We tried to clarify molecular/histological mechanisms why the  $\alpha$ SMA positivity was significantly correlated with the time intensity curve of CECT. The contrast medium of CECT infiltrates into the  $\alpha$ SMA-positive cancer stroma. A lot of active CAFs regulate the pancreatic cancer microenvironment and play an important role in the contrast medium infiltration.

**Corresponding author:** Shintaro Goto, Department of Pathology and Bioscience, Graduate School of Medicine, Hirosaki University, Japan, E-mail: sgoto0809@hirosaki-u.ac.jp

**Citation:** Goto S. (2019) Micro-Environment of Pancreatic Cancer and Its Clinicopathological Significance. BioMed Res J, 3(S1): 24.

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