



AB080. P052. Role of neutrophil extracellular traps (NETs) in pancreatic cancer liver metastasis

Shin Takesue, Kenoki Ohuchida, Hiromichi Nakayama, Kazuhiro Koikawa, Koji Shindo, Kohei Nakata, Taiki Moriyama, Yoshihiro Miyasaka, Takao Ohtsuka, Masafumi Nakamura

Kyushu University, Fukuoka, Japan

Background: Liver metastasis is the major cause of pancreatic ductal adenocarcinoma (PDAC) related death and preventing liver metastases may improve the patient's survival. Neutrophil extracellular traps (NETs) were identified in 2004 and are extracellular networks that consist of DNA released from neutrophils together with antimicrobial peptides and proteases derived from neutrophil granules. Recently, it was shown that NETs promote various human pathology, such as cancer-associated thrombosis and auto-immune disease and cancer, but the role of NETs in pancreatic cancer progression is not well known. This study aims to investigate the role of NETs in pancreatic cancer liver metastasis using genetically engineered mice that spontaneously develop PDAC and tumor intrasplenic injection mouse model that forms experimental liver metastases.

Methods: Two mouse models, spontaneous pancreatic

cancer mice KPCL (LSL-Kras G12D/+; LSL-Trp53 R172H/+; LSL-Luciferase; Pdx-1-Cre) mice and tumor splenic injection model were treated with DNase I, NETs inhibitor, and examined the influence of DNase I on invasion and metastasis of pancreatic cancer. Neutrophils isolated from bone marrow of C57BL/6 mouse were co-cultured with pancreatic cancer cells derived from KPC (LSL-Kras G12D/+; LSL-Trp53 R172H/+; Pdx-1-Cre) mouse.

Results: KPCL mice treated with DNase I from the 8 weeks of age had significantly longer survival time compared to the control group, and liver metastasis was suppressed. However, liver metastasis was suppressed in the group that started administration from the 13 weeks of age, the survival period was not extended. In the tumor intrasplenic injection model, neutrophils were recruited to the liver micrometastases, and liver metastasis formation was inhibited in the DNase I treated group. In vitro study revealed that cancer cells derived from KPC mice indirectly co-cultured with neutrophils promoted NETs formation.

Conclusions: DNase I, a NETs inhibitor, suppressed liver metastasis formation in KPCL mice and tumor intrasplenic injected model, suggesting that NETs promotes liver metastasis in pancreatic cancer.

doi: 10.21037/apc.2018.AB080

Cite this abstract as: Takesue S, Ohuchida K, Nakayama H, Koikawa K, Shindo K, Nakata K, Moriyama T, Miyasaka Y, Ohtsuka T, Nakamura M. Role of neutrophil extracellular traps (NETs) in pancreatic cancer liver metastasis. *Ann Pancreat Cancer* 2018;1:AB080. doi: 10.21037/apc.2018.AB080