AB036. P007. BM-derived cells differentiated into multilineage hematopoietic cells regulate invasion and proliferation of pancreatic cancer

Chika Iwamoto, Kenoki Ohuchida, Takashi Okumura, Kazuhiro Koikawa, Shin Takesue, Hiromichi Nakayama, Sho Endo, Shin Kibe, Yohei Ando, Koji Shindo, Kohei Nakata, Kohta Miyawaki, Masaharu Murata, Koichi Akashi, Masafumi Nakamura, Makoto Hashizume

Kyushu University, Fukuoka, Japan

Background: Pancreatic adenocarcinoma is characterized by a desmoplastic reaction, which provokes treatment resistance. Tumor-stroma interactions promote cancer malignancy. Cytokines secreted by tumor cells differentiate activated macrophages into tumor-associated macrophages (TAMs), which produce angiogenesis factor and cell growth factor to form tumor microenvironment. In breast cancer, a subset of stromal cells was descended from bone marrow (BM)-derived cells. While BM-derived cells seem to be involved in remodeling of microenvironment and tumor progression in pancreatic cancer, this mechanism remains unknown. We aimed to investigate an association between pancreatic cancer progression and BM-derived cells.

Methods: To establish the allogeneic BM transplantation models, BM-derived GFP+ cells were intravenously transplanted into KPC mice after sublethal irradiation. The phenotypic characterization and distribution of engrafted GFP+ cells were analyzed by flow cytometry or immunohistochemical staining. To evaluate invasive capacity and proliferation activity of pancreatic cancer cells (PCCs) co-cultured with BM-derived cells, we performed cell invasion assay and cell viability assay.

Results: The engraftment of BM-derived GFP^+ cells was detected in recipients' peripheral blood, BM, pancreas, liver, and ascites. The engrafted GFP^+ cells expressed CD45 consisting of a few $CD4^+$/$CD8^+$ T cells, a few natural killer (NK) cells, or macrophages. In recipients' pancreas, GFP^+ cells, $F4/80^+$ macrophages, and $CD163^+$ TAMs were accumulated around acinar-ductal metaplasia/pancreatic intraepithelial neoplasia (ADM/PanIN) and at invasive front. Invasive capacity of PCCs co-cultured with BM-derived macrophages significantly increased compared to the control. BM-derived lymphocytes inhibited the proliferation of PCCs. BM-derived GFP^+ cells showed a distribution similar to $aSMA^+$ cells, and a few GFP^+aSMA^+ cells were detected.

Conclusions: BM-derived lymphocytes, macrophages, and TAMs were engrafted in recipients' pancreas, and their distribution was biased. The present data also suggest that BM-derived macrophages have an insignificant effect on the proliferation of PCCs, while are involved in infiltration of PCCs.

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