



The role of stromal cells in anti-tumor immune responses

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ABSTRACT

Pancreatic ductal adenocarcinoma (PDAC) is a cancer of the exocrine pancreas with an aggressive prognosis (a 5-year survival rate of 6 months), resulting in more than 250,000 deaths per year. PDAC is the fourth most common cause of cancer-related mortality worldwide. PDAC is more resistant to chemotherapy than other types of cancer due to the dense fibrosis around it. Moreover, only 15% of patients who have PDAC tumors can have surgical resection. Consequently, the success of chemotherapy and surgery in PDAC treatments is limited, motivating researchers to turn to immunotherapy modalities. The dense fibrotic nature of the PDAC microenvironment makes it worthwhile to research the cancer-associated fibroblasts (CAF). The CAF cells play a role in the formation of fibrotic barriers, the altering of the anti-tumor immune response, and supporting to carcinogenesis. Many immune system elements, such as macrophages and cytotoxic T cells, play a role in the formation of the anti-tumor immune response. Macrophages play a particularly crucial role in that anti-tumor immune response but in two opposing manners, activating classically or in alternative ways. Macrophages that activate in alternative manners, the tumor associated macrophages (TAMs), have become a focus in cancer research in recent years due to their role in suppressing the anti-tumor response, in supporting angiogenesis and metastasis. However, there is no consensus on how the TAM cells are polarized from monocytes. This study aims to determine whether or not CAF cells play a role in the polarization of TAMs through CXCL12/ CXCR4 axis, and how this role affects survival and tumor volume in PDAC patients. If we explore that CAFs play a role in macrophage polarization via CXCL12 / CXCR4 axis in this study, we may suppress this pathway and gain clinical benefit from this inhibition in PDAC patients.

KEY WORDS: Cancer-associated fibroblasts; Tumor associated macrophages

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