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Editorial

What Is the Role of Immune Cells Contribute to the Occurrence of Programmed Cell Death (PCD) in the Tumor Microenvironment (TME)?

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Editorial

The tumor microenvironment (TME) plays decisive roles in tumor initiation, progression, metastasis, and response to therapies. The TME is a complex system that is composed of cancer cells, non-tumor cells (such as immune cells, etc.) and various extracellular factors. A large number of immune cells in the TME, including T cells, macrophages, bone marine-derived suppressor cells (MDSC) and etc., which have been shown to acquire growth signals and metabolic properties similar to cancer cells. Programmed cell death(PCD) plays an important role in tumorigenesis, development and metastasis. Currently, we know that pyroptosis occurs in almost all types of cancer [1]. Not only pyroptosis, but many other types of PCD are common in tumors. Tumor cells' activation of the PCD pathway may have a positive effect on multiple cancer types, and the PCD pathway has become a hot spot in cancer treatment. So what is the role of immune cells contributed to the occurrence of PCD in the TME? This question is frequently asked.

First, immune cells act as inducers of PCD. The interaction between immune cells and tumor cells is considered to be an important part of TME. Immune cells are involved in regulating the PCD of tumor cells. Pyroptosis is an important regulator of the TME, and there is a complex interaction between tumor-associated macrophages (TAMs) and tumor cells, which indirectly affects the pyroptosis process via the secretion of cytokines [2]. The CD8+ T cells are major killers of pathogens and neoplastic cells. The recent studies identified a new mechanism by which CD8+ T cells suppress tumor growth by inducing ferroptosis and pyroptosis, which provoked a review of the relationship between tumor cell death mechanisms and immune system activation

[3]. Of course, the complex mechanism by which immune cells regulate the multiple PCD of tumor cells remains to be further revealed.

Second, immune cells are influenced by PCD of tumor cells. There is growing evidence that tumors regulate the immune response of immune cells and tissues through PCD, and as a way to delay tumor-specific immune responses. TAMs were found to participate in ferroptosis-mediated immunosuppression [4]. Immune cells are affected by all forms of PCD in tumor cells, but the relevant studies are still not extensive.

In addition, immune cells can act as generators of PCD, while tumor cells act as inducers of this process. The study on PCD in the TME frequently concentrates on tumor cells, but neglects the PCD of immune cells. PCD can occur in both immune cells and tumor cells due to external intervention in the TME. Recently, several studies have revealed that L-kynurenine produced by gastric cancer cells indoleamine 2, 3-dioxygenase can induce ferroptosis in NK cells [5].

The role of immune cells in the occurrence of PCD in TME is complex and diverse. However, the interpretation of the role of immune cells contribute to the occurrence of PCD in TME also provides many new ideas for future cancer treatment.

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