



Preface to the series on tumor immune microenvironment in cancer progression and cancer therapy

The development of cancer is not only the growth and proliferation of a single transformed cell, but also the co-evolution of the surrounding environment. Cancer cells can alter the function of their microenvironment by secreting various chemokines, cytokines and other factors (1). This leads to the reprogramming of the surrounding cells, which plays a decisive role in the progression of the tumor. Growing evidence suggests that tumor microenvironment (TME) plays an important role in the development, invasion and metastasis of tumor (2). TME consists of immune cells, endothelial cells, smooth muscle cells, fibroblasts and factors released by cells, which is characterized by acidosis, hypoxia, nutrient deficiency, vascular hyperpermeability and drug retention. Due to the important role of TME, it is urgently needed to understand the impact of TME in cancer progression and cancer therapy.

Acidosis in TME promotes angiogenesis and invasion and plays a role in tumor progression and metastasis. In acidic TME, tumor-derived exosomes (TEs) play a pivotal role in the occurrence and development of tumors through the continuous exchange of molecular contents between tumor cells and stromal cells. TEs, whose assembly and release are regulated by TME, can induce the apoptosis of immune cells and enhance the immunosuppressive function. These exosomes are information carriers that transmit molecular information from tumor cells to other cells located proximal or distal (3). The study of the effects of acidic microenvironment on TEs and cells represents an emerging field of research that may provide new strategies for the ways to inhibit tumor progression.

Immune cells are an important part of TME and play a critical role in oncotherapy. There is mounting evidence to suggest that both the innate immune cells and adaptive immune cells are involved in tumor progression in TME. The cross-talk between the cancer cells and the immune cells ultimately leads to profound impacts on cancer progression and remodeling of the TME. Myeloid-derived suppressor cells (MDSCs) are produced in bone marrow and migrate to peripheral lymphoid organs and tumors, which are one of the major components of the TME (4). The main characteristic of these cells is their strong immunosuppressive activity. They can suppress the function of CD8⁺T cell and promote the expansion of regulatory T cells (Tregs) and M2 macrophages. Targeted therapy for MDSCs can destroy the immunosuppressive microenvironment and improve the therapeutic effect. The underlying mechanisms for the development, infiltration, and function of MDSCs remain relatively unexplored. Thus, further work is needed to restore the immune response in tumor-bearing environment by targeted MDSCs.

An in-depth understanding of the TME and underlying genetic factors may contribute to tumor therapy. MicroRNAs (miRNAs) play an important role in the regulation of gene expression because they can interact with a wide range of specific target genes. MiRNAs are produced and released by almost every cell type. Tumor cells and stromal cells cross-communicate through a variety of factors, including miRNAs, which serve as a target for antitumor therapy. Abnormally expressed miRNAs are reported to play pivotal roles in the development of different types of cancers. Both loss-of-function and gain-of-function approaches have been used as therapeutic options. Several pre-clinical studies showed that intratumoral injections of miRNAs directly into the primary site can enhance efficacy, specificity, and reduce side effects. New advances in miRNAs may contribute to the development of diagnostic and prognostic biomarkers, the identification of new drug targets, and the design of effective strategies for the personalized management of cancer (5).

The series on tumor immune microenvironment in cancer progression and cancer therapy includes articles analyzing the role of microenvironmental acidity and TEs, the immune cells such as MDSCs, and genetic factors such as miRNAs. The TME has profound impacts on cancer progression and remodeling of the TME has become a strategy to facilitate cancer therapy.

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Jia Wei

Jia Wei, MD, PhD

The Comprehensive Cancer Centre of Drum Tower Hospital, Medical School of Nanjing University & Clinical Cancer Institute of Nanjing University, Nanjing, China. (Email: weijia01627@hotmail.com)

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