CHARTING THE TUMOR MICROENVIRONMENT:

NAVIGATING COMPLEX SYSTEM INTERPLAY

The tumor microenvironment is a complex network of cancer, immune, vascular, and stromal cells, generally characterized by extracellular matrix (ECM) remodeling, tissue suppression, and hypoxia due to poor vascularization. These contribute to create favorable conditions for cancer-cell survival, proliferation, and mobility, resulting in tumor growth, invasion, and metastasis. Understanding the components of the tumor microenvironment and their interplay is essential to better target tumor growth and metastasis in the laboratory and clinic.

DENDRITIC CELLS AND MACROPHAGES

Dendritic cells (DCs) are sentinels that communicate with T cells and other immune cells, promoting immune responses by processing and presenting antigen to T cells. DCs can also promote tolerance by inhibiting T-cell responses. In the tumor microenvironment, DCs can be inhibited by factors produced by tumor cells or by other immune cells, which can impair their ability to prime T cells.

Macrophages are also present in the tumor microenvironment and can have different phenotypes depending on the microenvironment. M2-type macrophages can promote tumor growth by secreting cytokines that promote angiogenesis and ECM remodeling, while M1-type macrophages can promote tumor regression by secreting cytokines that activate T cells.

TUMOR INVASION AND METASTASIS

Tumor cells, either individually or collectively, create the processes and structures in the extracellular matrix (ECM) that enable them to move through tissues and organs. ECM remodeling by tumor cells can facilitate tumor cell migration, invasion, and metastasis. ECM remodeling is facilitated by the expression of enzymes such as matrix metalloproteinases (MMPs) and by the release of growth factors.

HYPOXIA

Hypoxia is a common feature of tumors and can be caused by a lack of blood flow or oxygen diffusion, leading to increased production of hypoxia-inducible factors (HIFs) and the activation of various signaling pathways that can promote tumor growth, angiogenesis, drug resistance, and metastasis.

THE VASCULATURE

The tumor vasculature is a network of vessels that supplies nutrients and oxygen to tumor cells. Tumor vessels can be leaky, which can promote the extravasation of tumor cells and the formation of metastases. The vasculature can also be a target for therapeutic intervention.

QUANTITATING IMMUNE-CANCER INTERACTIONS

Immunotherapy is the use of naturally occurring immune responses to treat cancer. Immunologic tests can be used to identify tumor-specific antigens and to monitor the response to immunotherapy. Immunohistochemistry is the conventional avenue for investigating the immune-cancer interactions, but it requires the detection of tumor antigens, cytokines, chemokines, and/or antibodies is required for optimal therapeutic effects in solid tumors.**

REFERENCES:

** This open the exploration of specific cancer types and their microenvironment in the context of immuno-oncology.
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