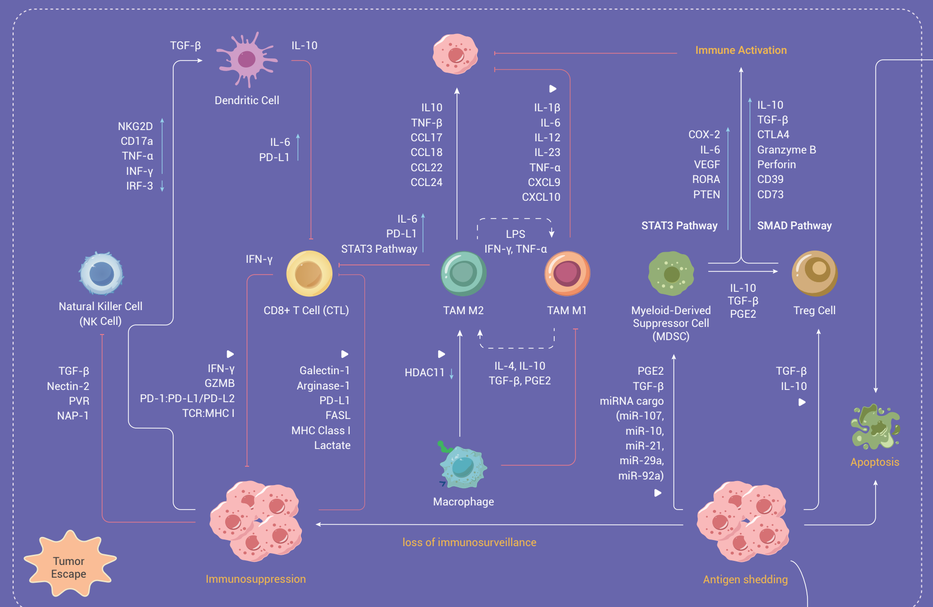
Tumor Microenvironment (TME)

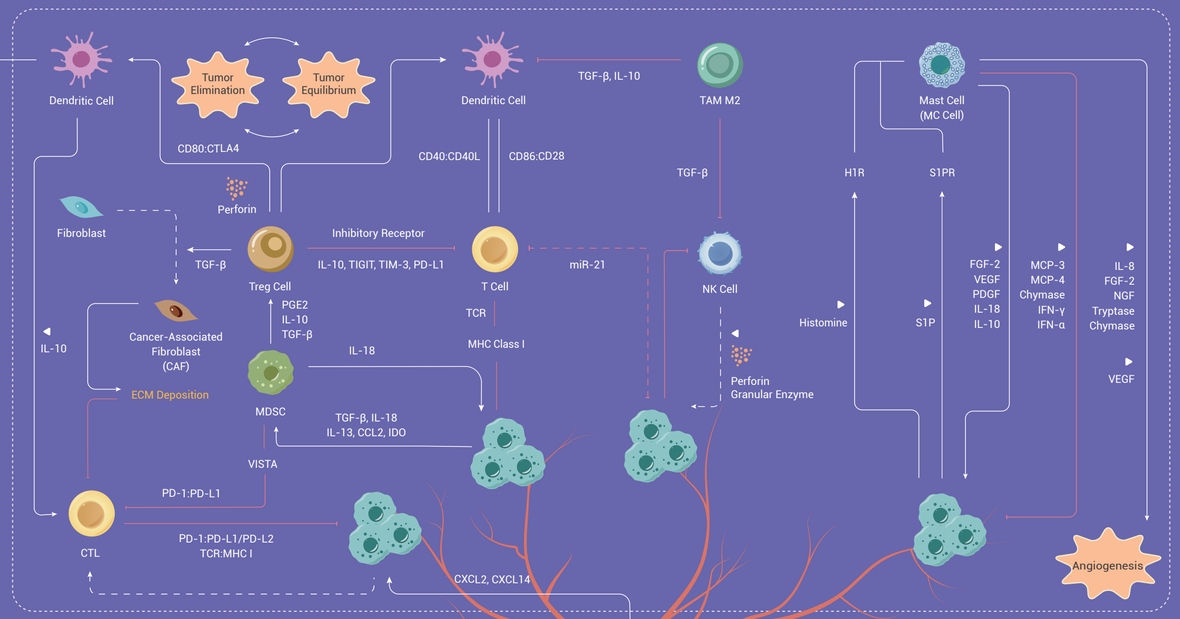
TME and Immunosuppression/ Tumor Escape

TME contains a variety of immunosuppressive cells, such as regulatory T cells (Tregs), bone myeloid-derived suppressor cells (MDSCs), and M2 macrophages. Immunosuppressive factors released by these cells inhibit the function of immune cells, leading to a decrease in tumor-infiltrating lymphocytes, thereby reducing immune surveillance of tumors. Meanwhile, immune escape pathways in the TME increase, and tumor epitope recognition antigens are shed, further inhibiting the anti-tumor immune response. Tumors gradually evolve the ability to evade immune attacks, going through three stages: "immune clearance", "immune balance", and "immune escape", ultimately enabling tumors to tolerate immune attacks and continue to grow in the body.



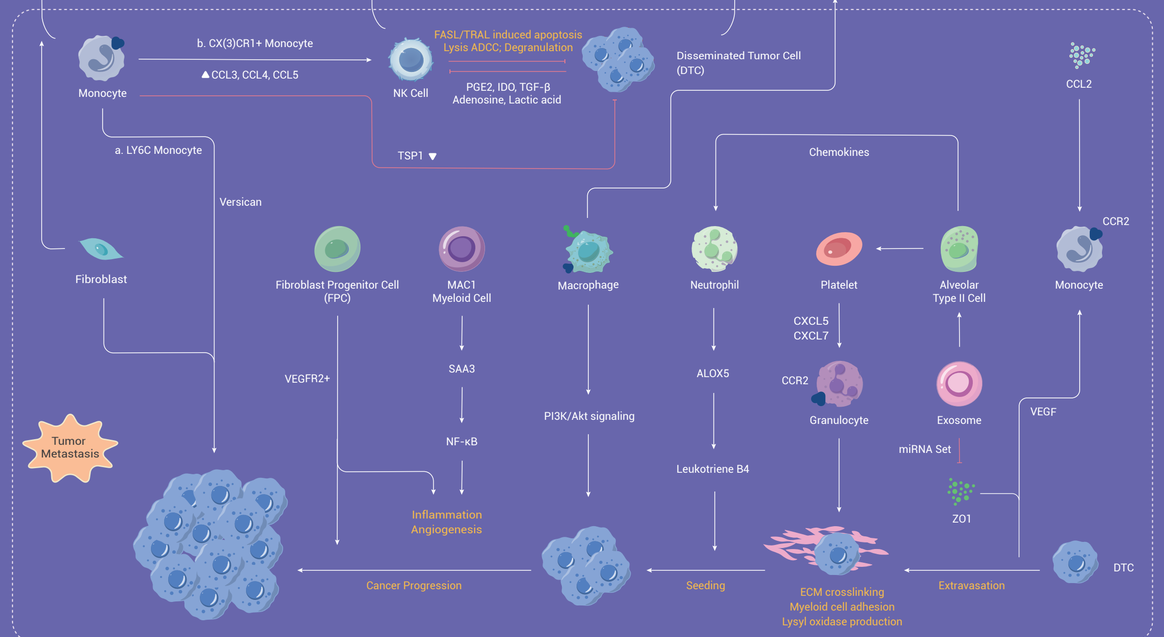
TME and Angiogenesis

TME has a complex relationship with angiogenesis, as factors such as hypoxia, acidity, and nutrient deprivation impair CAR-T cell proliferation and function, while also inducing oxidative stress that promotes the proliferation of cancer-associated fibroblasts (CAFs) and extracellular matrix (ECM) deposition, reducing cellular motility. The TME recruits CAFs and immune cells, influencing their secreted factors to facilitate new blood vessel formation by endothelial cells, thus modifying the surrounding microenvironment. Angiogenesis is primarily driven by vascular endothelial growth factor (VEGF), and an increased rate of angiogenesis in the TME results in vascular abnormalities, elevated interstitial pressure within tumors, and reduced immune cell infiltration and checkpoint inhibitor penetration.



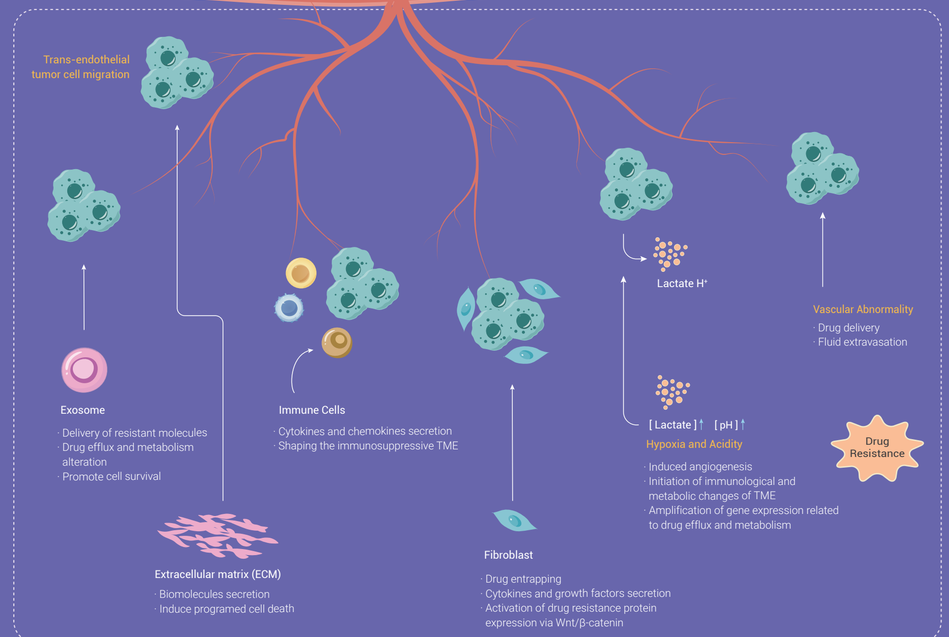
TME and Tumor Invasion/ Metastasis

TME mainly enhances the invasive ability of tumor cells through extracellular matrix (ECM) remodeling, immune regulation, and the activation of PI3K/Akt and other pathways. TME can also release factors that promote angiogenesis, leading to the formation of new blood vessels, thereby promoting tumor metastasis. TME can also change the matrix structure, providing support, and promote tumor cell invasion and metastasis. In addition, TME also promotes tumor invasion and metastasis by inhibiting the function of immune cells and reducing immune surveillance.



TME and Tumor Drug Resistance

TME mediates non-cell-autonomous mechanisms of drug resistance, enabling tumors to resist anti-tumor drugs in vivo. It contributes to this resistance through several mechanisms, including hypoxia, extracellular acidity, vascular abnormalities, changes in immune cell populations, cancer-associated fibroblasts (CAFs) and their secretions, exosomes, extracellular matrix, and other soluble factors. The TME releases drug-resistant factors, reduces drug permeability, and enhances tumor stem cell characteristics, thereby increasing drug resistance. Additionally, it inhibits immune cell function, reducing anti-tumor immune responses, and induces irregular blood vessels leading to uneven drug delivery, limiting chemotherapy effectiveness.



Alveolar type II cell · CAF · CTL · Dendritic Cell · DTC · Exosome · Fibroblast · FPC · MAC1 myeloid cell · Macrophage · Monocyte · MDSC · MC cell · Neutrophil · Granulocyte · NK cell · Platelet · TAM · TAM M1 · TAM M2 · Tumor stem cell · Treg cell