Tumor immune microenvironment

The tumor microenvironment (TME) is the cellular environment in which the tumor exists, including surrounding blood vessels, immune cells, fibroblasts, bone marrow-derived inflammatory cells, lymphocytes, signaling molecules and the extracellular matrix (ECM).

The tumor microenvironment (TME) could be simply characterized into cold (non T cell inflamed) or hot (T cell-inflamed tumor microenvironment), which is largely attributed to the levels of proinflammatory cytokine production and T cell infiltration

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With the advent of cancer immunotherapy, there has been a major improvement in patients' quality of life and survival. The growth of cancer immunotherapy has dramatically changed our understanding of the basics of cancer biology and has altered the standards of care (surgery, radiotherapy, and chemotherapy) for patients. Cancer immunotherapy has generated significant excitement with the success of chimeric antigen receptor (CAR) T cell therapy in particular. Clinical results using CAR-T for hematological malignancies have led to the approval of four CD19-targeted and one B-cell maturation antigen (BCMA)-targeted cell therapy products by the US Food and Drug Administration (FDA). Also, immune checkpoint inhibitors such as antibodies against Programmed Cell Death-1 (PD-1), Programmed Cell Death Ligand-1 (PD-L1), and Cytotoxic T-Lymphocyte-Associated Antigen 4 (CTLA-4) have shown promising therapeutic outcomes and long-lasting clinical effect in several tumor types and patients who are refractory to other treatments. Despite these promising results, the success of cancer immunotherapy in solid tumors have been limited due to several barriers, which include immunosuppressive tumor microenvironment (TME), inefficient trafficking, and heterogeneity of tumor antigens. This is further compounded by the high intra-tumoral pressure of solid tumors, which presents an additional challenge to successfully delivering treatments to solid tumors [1)].

The immunosuppressive tumor microenvironment (TME) of cancer strongly hinders the anti-tumor immune responses, thereby resulting in disappointing responses to immunotherapy. Chemoattractive and promotive traits of chemokines exerted on leukocytes have garnered interest in improving the efficiency of immunotherapy by increasing the infiltration of immune cells in the TME. In a study, a folic acid (FA) -modified gene delivery system based on the self-assembly of DOTAP, MPEG-PCL-MPEG, and FA-PEG-PCL-PEG-FA, namely F-PPPD, was developed to deliver plasmids encoding the immunostimulating chemokine CKb11. The delivery of plasmid CKb11 (pCKb11) by F-PPPD nanoparticles resulted in the high secretion of CKb11 from tumor cells, which successfully activated T cells, suppressed the M2 polarization of macrophages, promoted the maturation of dendritic cells (DCs), facilitated the infiltration of natural killer cells and inhibited the infiltration of immunosuppressive cells in tumor tissues. Administration of F-PPPD/pCKb11 also significantly suppressed the cancer progression. The study demonstrated a nanotechnology-enabled delivery of pCKb11, that remodeled the immunosuppressive TME, for cancer treatment [2)].

Glioma tumor immune microenvironment

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2)
Nie W, Yu T, Liu X, Wang B, Li T, Wu Y, Zhou X, Ma L, Lin Y, Qian Z, Gao X. Non-viral vector mediated CKb11 with folic acid modification regulates macrophage polarization and DC maturation to elicit immune response against cancer. Bioact Mater. 2021 Apr 6;6(11):3678-3691. doi: 10.1016/j.bioactmat.2021.03.031. PMID: 33898872; PMCID: PMC8056185.