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Therapeutic target of tumor microenvironment

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Abstract
As tumors grow, develop, angiogenesis, progress and metastasis, the tumor microenvironment (TME) changes or evolves. Targeting TME is a substantial matter in tumor biology. Targeting TME through multi-dimensional ways should be accepted to treat the cancers. Understanding how the tumor microenvironment treated by multiple ways are considered in this mini review. this could aid in the development of effective therapeutics to target cancer cell invasion and metastasis.

Keywords: therapeutic, target, tumor, microenvironment, angiogenesis

1. Introduction

Background

In tumor growth, angiogenesis and metastasis, Tumour microenvironment (TME) has a key roles (Tan *et al*., 2018) [9]. The tumor microenvironment (TME) is a heterogenous population of components composed of borders, blood vessels, lymph vessels, extracellular matrix (ECM), immune/inflammatory cells, secreted proteins, RNAs, small organelles, tumor cells and other associated or supporting cells (Guo and Deng, 2018) [4]. By affecting cancer cell metabolism, the tumor microenvironment regulates cancer invasion (Gould and Courtneidge, 2014) [3]. The aberrant expression of genes in tumor microenvironment (TME) has been associated with the pathogenesis of cancers (Md. N. Uddin *et al*., 2019; M. N. Uddin *et al*., 2019). So, targeting TME should be considered during the treatment of cancers. The aim of this mini review is to discuss about multiple target methods of TME.

Targeting stromal cells in tumor microenvironment

During the progression of tumor, TME recruited the stromal cells including vascular endothelial cells, pericytes, adipocytes, fibroblasts, osteoblasts, chondrocytes, the extracellular matrix (ECM) and bone-marrow mesenchymal stromal cells. Tumour stroma can promote resistance of cancer cells to therapies, eventually resulting in fatal disease (Valkenburg *et al*., 2018) [12]. Stromal cells in the TME dynamically interact with molecular components of tumor cells and can cooperate with them. These dynamic interactions alter the genotype and phenotype of cancer cells in the TME (Pienta *et al*., 2008) [8]. So, targeting stromal cells in TME is crucial for cancer treatment.

Targeting tumor microenvironment by nano therapy

Nanotechnology have brought new approaches to cancer diagnosis and therapy (Fernandes *et al*., 2018) [2]. Due to complexity of tumor microenvironment, the conventional drug delivery system fails to deliver the chemotherapeutics in effective concentration for cancer cell kill and is associated with debilitating side effects. This has prompted to exploit the alternative nanoparticulate strategy to achieve tumor specificity, if possible, improve therapeutic index and the pharmacokinetic profile of chemotherapeutic agents. Hence, Nano-chemotherapeutics can alter the Tumoral drug delivery by inducing perturbations in the tumor microenvironment. Thus, nanotechnology offers a versatile tool by enabling delivery of either single or combination of chemotherapeutics along with multiple targeting ligands to specifically target overexpressed receptors or enzymes or reductive environment, a common feature of tumor microenvironment. With growing number of clinical trials on Nanotherapy, different strategies combining nano-chemotherapeutics with radiotherapy and other allied therapies will translate into successful strategy for overcoming drug resistance.

Targeting tumour microenvironment by tyrosine kinase inhibitors (TKIs)

Recent works have demonstrated that beyond the direct action on cancer cells, tyrosine kinase inhibitors (TKIs) have been implicated in inactivation or normalization of Dysregulated TME components leading to cancer regression (Tan *et al*., 2018) [9]. Either through re-sensitizing the tumour cells or reversing the immunological tolerance microenvironment, the emergence of these TME modulatory mechanism of TKIs supports the combinatory use of TKIs with current chemotherapy or immunotherapy for cancer therapy. Therefore, an appropriate understanding on TME modulation by TKIs may offer another mode of action of TKIs for cancer treatment.

Modulating tumor-associated blood vessels

Tumor-associated blood vessels became permissive to T cell immigration (Hamzah *et al*., 2008) [3] and DC emigration (Jackaman *et al*., 2011) [6]. Transient normalisation of tumor vessels is reported to lead to better perfusion of the tumor bed by cytotoxic chemotherapy (Jain, 2005) and, likely, improved tumor penetration of antibodies and other important molecules. Therefore, a considered approach to the design of targeted therapy is needed to ensure that this stealthy approach can pave the way for further immune modulation, using standard cytotoxic chemotherapy or immunotherapy.

Trojan-horse targeting strategy

The non-specific uptake of the conventional actively-

targeted nano-vehicles by non-cancerous cells could lead to side effects. Recently, Trojan-horse targeting strategy was reported by Wu and Tan's group to reduce this risk. Fe3O4 nanocrystals-loaded albumin nanoparticles modified by folic acid and pH-sensitive polymers (PP-FA-AN-FN) were prepared for tumor imaging. PP-FA-AN-FN could hide or expose the targeting ligand (folic acid) of nanoparticles on demand. Similar to the "Pop-up" systems, this strategy is also reversible (Chen *et al*., 2017) [1]. After passing through the normal tissue, the ligands of the unused actively-targeted nanoparticles are shielded and eventually are effectively exploited in the tumor region.

Triggered drug release

Drug release is one of the most concerning issues for most passively- and actively-targeted nano-sized drug delivery systems and plays a critical role in tumor therapy as the tumor inhibition effect of most chemotherapeutics is dose-dependent. Although many nanoparticles and biomaterials have been developed to achieve perfect tumor-targeted delivery, drug release is still a common problem that needs to be solved. Liposomes and self-assembled nanoparticles are two promising nanocarriers because of their perfect biocompatibility, long circulation, and tumor targeting efficacy (Chen *et al*., 2017) [1]. Hence, novel platforms, including triggered drug release systems based on the tumor microenvironment have been developed to liberate the loading cargo at the right time and in the right place. The microenvironment stimuli-triggered drug release can mainly be divided into three types based on the mechanism: nanoparticle disassembly systems, sensitive-bond cleavage systems, and cap systems.

Conclusion

The tumor microenvironment is an active player during tumor progression. So, TME should be targeted by the above-mentioned ways to treat the cancers along with other chemical drugs.

References

1. Chen B, Dai W, He B, Zhang H, Wang X, Wang Y, Zhang Q. Current Multistage Drug Delivery Systems Based on the Tumor Microenvironment. Theranostics. 2017; 7:538–558. https://doi.org/10.7150/thno.16684
2. Fernandes C, Suares D, Yergeri MC. Tumor Microenvironment Targeted Nanotherapy. Front. Pharmacol, 2018, 9. https://doi.org/10.3389/fphar. 2018. 01230
3. Gould CM, Courtneidge SA. Regulation of invadopodia by the tumor microenvironment. Cell Adhes. Migr. 2014; 8:226–235. https://doi.org/10.4161/cam.28346
4. Guo S, Deng CX. Effect of Stromal Cells in Tumor Microenvironment on Metastasis Initiation. Int. J. Biol. Sci. 2018; 14:2083–2093. https://doi.org/10.7150/ ijbs. 25720
5. Hamzah J, Nelson D, Moldenhauer G, Arnold B, Hämmerling GJ, Ganss R. Vascular targeting of anti-CD40 antibodies and IL-2 into autochthonous tumors enhances immunotherapy in mice. J. Clin. Invest. 2008; 118:1691–1699. https://doi.org/10.1172/JCI33201
6. Jackaman C, Cornwall S, Graham PT, Nelson DJ. CD40-activated B cells contribute to mesothelioma tumor regression. Immunol. Cell Biol. 2011; 89:255–267. https://doi.org/10.1038/icb.2010.88
7. Jain RK. Normalization of tumor vasculature: an emerging concept in antiangiogenic therapy. Science. 2005; 307:58–62. https://doi.org/10.1126/science. 1104819
8. Pienta KJ, McGrego, N, Axelrod R, Axelrod DE. Ecological therapy for cancer: defining tumors using an ecosystem paradigm suggests new opportunities for novel cancer treatments. Transl. Oncol. 2008; 1:158–164.
9. Tan HY, Wang N, Lam W, Guo W, Feng Y, Cheng YC. Targeting tumour microenvironment by tyrosine kinase inhibitor. Mol. Cancer, 2018, 17. https://doi.org/10.1186/s12943-018-0800-6
10. Uddin Md N, Li M, Wang X. Identification of Transcriptional Signatures of Colon Tumor Stroma by a Meta-Analysis. J. Oncol. 2019. https://doi.org/10.1155 /2019/8752862
11. Uddin MN, Li M, Wang X. Identification of Transcriptional Markers and microRNA-mRNA Regulatory Networks in Colon Cancer by Integrative Analysis of mRNA and microRNA Expression Profiles in Colon Tumor Stroma. Cells, 2019, 8. https://doi.org/10.3390/cells8091054
12. Valkenburg KC, de Groot AE, Pienta KJ, Targeting the tumour stroma to improve cancer therapy. Nat. Rev. Clin. Oncol. 2018; 15:366–381. https://doi.org/10.1038/s41571-018-0007-1
13. Ashikujaman Syed. New Concepts of Tumour microenvironment. Int. J. Curr. Res. Med. Sci. 2019; 5(6):14-22.