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Plasma delivery systems for cancer treatment

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Cold atmospheric plasma (CAP) selectively kills tumor cells by generating reactive oxygen/nitrogen species (ROS/RNS), but its clinical application is limited by insufficient tissue penetration, attenuation of local active ingredients, and low efficiency of immune activation [1]. Our recent research focuses on the development of new delivery systems (such as portable devices, microneedle patches, injectable hydrogels) and combination therapies (immune checkpoint inhibitors, biomaterials, nanomaterials, etc.), aiming to enhance the local killing effect of CAP, activate local and systemic anti-tumor immune responses, and regulate the tumor microenvironment (TME), shown in Fig. 1.

Our study optimized the application of CAP through a multidisciplinary cross-strategy: 1) Innovative delivery system, a portable air-driven device, designed based on the lightning principle, directly acts on residual tumors after surgery and activates T cell immunity. The portable device inhibited postoperative recurrence in the 4T1 breast cancer model and prolonged survival by more than 50% [2]. Hollow microneedle patches deliver CAP and PD-L1 antibodies transdermally to enhance antigen presentation by dendritic cells (DCs) [3]. The microneedle patch combined with PD-L1 antibody reduced melanoma metastasis by 60%. Injectable hydrogels (such as Pluronic) load CAP active substances to achieve ROS/RNS sustained release and combined with immune checkpoint inhibitors (such as anti-PD-1) or ferroptosis inducers (RSL3) or biomaterials (trehalose) to prolong the local action time [4-6]. A single injection of alginate hydrogel reduced the tumor volume of the colon cancer model by 70%, induced the release of immunogenic cell death (ICD) markers (ATP, HMGB1), activated DC maturation and CD8+ T cell infiltration.

We investigate the mechanism synergy. In terms of immune regulation, CAP induces ICD to release tumor antigens, combined with immune checkpoint inhibitors (such as anti-PD-1/PD-L1) to block immunosuppressive signals and promote CD8+ T cell infiltration. In terms of metabolism and oxidative damage, RSL3 induces ferroptosis by inhibiting GPX4, and synergizes with CAP's ROS to enhance tumor cell apoptosis; trehalose amplifies the oxidative damage effect of CAP by activating the endoplasmic reticulum stress pathway. Immune microenvironment regulation, CAP treatment significantly increased the proportion of M1 macrophages in the tumor (more than 60%) and reduced the expression of immunosuppressive factors (TGF-β, IL-10). RSL3 combined with CAP enhanced the synergistic effect of ferroptosis and apoptosis by inhibiting the expression of anti-apoptotic proteins (Bcl-2, Mcl-1).

Current research has revealed the core advantages of the CAP combined delivery system: 1) Breaking through the penetration limitation of CAP through local sustained-release systems (hydrogels, microneedles), combined with immunotherapy or ferroptosis inducers to form a "local killing-systemic immune activation" model, significantly improving efficacy and reducing side effects; 2) The portable device is suitable for precision treatment after surgery; the injectable hydrogel is compatible with a variety of drugs and is suitable for personalized treatment of solid tumors and metastases; 3) Optimizing the loading efficiency of active ingredients (such as material design/drug design), exploring the synergistic mechanism of CAP and new therapies (such as pyroptosis, apoptosis), and promoting the clinical transformation of portable devices. Finally, we will present clinical results of plasma treating tumors.

References

[1] Z. T. Chen, et al, Mater. Today 54, 153 (2022)
[2] G.C. Chen#, Z.C. Chen#, et al, Sci. Adv. 7(36), eabg5686 (2021)
[3] G.C. Chen#, Z.T. Chen#, et al, PNAS 117(7), 3687 (2020)
[4] T.X. Fang, et al, Biomaterials 300, 122189 (2023)
[5] X.N. Cao, et al, Biomaterials 309, 122582 (2024)
[6] X.N. Cao, et al, J. Nanobiotechnology 23, 136 (2025)

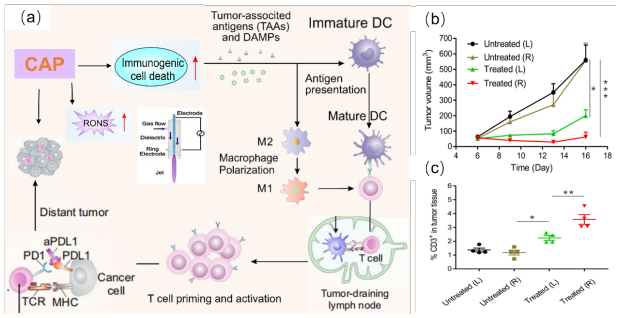

Figure 1: Schematic diagram of CAP-mediated cancer immunotherapy. a) CAP produces high concentrations of ROS/RNS, which increases the oxidative stress level of cancer cells. ROS/RNS induce ICD, release TAAs and DAMPs, promote DC maturation, promote the polarization of M2 phenotype macrophages to M1, enhance the presentation of TAAs to T cells, T lymphocytes infiltrate tumor tissues, activate T cell-mediated anti-tumor immune responses to tumor cells, aPD-1 inhibits the recognition of PD-1 and PD-L1 lymphocytes and tumor cells, further enhances the activity of T cells, and activated T cells enhance systemic anti-tumor responses and attack distant tumor cells; b) Left and right tumor growth curves of untreated and CAP-treated mice; c) CD3+T cells were detected in B16F10 tumors 3 days after treatment.