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Synergistic effect of tumor chemo-immunotherapy induced by leukocyte-hitchhiking thermal-sensitive micelles

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Some specific chemotherapeutic drugs are able to enhance tumor immunogenicity and facilitate antitumor immunity by inducing immunogenic cell death (ICD). However, tumor immunosuppression induced by the adenosine pathway hampers this effect. In this study, E-selectin-modified thermal-sensitive micelles are designed to co-deliver a chemotherapeutic drug (doxorubicin, DOX) and an A2A adenosine receptor antagonist (SCH 58261), which simultaneously exhibit chemo-immunotherapeutic effects when applied with microwave irradiation. After intravenous injection, the fabricated micelles effectively adhere to the surface of leukocytes in peripheral blood mediated by E-selectin, and thereby hitchhiking with leukocytes to achieve a higher accumulation at the tumor site. Further, local microwave irradiation is applied to induce hyperthermia and accelerates the release rate of drugs from micelles. Rapidly released DOX induces tumor ICD and elicits tumor-specific immunity, while SCH 58261 alleviates immunosuppression caused by the adenosine pathway, further enhancing DOX-induced antitumor immunity. In conclusion, this study presents a strategy to increase the tumor accumulation of drugs by hitchhiking with leukocytes, and the synergistic strategy of chemo-immunotherapy not only effectively arrested primary tumor growth, but also exhibited superior effects in terms of antimetastasis, antirecurrence and antirechallenge.

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