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ABSTRACT

Tumor vaccine has been one of the research hotspots for cancer immunotherapy in recent years. By introducing tumor antigens into the body, the patient's own immune system will be specifically activated to induce effective immune responses for controlling or eliminating the malignant tumor cells. In this study, a simple nanovaccine was developed to induce antigen-specific anti-tumor immune responses. Polycationic polyethylenimine (PEI) was utilized to co-deliver the antigen ovalbumin (OVA) and the adjuvant unmethylated cytosine-phosphate-guanine (CpG) by electrostatic binding. The positively charged PEI could be beneficial to augment the PEI/CpG/OVA nanovaccine uptake in dendritic cells (DCs) and facilitate the endosomal escape of the nanovaccine for antigen delivering into the cytoplasm. The nanovaccine showed significant stimulation on DCs' maturation *in vitro*, and it was further applied for *in vivo* anti-tumor immunotherapy. To enhance the tumor infiltration of the nanovaccine-generated tumor-specific T cells, hyaluronidase (HAase) was employed to increase the permeability of the tumor tissues by breaking down the hyaluronan (HA) in the extracellular matrix (ECM) of tumors. Highly enhanced *in vivo* anti-tumor therapeutic efficiency was achieved by combining the PEI/CpG/OVA nanovaccine with HAase, which was attributed to the increased quantity of OVA-specific T cells in tumor tissues. The combination of nanovaccine with HAase has offered a simple and efficient strategy for inducing powerful anti-tumor effect in cancer immunotherapy.