A rapid strategy to develop personalized cancer nanovaccines for different immunogenic tumors

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Background: Therapeutic cancer vaccines aim to train the immune system and elicit antitumor immune responses, which are expected to fill the unmet medical need of immune checkpoint inhibitors. Despite tremendous efforts over the past decades, it remains challenging to prepare personalized cancer vaccines using a facile and rapid approach due to tumor diversity. CpG-ODN is a promising immunoadjuvant in cancer immunotherapy, and many clinical trials have been performed or are ongoing. However, commonly used phosphorothioate-modified CpG ODN easily induces protein aggregation and its long-term side effects are concerned. Here, we designed hollow large-pore mesoporous organosilica with sulfide bond to simultaneously load unmodified CpG-ODN with guanine-quadruplex (G4) structures and different tumor antigens to prepare personalized cancer vaccines in a simple, fast, and effective way.
Methods: High-immunogenic E.G7-OVA lymphoma or low-immunogenic Lewis lung carcinoma (LLC) cells were subcutaneously inoculated into the left flanks to establish tumor-bearing mice. On days 4, 7, and 10 post tumor inoculation, cancer vaccines prepared using model antigen (OVA) or autologous tumor antigen (LLC tumor cell lysate) were subcutaneously injected into the right flanks of mice, respectively. Saline group, free tumor antigen group, free tumor antigen + CpG-ODN group, tumor antigen + organosilica group were used as controls. The size of tumors was monitored.
Results: Cancer vaccines against E.G7-OVA showed high loading efficiencies of >95% for both CpG-ODN and OVA, triggered antitumor immune response with high percentages of $CD4^+$, $CD8^+$, $tetramer^+CD8^+$ T cells in splenocytes, and effectively inhibited the growth of established tumor, compared with free OVA, free OVA + CpG-ODN, free OVA + organosilica groups. Cancer vaccines against LLC exhibited high loading efficiencies of >95% and >80% for CpG-ODN and LLC tumor cell lysate, activated antitumor immune response with high percentages of $CD4^+$ and $CD8^+$ T cells in splenocytes and $CD8^+$ T, NK and M1 cells in tumor sites, and effectively inhibited the growth of established tumor, compared with control groups.
Conclusions: Codelivery of CpG-ODN and different tumor antigens using hollow large-pore mesoporous organosilica elicits antitumor immunity against both high-immunogenic and low-immunogenic tumors.