1146 SELF-ASSEMBLY NEOANTIGEN PEPTIDES FOR PERSONALIZED CANCER VACCINES

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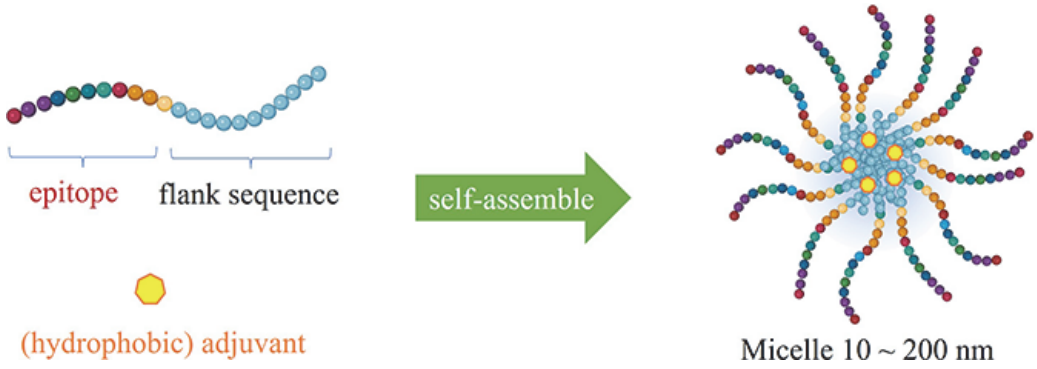
Background Cancer vaccines are one of the most important immunotherapies against tumor. In the past decades, the development neoantigen has greatly enhanced the specificity of tumor antigens and enable the design of 'personalized' cancer vaccine. However, the clinical success of neoantigen cancer vaccines is still limited by their poor in vivo distribution. In this project, we aim to develop a novel vaccine delivery system based on the self-assembly of synthetic long peptide (SLP) containing neoantigen epitopes to address the challenge of vaccine delivery.

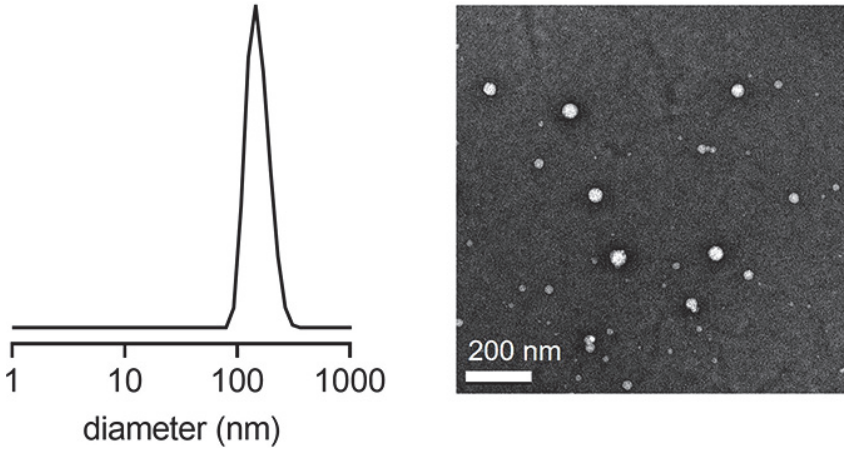
Methods Through decorating neoantigen peptides with pH-sensitive flanking sequence of optimized length, we can easily obtain the amphiphilic synthetic long peptides which are ready to co-assembly with molecular adjuvants in mild conditions (figure 1). The self-assembly neoantigens could greatly enhance the extracellular delivery including the localization of neoantigen and adjuvants in peripheral lymphoid organs, such as the lymph nodes, as well as the endocytosis with antigen-presenting cells, such as dendritic cells. For intercellular delivery, the pH-responsive nanoparticle can rapidly disassemble in the acidic environment of the endosome to enhance the escaping of antigens to cytoplasm, thus enhancing the antigen cross-presentation to CD8 T cells. Additionally, Self-assembly design maximizes the loading capacity of antigens and adjuvants, and the size of the particle can be optimized by adjusting the flanking peptide sequence and self-assembly conditions to meet the specific requirements of vaccine delivery. In summary, the self-assembly peptide neoantigen is potent candidate to address the challenge in neoantigen vaccine delivery.

Results The self-assembly of amphiphilic neoantigen peptides generates regular nanoparticle of 50~150 nm as measured by DLS, TEM, and SEM (figure 2). The particles remain stable under 4°C for more than one week. Once exposed to acidic condition (pH 5–6), the nanoparticles show disassembly behavior. For in vitro assays, the DC uptake assay showed greatly enhanced antigen and adjuvants endocytosis (figure 3). The self-assembly neoantigens exhibited equal DC maturation and enhanced antigen cross-presentation capability with soluble antigens. For in vivo assessments, the self-assembly neoantigen vaccine showed greatly enhanced lymph node localization (figure 4). In the therapeutic study with mice bearing different tumor models, the treatment of self-assembly neoantigen vaccine showed significantly suppressed tumor growth as well as greatly increased survival (figure 5).

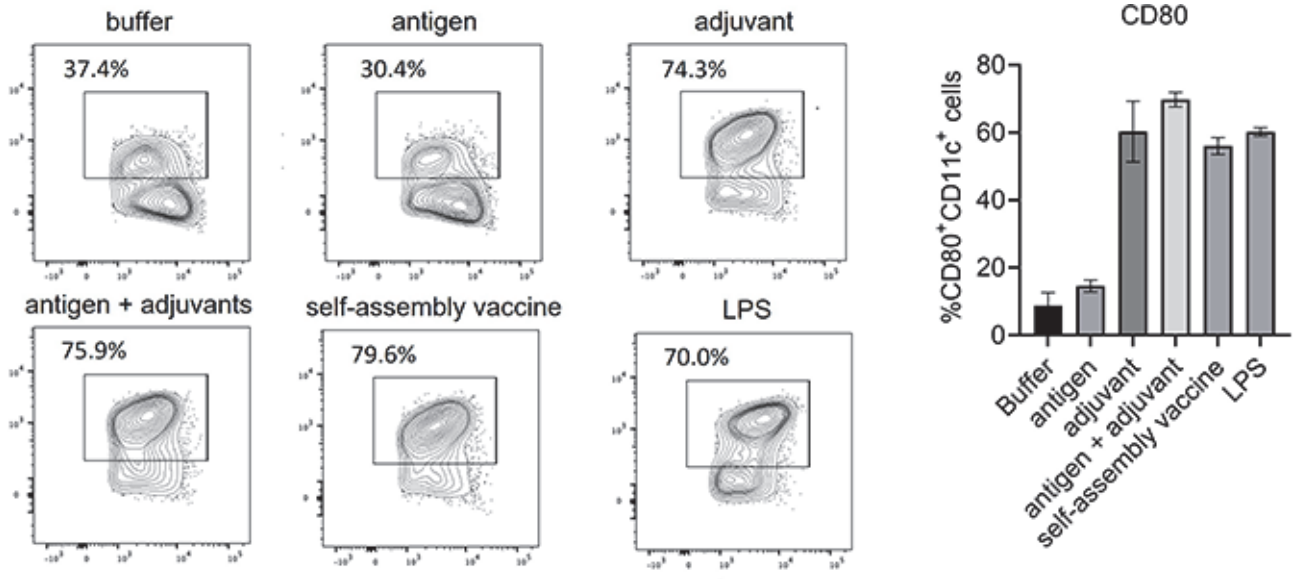
Conclusions In summary, the self-assembly neoantigen vaccine is an efficient delivery system for neoantigen and adjuvants through enhancing both extracellular and intracellular travelling. The safe and simple design has great potential for clinical application.



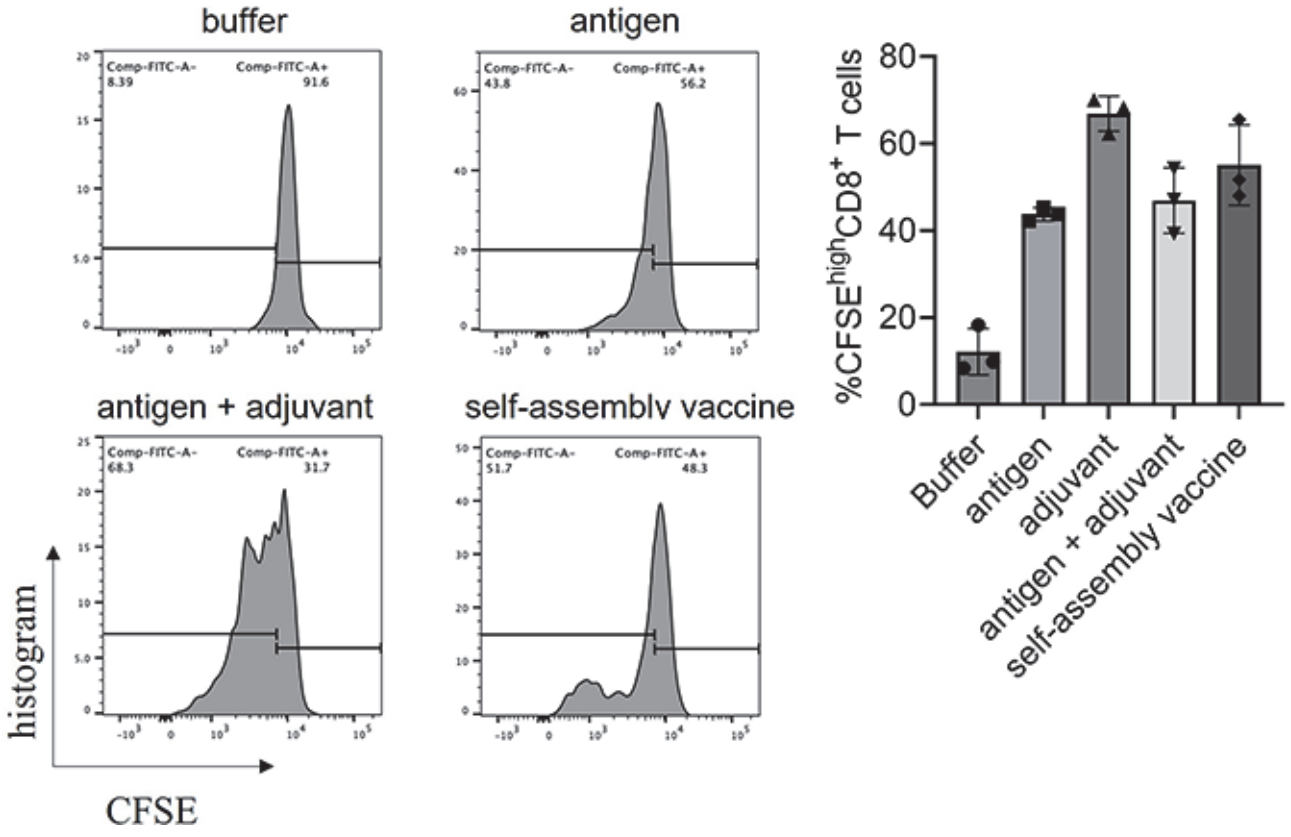
Abstract 1146 Figure 1



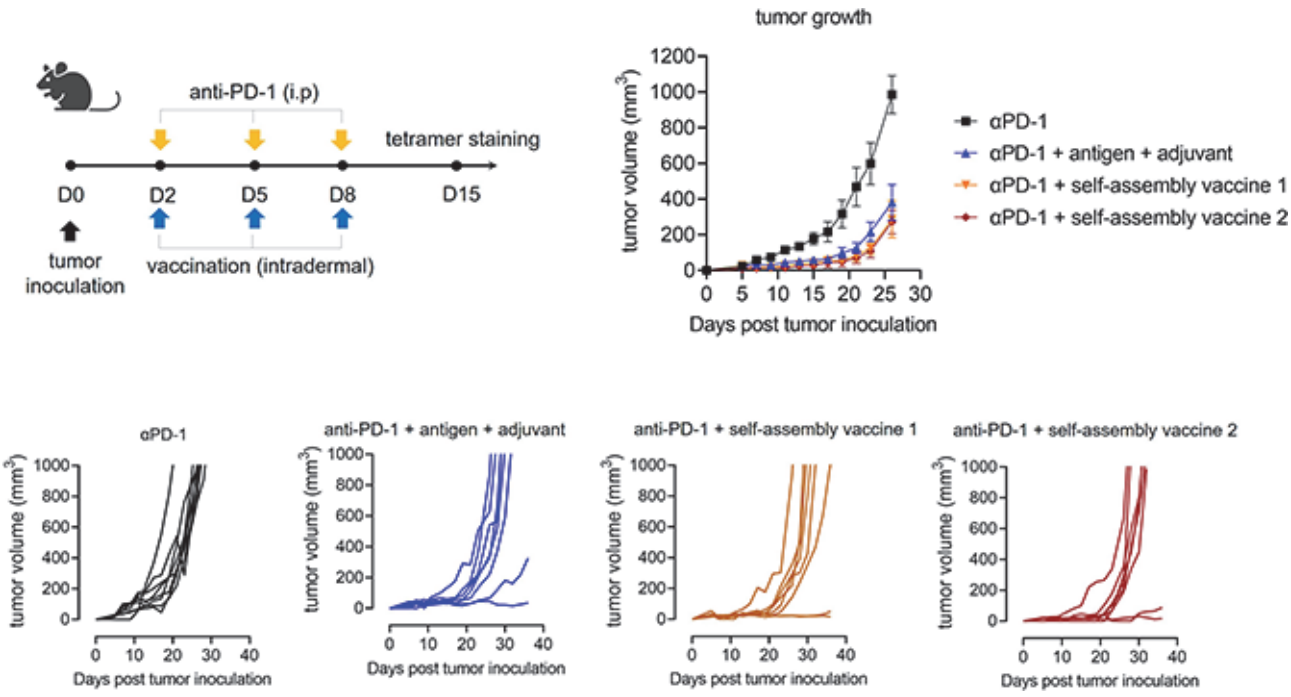
Abstract 1146 Figure 2



Abstract 1146 Figure 3



Abstract 1146 Figure 4



Abstract 1146 Figure 5

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