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Antigen targeting to Dendritic cells by sPD1-based vaccine amplifies CD8⁺ T cell immunity in mice

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Abstract

An effective vaccine to elicit a high frequency of protective CD8⁺ T cell immunity against intracellular pathogens such as HIV remains a continuous challenge. DNA vaccination is one of the most simple and effective methods of inducing specific cellular and humoral immunity against various human infections and cancer but with weak antigen immunogenicity. Here, we report a novel antigen targeting DNA vaccine strategy that exploits the binding of programmed death-1 (PD1) to its ligands expressed on dendritic cells by fusing soluble PD1 with HIV-1 Gag p24 antigen to increase antigen immunogenicity. As compared with non-targeting vaccines, the sPD1-based form can interact with DCs in vitro and enhance antigen specific immunity through DC-pulsed tail vein injection in vivo. In addition, the traditional DNA vaccination method of intramuscular immunization via electroporation (EP) of the fusion DNA was also tested in mice. The results showed that sPD1-based DNA elicited consistently higher frequencies of Gag-specific, broadly reactive and polyfunctional T cells in addition to robust anti-Gag antibody titers. The enhanced responses were attributed mainly to effective antigen dendritic cell-targeting, and were dose-dependent, long lasting and conferred significant protection against mucosal challenge in mice with vaccinia-Gag viruses. Meanwhile, sPD1-based DNA protects mice from a p24-expressed tumor challenge. Furthermore, the comparison between classic DC targeting strategy utilizing anti-DEC205 antibody with the same antigen ligation as well as soluble CTLA-4 fusion with antigen HIV-1 p24 demonstrated that the sPD1 is one of the most important DC targeting strategies which strongly induced antigen specific CD8⁺ T cells immunity in mice. The high frequency of durable and protective Gag-specific CD8⁺ T cell immunity induced by soluble PD1-based DNA/EP vaccination has important implications for vaccine development and immune therapy against virus infection and cancer.