1137 MHC CLASS II PEPTIDE ON A NANOPARTICLE CANCER VACCINE INDUCES ANTI-TUMOR IMMUNE RESPONSES

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Background Nanoparticle cancer vaccines provide advantages over conventional vaccines, including the ability to co-deliver antigens and adjuvants, protect them from degradation, and be preferentially taken up by dendritic cells; all of which can lead to better anti-tumor immune responses relative to non-nanoparticle formulations.[1] Nanoparticle materials can range from inorganic, to polymers, or as in our case, self-assembling proteins.[1] Most cancer vaccination strategies focus on stimulating CD8 T cell responses through major histocompatibility complex (MHC) Class I recognition.[2] However, recent studies highlight the importance of CD4 T cells in supporting effective anti-tumor immune responses.[3 4] We evaluate the hypothesis that a nanoparticle vaccine can induce a T helper type-1 (Th1) response against an MHC Class II peptide, with the goal of optimizing anti-tumor immunity by combining Class I and Class II peptides on a single nanoparticle.

Methods The E2 protein nanoparticle has been utilized as an effective delivery platform for Class I targeted cancer vaccines.[5] This self-assembling nanoparticle forms a hollow protein cage with exterior and interior surfaces available for conjugation,[5] and its ~30 nm diameter is in the optimal size range for dendritic cell uptake and drainage to the lymph nodes.[5 6] These characteristics make this nanoparticle particularly attractive as a vaccine delivery platform. In this study, an MHC class II (CT26ME1) peptide from the CT26 murine colon carcinoma, along with an adjuvant (CpG), were conjugated to the nanoparticle exterior or interior, respectively, enabling co-delivery of antigen and adjuvant. We evaluated murine (BALB/c) splenocytes for antigen-specific IFN-γ response by ELISpot and changes in immune cell subsets by flow cytometry.

Results The nanoparticles remained intact after antigen and adjuvant conjugation. Mice vaccinated with CpG-CT26ME1-E2 (nanoparticle carrying an MHC Class II peptide and adjuvant) showed significant increases in antigen-specific IFN-γ from splenocytes compared to PBS-treated mice, indicating a Th1 response elicited by the vaccine. CpG-CT26ME1-E2 vaccinated mice also exhibited overall higher dendritic cell counts in the spleens and lymph nodes, suggesting effective *in vivo* processing of the vaccine.

Conclusions Our results indicate that nanoparticles carrying an MHC Class II peptide can generate a Th1 immune response, even in Th2-biased BALB/c mice. Combined with previous studies on Class I targeted vaccines, our results suggest that co-delivery of Class I and Class II peptides, along with an adjuvant, on a single nanoparticle could stimulate a powerful antigen-specific immune response, a hypothesis currently being evaluated.

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Ethics Approval All animal studies were carried out under protocols approved by the Institute of Animal Care and Use Committee (IACUC) at the University of California, Irvine.

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