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Apoptosis inhibitor 5 (API5) induce cytotoxicity CD^{8+} T cells mediated anticancer effect through TLR4 signaling of dendritic cells

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Dendritic Cells (DCs) among innate immune system are important to induce adoptive immune response such as CD^{8+} cytotoxic T cells activation. Immunotherapy using dendritic cells is a promising one of cancer therapy. Because most of adjuvants that activate immune cells are derived from bacteria, restricted to the use of DC-based immunotherapy. Here we evaluate the use of apoptosis inhibitor 5 (API5), a damage-associated molecular pattern expressed by many human cancer cells, as a novel DC vaccine adjuvant. API5 regulating survival is generally localized at nuclear, upregulated in various cancer cells. We showed that API5 can prompt activation and maturation of DCs and activate NFkB by stimulating the Toll-like receptor signaling pathway. We also demonstrated that vaccination with API5-treated DCs pulsed with OVA, E7, or AH1-A5 peptides led to the generation of OVA, E7, or AH1-A5-specific CD^{8+} T cells and memory T cells, which is associated with long term tumor protection and antitumor effects in mice, against EG.7, TC-1, and CT26 tumors. Additionally, we determined that API5-mediated DC activation and immune stimulation are dependent on TLR4. Lastly, we showed that the API5 protein sequence fragment that is proximal to its leucine zipper motif is responsible for the adjuvant effects exerted by API5. In conclusion, our results provide evidence that support the use of API5 as a promising adjuvant for DC-based therapies, which can be applied in combination with other cancer therapies. Most notably, our results further support the continued investigation of human-based adjuvants.

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