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Immuno-modulators enhance antigen-specific immunity and anti-tumor effects of mesothelin-specific chimeric DNA vaccine through promoting DC maturation

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Abstract

As a tumor antigen, mesothelin (MSLN) can be identified in various malignancies. MSLN is potential for antigen-specific cancer vaccines. We generated a novel chimeric DNA vaccine using antigen-specific connective tissue growth factor lined with MSLN (CTGF/MSLN). The anti-tumor effects of the CTGF/MSLN DNA vaccine combined with anti-CD40 Ab and toll-like receptor 3 ligand–poly(I:C) were validated in an MSLN-expressing model. CTGF/MSLN DNA with anti-CD40Ab and poly(I:C) vaccinated mice demonstrated potent anti-tumor effects with longer survival and less tumor volumes. An increase in MSLN-specific CD8⁺ T cells and anti-MSLN Ab titers was also noted in CTGF/MSLN DNA with anti-CD40Ab and poly(I:C) vaccinated mice. The CTGF/MSLN DNA vaccine combined with immuno-modulator EGCG also generated potent anti-tumor effects. Immuno-modulators could enhance the antigen-specific anti-tumor effects of CTGF/MSLN DNA vaccine through promoting the DC maturation. In addition, MSLN-specific cell-based vaccine with AAV-IL-12 and the CTGF/MSLN DNA vaccine with anti-CD40Ab/polyp(I:C) generated more potent anti-tumor effects than the other combinational regimens. The results indicate that an MSLN-specific DNA vaccine combined with immuno-modulators may be an effective immunotherapeutic strategy to control MSLN-expressing tumors including ovarian and pancreatic cancers, and malignant mesothelioma.

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