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RESEARCH ARTICLE

Development of Membrane-Bound GM-CSF and IL-18 as an Effective Tumor Vaccine

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Abstract

The development of effective adjuvant is the key factor to boost the immunogenicity of tumor cells as a tumor vaccine. In this study, we expressed membrane-bound granulocyte-macrophage colony-stimulating factor (GM-CSF) and interleukin-18 (IL-18) as adjuvants in tumor cells to stimulate immune response. B7 transmembrane domain fused GM-CSF and IL-18 was successfully expressed in the cell membrane and stimulated mouse splenocyte proliferation. Co-expression of GM-CSF and IL-18 reduced tumorigenesis ($P<0.05$) and enhanced tumor protective efficacy ($P<0.05$) significantly in comparison with GM-CSF alone. These results indicated that the combination of GM-CSF andIL-18 will enhance the immunogenicity of a cell-based anti-tumor vaccine. This membrane-bound approach can be applied to other cytokines for the development of novel vaccine strategies.

Introduction

A major obstacle in tumor cell vaccine technology is inefficient stimulation of an immune response to induce anti-tumor effects. The co-administration of cytokines is a possible approach for the enhancement of anti-tumor immunity. Various cytokines have been tested for their host immune stimulation activity for cancer treatment, such as IL-2, GM-CSF, and INF-α[1]. Among these, GM-CSF has been widely studied and has shown promising anti-tumor results in many tumor models, such as melanoma cells[2], bladder cancer cells[3], murine leukemia[4], etc. GVAX (Cell Genesys) is a tumor vaccine comprised of genetically modified tumor cells engineered to secrete GM-CSF. It has been studied in a number of cancer types in preclinical and clinical trials[5], and demonstrated promising results in both phase I and II clinical trials of pancreatic and prostate cancer patients [6–8]. However, a phase III