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# Generation of interleukin-13 receptor alpha2 antigen expressing modified vaccinia ankara recombinant virus for potential cancer immunotherapy

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Genetically modified recombinant poxviruses have shown promise in preclinical models of cancer immunotherapy due to their ability to induce effective cell-mediated immunity against target tumor-associated antigens (TAA). One such vector, recombinant Modified Vaccinia Ankara (MVA), is capable of expressing foreign genes in infected host cells. MVA is replication restricted in most mammalian cells exemplifying a unique safety profile. We have demonstrated that the interleukin-13 receptor  $\alpha 2$  (IL-13R $\alpha 2$ ) is selectively expressed in various solid tumors but not in normal tissues making it a promising TAA. Prophylactic and therapeutic vaccination with a plasmid vector expressing IL-13R $\alpha 2$  caused only partial regression of established tumors [1], suggesting that host immune responses against IL-13R $\alpha 2$  needed further enhancement. Thus, we constructed a recombinant MVA (rMVA-IL13R $\alpha 2$ ) expressing both IL-13R $\alpha 2$  and a green fluorescent protein (GFP) reporter gene. Purified virus titration by immunostaining using anti-vaccinia antibody and anti-IL-13R $\alpha 2$  antibody confirmed the identity and purity of the recombinant MVA. Western Blot analysis showed the presence of IL-13R $\alpha 2$  protein (65 kDa). Flow cytometric analysis of IL-13R $\alpha 2$  negative T98G glioma cells infected with rMVA-IL13R $\alpha 2$  virus (T98G-IL13R $\alpha 2$ ) demonstrated surface expression of IL-13R $\alpha 2$ , indicating the infectivity potential of the recombinant virus. Incubation of T98G-IL13R $\alpha 2$  cells with varying concentrations (0-100 ng/ml) of IL13-PE (interleukin-13 fused to truncated *Pseudomonas* exotoxin [2]) resulted in depletion of GFP<sup>+</sup> T98G-IL13R $\alpha 2$  cells in a concentration-dependent manner.

Higher concentrations of IL13-PE (10-1000 ng/ml) also inhibited the protein synthesis in T98G-IL13R $\alpha 2$  compared to cells infected with control pLW44-MVA. We further observed that IL13-PE treatment of rMVA-IL13R $\alpha 2$  infected chicken fibroblast, DF-1 cells led to a reduction in virus titer compared to untreated cells. These results indicate that rMVA-IL13R $\alpha 2$  virus can successfully infect mammalian cells and express IL-13R $\alpha 2$  in a biologically active form on the cell surface. The immunization studies of rMVA-IL13R $\alpha 2$  are ongoing in a syngeneic mouse model of metastatic breast carcinoma. Based on *in vitro* results, we expect the rMVA-IL13R $\alpha 2$  to be a useful agent in tumor immunotherapy as a vaccine alone and in combination with other therapeutic agents to eradicate metastatic tumors.

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## References

1. Nakashima H, Terabe M, Husain SR, Puri RK: A novel combination immunotherapy for cancer by IL-13R $\alpha 2$ -targeted DNA vaccine and immunotoxin in murine tumor models. *J Immunol* 2011, **187**:4935-4946.
2. Husain SR, Puri RK: Interleukin-13 receptor-directed cytotoxin for malignant glioma therapy: from bench to bedside. *J Neuro-Oncol* 2003, **65**:37-48.

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