자유연제 1-1

DISC-GMCSF(GM-CSF Gene Transduced Defective Infectious Single Cycle Herpes Virus) Gene Therapy in Established SCCVII Squamous Cell Carcinoma Model

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Background : Over the past five years, preclinical studies evaluating viral-vector-mediated gene transfer in the treatment of head and neck cancer have reported promising results. The main goal of this study was to evaluate the efficacy of intra-tumoral treatment with DISC virus (defective infectious single cycle herpes virus) carrying a GM-CSF immunomodulatory genes as cancer gene therapy.

Method : We used the SCCVII squamous cell carcinoma model. We determinated the in vivo GM-CSF production by ELISA method and evaluated the in vivo effects of DISC-GMCSF on established tumor model. One of the following preparations was injected every two days to a total of three-dose intratumorally. Group I (control) : PBS alone, group II: heat inactivated DISC-GMCSF, group III : DISC-GMCSF. To prove the specific anti-tumor response, we analyzed surface phenotype of tumor infiltrating cells. Flow cytometric analysis was performed using FACScan.

Result : Intratumoral injection of the DISC-GMCSF resulted in effective in vivo production of the cytokine (4,500 pg/0.5g tumor tissue), but as the progeny of the DISC virus could not infect other host cells, effective cytokine production time was limited. However the DISC vector was safe and also allowed the possibility to administer repeated treatment as needed. Effect of DISC-GMCSF injection on established tumor model showed that the greatest inhibition of tumor growth was seen in the DISC-GMCSF treated group (control vs DISC-GMCSF, $p<0.001$). It was interesting to note from our in vivo analysis of tumor infiltrating cells that treatment of flank tumors with the DISC-GMCSF virus resulted in a significant increase in the percentage of CD8+ cells within the tumor (control vs DISC-GMCSF, $p<0.05$).

Conclusion : Intratumoral injection of DISC-GMCSF significantly suppressed the tumor growth and induced immune effector cells. The results demonstrate the gene transfer to be effective anti-cancer therapy.

KEY WORDS : DISC virus · GM-CSF · Gene therapy · Tumor vaccine · Head and Neck cancer