Antitumor Effects of Canine Adipose Tissue-Derived Mesenchymal Stem Cell Based IFN-β Gene Therapy and Cisplatin in a Mouse Melanoma Model

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Purpose: Adult stem cells have been demonstrated as a potential source for cell mediated gene therapy of cancer. The purpose of this study is to generate engineered canine adipose tissue-derived mesenchymal stem cells (cAT-MSCs) producing mouse IFN-β using lentivirus vector system for the treatment of cutaneous melanoma in an immunocompetent mouse model.

Material and methods: Melanoma-bearing animal model developed by injection of B16F10 cells into 6-week-old C57BL/6 mice subcutaneously. Fourteen days later, cisplatin injected intratumorally and 3 days later from this time, unengineered cAT-MSCs and IFN-β transduced cAT-MSCs were subcutaneously injected.

Results: Although in both treatments were significantly inhibited tumor growth and increased survival of B16 melanoma model, the combined treatment with IFNβ-cAT-MSCs was resulted in a greater inhibition of tumor growth than both unengineered cAT-MSCs combination group and cisplatin alone group. Interestingly, it was observed that subcutaneously injected xenogeneic AT-MSCs migrate to tumor sites and no clinical signs were found with multiple injections in mouse melanoma model. These results suggest that locally injected IFNβ-cAT-MSCs and cisplatin suppress the growth of tumor, presumably through the local production of IFN-β in the tumor microenvironment. Also, these data support the fact that canine originated AT-MSCs may be an effective cellular vehicle having an advantage of targeted delivery of therapeutic proteins to cancer site and antitumor effect in itself.

Conclusion: In conclusion, combination treatment of IFNβ-cAT-MSCs and cisplatin is considered as a potentially effective therapeutic protocol for melanoma.

Key words: IFN-β, adipose tissue-derived mesenchymal stem cells (cAT-MSCs), melanoma, dog

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