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论著

微囊化小鼠白介素-12基因工程细胞的长效抗肿瘤作用

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摘要 目的 探讨通过微囊化能否获取长效抗肿瘤的小鼠白介素-12(mIL-12)基因工程细胞。方法 构建pcDNA3.1/mIL-12重组表达质粒，然后稳定转染CHO细胞，采用海藻酸钠微囊制作技术，将mIL-12基因修饰的CHO细胞包裹。观察微囊化mIL-12基因工程细胞的mIL-12释放，并将微囊化细胞植入荷瘤小鼠体内，测定小鼠的抗肿瘤免疫功能及抑瘤效应。结果 微囊化mIL-12基因工程细胞产生的mIL-12蛋白可自由透过微囊膜。植入荷瘤小鼠体内21 d后，微囊化mIL-12基因工程细胞治疗组血清中mIL-12，mIL-2及mIFN-γ水平分别为 （549±53），（180±29）和（1008±156）ng·L^{-1}，而mIL-4，mIL-10水平则显著降低。脾脏细胞毒T淋巴细胞(CTL)活性及自然杀伤细胞(NK)活性均显著增高，肿瘤生长受到显著性抑制，荷瘤小鼠的存活期明显延长。 结论 微囊化mIL-12基因工程细胞在体内可持续、稳定地释放mIL-12，能激发机体产生持久而强大的抗肿瘤免疫反应，对实验小鼠产生明显的抗肿瘤效应并延长其生存期。

关键词 细胞微囊化 白介素 基因疗法 肿瘤

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Long term anti tumor effects of microencapsulated murine interleukins-12 engineered cells

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Abstract

AIM To investigate if long-term antitumoric murine interleukin-12(mIL-12) gene- engineering cells could be obtained by microencapsulation. **METHODS** Reconstructed plasmid pcDNA3.1/mIL-12 was transfected into CHO cells stably by Superfect^{TM}, then CHO/pcDNA3.1/ mIL-12 cells were encapsulated in alginate microcapsules. mIL- 12 release from the microencapsulated CHO/pcDNA3.1/mIL- 12 cells was confirmed using ELISA assay. Microencapsulated CHO/pcDNA3.1/mIL-12 cells were transplanted subcutaneously into the tumor-bearing mice with CT26 cells. The anti- tumor immunoreaction responses and the anti-tumor activities of the microencapsulated CHO/pcDNA3.1/mIL- 12 cells were evaluated. **RESULTS** mIL- 12 protein could release freely from the microencapsulated CHO/ pcDNA3.1/mIL-12 cells. After the microencapsulated CHO/pcDNA3.1/mIL- 12 cells were transplanted subcutaneously into the tumor- bearing mice for 21 d, the serum average concentrations of mIL-12, mIL- 2 and mIFN-γ in the mice treated with microencapsulated CHO/pcDNA3.1/mIL- 12 cells were（549±53）,（180±29）and （1008±156）ng·L^{-1}, respectively, but the serum concentrations of mIL-4 and mIL- 10 were decreased significantly compared to the controls. The cytotoxicity of the CTL from the splenocytes and the NK activity were significantly higher in the mice treated with microencapsulated CHO/pcDNA3.1/mIL-12 cells. Moreover, mIL- 12 released from the microencapsulated CHO/pcDNA3.1/mIL-12 cells continuously and stably brought a significantly inhibition of tumor proliferation and a prolonged survival time of tumor-bearing mice. **CONCLUSION** The results showed that microencapsulated CHO/pcDNA3.1/mIL- 12 cells expressed significant antitumor effects in the experimental tumor- bearing mice by activating anti-tumor immune responses *in vivo*.

Key words microencapsulated cells interleukins gene therapy tumor

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