

87-92. 载IL-2磁性纳米粒的制备及其联合体外磁场在肿瘤组织中的靶向富集作用[J]. 沈爱蓉, 郭全义, 袁玫, 王桂琴, 卢世璧. 中国肿瘤生物治疗杂志, 2013, 20(1)

载IL-2磁性纳米粒的制备及其联合体外磁场在肿瘤组织中的靶向富集作用 [点此下载全文](#)

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基金项目: 国家高技术研究发展计划(863计划)资助项目(No. 2007AA021806)

DOI: 10.3872/j.issn.1007-385X.2013.1.015

摘要:

目的: 以Fe<sub>3</sub>O<sub>4</sub>磁性纳米粒(Fe<sub>3</sub>O<sub>4</sub> magnetic nanoparticle, Fe<sub>3</sub>O<sub>4</sub>-MNP)和聚乳酸-聚乙醇酸共聚物(poly lactide-co-glycolide, PLGA)为材料, 制备载IL-2磁性纳米颗粒(IL-2-loaded magnetic nanoparticle, IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA), 观察其在肿瘤免疫治疗中的靶向富集作用。方法: 采用复乳法制备IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA, 激光粒度分析仪和扫描电镜观察其大小和形态。ELISA检测IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA的包封率、体外释药特性; MTT法检测其释放IL-2的生物学活性。构建S180肉瘤细胞小鼠肿瘤模型, 研究其瘤体内注射联合体外磁场对S180细胞移植瘤生长的影响, 普鲁士蓝染色观察IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA在肿瘤组织以及肝脏和肾脏组织中的富集和分布。结果: 成功制备了IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA, IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA呈圆球形, 平均粒径为(697±0.51) nm, 包封率为(83.76±1.24)%。IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA突释期释放的IL-2质量浓度为100 ng/ml, 第15 d后质量浓度为180 ng/ml, 并且保持原有生物学活性的85%~55%。在肿瘤组织中, IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA联合体外磁场组可见大量的普鲁士蓝染色阳性IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA颗粒沉积, IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA组只有少量的IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA阳性颗粒沉积; 两组肝脏中均可偶见少量阳性颗粒沉积, 而肾脏几乎未见IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA颗粒沉积。结论: 载IL-2磁性纳米颗粒IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA具有缓释IL-2的功能, 联合体外磁场可有效富集于肿瘤组织中。

关键词: [IL-2](#) [磁性纳米颗粒](#) [聚乳酸-聚乙醇酸共聚物](#) [药物缓释](#) [S180肉瘤](#) [肿瘤靶向富集](#)

Preparation of IL-2-loaded magnetic nanoparticle and its targeting accumulation in tumor tissues combining with external magnetic field [Download Fulltext](#)

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Fund Project: Project supported by the National High Technology Research and Development Program (863 Program) (No. 2007AA021806)

Abstract:

Objective: To prepare IL-2-loaded magnetic nanoparticle (IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA) with Fe<sub>3</sub>O<sub>4</sub> magnetic nano-particle (Fe<sub>3</sub>O<sub>4</sub>-MNP) and poly lactide-co-glycolide (PLGA), and to investigate its targeted accumulation function in tumor immunotherapy. Methods: The double emulsion method was employed for preparation of IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA, its size and morphology were observed with a laser particle size analyzer and under a scanning electron microscope, respectively. In addition, the drug encapsulation efficiency and releasing characteristics of IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA in vitro were measured with ELISA. The biological activity of the IL-2 released from the IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA was evaluated by MTT assay. Sarcoma 180 cell-transplanted tumor mouse model was established to study the effect of IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA in combination with external magnetic field on the growth of Sarcoma 180 tumors. The tumor, liver and kidney tissues were examined by Prussian blue staining to determine the accumulation and distribution of the IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA in the tissue sections. Results: IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA was constructed successfully, and was spherical with a mean diameter of (697±0.51) nm as well as a drug encapsulation efficiency of (83.76±1.24)%. In the drug release test in vitro, the mass concentration of released IL-2 was 100 ng/ml during the burst release phase and rose to 180 ng/ml at the end of 15 d. Moreover, the released IL-2 remained 85%-55% of its original activity during the releasing period. A strong IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA positive reaction was observed in IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA-treated mice combined with an external magnetic field, but only a weak reaction in mice injected with IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA alone. Furthermore, in both groups, Prussian blue-stained liver showed occasionally light IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA positive staining, while IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA positive reaction was rarely detected in the kidneys. Conclusion: IL-2 loaded magnetic nanoparticle IL-2-Fe<sub>3</sub>O<sub>4</sub>-PLGA has controlled IL-2-release function and targeting accumulation capability in tumor tissues when combined with an external magnetic field.

Keywords: [IL-2](#) [magnetic nanoparticle](#) [PLGA](#) [controlled release of drug](#) [sarcoma S180](#) [tumor targeted accumulation](#)

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