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趋化因子SLC和免疫佐剂CpG-ODN联合应用对小鼠移植黑素瘤的疗效

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摘要：

目的：探讨次级淋巴组织趋化因子（seccondary lymphoid tissue chemokine, SLC）和CpG寡聚脱氧核苷酸（CpG oligodeoxynucleotide, CpG ODN）联合应用对小鼠移植黑素瘤的治疗效果及其可能机制。方法：制备SLC Fc融合蛋白，体外检测SLC Fc对小鼠淋巴细胞的趋化效应。建立小鼠黑素瘤移植模型，随机分生理盐水对照组、CpG ODN组、SLC Fc组以及SLC Fc+CpG ODN组共4组。观察治疗后各组小鼠肿瘤的生长情况，流式细胞术检测移植瘤组织中淋巴细胞的种类和浸润情况。结果：成功制备SLC Fc蛋白，SLC Fc对小鼠淋巴细胞具有剂量依赖性（0.03、0.3和 3 μg/L ）趋化作用。瘤内注射SLC Fc和(或)CpG ODN明显抑制肿瘤的生长，联合治疗组瘤体明显小于对照组（ P <0.01），并且小鼠存活时间也明显延长。联合治疗组瘤体内CD4 +、CD8 +T淋巴细胞和CD11c +树突状细胞较对照组显著增多（ P <0.05， P <0.01），并且其肿瘤引流淋巴结也明显增大。结论：SLC和CpG ODN联合应用对小鼠移植黑素瘤有抑制作用，其机制与趋化CD4 +T、CD8 +T细胞和促进DCs增殖有关。

关键词：次级淋巴组织趋化因子 CpG寡聚脱氧核苷酸 黑素瘤 抗肿瘤免疫

Therapeutic effect of chemokine SLC combined with immune adjuvant CpG-ODN in treatment of implanted mouse melanoma

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Abstract:

Objective:To study the therapeutic effect of secondary lymphoid tissue chemokine (SLC) combined with CpG oligodeoxynucleotide (CpG ODN) in treatment of implanted mouse melanoma and the possible mechanism. Methods:SLC Fc fusion protein was prepared and its chemotaxis of lymphocytes was detected by chemotaxis assay. Implanted melanoma mouse models were established and randomly divided into 4 groups: control group, SLC Fc group, CpG ODN group, and SLC Fc+CpG ODN group. The growth of implanted tumors in each group was observed after treatment. Subtype and infiltration of lymphocytes in implanted tumor tissues were examined by flow cytometry. Results:SLC Fc protein was successfully prepared, and it dose dependently attracted lymphocytes (0.03, 0.3, and 3 μg/L). Intra tumor injection SLC Fc and CpG ODN alone or in combination significantly inhibited growth of B16 implanted tumors. Tumor size in SLC Fc+CpG ODN group was significantly smaller than that in control group (P <0.01), and animals in SLC Fc+CpG ODN group survived longer. Tumor infiltrated CD4 + T, CD8 + T, and dendritic cells (DCs) in SLC Fc+CpG ODN group were markedly increased as compared with those in control group (P <0.05), and tumor draining lymph nodes were dramatically enlarged. Conclusion:SLC combined with CpG ODN can inhibit the growth of implanted melanoma by attracting CD4 + T and CD8 + T and promoting proliferation of DCs.

Keywords:secondary lymphoid tissue chemokine (SLC) CpG ODN melanoma antitumor immunity