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基础研究

组织特异性CD/5-FC系统对大肠癌的原位基因治疗

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Antitumor Effect of Cytosine Deaminase Genetherapy in Situ Human Colon Carcinoma in Nude Mice

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摘要

目的 探讨癌胚抗原(carcinoembryonic antigen,CEA)组织特异性胞嘧啶脱氨基酶基因对不同分泌CEA大肠癌组织的靶向杀伤作用. 方法 脂质体法将CEA组织特异性逆转录病毒载体G1CEACDNa在PA317细胞中进行包装,大肠癌细胞LoVo和SW480分别接种到BALB/c裸鼠大腿皮下,成瘤2周后,瘤内多点注射法行原位基因转染,每天腹腔注射500mg/kg的5-FC(5-fluorocytosine),观察治疗效果. 结果 病毒滴度为5.6×106CFU/L.经多次注射法转染,目的基因在肿瘤组织中能有效表达,治疗21天后,基因治疗组有明显的抑瘤作用,但对LoVo细胞肿瘤的抑瘤作用明显大于对SW480细胞肿瘤. 结论 CEA组织特异性CD/5-FC系统对LoVo细胞肿瘤的抑瘤作用更明显.

关键词: 癌胚抗原 胞嘧啶脱氨基酶 5-氟胞嘧啶 大肠癌 基因治疗

Abstract: Objective To investigate the antitumor effect of genetherapy in situ of carcinoembryonic antigen (CEA) tissue-specific cytosine deaminase (CD) /5-fluorocytosine (5-FC) system on human colorectal carcinoma in nude mice. Methods Recombinant ret roviral vector G1CEACDNa was packaged in PA317 cells with lipofectamine technique and then the cells were selectively cultured in G418 and the viral supernatant was harvested. The human colorectal carcinoma cell lines LoVo and SW480 were injected into flanking Balb/c nude mice respectively. 0. 2ml viral supernatant was injected into tumors daily for 3ds and 500 mg/ kg 5-FC was givenip daily for 21ds when the tumors were palpable. All the mice were sacrificed at the end of the t reatment , and then PCR and RT-PCR were performed to detect the expression of targeted gene in carcinoma tissue. Results The virus titer of G1CEACDNa was 5. 6 ×10 ^{6} CFU (colony forming unit , CFU) / L. The targeted genes were detected in tumor tissues. The weight of the LoVo cell tumor were 111. 52 ±25. 89 mg (P < 0. 01 , t = 4. 035 , n = 5 than that in the cont rol group s) and the weight of the SW480 cell tumor were 685. 44 ±240. 38mg (P < 0. 01 , t = 3. 670 , n = 5 than that in the parent groups) following administ ration of 5-FC systemically. Conclusion The CEA tissue-specific CD/5-FC system has an obvious targeting anti-tumor effect on human colorectal carcinoma LoVo cell tumor and SW480 cell tumor , but the killing effect on the LoVo cell tumor is stronger than that on the SW480 cell tumor.

Key words: CEA Cytosine Deaminase 5-Fluorocytosine Colorectal Carcinoma Genetherapy

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