

论著

HSV-1型载体介导IL-1R α 关节腔内注射治疗兔膝关节炎

吴仪¹, 李建明¹, 孔瑛², 陈丁², 刘博², 王万春²

1. 长沙医学院外科, 长沙 410219;
2. 中南大学湘雅二医院骨科, 长沙 410011

摘要:

目的: 探讨单纯疱疹病毒1(HSV-1)型载体介导白细胞介素1受体拮抗基因(IL-1R α)局部治疗兔膝关节炎的作用。方法: 采用改良Hulth法构建兔负重膝关节炎模型;造模成功后利用基因重组技术构建IL-1R α 基因单纯疱疹病毒1型表达载体(pHSV-IL-1R α -LacZ),行兔膝关节腔内注射4周;手术造模和基因治疗后,抽取关节腔灌注液,采用ELISA分析IL-1R α 和IL-1的表达;采用HE染色和甲苯胺蓝染色方法观察局部治疗效果,pHSV-LacZ空白载体设为对照组。结果: 手术造模治疗组注射pHSV-IL-1R α -LacZ后能明显持续抑制IL-1表达水平,且对膝关节软骨炎进展显著性抑制,与对照组比较,差异具有统计学意义($P<0.05$)。结论: pHSV-LacZ是关节腔内局部基因治疗兔膝关节炎模型的理想基因运输体。关节腔内持续表达的IL-1R α 可能通过拮抗IL-1的作用治疗兔膝关节炎。

关键词: 骨性关节炎 IL-1R α 单纯疱疹病毒1型载体 基因治疗

HSV-1 based vector mediated IL-1R α gene for knee osteoarthritis in rabbits

WU Yi¹, LI Jianming¹, KONG Ying², CHEN Ding², LIU Bo², WANG Wanchun²

1. Department of Surgery, Changsha Medical College, Changsha 410219;
2. Department of Orthopedics Surgery, Second Xiangya Hospital, Central South University, Changsha 410011, China

Abstract:

Objective: To investigate the effect and mechanism of herpes simplex virus type 1 (HSV-1) based vector mediated interleukin-1 receptor antagonist (IL-1R α) gene for knee osteoarthritis in rabbits. Methods: HSV-1 vectors containing IL-1R α genes were constructed and injected into the joint space of the osteoarthritis knee in rabbits for 4 weeks. The rabbits were sacrificed, and the knees were lavaged, dissected and the effect of transgene expression was analyzed. Levels of IL-1R α and IL-1 expression in the recovered lavage fluids were measured with a cytokine ELISA kit. Cartilage from the lesion areas of medial femoral condyle and synovium were observed with hematoxylin and eosin (cartilage and synovium) and toluidine blue (cartilage). The blank control group was injected pHSV-LacZ vector into rabbit knees.

Results: Intra-articular delivery of pHSV-IL-1R α -LacZ resulted in a significant inhibition of IL-1 level and cartilage degradation compared with those in the blank control group ($P<0.05$).

Conclusion: pHSV-LacZ is an ideal vector to mediate intra-articular gene delivery in the rabbit model of osteoarthritis. Continuous intra-articular expression of IL-1R α can treat knee osteoarthritis by inhibiting IL-1.

Keywords: osteoarthritis IL-1R α herpes simplex virus type 1 vector gene therapy

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通讯作者: 王万春,Email: wwc1962@yahoo.com.cn

作者简介: 吴仪,硕士研究生,讲师,主要从事骨科临床与基础方面研究。

作者Email: wwc1962@yahoo.com.cn

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