中国病理生理杂志 2005 21 (9): 1669-1674 ISSN: 1000-4718 CN: 44-1187/R

论著

肿瘤坏死因子受体Ⅱ196位点基因多态性与SLE相关性及功能研究

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收稿日期 2004-7-9 修回日期 2004-12-6 网络版发布日期 2009-10-18 接受日期 2004-12-6

摘要 目的：调查中国汉族人群肿瘤坏死因子受体Ⅱ（TNFRⅡ）196位基因多态性与SLE的关系并构建野生和突变的逆转录病毒载体以研究其功能差异。 方法： 利用聚合酶链反应-限制性片段长度多态性（PCR-RFLP）方法检测了106例SLE和119例健康人TNFRⅡ196位的基因型。扩增TNFRⅡ196M cDNA 克隆到PMD18-T载体上，定点突变为TNFRⅡ196R,然后亚克隆到逆转录病毒载体PLXSN上(PLXSN-TNFRⅡ196M和PLXSN-TNFRⅡ196R)并分别转染大鼠系膜细胞，以 ELISA法观察对系膜细胞产生IL-6的影响。 结果： (1)SLE组TNFR Ⅱ196R等位基因型明显高于正常组（35.2% vs 14.3%,P<0.05）；(2)成功构建野生型和突变型重组逆转录病毒载体；（3）rhTNFα刺激后196R型转染系膜细胞产生IL-6明显高于196M型(P<0.05)。 结论： TNFRⅡ196R与中国汉族人群SLE相关，其可以高效转导TNFα的信号，可能参与SLE发病。

关键词 红斑狼疮,系统性； 肿瘤坏死因子受体Ⅱ； 白细胞介素6

分类号 R363

Association and function study of tumor necrosis factor receptorⅡ position 196 polymorphism with systemic lupus erythematosus

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Abstract

<FONT face=Verdana>AIM: To investigate the association of gene polymorphism at position 196 of tumor necrosis factor receptor Ⅱ (TNFRⅡ) with systemic lupus erythematosus (SLE) in Chinese, and establish recombinant retroviral vector to analyze the function of the TNFRⅡ 196M/R. METHODS: The genotype at position 196 of TNFRⅡ was determined by PCR-RFLP in 106 SLE patients and 119 healthy controls in china. Human TNFRⅡ196M cDNA were amplified by PCR and cloned into PMD18-T vector. Then, PMD18-TNFRⅡ196R was induced by site-directed mutagenesis. The recombinant T vector, PMD18-TNFRⅡ196M and PMD18-TNFRⅡ196R, were subcloned into retroviral vector PLXSN. Both normal and variant were transfected into rat mesangial cell. The effects of TNFα on production of sTNFRⅡ and IL-6 were study by ELISA. RESULTS: (1) The frequency of TNFRⅡ196R allele was significantly higher than those in controls (35.2% vs 14.3%, P<0.05); (2) The recombinant retroviral vector (PLXSN-TNFR 196M and PLXSN-TNFR 196R) was constructed successfully; (3) rhTNFα caused a significant increase in IL-6 production by rat mesangial cells transfected with PLXSN-TNFRⅡ196R than that with TNFRⅡ196M. CONCLUSION: These data indicate that TNFRⅡ196R allele is associated with SLE in the Chinese. TNFRⅡ196R transduces the signals of TNFα more effectively than TNFRⅡ196M, which may be involved in the pathogenesis of SLE. </FONT>

Key words Lupus erythematosus systemic Tumor necrosis factor receptor Ⅱ Interleukin-6

DOI: 1000-4718

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