

论著

Toll样受体4在宫颈细胞系和宫颈上皮病变中的表达及与HPV16感染的关系

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**摘要:** 目的: 检测Toll样受体4 (Toll-like receptor 4, TLR4) 在宫颈细胞系和宫颈病变组织中的表达, 探讨TLR4在宫颈病变进展中的作用及与人乳头状瘤病毒 (human papillomavirus 16, HPV16) 感染的关系。方法: 用RT-PCR检测H8, SiHa, Caski细胞中HPV16 E6基因的mRNA含量; Western 免疫印迹测定3种细胞系中TLR4蛋白含量; 免疫组织化学检测127例慢性宫颈炎、宫颈上皮内瘤变 (cervical intra-epithelial neoplasia, CIN) 以及宫颈鳞癌组织石蜡切片中TLR4蛋白的表达。抽提石蜡组织总DNA, 用PCR方法检测组织中HPV16的感染情况。结果: Caski和SiHa细胞中HPV16 E6基因mRNA含量和TLR4蛋白表达明显高于H8正常对照 ( $P<0.05$ ), 且Caski细胞中HPV16 E6基因mRNA含量和TLR4蛋白表达也显著高于SiHa细胞 ( $P<0.05$ ); TLR4在慢性宫颈炎, CIN和宫颈鳞癌组织的表达分别为32.0%, 59.4%和77.8%, 随着宫颈上皮病变加重TLR4表达增强 ( $P<0.01$ ), 并且与宫颈癌分化程度有关 ( $P<0.01$ ); HPV16在宫颈病变组织中的表达随着病理分级逐渐增高, 在慢性宫颈炎、CIN和宫颈鳞癌组织中分别为8.0%, 48.4%和81.0% ( $P<0.01$ ); 在CIN和宫颈鳞癌组织中TLR4与HPV16相关 ( $r=0.303, P<0.05; r=0.633, P<0.05$ )。结论: HPV16感染可以上调TLR4在宫颈上皮病变中的表达, TLR4与HPV16共同作用对宫颈上皮从炎症发展到CIN至宫颈癌过程中发挥重要作用。

**关键词:** 宫颈细胞系 宫颈病变 Toll样受体4 人乳头状瘤病毒16

Expression of Toll-like receptor 4 in cervical cell lines and cervical lesions and its relation to HPV16 infection

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**Abstract:** Objective: To explore the relation between human papillomavirus (HPV16) infection and expression of Toll-like receptor 4 (TLR4) in cervical cell lines and cervical lesion tissues and to investigate the effect of TLR4 on cervical cancer progression. Methods: Expression of HPV16 E6 mRNA was detected by RT-PCR. Western blot and immunohistochemistry were used to detect the expression of TLR4 in H8, SiHa, Caski cell lines and formalin-fixed and paraffin-embedded cervical tissue specimens with cervicitis, cervical intraepithelial neoplasia (CIN) and cervical squamous cell carcinoma (CSCC). DNA was extracted from paraffin-embedded cervical cancer tissues and HPV16 genes were detected. Results: The differentiation expression of HPV16 E6 mRNA and TLR4 in SiHa and Caski was significantly higher than that of normal cervical cell H8 ( $P<0.05$ ). The positive expression rates of TLR4 and HPV16 in chronic cervicitis, CIN, and cervical cancer were 32.0%, 59.4%, and 77.8% ( $P<0.01$ ) and 8.0%, 48.4%, and 81.0% ( $P<0.01$ ), respectively. Up-regulation of TLR4 was correlated with tumor differentiation ( $P<0.01$ ), but not with FIGO stages or lymph node metastasis ( $P>0.05$ ). The expression of TLR4 was significantly correlated with HPV16 infection in CIN and CSCC ( $r=0.303, P<0.05, r=0.633, P<0.05$ ). Conclusion: High expression of TLR4 may play important roles in the development and progression of CIN and CSCC, and the expression of TLR4 can be up-regulated by HPV16 infection.

**Keywords:** cervical cell lines cervical lesion Toll-like receptor 4 HPV16

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