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WT1在儿童横纹肌肉瘤中作用的初步研究

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The Role of WT1 Gene in Childhood Rhabdomyosarcoma

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摘要 探讨WT1基因在儿童横纹肌肉瘤(Rhabdomyosarcoma, RMS)发生、发展过程中的生物学作用及其与临床预后的关系,为WT1疫苗的应用提供理论依据。方法:应用普通和实时定量PCR技术检测WT1 mRNA在37例RMS中的相对表达量,采用免疫组织化学染色方法观察WT1蛋白在61例RMS中的表达情况。利用Mann-Whitney检验分析WT1 mRNA及蛋白在不同病理类型RMS病例中表达的差异性,采用Kaplan-Meier生存曲线和Log-rank检验评估WT1 mRNA及蛋白表达水平与生存率的关系。结果:与胚胎型组和转移阴性组比较,非胚胎型RMS组和转移阳性组中WT1 mRNA及蛋白表达水平较高($P<0.05$)。37例RMS中的WT1 mRNA相对表达量中位数为 2.20×10^{-3} ,以其为阈值分为低表达组和高表达组,Log-rank检验提示高表达组生存率较低($P=0.001$)。61例RMS中,依据阳性细胞的比例,将WT1蛋白表达水平分为低、中及高三组,Log-rank检验显示,低表达组与中表达组之间生存率差异无统计学意义($P=0.185$),但低表达组与高表达组之间、中表达组与高表达组之间差异存在统计学意义(P 均 <0.05)。结论:WT1在儿童RMS发生发展中具有致癌效应,WT1疫苗在儿童RMS治疗有潜在应用价值。

关键词: 横纹肌肉瘤 WT1基因 免疫治疗 儿童

Abstract: To elucidate the role of WT1 gene in the development of childhood rhabdomyosarcoma (RMS) and determine whether WT1 vaccines are applicable to RMS. Methods: WT1 mRNA expression was investigated in the tumor tissue of 37 RMSs using conventional and real-time RT-PCR. Immunohistochemistry was utilized to observe WT1 protein expression in 61 RMSs. Mann-Whitney Test was employed for the comparison of WT1 mRNA or protein expression in embryonal versus non-embryonal subtype and non-metastasis versus metastasis group. The effect of WT1 mRNA or the protein expression on survival was analyzed using Kaplan-Meier survival curve and Log-Rank Test. Results: Compared with the embryonal subtype and non-metastasis group, a higher elevation of WT1 mRNA or protein expression in non-embryonal and metastasis group was observed ($P < 0.05$). The median of relative WT1 mRNA expression in 37 RMSs was 2.20×10^{-3} , which was defined as the threshold value. The RMSs were divided into two groups: high and low WT1 mRNA expression groups. Survival analysis indicated that the high WT1 mRNA level worsened the prognosis ($P = 0.001$). Based on the ratio of positive cells in RMSs, the WT1 protein expression was grouped into three levels, namely, low, middle, and high groups. No significant difference between low and middle group ($P = 0.185$) was observed. However, significant difference appeared in low versus high group and in middle versus high group ($P = 0.000$ and $P = 0.000$). Conclusion: WT1 may act as an oncogene in childhood RMS, and immunotherapy using peptide vaccines against WT1 may be applicable for RMS.

Key words: Rhabdomyosarcoma Wilms tumor gene Immunotherapy Children

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