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Nucleostemin基因特异性短发夹状干扰RNA在裸鼠移植瘤模型体内的抗白血病作用

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Anti-leukemia Effects of Nucleostemin Specific Short Hairpin RNA（NS-shRNA） in Nude Mice Xenograft Tumor Model

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摘要 目的探讨核干细胞因子（NS）特异性短发夹状干扰RNA（NS-shRNA）在裸鼠移植瘤模型体内的抗白血病作用。方法对数生长期HL-60细胞接种于裸鼠皮下使其致瘤并洗脱，体外传至第5代再次接种裸鼠，Transwell法验证HL-60细胞体外侵袭力，建立高致瘤性HL-60白血病细胞异种移植瘤裸鼠模型。腹腔注射体外合成的NS-shRNA脂质包裹体，观察治疗前后瘤体体积、重量的变化，组织切片、HE染色观察肿瘤细胞学改变，免疫组织化学检测瘤体细胞内NS蛋白含量，TdT介导的dUTP缺口末端标记技术（Tunel）检测细胞凋亡情况。结果制备的高致瘤性HL-60细胞使30只裸鼠均形成异种移植瘤，成瘤率为100%，瘤体大小均一。腹腔注射NS-shRNA脂质包裹体13天后，治疗组裸鼠移植瘤体积增长率为207.1%，阴性和空白对照组分别为497.1%和569 6%。治疗组瘤体重量为（1.18±0.27）g，阴性和空白对照组为（2.04±0.73）g和（2.35±0.41）g。切片观察治疗组有大量斑片状组织结构破坏，并出现“凋亡特征”样细胞改变。免疫组织化学检测治疗组移植瘤细胞NS蛋白阳性率和积分值分别为（71.59±1.80）%和（110.26±13.46），阴性对照组为（90.72±1.47）%和（195.11±9.71），空白对照组为（97.33±1.76）%和（220.93±16.54），与阴性和空白对照组相比，NS蛋白表达抑制率分别为43 5%和50 1%。Tunel法检测治疗组移植瘤内出现较多凋亡细胞。结论NS-shRNA在裸鼠移植瘤模型体内具有抗白血病作用，其作用机制之一可能是通过下调NS表达诱发白血病细胞凋亡增加。

关键词： 核干细胞因子 短发夹状干扰RNA 裸鼠移植瘤 白血病 HL-60细胞

Abstract： ObjectiveTo investigate the anti-leukemia role of Nucleostemin（NS）specific short hairpin RNA （NS-shRNA） in nude mice xenograft tumor model. MethodsHL-60 leukemia cells at logarithmically growing phases were subcutaneouly inoculated into nude mice to make them oncogenic, then cells which were eluted, were cultured to the fifth generation. The invasiveness of HL-60 cells was detected by Transwell test. The heterogeneic nude mice xenograft tumor model of high-oncogenic HL-60 leukemia cells were established through implanting of high-invasive cells. NS-shRNA was synthesized in vitro, and intraperitoneally injected into the mice. The volumes and weights of the tumor were measured, and tumor samples were stained by HE. NS protein expression was detected by immunocytochemistry, and the apoptotic cells of HL-60 were examined by Tunel technique. ResultsA heterogeneic nude mice xenograft tumor model with high-oncogenic HL-60 leukemia cells were successfully established with uniform tumor volumes. After treated by NS-shRNA for 13 days, the tumor volumes, weight and NS protein in the tumor cells were statistically lower than those in control group. Large destroy of tumor tissue and “apoptosis character” changes appeared in treated group. A great deal of apoptotic cells were observed in tumor tissue after therapy, detected by Tunel technique. ConclusionThe anti-leukemia effects of NS-shRNA in nude mice xenograft tumor model were

significant. One of the mechanisms was probably that down-regulation of NS expression induce the apoptosis of leukemia cells.

Key words： Nucleostemin Specific short hairpin RNA Nude mice xenograft tumor Leukemia HL-60 cell

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