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基础研究

靶向HER-2 mRNA 反义硫代寡核苷酸体外抗乳腺癌活性研究

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Inhibitory Effect of Antisense Ol igodeoxynucleotides Targeting HER-2 mRNA on Prol iferation of Breast Cancer Cell Line in Vitro

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摘要

目的 研究以HER2 mRNA为靶点的反义硫代脱氧寡核苷酸（S-ODNs）HA6722对HER-2过表达乳腺癌细胞株MDA-MB-453体外增殖的抑制作用，及HA6722对肿瘤细胞HER-2表达的影响。方法 选择HER2过表达的MDA-MB-453细胞与HER2低表达的MDA-MB-231细胞，MTT法观察S-ODNs对肿瘤细胞增殖的影响，免疫细胞化学（ICC）与RT-PCR方法研究S-ODNs对细胞HER2蛋白及mRNA表达的影响。结果 HA6722可以剂量依赖方式抑制MDA-MB-453细胞的体外增殖，IC50值（41．8±8．1nmol·L^{-1}，n=5，mean±s）显著低于对照序列Scramble6722（IC50=489．4±12．1nmol·L^{-1}，n=5，P〈0．01）。HA6722在蛋白水平与mRNA水平显著抑制MDA-MB-453细胞中HER-2的表达；HA6722对MDA-MB-231细胞的体外增殖无显著影响（IC50=476．7±17．6nmol·L^{-1}，n=5，P〉0．05）。结论 HA6722可序列特异性地抑制HER-2过表达乳腺癌细胞的体外增殖，其抑制增殖作用与靶细胞HER-2表达下调有关。

关键词： 反义 寡核苷酸 乳腺癌 HER2 mRNA

Abstract: Objective To study the inhibitory effects of HER2 specific antisense oligodeoxynucleotide HA6722 on the HER2 overexpression human breast cancer cell line ,MDA-MB-453 , and to ascertain the mechanism through which HA6722 works. Methods MDA-MB-453 and MDA-MB-231 cell lines , which are HER2 over-and normal-espression , respectively , were set as our experimental cells. Inhibitory effects of HA6722 on these cells were detected by means of methyl thiazolyl blue (MTT) , HER2 protein p^{185} and HER2 mRNA were detected by immunocytochemistry and RT2PCR. Results Compared with its control sequence Scramble6722 , HA6722 could inhibit the growth of MDA2MB2453 cell in vit ro in a dose2 dependent manner , the IC50 value of HA6722 (41. 8 ±8. 1nmol • L^{-1} n = 5) was significantly lower than that of scramble6722 (IC50 = 489. 4 ±12. 1 nmol • L^{-1} , n = 5 , P < 0. 01) . Furthermore , HA6722 could inhibit the expression of HER2 in MDA-MB-453 cells markedly at protein and mRNA level. On the other hand , HA6722 had no effect s on the proliferation of MDA2MB2231 cell (IC50 = 476. 7 ±17. 6nmol • L^{-1},n = 5 , P > 0. 05) . Conclusion Antisense oligodeoxynucleotide HA6722 could inhibit the growth of breast cancer cell which is HER2 overexpression in sequence specific manner , and the inhibitory effects correlated with the down-regulation of HER2 in targeting cells.

Key words: Antisense Oligodeoxynucleotide Breast carcinoma HER2 mRNA

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