

论著

神经调节因子对MDA-MB-231细胞mtp53和HIF-1 α 的影响及意义

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摘要

目的: 探讨在ErbB2非过表达乳腺癌细胞MDA-MB-231中, 神经调节因子(NRGs)/ErbB2信号通路对突变型p53(mtp53)和缺氧诱导因子-1 α (HIF-1 α)的影响及意义。方法: 免疫细胞化学法和Western blotting检测MDA-MB-231细胞中神经调节因子(NRG)的表达。应用ErbB2受体功能抑制剂AG825处理MDA-MB-231细胞, MTT法检测细胞的增殖抑制作用; 流式细胞术检测细胞周期和细胞凋亡; Western blotting检测mtp53、HIF-1 α 蛋白表达; RT-PCR检测HIF-1 α mRNA的表达。结果: 神经调节因子在乳腺癌细胞MDA-MB-231呈显著表达, Western blotting实验可见分子量44 kD的NRG抗体阳性反应条带。应用ErbB2受体功能抑制剂AG825后, MDA-MB-231细胞生长受到抑制, 作用呈时效、量效依赖关系(P<0.01); 细胞周期阻滞在G0/G1期; 细胞凋亡增加(P<0.05); mtp53、HIF-1 α 蛋白表达减少(P<0.05); HIF-1 α mRNA表达减少(P<0.05)。结论: ErbB2非过表达乳腺癌细胞MDA-MB-231存在神经调节因子分泌, 可能通过神经调节因子自分泌或旁分泌配体作用方式使ErbB2受体信号转导处于激活状态, 上调mtp53和HIF-1 α 的表达, 促进肿瘤细胞的增殖、存活能力和抑制凋亡。

关键词 [ErbB2通路](#); [神经调节蛋白类](#); [突变型p53](#); [缺氧诱导因子-1 \$\alpha\$](#)

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Effect of neuregulins on mtp53 and HIF-1 α in MDA-MB-231 cells

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Abstract

<P>AIM: To explore the effect and significance of neuregulins /ErbB2 receptor signal transduction pathway on mtp53 and hypoxia-inducible factor-1 α (HIF-1 α) in none-overexpression ErbB2 breast cancer cell MDA-MB-231. METHODS: The expression of neuregulin was detected by immunocytochemistry and Western blotting. MDA-MB-231 cells were treated with ErbB2 kinase inhibitor AG825. Proliferation was measured by MTT assay. The cell cycle and apoptosis were determined by flow cytometry. The expressions of mtp53 and HIF-1 α were detected by Western blotting. The mRNA expression of HIF-1 α was detected by RT-PCR. RESULTS: MDA-MB-231 cells expressed a relative higher level of neuregulin. In the results of Western blotting, the positive reaction band was found in 44 kD which coincides with the molecular weight of neuregulin. When MDA-MB-231 cells were treated with AG825, the proliferation was inhibited in time and dose dependent manners (P<0.01). The cell cycle was arrested in G0/G1 phase (P<0.05). The apoptosis rate was increased (P<0.05). The protein expression levels of mtp53 and HIF-1 α were decreased (P<0.05), and the mRNA level of HIF-1 α

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was also decreased ($P < 0.05$). CONCLUSION: Our study indicates that neuregulins are synthesized in MDA-MB-231 cells as transmembrane proteins. Neuregulins activate ErbB2 receptor signal transduction pathway by ligand autocrine or paracrine actions, and play an important role in proliferation of non-overexpression ErbB2 breast cancer cell MDA-MB-231. Proliferation and survivorship, and inhibition apoptosis can be induced with up-regulation of mtp53 and HIF-1 α level.

Key words [ErbB2 pathway](#) [Neuregulins](#) [Mutant p53](#) [Hypoxia-inducible factor-1 \$\alpha\$](#)

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