

论文

腺病毒介导的NEP基因对Aβ25-35诱导的SK-N-SH细胞凋亡的抑制作用

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摘要:

目的 研究脑中内肽酶(NEP)基因外源表达对神经毒性物质β-淀粉样肽(Aβ25-35)诱导损伤的SK-N-SH细胞凋亡的抑制作用。方法 用脂质体法将含NEP的腺病毒载体转染高代次293细胞,制备高滴度病毒载体,感染Aβ25-35处理的外源损伤的人神经母细胞瘤细胞(SK-N-SH细胞),采用MTT法检测细胞存活率,采用流式细胞术分析细胞凋亡状态和细胞内活性氧水平,采用RT-PCR和Western blot法检测凋亡相关基因bcl-2及bax的表达情况。结果 细胞存活率及流式细胞术检测结果显示,NEP高表达可明显减轻Aβ25-35诱导的细胞凋亡及减低细胞内活性氧水平,RT-PCR和Western blot结果显示,NEP对Aβ25-35诱导的细胞凋亡的抑制作用可能是通过减少促凋亡基因bax的表达以及降低细胞内活性氧水平来实现的。结论 NEP对Aβ25-35诱导的神经细胞损伤具有一定保护作用,其作用机制可能与凋亡相关基因有关。

关键词: 内肽酶类;腺病毒,人;淀粉样β蛋白;细胞凋亡;阿尔茨海默病

Inhibitory effects of NEP mediated by adenovirus vector on amyloid beta peptide-induced SK-N-SH cell apoptosis

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Abstract:

Objective To investigate the inhibitory effects of neprilysin(NEP) on SK-N-SH cell apoptosis induced by neurotoxic amyloid beta peptide(Aβ25-35). Methods The adenovirus vector carrying NEP was transfected into human embryonic kidney 293 cells by using LipofectaminTM 2000 and the adenovirus expressing exogenous genes was generated. Then the person nerve metrocyte lump cell SK-N-SH cells induced by Aβ25-35 were infected. Cell survival rate was measured by MTT. Cell apoptosis rate and level of intracellular ROS were measured by flow cytometry. Expressions of the apoptosis associated genes bax and bcl-2 in cells were detected by RT-PCR and Western blot. Results MTT and flow cytometry indicated that expression of NEP reduced cell apoptosis rate and level of intracellular ROS induced by Aβ25-35. RT-PCR and Western blot showed that the inhibitory effect of NEP on Aβ25-35-induced apoptosis might be exerted by reducing the expression level of bax and the level of intracellular ROS. Conclusion Expression of NEP may exert a neuro-protective effect on SH-N-SK cells induced by neurotoxic Aβ25-35, which might be associated with apoptosis-associated genes.

Keywords: Endopeptidases; Adenoviruses, human; Amyloid beta protein; Apoptosis; Alzheimer disease

收稿日期 2009-11-03 修回日期 网络版发布日期

DOI:

基金项目:

高等学校博士点科研基金资助项目(20050422045);山东省科技发展计划项目(2009GG10002012)

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