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APOE基因亚型及其短肽COG1410对神经细胞损伤后早期凋亡的影响

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Title: Effect of APOE alleles and apoE-mimetic peptide COG1410 on early neuron apoptosis after *in vitro* traumatic brain injury

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关键词: [载脂蛋白E](#); [短肽](#); [创伤性脑损伤](#); [体外模型](#); [早期凋亡](#)

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摘要: 目的 探讨载脂蛋白E(APOE代表基因, apoE代表蛋白)亚型特异性及其短肽与早期凋亡的相关性,以期明确APOE亚型影响脑创伤病情转归及预后的病理机制。方法 采用稳定表达人APOE各等位基因的APOE敲除鼠的神经干细胞,优化诱导分化条件,构建神经元/胶质细胞共培养体系及细胞划痕损伤模型。通过Annexin V/PI联合流式细胞技术检测损伤后各组细胞早期凋亡率,分析人APOE各等位基因及其短肽影响继发性神经细胞损伤的差异。结果 成功构建携带人源性APOE各亚型的细胞划痕损伤模型;伤后24 h时间点各组细胞早期凋亡率较6、12 h明显增高($P<0.05$),且人APOE ϵ 4组较其余亚型组早期凋亡率明显增高($P<0.05$)。在伤后24 h apoE短肽COG1410可显著降低各亚型组早期凋亡率($P<0.01$)。结论 APOE ϵ 4携带者可能通过早期凋亡导致脑创伤急性期病情加重。而apoE短肽COG1410可通过降低早期凋亡发挥神经保护作用。

Abstract: Objective To elucidate the mechanism mediating the effects of apolipoprotein E (APOE for gene, apoE for protein) alleles and apoE-mimetic peptide COG1410 on early apoptosis in an *in vitro* model of experimental traumatic brain injury. Methods Eukaryotic expression vectors carrying individual APOE alleles (ϵ 2, ϵ 3, ϵ 4) were transferred into neural stem cells (NSCs) derived from APOE knockout mice. An *in vitro* neuronal/glial co-culture model of mechanical injury was developed using a controlled scratch. Flow cytometry was performed to analyze the correlations among APOE genotypes, apoE-mimetic peptide COG1410 and early apoptosis. Results Early apoptosis after injury was observed in all groups, which was significantly higher at 24 h after injury than at 6 h and 12 h after injury ($P<0.05$). The group transfected with APOE ϵ 4 showed more significant early apoptosis 24 h after injury as compared to the groups transfected with APOE ϵ 2 or APOE ϵ 3 ($P<0.05$). Furthermore, decreases of early apoptosis were detected in the groups treated with apoE-mimetic peptide COG1410 at 24 h after injury ($P<0.01$). Conclusion APOE ϵ 4-transfected NSCs showing a higher rate of early apoptosis indicates that the patients with APOE ϵ 4 may suffer aggravation of brain trauma in acute stage due to early apoptosis. Our results also identify the early neuroprotective effect of apoE-mimetic peptide COG1410.

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