

论著

# 大鼠MSCs体外诱导分化为神经元样细胞过程中发生细胞凋亡的机制研究

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**摘要** 目的: 探讨体外诱导大鼠骨髓间充质干细胞(MSCs)向神经元样细胞分化过程中凋亡发生的机制。方法: 分离纯化大鼠骨髓间充质干细胞, 随机分为3组: 对照组为单纯 $\beta$ -巯基乙醇诱导分化组; NEK1/2抑制剂1, 4-二氨基-2,3-氧基-1,4-双[2-氨基苯基硫代]丁二烯(U0126)组为自预诱导开始在加入 $\beta$ -巯基乙醇的同时加入10  $\mu$ mol/L U0126; 蛋白激酶PKC激动剂氟波酯(PMA)组为自预诱导开始在加入 $\beta$ -巯基乙醇的同时分别加入30 nmol/L、120 nmol/L与300 nmol/L PMA。诱导5 h后终止反应, MTT法检测细胞活性, 免疫细胞化学检测神经元特异性巢蛋白nestin及凋亡相关蛋白caspase、Bcl-2、Bax的表达情况, TUNEL法检测细胞凋亡指数。结果: 诱导后5 h与对照组相比, U0126组神经元样细胞的活性、nestin的表达、Bcl-2蛋白阳性表达率均出现增强或升高( $P<0.05$ ), 细胞凋亡指数降低( $P<0.05$ ); 300 nmol/L PMA组则显著抑制神经元样细胞的活性和nestin的表达( $P<0.05$ ), 增强Bax并降低Bcl-2的表达( $P<0.05$ ), 细胞凋亡指数明显升高( $P<0.05$ )。结论: 大鼠MSCs诱导分化为神经元样细胞过程中发生凋亡机制涉及MAPK及PKC信号途径。

**关键词** [骨髓间充质干细胞](#); [神经元](#); [细胞凋亡](#); [信号转导](#)

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## Apoptotic mechanism of neuron-like cells differentiated from adult rat mesenchymal stem cells in vitro

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### Abstract

<FONT face=Verdana>AIM: To investigate the mechanism of apoptosis during the process of adult rat mesenchymal stem cells (MSCs) differentiating into neuron-like cells in vitro. METHODS: The MSCs were isolated primarily from adult rats bone marrow by density gradient and then expanded in medium as undifferentiated cells for 3-5 generations. The MSCs were divided into three groups at random. The control group was induced with  $\beta$ -mercaptoethanol ( $\beta$ -ME). Meanwhile, the U0126 group was given  $\beta$ -ME and U0126 (10  $\mu$ mol/L) added at the beginning of induction. The PMA groups were treated with  $\beta$ -ME and different concentrations of PMA since pre-induction. The effects of U0126 and PMA on the activity of neuron-like cells were observed by MTT. The effects of U0126 and PMA on the expression of neuron specific marker nestin and expression of apoptosis-related protein caspase, Bcl-2, Bax in neuron-like cells were detected by using immunocytochemistry method. TUNEL technique was used to detect apoptosis index. RESULTS: Compared to control group, neuron viability, nestin and Bcl-2 increased and neuron apoptosis decreased in U0126 group ( $P<0.05$ ). The activity of neuron-like cells, the expression of nestin and Bcl-2 in experiment group treated with 300 nmol/L PMA decreased ( $P<0.05$ ), while Bax protein expression and apoptosis index increased ( $P<0.05$ ). CONCLUSION: Both MAPK and PKC signal pathways may be involved in the differentiation of MSCs into neuron-like cells as well as the apoptotic process in differentiated neuron-like cells.</FONT>

**Key words** [Bone marrow mesenchymal stem cells](#) [Neurons](#) [Apoptosis](#) [Signal transduction](#)

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