[1]王翠琴,张广宇,彭越,等.大鼠骨髓间充质干细胞神经分化过程中哺乳动物雷帕霉素靶蛋白分布的变化及意义[J].第三军医大学学报,2013,35(13):1345-1349.

Wang Cuiqin,Zhang Guangyu,Peng Yue,et al.Distribution and significance of mammalian target of rapamycin during differentiation of rat bone marrow mesenchymal stem cells into neurons[J].J Third Mil Med Univ,2013,35(13):1345-1349.

点击复制

导航/NAVIGATE
本期目录/Table of Contents
下一篇/Next Article
上一篇/Previous Article

工具/TOOLS
引用本文的文章/References
下载 PDF/Download PDF(1252KB)
立即打印本文/Print Now
查看/发表评论/Comments
导出

统计/STATISTICS
摘要浏览/Viewed 206
全文下载/Downloads 104
评论/Comments

RSS XML

大鼠骨髓间充质干细胞神经分化过程中哺乳动物雷帕霉素靶蛋白分布的变化及意义(PDF)

分享到:

《第三军医大学学报》[ISSN:1000-5404/CN:51-1095/R] 卷: 35 期数: 2013年第13期 页码: 1345-1349 栏目: 论著 出版日期: 2013-07-15

Title: Distribution and significance of mammalian target of rapamycin during differentiation of rat bone marrow mesenchymal stem cells into neurons

作者: 王翠琴; 张广宇; 彭越; 彭涛; 贾延劼
郑州大学第一附属医院神经内科

Author(s): Wang Cuiqin; Zhang Guangyu; Peng Yue; Peng Tao; Jia Yanjie
Department of Neurology, First Affiliated Hospital, Zhengzhou University, Zhengzhou, Henan Province, 450052, China

关键词: 骨髓间充质干细胞; 诱导; 神经细胞; mTOR; 雷帕霉素

Keywords: bone marrow mesenchymal stem cells; induction; neurons; mTOR; rapamycin

分类号: R322.8; R329.21; R979.5

文献标志码: A

摘要: 目的 探讨大鼠骨髓间充质干细胞神经分化过程中哺乳动物雷帕霉素靶蛋白（mammalian target of rapamycin, mTOR）分布的变化及意义。 方法 常规体外培养大鼠MSCs，采用β-巯基乙醇诱导MSCs分化为神经细胞。实验分MSCs空白对照组、二甲基亚砜（DMSO）阴性对照组、β-巯基乙醇诱导组、不同浓度雷帕霉素干预组、不同浓度雷帕霉素干预+β-巯基乙醇诱导组。采用免疫荧光法检测诱导前后mTOR在细胞内的分布，激光共聚焦显微镜观察照相；Western blot法检测诱导前后神经细胞相关蛋白和mTOR通路蛋白的表达。 结果 ①诱导前mTOR主要在MSCs细胞核内点状分布，细胞质也有少量的分布；诱导后核内荧光信号减弱，mTOR向细胞质转移。雷帕霉素处理后，随着雷帕霉素浓度的提高（10~30 μmol/L），mTOR向细胞质转移越明显。雷帕霉素浓度超过50 μmol/L后，细胞形态变圆，部分细胞脱壁，死亡率显著增加(P<0.05)。 ②β-巯基乙醇可诱导骨髓间充质干细胞分化为神经细胞，诱导后神经细胞Tau蛋白、MAP-2蛋白表达显著增加。雷帕霉素（10~30 μmol/L）干预后，随着雷帕霉素浓度（10~20 μmol/L）的提高，Tau蛋白、MAP-2蛋白表达逐渐增加，30 μmol/L时Tau蛋白、MAP-2蛋白表达下降(P<0.05)。 ③Western blot检测结果提示，诱导前后总mTOR表达不变；磷酸化mTOR、磷酸化p70S6K、磷酸化4EBP1诱导后较诱导

前表达下降(P<0.05)，雷帕霉素干预后下调更加显著(P<0.05)。　结论　mTOR在MSCs神经分化过程中由细胞核内向细胞质转移，活性下降，表达下调，提示mTOR在MSCs神经分化过程中可能发挥了重要作用。

Abstract: Objective To investigate the distribution and significance of mammalian target of rapamycin (mTOR) during the differentiation of rat bone marrow mesenchymal stem cells (MSCs) into neurons. Methods Rat MSCs were cultured by conventional method *in vitro*, and were induced by β-mercaptoethanol (β-ME) to differentiate into neurons. The MSCs were divided into a MSCs blank control group, a dimethyl sulfoxide (DMSO) negative control group, a β-ME induction group, different concentrations of rapamycin intervention groups, and different concentrations of rapamycin intervention + β-ME induction groups. Immunofluorescence and laser confocal microscopy were used to observe the intracellular distribution of mTOR before and after induction. Western blotting was used to detect the expression of neuron-related proteins and mTOR before and after induction. Results (1) Before β-ME induction, mTOR were mainly distributed in the cell nucleus like spots, and a small amount was distributed in the cytoplasm. After β-ME induction, the nuclear fluorescence signal reduced, and mTOR translocated into the cytoplasm. After rapamycin treatment, mTOR translocation to the cytoplasm became more obvious along with the increase of rapamycin concentration (10 to 30 μmol/L). When the concentration of rapamycin was more than 50 μmol/L, the morphology of MSCs became round, some cells detached, and the cell death rate was significantly increased (*P*<0.05). (2) MSCs were induced by β-ME to differentiate into neurons and the expression of Tau and MAP-2 increased significantly. After rapamycin treatment, the expression of Tau and MAP-2 gradually increased along with the increase of rapamycin concentration (10 to 20 μmol/L). When the concentration reached 30 μmol/L, the expression of Tau and MAP-2 was down-regulated (*P*<0.05). (3) Western blotting results suggested that the total expression of mTOR was the same before and after β-ME induction. The expression of phospho-mTOR, phospho-p70S6K and phospho-4EBP1 was significantly decreased after β-ME induction (*P*<0.05), and the decrease became more significant after rapamycin treatment (*P*<0.05). Conclusion During the induction of MSCs differentiation into neurons, mTOR translocated into cytoplasm from cell nucleus, and the expression of mTOR declines. mTOR may play an important role in regulating MSCs differentiation into neurons.

参考文献/REFERENCES:

王翠琴，张广宇，彭越，等. 大鼠骨髓间充质干细胞神经分化过程中哺乳动物雷帕霉素靶蛋白分布的变化及意义[J].第三军医大学学报,2013,35(13):1345-1349.

相似文献/REFERENCES:

[1]张蕾,陈沅,田杰,等.心肌细胞介导骨髓间充质干细胞的心肌样分化[J].第三军医大学学报,2005,27(16):1681.

[2]王颖楠,范雪梅,赵敏,等.脱细胞膀胱基质复合大鼠骨髓间充质干细胞体外构建组织工程化吊带治疗压力性尿失禁的初步研究[J].第三军医大学学报,2012,34(22):2269.

Wang Yingnan,Fan Xuemei,Zhao Min,et al.Preliminary study on the construction of a tissue-engineered sling with BMSCs and UBM in vitro for treating stress urinary incontinence[J].J Third Mil Med Univ,2012,34(13):2269.

[3]罗茜,王斌,雷增杰,等.肝星状细胞具有向肝细胞样细胞分化的干细胞潜能[J].第三军医大学学报,2013,35(07):604.

Luo Xi,Wang Bin,Lei Zengjie,et al.Hepatic stellate cells might possess potential capabilities of stem cells to differentiate into hepatocyte-like cells in vitro[J].J Third Mil Med Univ,2013,35(13):604.

[4]周长立,任先军,蒋涛,等.Wnt7a基因对大鼠骨髓间充质干细胞增殖及向神经元样细胞分化的影响[J].第三军医大学学报,2013,35

(08):702.

Zhou Changli,Ren Xianjun,Jiang Tao,et al.Wnt7a gene stimulates mesenchymal stem cell proliferation and differentiation into neuron-like cells[J].J Third Mil Med Univ,2013,35(13):702.

[5]郝磊,邹仲敏,王军平,等.hPDGF-A/hBD2双基因共表达腺病毒载体的构建及表达[J].第三军医大学学报,2007,29(10):859.

HAO Lei,ZOU Zhong-min,WANG Jun-ping,et al.Construction and identification of recombinant adenovirus expressing hPDGF-A and hBD2[J].J Third Mil Med Univ,2007,29(13):859.

[6]郭书权,吴雪晖,许建中,等.两种方法分离小型猪骨髓间充质干细胞的比较[J].第三军医大学学报,2007,29(10):988.

[7]黄文秋,黄宏,徐祥,等.mTOR及其下游信号通路在骨髓间充质干细胞氧化应激损伤中的变化及作用[J].第三军医大学学报,2013,35(02):114.

Huang Wenqiu,Huang Hong,Xu Xiang,et al.Changes and roles of mTOR and its downstream signaling passway in mouse bone marrow stem cells with oxidative stress injury[J].J Third Mil Med Univ,2013,35(13):114.

[8]冯一梅,徐辉,邹仲敏,等.hPDGF-A/hBD2双基因转染对大鼠骨髓间充质干细胞生物学特性的影响[J].第三军医大学学报,2008,30(06):472.

FENG Yi-mei,XU Hui,ZOU Zhong-min,et al.Effects of hPDGF-A/hBD2 genes transfection on rat bone marrow mesenchymal stem cells[J].J Third Mil Med Univ,2008,30(13):472.

[9]姚青,宋治远,马显光.脉冲微交流电刺激促进体外诱导大鼠骨髓间充质干细胞向心肌分化[J].第三军医大学学报,2008,30(05):410.

YAO Qing,SONG Zhi-Yuan,MA Xian-guang.Electrical stimulation promotes the differentiation of rat bone marrow mesenchymal stem cells to cardiomyocyte induced by 5-azacytidine in vitro[J].J Third Mil Med Univ,2008,30(13):410.

[10]朱淑霞,李永华,宋治远,等.电磁场促进骨髓间充质干细胞体外诱导分化时细胞增殖[J].第三军医大学学报,2008,30(05):421.

ZHU Shu-xia,LI Yong-hua,SONG Zhi-yuan,et al.Pulsed electromagnetic fields improve proliferation of rat marrow mesenchymal stem cells induced by 5-azacytidine[J].J Third Mil Med Univ,2008,30(13):421.

[11]段江洁,王蓓,张建华,等.胎儿肠壁结缔组织诱导骨髓间充质干细胞向肠上皮细胞的分化[J].第三军医大学学报,2008,30(18):1718.

DUAN Jiang-jie,WANG Bei,ZHANG Jian-hua,et al.Bone marrow-derived mesenchymal stem cells differentiate into epithelial cells induced by fetal intestinal connective tissue[J].J Third Mil Med Univ,2008,30(13):1718.

更新日期/Last Update: 2013-07-01