[an error occurred while processing this directive]

山东大学学报(医学版) 2013, 51(10) 1-4 DOI: ISSN: 1671-7554 CN: 37-1390/R

基础医学

辛伐他汀对转β分泌酶HEK293细胞RhoA/ROCK途径及Aβ42生成的影响

刘郡1，朱天瑞2，李晓红2

1.山东大学医学院， 济南 250012； 2.山东大学附属济南市中心医院神经内科， 济南 250013

摘要：

目的 观察辛伐他汀(Sim)通过RhoA/ROCK途径对转β分泌酶(BACE1)-HEK293细胞分泌β-淀粉样蛋白(Aβ)的影响。方法 体外培养BACE1-HEK293细胞，在保证培养环境胆固醇充足的条件下分为对照组、1μmol/L Sim组、1μmol/L Sim+250μmol/L甲羟戊酸(Mev)组、5μmol/L Sim组、5μmol/L Sim +250μmol/L Mev组对细胞进行处理。MTT检测细胞存活率；ELISA检测Aβ42分泌量；Western blotting检测细胞膜RhoA及细胞浆磷酸化肌球蛋白磷酸酶肌球蛋白结合亚基(p-MYPT1)表达量。结果 MTT显示各组细胞存活率无差异(P>0.05)；1μmol/L Sim组和5μmol/L Sim组细胞分泌Aβ42较对照组减少(P<0.05)；两组细胞膜上RhoA及细胞浆p-MYPT1含量较对照组显著降低(P<0.01)，分别加入250μmol/L Mev后能对抗Sim的作用(P<0.01)。结论 Sim可以通过降低胆固醇以外的途径减少RhoA蛋白的细胞膜定位和下游激酶ROCK的活化，抑制细胞Aβ42的分泌。

关键词： β-淀粉样蛋白；辛伐他汀；RhoA蛋白；Rho激酶；甲羟戊酸

Effects of simvastatin on RhoA/ROCK pathway and secretion of Aβ42 in β-secretase transferred HEK293 cells

LIU Jun1, ZHU Tian-rui2, LI Xiao-hong2

1. School of Medicine, Shandong University, Jinan 250012, China;
2. Department of Neurology, Jinan Central Hospital Affiliated to Shandong University, Jinan 250013, China

Abstract:

Objective To observe the effect of simvastatin (Sim) on the production of beta-amyloid peptide (Aβ) via RhoA/ROCK pathway. Methods HEK293 cells transferred with β-secretase(BACE1) were cultured in vitro with cholesterol sufficient culture medium and divided into five groups: control group, 1μmol/L Sim group, 1μmol/L Sim +250μmol/L mevalonic acid(Mev) group, 5μmol/L Sim group, 5μmol/L Sim + 250μmol/L Mev group. MTT was employed to identify the vitality of the cells; ELISA was used for detecting extracellular Aβ42; Western blotting was employed to detect the expression of RhoA in cell membrane and phosphorylated myosin-binding subunit of myosin phosphatase (p-MYPT1) in cytoplasm. Results All treatment groups had no effects on the vitality of BACE1-HEK293 cells(P>0.05). Compared with control group, the secreted Aβ42 was decreased in 1μmol/L and 5μmol/L Sim groups (P<0.05). The expression of RhoA in cell membrane and p-MYPT1 in cytoplasm were both decreased in 1μmol/L and 5μmol/L Sim groups(P<0.01), and 250μmol/L Mev could reversed the effect of Sim(P<0.01). Conclusion Simvastatin decreases not only the RhoA in cell membrane together with p-MYPT1 in cytoplasm, but also the secretion of Aβ42 via cholesterol-independent mechanism.

Keywords: Beta-amyloid peptide; Simvastatin; RhoA protein; Rho kinase; Mevalonic acid

收稿日期 2012-12-19 修回日期 网络版发布日期

DOI:

基金项目:

山东省自然科学基金(Y2008C103)；济南市科技发展计划项目(200807032)

通讯作者: 李晓红， E-mail:lxh5231@126.com

作者简介:
作者Email:

参考文献:

本刊中的类似文章