中国药理学与毒理学杂志 2009 23 (5): 368-374 ISSN: 1000-3002 CN: 11-1115/R

论著

# 普伐他汀对高糖培养肾小球系膜细胞P38促分裂原活化蛋白激酶信号通路的影响

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收稿日期 2008-12-29 修回日期 网络版发布日期 2009-9-30 接受日期 2009-5-13

摘要 目的 探讨普伐他汀对高糖培养大鼠肾小球系膜细胞（MC）p38促分裂原活化蛋白激酶（p38MAPK）信号传导通路的影响。方法 大鼠MC分别培养在正常糖5.5 mmol·L$^{-1}$(正常对照组)，高糖25 mmol·L$^{-1}$(高糖组)，葡萄糖25 mmol·L$^{-1}$+p38MAPK特异性抑制剂SB203580(SB) 10 μmol·L$^{-1}$，及葡萄糖25 mmol·L$^{-1}$+普伐他汀（PV） 100 μmol·L$^{-1}$。ELISA法检测培养上清液Ⅳ型胶原(Col-Ⅳ)、纤连蛋白(FN)含量； Phospho-ELISA法检测胞浆及胞核内p38MAPK和磷酸化p38MAPK（p-p38MAPK）蛋白的表达；以及RT-PCR法检测p38MAPK mRNA的表达。结果 与正常对照组比较，高糖组MC合成基质蛋白Col-Ⅳ，FN增多；胞浆及胞核内p-p38MAPK的表达增加。SB或PV干预能部分或完全逆转这一变化。与高糖组比较，SB干预后，上清液中Col-Ⅳ含量下降〔48 h：(21.19±3.21) *vs* (16.75±1.93)μg·L$^{-1}$，*n*=6，*P*<0.05〕、FN减少〔48 h：(13.47±1.27) *vs* (12.01±0.85)μg·L$^{-1}$，*n*=6，*P*<0.05〕；胞浆及胞核内p-p38MAPK表达显著下调。PV干预后，上清液中Col-Ⅳ含量下降〔48 h：(21.19±3.21) *vs* (14.97±3.04)μg·L$^{-1}$，*n*=6，*P*<0.05〕、FN减少〔48 h：(13.57±1.27) *vs* (11.99±0.98)μg·L$^{-1}$，*n*=6，*P*<0.05〕；胞核内p-p38MAPK表达显著下调，但对胞浆内p-p38MAPK的表达则无显著影响。各组总p38MAPK蛋白水平及p38MAPK mRNA表达则没有明显改变。结论 PV能够显著下调高糖培养的MC胞核内p38MAPK信号传导通路的活化，进而减少胞外基质合成，达到对糖尿病肾病的治疗作用。

关键词 普伐他汀 糖尿病性肾病 肾小球系膜细胞 p38促分裂原活化蛋白激酶

分类号 R966，R972.6



# Effects of pravastatin on signal passway of p38 mitogen-activated protein kinase in glomerular mesangial cells incubated with high concentration of glucose

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**Abstract**

**AIM** To investigate effects of pravastatin(PV) on the signal passway of p38 mitogen-activated protein kinase (p38MAPK) in glomerular mesangial cells (MC) incubated in high concentration of glucose. **METHODS** MC were incubated in media containing glucose 5.5 mmol·L$^{-1}$ (control), high glucose(HG) 25 mmol·L$^{-1}$, glucose 25 mmol·L$^{-1}$+SB203580(specific inhibitor of p38MAPK) 10 μmol·L$^{-1}$ (SB+HG), glucose 25 mmol·L$^{-1}$+PV 100 μmol·L$^{-1}$ (PV+HG), respectively. Fibronectin (FN) and type Ⅳ collagen (Col-Ⅳ) in supernatant were determined by ELISA method. Protein expressions of p38MAPK and phospho-p38MAPK in cytoplasm and nuclei were detected by phospho-ELISA method. The mRNA expression of p38MAPK was detected by semi-quantitative reverse transcription polymerase chain reaction (RT-PCR). **RESULTS** Compared with control group, there are increased Col-Ⅳ and FN in supernatant in HG group; there are increased phospho-p38MAPK in nuclei and cytoplasm in HG group, too. These changes could be partly or fully reversed by treatment of SB or PV. Compared with HG group, (SB+HG) or (PV+HG) group showed decreased Col-Ⅳ 〔48 h：(21.19±3.21) *vs* (16.75±1.93), (14.97±3.04)μg·L$^{-1}$, *n*=6, *P*<0.05〕 and FN 〔48 h：(13.47±1.27) *vs* (12.01±0.85), (11.99±0.98)μg·L$^{-1}$, *n*=6, *P*<0.05〕. Phospho-p38MAPK in nuclei and cytoplasm could be decreased by treatment of SB. However, phospho-p38MAPK in nuclei but not cytoplasm could be decreased by treatment of PV. There was no significant difference of the total protein expressions and mRNA of p38MAPK among 4 groups. **CONCLUSION** PV could down-regulate the activities of signal passway of p38MAPK in nuclei of MC incubated in high concentration of glucose, decrease synthesis of extracellular matrix and result in the treatment of diabetic nephropathy.

**Key words** pravastatin diabetic nephropathy mesangial cells p38 mitogen-activated protein kinases

DOI: 10.3867/j.issn.1000-3002.2009.05.006

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