[an error occurred while processing this directive]

山东大学学报(医学版) 2013, 51(9) 35-39 DOI: ISSN: 1671-7554 CN: 37-1390/R

基础医学

二甲双胍抑制人前列腺癌细胞上皮间质转化及其作用机制

张晶1，王林2，3，夏平钿3，秦晓敏4，韩博3，4，郭秀丽1

1.山东大学药学院药理学教研室, 济南 250012； 2.山东省医学科学院，济南 250012；
3.山东大学医学院病理学教研室, 济南 250012； 4.山东大学齐鲁医院病理科, 济南 250012

摘要：

目的 研究二甲双胍对前列腺癌Vcap细胞增殖、侵袭及上皮间质转化（EMT）的影响，初步探讨microRNA (miRNA) 相关的作用机制。方法 以PBS处理组作为对照，使用不同浓度二甲双胍(1~50mmol/L) 处理前列腺癌Vcap细胞，MTS比色法检测细胞的增殖能力；流式细胞术分析二甲双胍对Vcap细胞周期分布的影响；划痕和侵袭小室实验分别检测5mmol/L二甲双胍和miR30a对细胞迁移和侵袭能力的作用；使用RT-PCR和Western blotting测定5mmol/L二甲双胍对Vcap细胞上皮指标物（E-cadherin、β-catenin）和间质指标物（Vimentin、Snail）mRNA和蛋白表达水平的影响；使用RT-PCR检测miR30a、miR143、miR185、miR196、miR205的表达水平变化。结果 二甲双胍抑制前列腺癌Vcap细胞的增殖，且呈浓度和时间依赖性。5mmol/L 二甲双胍明显影响Vcap细胞的周期分布并显著抑制Vcap细胞的迁移和侵袭能力。二甲双胍在mRNA和蛋白水平上，显著上调Vcap细胞中E-cadherin 和β-catenin的表达(P均<0.05) ，下调Vimentin和N-cadherin的表达(P均<0.05)。进一步的实验发现，二甲双胍显著上调miR30a的表达水平 (P<0.05)，而后者可显著抑制Vcap细胞的增殖和EMT的发生。结论 二甲双胍明显抑制前列腺癌Vcap细胞的增殖、侵袭能力和上皮间质转化的过程。该过程可能涉及二甲双胍对miR30a的表达的上调。

关键词： 二甲双胍；上皮间质转化；前列腺肿瘤；Vcap；miR30a

Inhibition of epithelial-mesenchymal transition by metformin in prostate cancer cells and correlative mechanisms

ZHANG Jing1， WANG Lin2，3， XIA Ping-tian3， QIN Xiao-min4， HAN Bo3，4， GUO Xiu-li1

1. Department of Pharmacology, School of Pharmacology, Shandong University, Jinan 250012, China；
2. Shandong Academy of Medicinal Sciences, Jinan 250012, China;
3. Department of Pathology, School of Medicine, Shandong University, Jinan 250012, China;
4.Department of Pathology, Qilu Hospital, Shandong University, Jinan 250012, China

Abstract:

Objective To investigate the effects of metformin on proliferation, invasion and epithelial-mesenchymal transition (EMT) of prostate cancer Vcap cells and the possible miRNA-based mechanisms. Methods Vcap cells that were treated with PBS were used as control group. MTS assay was used to determine cellular proliferation of Vcap cells treated by metformin with various concentrations (1-50mmol/L). Flow cytometric analysis was performed to detect cell cycle distributions. Wound healing assay and martrigel invasion assay were performed to evaluate invasive capacity of cancer cells treated by 5mmol/L metformin and miR30a; RT-PCR and Western blotting were used to detect mRNA and protein expression levels of epithelium markers (β-catenin, E-cadherin) as well as mesenchymal marker (Vimentin, N-cadherin). RT-PCR was used to detect the expression levels of miR30a, miR143, miR185, miR196b and miR205. Results Metformin significantly inhibited proliferation of Vcap cells in a dose- and time-dependent manner. 5mmol/L metformin significantly influenced cell cycle distribution and inhibited invasiveness and motility capacity of Vcap cells. Metformin upregulated expression of E-cadherin (P<0.05) and β-catenin (P<0.05), but downregulated Vimentin (P<0.05) and N-cadherin (P<0.05) expression at mRNA and protein levels in Vcap cells. Significant upregulation of miR30a expression levels by metformin was identified (P<0.05) and further experiments confirmed that miR30a significantly inhibited proliferation and EMT of Vcap cells. Conclusion Metformin significantly inhibits cell proliferation, invasion and EMT in prostate cancer Vcap cells. This process may involve upregulation of miR30a by metformin.

Keywords: Metformin; Epithelial-mesenchymal transition; Prostatic neoplasia; Vcap; miR30a

收稿日期 2013-07-16 修回日期 网络版发布日期

DOI:

基金项目:

国家自然科学基金(81072110)

通讯作者: 郭秀丽，E-mail: guoxl@sdu.edu.cn

作者简介:

作者Email:

参考文献：

本刊中的类似文章