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基础研究

高浓度葡萄糖条件下罗格列酮对NIT-1细胞FOXO1、TSC2基因表达及细胞分泌功能的影响

乔伟, 刘丹, 孙情, 梁瑜祯, 冯乐平

1.桂林医学院生物技术学院实验教学中心|广西 桂林541004； 2.广西医科大学第一附属临床医院代谢糖尿病中心|广西 南宁 530021

摘要：

目的：研究罗格列酮在不同浓度葡萄糖条件下，对胰岛β细胞增殖凋亡与胰岛素分泌以及叉头转录因子-1(FOXO1)和结节性硬化症-2(TSC2)表达的影响。方法： 将 NIT-1细胞按每孔5×10个放置于24孔细胞培养板，培养48 h后随机分为各处理组：5.6、7.8、11.1、16.7、22.2 和27.6 mmol/L葡萄糖组，继续培养24 h后再分别施加1×10^{-5}mol/L罗格列酮，分别于干预24和48 h后取细胞培养上清液，采用放射免疫法检测胰岛素水平和免疫荧光法检测细胞增殖情况，RT-PCR半定量法检测FOXO1和TSC2 mRNA表达水平。 结果：①$1\times10^{-6}$～1×10^{-5} mol/L罗格列酮可以分别在不同浓度葡萄糖培养条件下使胰岛NIT-1细胞增殖 （P<0.05） ,且这种变化趋势随剂量的增加而增加（即1×10^{-5} mol/L罗格列酮组＞1×10^{-6} mol/L罗格列酮组＞1×10^{-7} mol/L罗格列酮组）。1×10^{-5} mol/L的罗格列酮干预后，可见细胞凋亡百分率增加趋势随着葡萄糖浓度不断升高；②在同一浓度罗格列酮作用下，当葡萄糖浓度为11.1 mmol/L时，胰岛素分泌水平最高，高于其他各组（均P<0.05），随着葡萄糖浓度增加，胰岛素分泌量逐渐下降（11.1 mmol/L葡萄糖组>16.7 mmol/L葡萄糖组>22.5 mmol/L葡萄糖组>27.6 mmol/L葡萄糖组），而葡萄糖为5.6 mmol/L时，胰岛素分泌量最低；③ 在1×10^{-5} mol/L罗格列酮干预后，FOXO1和TSC-2 mRNA的表达水平均较未干预组明显下降，且呈现出5.6 mmol/L组＜11.1 mmol/L组＜16.7 mmol/L组＜22.5 mmol/L组＜27.6 mmol/L组的变化趋势，而且葡萄糖浓度＞16.7 mmol/L的各组均较前面小剂量葡萄糖组（≤11.1 mmol/L各组）表达明显。结论：罗格列酮可以通过直接影响胰岛β细胞内FOXO1和TSC2表达促进胰岛β细胞的增殖及影响细胞胰岛素分泌功能，提示通过调控FOXO1和TSC2表达，可以直接影响胰岛β细胞的生物学功能，如分泌功能、细胞的增殖与凋亡以及改善胰岛素抵抗状况。

关键词： 葡萄糖；胰岛β细胞；结节性硬化症-2基因；叉头转录因子-1基因；罗格列酮

Effects of rosiglitazone on expressions of FOXO1 and TSC2 gene and cell secretory function of NIT-1 cells after treated with high concentration glucose

QIAO Wei, LIU Dan, SUN Qing, LIANG Yu-Zhen, FENG Le-Ping

1. Experiment Teaching Center|School of Biotechnology,Guilin Medical College,Guilin 541004,China;2. Diabetes Research Center,First Affiliated Hospital|Guangxi Medical University,Nanning 530021,China

Abstract:

Abstract:Objective To study the effects of rosiglitazone on FOXO1 and TSC2 gene expressions,insulin secretory function,cell proliferation and apoptosis of pancreatic β cells under high concentration glucose condition.Methods The NIT-1 cells were put into plates (5×10 cells /well) and cultivated for 48 h,then they were randomly divided into treatment groups containing different concentrations of glucose as ollows:5.6,7.8,11.1,16.7,22.2,and 27.6 mmol/L groups. After cultivated for 24 h,they were intervented by 10^{-5} mmol/L rosiglitazone for next 24 and 48 h,then the supernatant was collected.The insulin level was evaluated by radio-immunity technique,the cell proliferation and apoptosis were detected by immunofluorescence staining and MTT assay respectivly.The expressions of FOXO1 and TSC2 mRNA were detected by semi-quantitative RT-PCR assay.Results ① Under different concentrations of glucose，after treated with 10^{-6}-10^{-5} mol/L rosiglitazone the proliferation of pancreatic β cells (NIT-1 cell line) was found(P<0.05)and the apoptotic rate of cells was increased in a dose-dependent manner （1×10^{-5} mol/L rosiglitazone group＞1×10^{-6} mol/L rosiglitazone group＞1×10^{-7} mol/L rosiglitazone group）.② When under same dose of glucose,the insulin secretion level in 11.1 mmol/L group was much higher than those in other groups(P<0.05),but the insulin secretion level was reduced gradually following the decrease of glucose concentration(11.1 mmol/Lgroup＞16.7 mmol/L group＞22.5 mmol/L group＞27.6 mmol/L group).The insulin secretion level in 5.6 mol/L group was the lowest.③ After intervention of 10^{-5} mol/L rosiglitazone,the expression levels of both FOXO1 and TSC2 mRNA were significantly lower than those in control group (5.6 mmol/L group＜11.1 mmol/L group＜16.7 mmol/L group＜22.5 mmol/L group＜ 27.6 mmol/L group).When the glucose concentration was over 16.7 mol/L,the expressions of FOXO1 and TSC2 mRNA were obviously higher than those in the groups with glucose concentration ≤11.1 mmol/L after the intervention of 10-5 mol/L rosiglitazone.Conclusion Rosiglitazone can improve the secretion function of pancreatic β cells and cell proliferation and alleviate

insulin resistance by directly regulating FOXO1 and TSC2 expressions.

Keywords: glucose;pancreatic &beta cells;tuberous sclerosis complex2;forkhead box O1;rosiglitazone

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通讯作者: 梁瑜祯（Tel：0771-3277215，E-mail：liangyuzhen26@yahoo.com.cn）； 冯乐平（Tel：0773-5895380，E-mail：lpfeng1226@163.com）

作者简介: 乔 伟（1962-）|女|吉林省长春市人|高级工程师|主要从事细胞分子生物学研究。

作者Email: liangyuzhen26@yahoo.com.cn;lpfeng1226@163.com

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