[1]赖姝婕,王军,王斌,等.沉默PKCδ表达对L02肝细胞脂肪变性和内质网应激的影响[J].第三军医大学学报,2014,36(07):650-654.

Lai Shujie,Wang Jun,Wang Bin,et al.PKCδ silencing suppresses endoplasmic reticulum stress and attenuates fatty degeneration in steatotic L02 hepatocytes[J].J Third Mil Med Univ,2014,36(07):650-654.

沉默PKCδ表达对L02肝细胞脂肪变性和内质网应激的影响(PDF)

《第三军医大学学报》[ISSN:1000-5404/CN:51-1095/R] 卷: 36 期数: 2014年第07期 页码: 650-654 栏目: 论著 出版日期: 2014-04-15

Title: PKCδ silencing suppresses endoplasmic reticulum stress and attenuates fatty degeneration in steatotic L02 hepatocytes

作者: 赖姝婕; 王军; 王斌; 魏艳玲; 熊吉; 李青; 李砚; 樊丽琳; 陈东风

第三军医大学大坪医院野战外科研究所消化内科

Author(s): Lai Shujie; Wang Jun; Wang Bin; Wei Yanling; Xiong Ji; Li Qing; Li Yan; Fan Lilin; Chen Dongfeng

Department of Gastroenterology, Institute of Surgery Research, Daping Hospital, Third Military Medical University, Chongqing, 400042, China

关键词: 非酒精性脂肪性肝炎; 蛋白激酶C; 肝细胞脂肪变性; 内质网应激

Keywords: non-alcoholic steatohepatitis; protein kinase Cδ; steatotic hepatocyte ; endoplasmic reticulum stress

分类号: R322.47; R329.25; R363.21

文献标志码: A

摘要: 目的 研究蛋白激酶C δ亚型（protein kinase Cδ,PKCδ）与肝细胞脂肪变性、内质网应激的关系，探讨其在非酒精性脂肪性肝炎（non-alcoholic steatohepatitis，NASH）发病机制中的作用。 方法 用混合脂肪酸构建人正常肝细胞L02脂肪变性模型，油红O染色和甘油三酯（TG）试剂盒检测细胞脂变程度，实时荧光定量PCR检测PKCδ、Bip、XBP-1s mRNA表达，Western blot检测其蛋白表达。通过siRNA瞬时转染技术沉默PKCδ在L02细胞中的表达后观察上述指标表达变化。 结果 油酸和棕榈酸酯2∶1混合比例能够成功诱导肝细胞脂肪变性，与对照组单个细胞脂变面积(14.47±9.28)和TG含量(2.30±0.62)μg/mg相比，脂肪酸16 h组脂变面积（333.06±42.36）和TG含量(30.86±6.24)μg/mg均显著增加（P<0.05）。脂肪酸组肝细胞PKCδ、Bip、XBP-1s mRNA和蛋白表达水平较对照组显著升高（P<0.05），具有时间依赖性。在相同脂肪酸诱导液处理的条件下，PKCδ siRNA转染组细胞脂变程度（30.92±1.29）%较对照组（55.32±6.58）%明显减轻（P<0.05），且PKCδ siRNA转染组Bip、XBP-1s的表达较对照siRNA转染组明显降低。 结论 PKCδ在NASH形成发展中发挥重要作用，沉默PKCδ能够通过抑制内质网应激减轻肝细胞脂肪变性程度。

Abstract: Objective To investigate the relationship of the expression of protein kinase Cδ (PKCδ) with fatty degeneration and endoplasmic reticulum stress in the steatotic hepatocytes, and investigate the role of PKCδ in pathogenesis of non-alcoholic steatohepatitis (NASH). Methods The steatosis model of human L02 hepatocytes was established by induction with fatty acid mixture. Triglyceride (TG) kit was used to measured lipid accumulation in the hepatocytes with Oil Red O staining. The expression of PKCδ, binding immunoglobulin protein (Bip), and spliced X-box binding protein 1 (XBP-1) at mRNA and protein levels were analyzed by real-time PCR and Western blotting respectively. After transient transfection of PKCδ siRNA was used to knock down PKCδ expression in L02 cells, the above expression was detected again. Results Fatty acid mixture (oleate-to-palmitate at 2∶1) induced hepatic steatosis, the average LD area per cell of fatty acid 16 h group was 333.06±42.36 pixels, which was apparently more than that of the control group (14.47±9.28), and TG content was significantly higher than in control group (30.86±6.24 *vs* 2.30±0.62 μg/mg, P<0.05). Fatty acid mixture up-regulated the expression of PKCδ, Bip and XBP-1 in a time-dependent manner (P<0.05). Knock-down of PKCδ gene expression led to a reduction in both lipid accumulation [(30.92±1.29)% *vs* (55.32±6.58)%, P<0.05] and the expression of Bip and XBP-1 during fatty acid mixture-induced hepatic steatosis. Conclusion PKCδ may play an important role in the prognosis of NASH. Silencing the gene expression of PKCδ can reduce the degree of

fatty degeneration and endoplasmic reticulum stress.

参考文献/REFERENCES:

赖姝婕，王军，王斌，等. 沉默PKCδ表达对L02肝细胞脂肪变性和内质网应激的影响[J].第三军医大学学报,2014,36(7):650-654.

相似文献/REFERENCES:

[1]刘波,吴小翎,张霞,等.福辛普利对非酒精性脂肪性肝炎大鼠肝纤维化的作用[J].第三军医大学学报,2012,34(16):1646.
Liu Bo,Wu Xiaoling,Zhang Xia,et al.Effects and mechanism of fosinopril on hepatic fibrosis in rats with nonalcoholic steatohepatitis[J].J Th Mil Med Univ,2012,34(07):1646.

[2]魏勇,顾健腾,鲁开智,等.瑞芬太尼对肝细胞缺氧复氧损伤保护作用的机制研究[J].第三军医大学学报,2007,29(20):1976.
WEI Yong,GU Jian-teng,LU Kai-zhi,et al.Remifentanyl protects hepatocytes against anoxia-reoxygenation injury[J].J Third Mil Med Univ,200 (07):1976.

[3]向飞,张琼,褚志刚,等.蛋白激酶C在腺苷A1受体调控缺氧心肌细胞线粒体通透性转换孔开放中的表达和作用[J].第三军医大学学报,2007,29(12):1135.
XIANG Fei,ZHANG Qiong,CHU Zhi-gang,et al.Role of protein kinase C in adenosine A1 receptor regulating opening of mitochondria permeability transition pore in hypoxic cardiac myocytes[J].J Third Mil Med Univ,2007,29(07):1135.

[4]陈渝,邓忠良.蛋白激酶C在人骨肉瘤细胞多药耐药中的作用及机制[J].第三军医大学学报,2011,33(18):1900.
Chen Yu,Deng Zhongliang.Effect of protein kinase C on multidrug resistance in human osteosarcoma cells and its underlying mechanism[J] Third Mil Med Univ,2011,33(07):1900.

[5]韩京,冉新泽,艾国平,等.去甲肾上腺素促进骨髓间充质干细胞增殖的研究[J].第三军医大学学报,2009,31(23):2295.
HAN Jing,RAN Xin-ze,AI Guo-ping,et al.Norepinephrine improves bone marrow mesenchymal stem cells proliferation through AR/PKC-dependent signaling[J].J Third Mil Med Univ,2009,31(07):2295.

[6]闵敏,陈东风,王军,等.葡萄糖调节蛋白78在大鼠非酒精性脂肪性肝炎中的表达及意义[J].第三军医大学学报,2009,31(01):79.
MIN Min,CHEN Dong-feng,WANG Jun,et al.Expression and significance of glucose regulated protein GRP78 in nonalcoholic steatohepatitis rats[J].J Third Mil Med Univ,2009,31(07):79.

[7]王少雄,杨剑,陈彩宇,等.多巴胺D1受体通过PKC途径调节肾近曲小管上皮肾胺酶的表达[J].第三军医大学学报,2011,33(24):2558.
Wang Shaoxiong,Yang Jian,Chen Caiyu,et al.Dopamine D1-like receptors regulate renalase in renal proximal tubule cells through PKC pathv in vitro[J].J Third Mil Med Univ,2011,33(07):2558.

[8]王聪丽,邱小华,蔡颖,等.脂多糖干预气道上皮细胞细胞因子及蛋白激酶C的表达[J].第三军医大学学报,2013,35(17):1792.
Wang Congli,Qiu Xiaohua,Cai Ying,et al.Expression of protein kinase C and cytokine in airway epithelial cells interfered by LPS[J].J Third M Med Univ,2013,35(07):1792.

更新日期/Last Update: 2014-04-03