肾脏细胞CD36在炎症因子诱导的脂肪酸摄取及脂质沉积中的作用

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摘要 慢性炎症和脂质代谢紊乱是慢性肾病的重要特征, 炎症因子影响肾脏细胞脂质代谢的作用机制尚不清楚, 该研究旨在探讨炎症因子是否通过上调脂肪酸转运酶CD36的表达促进肾脏细胞脂肪酸摄取及脂质沉积。通过给予HMCs及HK2细胞肿瘤坏死因子(tumor necrosis factor-α, TNF-α)和白介素6(interleukin-6, IL-6)刺激处理24 h, 应用qRT-PCR检测*CD36*的表达量, 酶法检测HK2细胞内的甘油三酯(triglycercide, TG)水平。构建CD36过表达的细胞模型, 使用荧光标记脂肪酸, 观测细胞对外源性脂肪酸的摄取速率。然后利用小RNA干扰技术, 构建CD36低表达的细胞模型, 检测CD36低表达时细胞脂肪酸摄取速率及胞内甘油三酯、游离脂肪酸(free fatty acid, FFA)含量, 葡萄糖调节蛋白78(*GRP78*)及内质网跨膜激酶(*IRE1*)的mRNA表达量。结果显示, 炎性因子TNF-α和IL-6促进HMCs及HK2细胞TG的累积增加, 并刺激细胞CD36的表达; CD36过表达促进HMCs及HK2细胞对FFA的摄取。当CD36表达被干扰后, 炎性因子诱导的肾脏细胞TG及FFA的累积增加、FFA的摄取速率、细胞内*GRP78*、*IRE-1*的mRNA表达量及ROS含量均受到了抑制。该项研究表明, 在HMCs及HK2细胞中, 炎症因子可能通过促进CD36表达, 导致细胞对FFA摄取增多, 进而引起细胞脂质积聚; 干预CD36能够改善炎性因子引起的脂质积聚、内质网应激以及细胞损伤, 提示CD36可作为慢性肾脏疾病的潜在治疗靶点。

关键词 炎症; 脂肪酸转运酶CD36; 肾脏细胞; 脂质沉积

The Role of Renal Cell CD36 in Inflammatory Factor-Induced Fatty Acid Uptake and Lipid Deposition

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Abstract Chronic inflammation and lipid metabolism disorder are important features of chronic kidney disease. The mechanism of how inflammatory factors affect lipid metabolism in renal cells is not clear. This study aims to explore whether inflammatory factors promote fatty acid uptake and lipid deposition in renal cells by up-regulating the expression of fatty acid transporter CD36. First, HMCs and HK2 cells were treated by TNF-α (tumor necrosis factor-α) and IL-6 (interleukin-6) respectively for 24 h. TG (triglycerides) were detected by enzymatic detection. The mRNA expression level of *CD36* was detected the by qRT-PCR. Next, CD36 overexpression cell model was established, fatty acids was fluorescent labeled to observe the uptake rate the of exogenous fatty acids. Then,

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small RNA interference technique was used to construct a cell model with low expression of CD36. Intracellular TG, intracellular FFA (free fatty acid), *GRP78* (glucose regulated protein 78) and *IRE1* (inosital-requiring enzyme 1) mRNA expression level were detected respectively. The results showed TNF-α and IL-6 promoted the accumulation of TG in HMCs and HK2 cells and stimulate the expression of CD36. Meanwhile, CD36 overexpression promoted FFA uptake in HMCs and HK2 cells. When CD36 expression was interfered, accumulation of TG and FFA, uptake rate of FFA and ERS (endoplasmic reticulum stress) induced by inflammatory cytokines were inhibited. In conclusion, inflammatory cytokines promotes CD36 expression in HMCs and HK2 cells, leading to increased uptake of FFA and lipid accumulation. Inhibition of CD36 expression may alleviate lipid accumulation and ERS induced by inflammatory cytokines. These results suggest that CD36 may be a potential therapeutic target for chronic renal disease.

Keywords inflammation; fatty acid transporter CD36; renal cells; lipid deposition

慢性肾病(chronic kidney disease, CKD)是指肾脏结构或功能受损超过三个月, 随之产生的机体血液、尿液指标及肾脏结构和功能障碍的疾病[1]。近年来, CKD在我国的发病率高达10.8%[2], 研究发现, 慢性炎症是进行性肾损伤的主要原因[3], 该课题组[4-7]的早期研究揭示了慢性炎症在脂质代谢紊乱中的作用, 发现慢性炎症通过破坏脂质流入和流出的平衡导致肝脏内脂质积聚。然而, 炎症对肾脏的异位性脂质沉积的影响尚不清楚。在炎症浸润的同时, CKD患者常伴随不同程度的脂代谢紊乱。脂代谢紊乱可以通过促进肾脏动脉粥样硬化及对肾脏细胞的直接毒性作用, 从而加速CKD的进展。细胞不仅通过被动扩散, 也可以通过脂肪酸转运受体介导机制来吸收游离脂肪酸(free fatty acid, FFA), 其中最具代表性的就是脂肪酸转位酶CD36[8]。CD36作为调节脂肪酸摄取的一个重要蛋白, 在脂肪酸的跨膜转运中起主导作用。CD36在肾脏近端和远端小管上皮细胞、足细胞、系膜细胞和微血管内皮细胞、间质巨噬细胞等中均有表达。近来研究表明, 在CKD患者中*CD36*的基因表达增高[9-10], 提示CD36在肾脏疾病的发病中起着重要作用。

该课题组前期研究证实, 炎症能够刺激肾脏CD36的表达增高, 但CD36是否直接参与炎症诱导的肾脏细胞脂质积聚及其作用机制还未清楚。该项研究使用长链脂肪酸及炎症因子TNF-α和IL-6处理肾脏细胞模拟体内炎症状态, 观察在炎症因子刺激下, 细胞对外源性脂肪酸的摄取、胞内脂质积聚及CD36表达的影响; 然后利用过表达质粒及小RNA干扰技术分别构建CD36过表达及干扰的细胞模型, 进一步阐明炎症因子刺激下, CD36在肾脏细胞脂肪酸摄取及脂质沉积中的作用。

1 材料与方法

1.1 实验材料

1.1.1 细胞及质粒 HK2细胞、HMCs细胞及CD36过表达质粒均为本实验室保存, 由英国UCL大学皇家自由医学院肾病中心惠赠。

1.1.2 主要试剂和仪器 RPMI-1640细胞培养基及胎牛血清购自美国HyClone公司; 牛血清白蛋白(不含脂肪酸)及软脂酸购自英国Sigma公司; Trizol RNA抽提试剂、SYBR Green PCR Master Mix及逆转录试剂盒购自日本TaKaRa公司; TG检测试剂盒购自南京建成生物工程研究所; 肿瘤坏死因子α及白介素6购自以色列Peprotech公司; 荧光标记脂肪酸(BODIPY FL C16)购自美国Invitrogen公司; 转染试剂X-treme GENE HP DNA Transfection Reagent和X-treme GENE SiRNA Transfection Reagent购自瑞士Roche公司; 2',7'-二氯荧光素二醋酸盐荧光探针购自美国AAT Bioquest公司; PCR引物由北京六合华大基因科技公司合成; CD36 siRNA由上海吉玛制药有限公司构建。

荧光定量PCR仪购自美国Bio-Rad公司; 倒置显微镜及荧光显微镜购自德国Carl Zeiss公司; 酶标仪购自美国BioTek公司。

1.2 方法

1.2.1 细胞培养 HMCs细胞在RPMI-1640中培养, 其中含有10%胎牛血清、1%胰岛素转铁蛋白亚硒酸钠、100 U/mL青霉素、100 μg/mL链霉素。HK2细胞在RPMI-1640中培养, 其中含有10%胎牛血清、100 U/mL青霉素、100 μg/mL链霉素。细胞都置于37 °C、5% CO_2培养箱中培养, 1~2天换液, 3~4天传代。

1.2.2 实验分组 待细胞生长汇合度为70%~80%时, 用含0.2% BSA(不含脂肪酸)的无血清RPMI-1640培养基处理, 24 h后再按照以下处理分为3个组。(1) Control组: 0.2% BSA+0.04 mmol/L软脂酸+PBS; (2) TNF-α组: 0.2% BSA+0.04 mmol/L软脂酸+25 ng/mL TNF-α; (3)IL-6组: 0.2% BSA+0.04 mmol/L软脂酸+20 ng/mL IL-6。以上3组处理24 h后收集细胞进行下一步检测。

1.2.3 质粒瞬时转染 当细胞融合度为30%~50%时, 在50 μL DMEM培养基中缓慢滴加0.5 μgDNA, 然后加入1.5 μL DNA Transfection Reagent, 用移液器吹打混匀, 室温孵育15~30 min(15~25 ℃), 将转染复合物逐滴加入到细胞中, 7~8 h在显微镜下观察转染效率。

1.2.4 实时荧光定量PCR检测mRNA的表达 使用RNAiso Plus提取细胞总RNA, 然后用PrimeScript® RT reagent Kit将总RNA反转录成cDNA, 反转录条件是: 37 ℃ 15 min, 85 ℃ 5 s, 保存于−20 ℃。再以cDNA为模板, 实时荧光定量PCR检测基因的mRNA表达水平。使用PowerSYBR Green PCR Master Mix试剂盒进行扩增, 反应条件: 50 ℃预热2 min, 95 ℃预变性5 min; 95 ℃变性20 s, 55 ℃退火延伸20 s, 40个循环。反应体系为25 μL, 用*ΔΔCt*计算基因的表达水平, 公式如下: *ΔCt*=目的基因*Ct*值−*β-actin*基因*Ct*值, *ΔΔCt*=实验组*ΔCt*−对照组*ΔCt*, 实验组相对于对照组基因表达水平的倍数=$2^{-\Delta\Delta Ct}$。设计的引物序列见表1。

1.2.5 TG及FFA含量的测定 使用6孔板接种细胞(每孔接种约5×10^{5}个), 经过实验处理后, 收集细胞并提取细胞脂质, 然后收集细胞上清液, 在真空条件下进行干燥。用比色法检测其TG含量, ELISA法检测FFA的含量; 再分别计算TG、FFA与细胞总蛋白量的比值, 得出各组TG及FFA的相对含量。

1.2.6 细胞FFA动态观察 使用24孔培养板接种细胞(40%融合度), 在无血清培养基中饥饿24 h, 再加入炎症因子处理24 h。去除培养基, PBS洗3次, 开始照相(无需PA培养为背景)。于0 s开始, 加入浓度为0.02 mmol/L BODIPY FL C16, 荧光显微镜下excitation/emission=505 nm/510 nm, 每隔4 s照相一次, 共观察5 min, 收集保存图片。

1.2.7 ROS含量测定 在细胞中加入10 μmol/L 2',7'-二氯荧光素二醋酸盐荧光探针(dichlorofluorescin diacetate, DCFH-DA) 37 ℃孵育40 min。然后使用ROS测定试剂盒检测细胞的相对荧光强度(RFU), 检测的激发波长为488 nm, 发射波长为520 nm, 最后得出ROS的相对含量测定值(试验组的荧光强度测定值与对照组的比值)。

1.2.8 统计学分析 所有数据采用GraphPad Prism 5统计分析软件进行处理, 所得到的数值均以$\bar{x}\pm s$表示, 两样本均数间的比较使用独立样本*t*检验, 检验水准为α=0.05。

2 结果

2.1 炎性因子诱导肾脏细胞中TG累积增加及CD36表达增高

使用炎症因子TNF-α和IL-6分别处理HMCs及HK2细胞后, 细胞中TG的含量与对照组相比均显著增高, (*P*<0.01, 图1)。同时, HMCs及HK2细胞中*CD36*的mRNA表达水平均显著增高(*P*<0.01, 图1)。

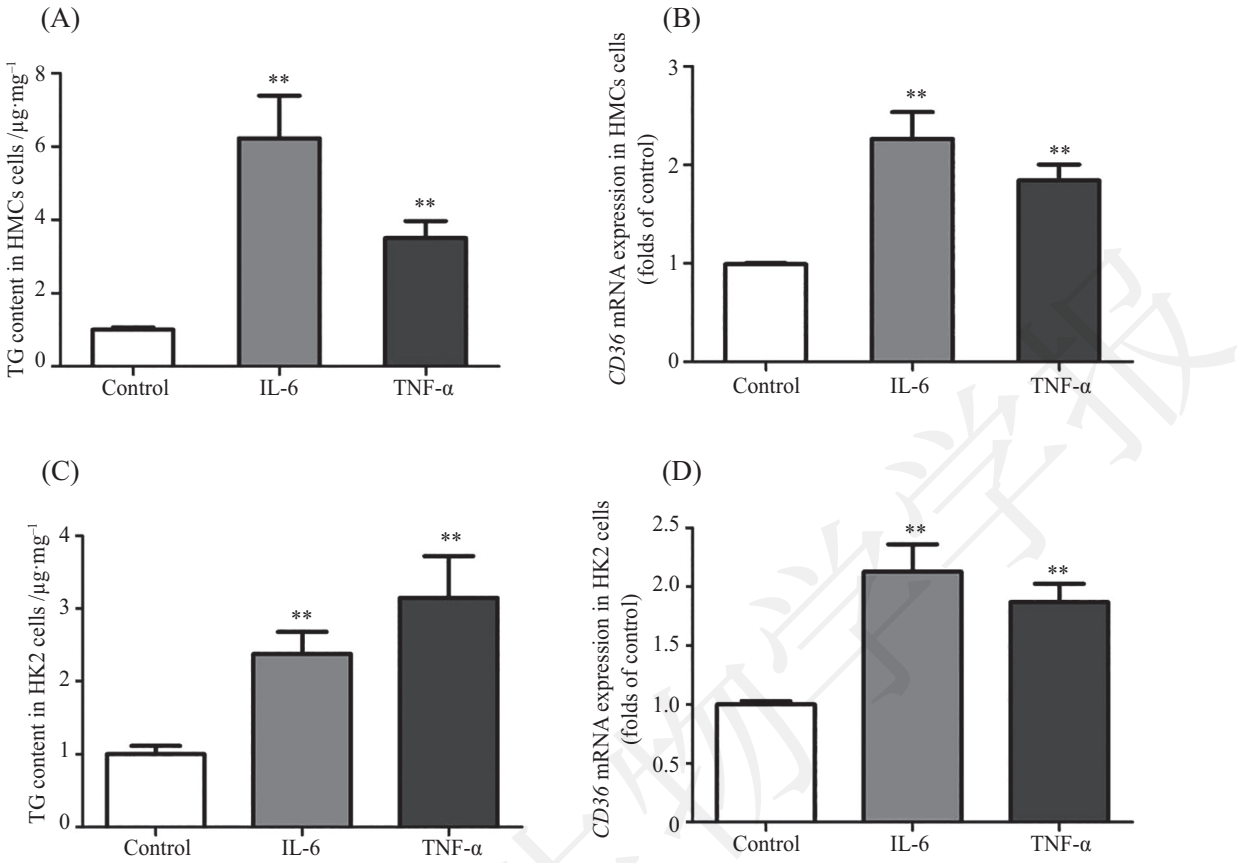
2.2 CD36过表达促进肾脏细胞FFA动态摄取

利用质粒过表达技术, 分别构建CD36过表达的HMCs及HK2细胞模型, 然后测定肾脏细胞对FFA的摄取能力。结果显示, 与对照组相比, CD36OE-

表1 qRT-PCR引物序列

Table 1 qRT-PCR primer sequence

基因名 Name	序列(5′→3′) Sequence (5′→3′)
CD36	Forward: TTC CTG CAG CCC ATG GT
	Reverse: GTC AGC CTC TGT TCC AAC TGA TAG
GRP78	Forward: CCG GCG CGA GGT AGA AA
	Reverse: TCA ATT CTT GCT TGA TGC TGA GA
IRE-1	Forward: CGA TGC CCT GAG GCT CTT T
	Reverse: TGG ATG CCA CAG GAT TCC AT
β-actin	Forward: CCT GGC ACC CAG CAC AAT
	Reverse: GCC GAT CCA CAC GGA GTA



A: 酶法检测HMCs细胞中TG含量; B: qRT-PCR检测HMCs细胞中*CD36*的mRNA表达量; C: 酶法检测HK2细胞中TG含量; D: qRT-PCR检测HK2细胞中*CD36*的mRNA表达量。**P<0.01, 与Control组比较。

A: enzymatic method was used to detect TG content in HMCs cells; B: qRT-PCR was used to detect *CD36* mRNA expression level in HMCs cells; C: enzymatic method was used to detect TG content in HK2 cells; D: qRT-PCR was used to detect *CD36* mRNA expression level in HK2 cells. **P<0.01 compared with Control group.

图1 炎性因子刺激下肾脏细胞内TG含量及*CD36* mRNA表达量

Fig.1 TG content and *CD36* mRNA expression levels in renal cells under inflammatory conditions

表2 荧光显微镜观察CD36过表达时HMCs细胞中FFA动态摄取速率

Table 2 Fluorescence microscope was used to observe FFA uptake rate with CD36 overexpression in HMCs cells

组别 Group	0 s	28 s	84 s	140 s	196 s
NC	0.000±0.004	16.909±3.381	32.482±5.953	37.147±4.846	38.829±4.286
CD36 OE	0.000±0.005	32.943±5.002**	46.632±6.974*	55.453±3.319**	60.441±9.186**

*P<0.05, **P<0.01, 与NC组比较。

*P<0.05, **P<0.01 compared with NC group.

HMCs组及CD36OE-HK2细胞组脂肪酸的动态摄取量均明显增加(P<0.05, 表2~表3)。

2.3 CD36干扰抑制炎症因子诱导的肾脏细胞FFA动态摄取

在炎症因子作用下, HMCs及HK2细胞对照组(NC组)脂肪酸的动态摄取量明显增加(P<0.05, 表4~表7)。而当CD36的表达下调之后, CD36 siRNA组炎症因子引起的HMCs及HK2细胞的脂肪酸动态摄取量增加的现象得到了改善(P<0.05, 表4~表7)。

2.4 CD36干扰抑制炎症因子诱导的肾脏细胞脂质积聚

炎症因子TNFα和IL-6处理HMCs及HK2细胞后, HMCs及HK2细胞中TG及FFA的含量均增高(P<0.05, 图2), 而当CD36的表达下调之后, 炎症因子引起的

表3 荧光显微镜观察CD36过表达时HK2细胞中FFA动态摄取速率

Table 3 Fluorescence microscope was used to observe FFA uptake rate with CD36 overexpression in HK2 cells

组别 Group	0 s	28 s	84 s	140 s	196 s
NC	0.000±0.003	17.394±3.290	31.159±6.467	35.698±6.906	38.127±6.423
CD36 OE	0.000±0.004	33.480±9.219*	49.893±5.544**	58.059±6.645**	62.337±7.916**

*P<0.05, **P<0.01, 与NC组比较。

*P<0.05, **P<0.01 compared with NC group.

表4 荧光显微镜观察CD36低表达时IL-6刺激下HMCs细胞FFA动态摄取速率

Table 4 Fluorescence microscope was used to observe FFA uptake rate induced by the inflammatory factor IL-6 with CD36 low expression in HMCs cells

组别 Group	0 s	28 s	84 s	140 s	196 s
NC siRNA	0.000±0.500	17.200±4.480	31.500±4.100	37.300±3.500	38.900±2.700
NC siRNA+IL-6	0.000±0.400	35.400±6.500*	57.700±9.841*	71.200±8.000*	79.300±7.506*
CD36 siRNA+IL-6	0.000±0.400	11.200±4.100#	33.400±5.600#	37.500±4.700#	38.200±3.400#

*P<0.01, 与NC siRNA组比较; #P<0.01, 与NC siRNA+ IL-6组比较。

*P<0.01 compared with NC siRNA group; #P<0.01 compared with NC siRNA+IL-6 group.

表5 荧光显微镜观察CD36低表达时TNF-α刺激下HMCs细胞FFA动态摄取速率

Table 5 Fluorescence microscope was used to observe FFA uptake rate induced by the inflammatory factor TNF-α with CD36 low expression in HMCs cells

组别 Group	0 s	28 s	84 s	140 s	196 s
NC siRNA	0.000±0.400	9.000±3.600	19.100±7.800	22.100±7.000	21.500±3.400
NC siRNA+TNF-α	0.000±1.000	42.500±5.000*	56.300±4.300*	63.000±5.445*	75.200±4.700*
CD36 siRNA+TNF-α	0.000±1.400	21.800±7.400#	33.400±4.300#	37.500±4.700#	38.200±3.400#

*P<0.01, 与NC siRNA组比较; #P<0.01, 与NC siRNA+TNF-α组比较。

*P<0.01 compared with NC siRNA group; #P<0.01 compared with NC siRNA+TNF-α group.

表6 荧光显微镜观察CD36低表达时IL-6刺激下HK2细胞FFA动态摄取速率

Table 6 Fluorescence microscope was used to observe FFA uptake rate induced by the inflammatory factor IL-6 with CD36 low expression in HK2 cells

组别 Group	0 s	28 s	84 s	140 s	196 s
NC siRNA	0.000±0.500	18.400±4.200	27.000±4.300	32.200±3.800	38.400±3.400
NC siRNA+IL-6	0.000±0.400	60.200±7.500*	88.000±8.800*	109.800±11.400*	107.100±10.600*
CD36 siRNA+IL-6	0.000±0.400	13.400±3.200#	23.200±6.600#	37.600±7.800#	42.000±8.200#

*P<0.01, 与NC siRNA组比较; #P<0.01, 与NC siRNA+ IL-6组比较。

*P<0.01 compared with NC siRNA group; #P<0.01 compared with NC siRNA+IL-6 group.

HMCs及HK2细胞中TG及FFA含量增高得到了抑制(P<0.05, 图2)。

2.5 CD36干扰抑制炎症因子诱导的*GRP78*和*IRE-1*的mRNA表达

脂质积聚能够引起内质网应激, 并造成细胞损伤。炎症因子TNFα和IL-6处理HMCs及HK2细胞后, HMCs及HK2细胞中*GRP78*和*IRE-1*的mRNA表达量均增高(P<0.05, 图3)。而当CD36的表达下调之后, 炎症因子引起的HMCs及HK2细胞中*GRP78*和*IRE-1*的mRNA表达量增高得到了抑制(P<0.05, 图3)。

2.6 CD36干扰抑制肾脏细胞损伤

炎症因子TNFα和IL-6处理HMCs及HK2细胞后,

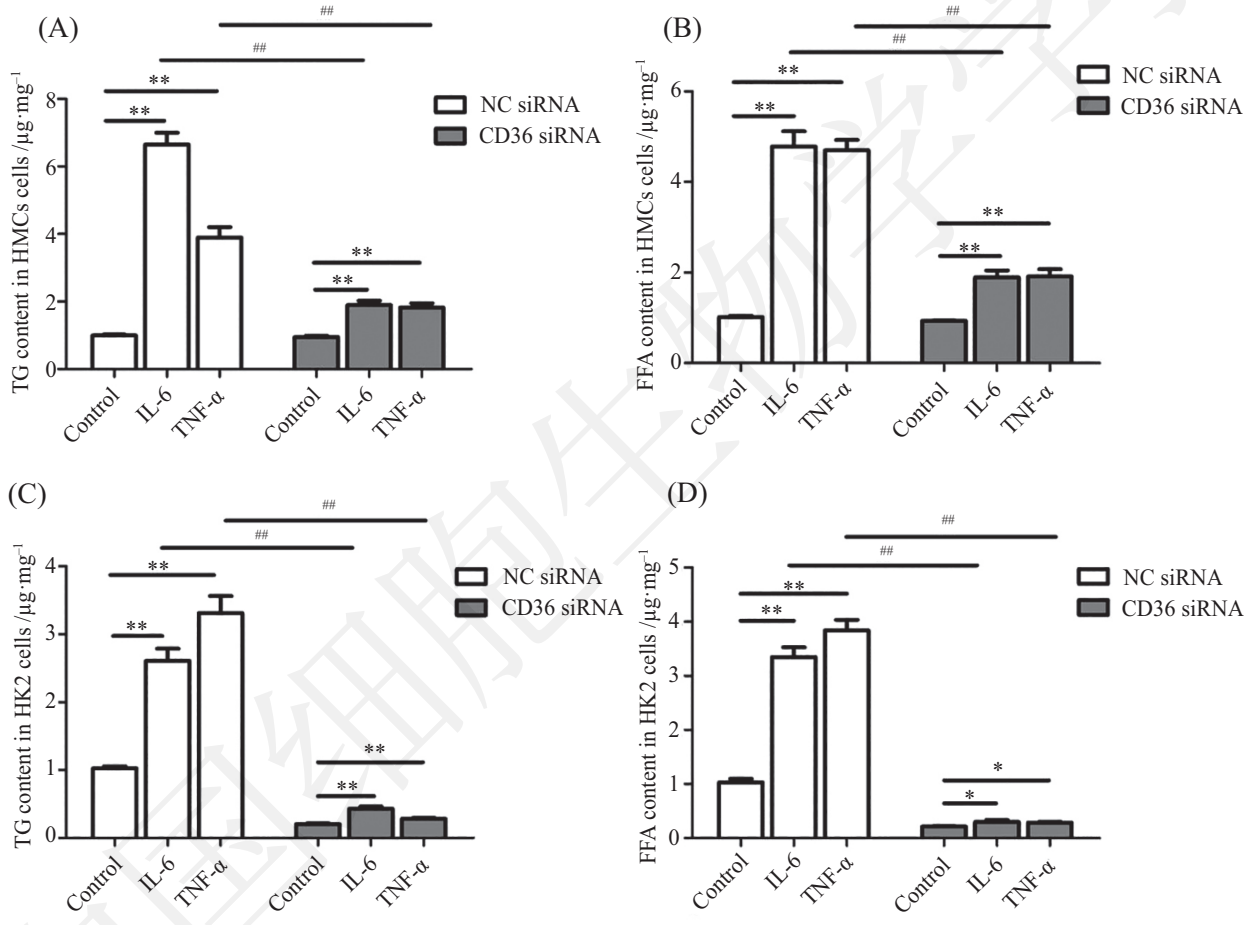
表7 荧光显微镜观察CD36低表达时TNF-α刺激下HK2细胞FFA动态摄取速率

Table 7 Fluorescence microscope was used to observe FFA uptake rate induced by the inflammatory factor TNF-α with CD36 low expression in HK2 cells

组别 Group	0 s	28 s	84 s	140 s	196 s
NC siRNA	0.000±0.500	12.400±3.400	24.400±3.800	30.000±4.100	32.200±5.100
NC siRNA+TNF-α	0.000±0.600	37.200±6.200*	67.900±9.100*	78.100±15.600*	90.200±8.500*
CD36 siRNA+TNF-α	0.000±0.600	15.600±5.100#	31.000±6.300#	37.100±6.700#	43.200±8.500#

*P<0.01, 与NC siRNA组比较; #P<0.01, 与NC siRNA+TNF-α组比较。

*P<0.01 compared with NC siRNA group; #P<0.01 compared with NC siRNA+TNF-α group.



A: 酶法检测HMCs细胞中TG含量; B: ELISA检测HMCs细胞中FFA含量; C: 酶法检测HK2细胞中TG含量; D: ELISA检测HK2细胞中FFA含量。*P<0.05, **P<0.01, 与Control组比较; ##P<0.01, 与NC siRNA组比较。

A: enzymatic method was used to detect TG content in HMCs cells; B: ELISA was used to detect FFA content in HMCs cells; C: enzymatic method was used to detect TG content in HK2 cells; D: ELISA was used to detect FFA content in HK2 cells. *P<0.05, **P<0.01 compared with Control group; ##P<0.01 compared with NC siRNA group.

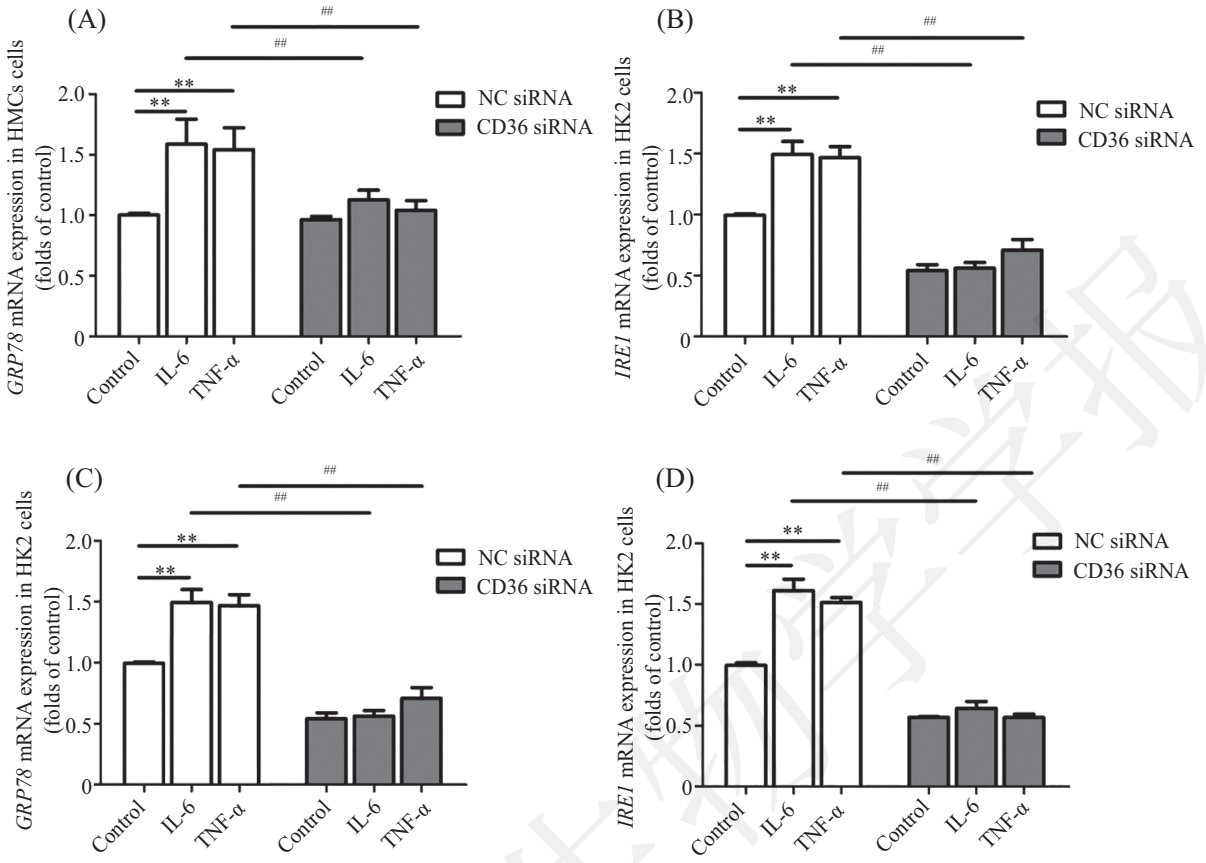
图2 CD36低表达时炎性因子刺激下肾脏细胞TG及FFA的含量

Fig.2 TG and FFA levels in renal cells under inflammatory conditions with low expression of CD36

HMCs及HK2细胞中ROS的表达量均增高(P<0.05, 图4)。而当CD36的表达下调之后, 炎症因子引起的*ROS*的mRNA表达量增高得到了抑制(P<0.05, 图4)。

3 讨论

近年来, 代谢综合征(metabolic syndrome, MS)被认为是影响机体健康的一项慢性因素, 有研究指

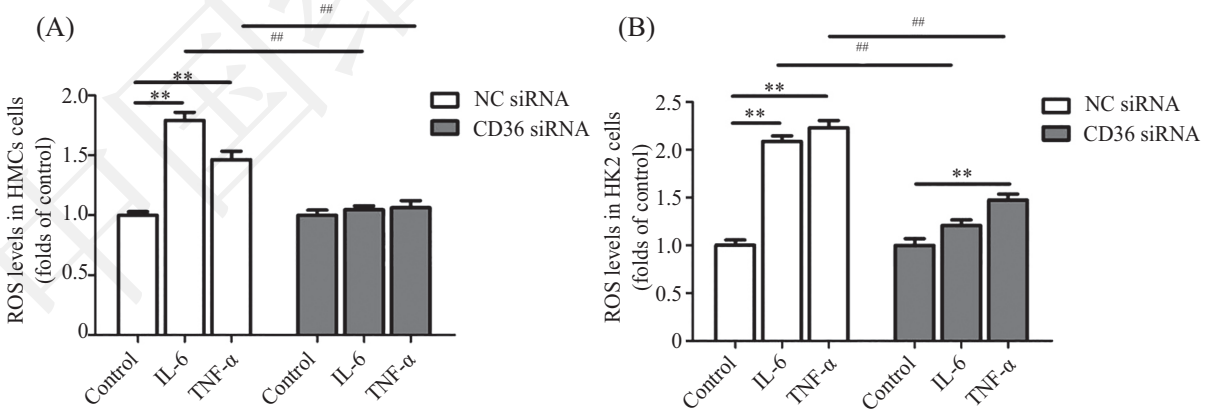


A: qRT-PCR检测HMCs细胞中*GRP78*的mRNA表达量; B: qRT-PCR检测HMCs细胞中*IRE1*的mRNA表达量; C: qRT-PCR检测HK2细胞中*GRP78*的mRNA表达量; D: qRT-PCR检测HK2细胞中*IRE1*的mRNA表达量。**P<0.01, 与Control组比较; ##P<0.01, 与NC siRNA组比较。

A: qRT-PCR was used to detect *GRP78* mRNA expression level in HMCs cells; B: qRT-PCR was used to detect *IRE1* mRNA expression level in HMCs cells; C: qRT-PCR was used to detect *GRP78* mRNA expression level in HK2 cells; D: qRT-PCR was used to detect *IRE1* mRNA expression level in HK2 cells. **P<0.01 compared with Control group; ##P<0.01 compared with NC siRNA group.

图3 CD36低表达时炎性因子刺激下肾脏细胞*GRP78*及*IRE-1*的mRNA表达量

Fig.3 *GRP78* and *IRE-1* mRNA expression levels in renal cells under inflammatory conditions with low expression of CD36



A: DCFH-DA检测HMCs细胞中ROS的含量; B: DCFH-DA检测HK2细胞中ROS的含量。**P<0.01, 与Control组比较; ##P<0.01, 与NC siRNA组比较。

A: DCFH-DA was used to detect ROS level in HMCs cells; B: DCFH-DA was used to detect ROS level in HK2 cells. **P<0.01 compared with Control group; ##P<0.01 compared with NC siRNA group.

图4 CD36低表达时炎性因子刺激下肾脏细胞ROS含量

Fig.4 ROS levels in renal cells under inflammatory conditions with low expression of CD36

出, CKD是MS在肾脏疾病中的表型[11]。已有研究证实, 在MS发展过程中, 长链不饱和脂肪酸以TG的形式异常沉积于非脂肪细胞中[12], 从而导致脂毒性, 进一步影响细胞的正常生理功能, 造成脂代谢紊乱。然后血液循环中的白蛋白结合游离脂肪酸, 经过肾小球滤过, 从而产生肾小管炎症及损伤, 促进CKD的发展[13]。该研究利用炎性因子与棕榈酸共同作用于肾脏细胞的方式, 模拟了体内的炎症状态, 进行了一系列的实验阐明炎症因子在肾脏脂质异位沉积中的作用。

脂肪酸在体内的平衡主要是脂肪酸的摄取、内源性合成以及TG外排共同作用的结果, 如果其中某一环节发生异常, 就会导致脂肪酸代谢紊乱[14-15]。细胞脂毒性涉及到非酯化FFA和TG的积累, 也是器官功能障碍的原因之一, 研究表明, 异位脂质与肾系膜和上皮细胞的结构和功能变化有关。该实验观察到在炎症状态下肾脏细胞的FFA及TG的含量明显增加, 并且炎症因子能够促进肾脏细胞对FFA的摄取增加, 这就提示炎症有可能通过促进脂肪酸摄取引起肾脏细胞的胞内脂质异位沉积。

CD36属于清道夫受体家族, 是一种广泛存在于各组织及细胞的膜糖蛋白[16-17], 在长链脂肪酸的跨膜转运中发挥着重要作用。CD36突变患者的心肌对长链脂肪酸的摄取能力明显降低。同时, CD36能够通过激活炎症通路调节炎症反应[18], 该课题组最近的研究表明, 炎症能够通过激活mTOR信号通路增加肝脏CD36的翻译效率[19]。CD36作为炎症反应的促进因子, 其与肾脏疾病的关系越来越清楚。在该实验中观察到, 炎性因子能够刺激CD36的表达增高。为了证实CD36在其中的作用, 未加炎症因子的状态下, 将肾脏细胞CD36过表达后, 肾脏细胞对FFA的摄取量也明显增加。进一步地, 当细胞内CD36的表达被干扰后, 细胞对FFA的摄取量降低, 并且能够改善炎性因子引起的细胞内质网应激、细胞损伤以及细胞内FFA及TG含量增加的情况。已有研究表明, CD36能够调节线粒体脂肪酸的转运及β氧化, 并且与细胞间ROS的产生有关, 从而造成细胞损伤。该研究表明, 抑制CD36的表达能够降低炎症诱导的肾脏细胞内ROS的产生, 从而降低炎症造成的细胞损伤。

综上所述, 炎症因子能够促进肾脏细胞中CD36的表达增加使得肾脏细胞对外源性FFA的摄取增加, 引起细胞内的TG及FFA的累积增加, 从而造成细胞内脂质沉积以及细胞脂毒性, 并启动了细胞应激反应及细胞损伤。该论文初步探讨了CD36在CKD中的作用, 同时提示CD36可能作为治疗CKD的一个潜在靶点。

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