LncRNA RMST靶向miR-27a-3p影响过氧化氢诱导心肌细胞损伤

徐玲 许朝祥 林晓欣 卢辉耀 蔡银链*

(福建医科大学附属第二医院心血管内科, 泉州 362000)

摘要 为了探讨LncRNA RMST对过氧化氢(H_2O_2)诱导的心肌细胞损伤的影响及其可能的作用机制, 该研究采用H_2O_2诱导大鼠心肌细胞H9C2建立细胞氧化损伤模型, 随机分组: si-NC+200 μmol/L H_2O_2组(即培养基中加入200 μmol/L H_2O_2干预2 h)、si-LncRNA RMST+200 μmol/L H_2O_2组、miR-NC+200 μmol/L H_2O_2组、miR-27a-3p+200 μmol/L H_2O_2组、anti-miR-NC+si-LncRNA RMST+200 μmol/L H_2O_2组、anti-miR-27a-3p+si-LncRNA RMST+200 μmol/L H_2O_2组。qRT-PCR法检测LncRNA RMST和miR-27a-3p的表达量; 利用相应试剂盒检测细胞培养液中LDH的水平, 以及细胞内MDA、SOD的水平; 流式细胞术检测细胞凋亡率; 双荧光素酶报告实验检测LncRNA RMST和miR-27a-3p的靶向关系; Western blot法检测Cleaved-caspase-3、Bax蛋白表达量。结果显示, 与si-NC+200 μmol/L H_2O_2组比较, si-LncRNA RMST+200 μmol/L H_2O_2组中的MDA、LDH的水平、细胞凋亡率以及Cleaved-caspase-3、Bax蛋白水平降低(P<0.05), SOD的水平升高(P<0.05); LncRNA RMST可靶向调节miR-27a-3p的表达; 与miR-NC+200 μmol/L H_2O_2组比较, miR-27a-3p+200 μmol/L H_2O_2组中的MDA、LDH的水平、细胞凋亡率以及Cleaved-caspase-3、Bax蛋白水平降低(P<0.05), SOD的水平升高(P<0.05); 与anti-miR-NC+si-LncRNA RMST+200 μmol/L H_2O_2组比较, anti-miR-27a-3p+si-LncRNA RMST+200 μmol/L H_2O_2组MDA、LDH的水平、细胞凋亡率以及Cleaved-caspase-3、Bax蛋白水平升高(P<0.05), SOD的水平降低(P<0.05)。这提示, 干扰LncRNA RMST表达可通过靶向miR-27a-3p抑制心肌细胞氧化应激反应及凋亡进而减轻H_2O_2诱导的心肌细胞损伤。

关键词 LncRNA RMST; miR-27a-3p; 过氧化氢; H9C2心肌细胞; 细胞凋亡

Study on the Mechanism of LncRNA RMST Affects the Mechanism of Hydrogen Peroxide-Induced Cardiomyocyte Damage by Targeting miR-27a-3p

XU Ling, XU Chaoxiang, LIN Xiaoxin, LU Huiyao, CAI Yinlian*

(*The Second Affiliated Hospital of Fujian Medical University, Quanzhou 362000, China*)

Abstract To explore the effect of LncRNA RMST on the damage of cardiomyocytes induced by hydrogen peroxide (H_2O_2) and its possible mechanism, H_2O_2 was used to induce rat cardiomyocyte H9C2 to establish a cell oxidative damage model. si-NC, si-LncRNA RMST, miR-NC, miR-27a-3p mimics, anti-miR-NC and si-LncRNA RMST, anti-miR-27a-3p and si-LncRNA RMST were transfected into H9C2 cells and added. The medium contain-

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*通讯作者。Tel: 13960355255, E-mail: caimiss7610@163.com

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*Corresponding author. Tel: +86-13960355255, E-mail: caimiss7610@163.com

ing 200 μmol/L H_2O_2 was intervened for 2 h, which were recorded as si-NC+200 μmol/L H_2O_2 group, si-LncRNA RMST+200 μmol/L H_2O_2 group, miR-NC+200 μmol/L H_2O_2 group, miR-27a-3p+200 μmol/L H_2O_2 group, anti-miR-NC+si-LncRNA RMST+200 μmol/L H_2O_2 group, anti-miR-27a-3p+si-LncRNA RMST+200 μmol/L H_2O_2 group. qRT-PCR method was used to detect the expression of LncRNA RMST and miR-27a-3p. The level of LDH in the cell culture fluid, as well as the levels of MDA and SOD in the cells were tested by using kits. Flow cytometry was used to detect the rate of apoptosis. The dual luciferase reporter experiment was used to detect the targeting relationship between LncRNA RMST and miR-27a-3p. Western blot method was used to detect the expression of Cleaved-caspase-3 and Bax protein. Compared with the si-NC+200 μmol/L H_2O_2 group, the levels of MDA and LDH in the si-LncRNA RMST+200 μmol/L H_2O_2 group were decreased (P<0.05), the rate of apoptosis and the protein levels of Cleaved-caspase-3 and Bax were decreased (P<0.05), while the level of SOD was increased (P<0.05). LncRNA RMST could target the expression of miR-27a-3p. Compared with the miR-NC+200 μmol/L H_2O_2 group, the levels of MDA and LDH in the miR-27a-3p+200 μmol/L H_2O_2 group were decreased (P<0.05), the rate of cell apoptosis and the protein levels of Cleaved-caspase-3, Bax were decreased (P<0.05), while the level of SOD was increased (P<0.05). Compared with the anti-miR-NC+si-LncRNA RMST+200 μmol/L H_2O_2 group, the levels of MDA and LDH in the anti-miR-27a-3p+si-LncRNA RMST+200 μmol/L H_2O_2 group were increased (P<0.05), the apoptosis rate and the protein levels of Cleaved-caspase-3 and Bax were increased (P<0.05), while the level of SOD was decreased (P<0.05). Interfering with the expression of LncRNA RMST could inhibit the oxidative stress response and apoptosis of cardiomyocytes by targeting miR-27a-3p, thereby reducing the damage of cardiomyocytes induced by H_2O_2.

Keywords LncRNA RMST; miR-27a-3p; hydrogen peroxide; H9C2 cardiomyocytes; cell apoptosis

急性心肌梗死是临床常见的心血管疾病之一, 可引起心肌缺氧及缺血进而损伤心肌组织, 活性氧自由基生成量增加时氧化应激反应加剧可破坏心血管结构及功能进而造成心肌组织损伤, 因而抑制氧化应激反应对保护心肌组织及降低急性心机梗死等心血管疾病发生率具有重要意义[1]。过氧化氢(hydrogen peroxide, 即H_2O_2)属于氧自由基并可促进心肌细胞凋亡进而诱导心肌细胞氧化损伤, 长链非编码RNA(LncRNA)是一类与生理病理功能密切相关的非编码RNA分子, 可调控细胞增殖、凋亡等生物学过程, 并可参与心血管疾病发生及发展过程, 还可调控心肌细胞生物学过程而参与心肌细胞损伤[2-4]。LncRNA RMST在氧糖剥夺诱导的脑微血管内皮细胞中表达上调, 并可通过调节miR-204-5p/VCAM1轴而促进脑微血管内皮细胞损伤[5]。但LncRNA RMST对H_2O_2诱导的心肌细胞损伤的影响尚未可知。生物信息学预测显示LncRNA RMST与miR-27a-3p存在结合位点, 缺氧诱导的人源心肌细胞中miR-27a-3p表达下调, 但上调其表达可促进细胞增殖、迁移及侵袭, 而抑制细胞凋亡[6]。然而LncRNA RMST/miR-27a-3p在H_2O_2诱导的心肌细胞损伤中的作用机制尚未阐明。因此, 本研究采用H_2O_2诱导大鼠心肌细胞H9C2建立细胞氧化损伤模型, 探讨LncRNA RMST是否可通过靶向调控miR-27a-3p影响H_2O_2诱导的心肌细胞损伤。

1 材料与方法

1.1 材料与试剂

大鼠心肌细胞H9C2购自上海中乔新舟生物科技有限公司(货号: ZQ0102); H_2O_2购自上海国药集团(货号: 10011218); DMEM培养基(货号: C11995500)与胎牛血清(货号: 16000044)购自美国Gibco公司; Lipofectamine 2000(货号: 11668)、Trizol试剂(货号: 15596018)购自美国Invitrogen公司; 反转录试剂(货号: FP313-01)与SYBR Green试剂盒(货号: FP204)购自北京天根生化科技有限公司; LncRNA RMST小分子干扰RNA(si-LncRNA RMST)及其阴性对照(si-NC)、miR-27a-3p寡核苷酸模拟物(miR-27a-3p mimics)及阴性对照mimic NC序列(miR-NC)、miR-27a-3p特异性寡核苷酸抑制剂(anti-miR-27a-3p)及其阴性对照(anti-miR-NC)购自广州市锐博生物科技有限公司; MTT试剂(货号: M1020)、凋亡检测试

剂盒(货号: CA1020-20)购自北京索莱宝科技有限公司; MDA(货号: A003-1-2)、LDH(货号: A020-2-2)、SOD(货号: A001-3-2)的检测试剂盒购自南京建成生物工程研究所; 兔抗鼠Cleaved-caspase-3(货号: sc-7272)、Bax抗体(货号: sc-7480)与HRP标记的山羊抗兔二抗(货号: sc-69786)购自美国Santan Cruz公司。

1.2 方法

1.2.1 MTT检测细胞活力 取H9C2细胞接种于96孔板(密度为5×10^{3}个/孔), 分别加入含有不同浓度H_2O_2(50 μmol/L、100 μmol/L、200 μmol/L)的培养基内培养2 h(50 μmol/L H_2O_2组、100 μmol/L H_2O_2组、200 μmol/L H_2O_2组)[7], 每孔加入质量浓度为5 mg/mL的MTT溶液20 μL, 于37 °C培养箱内继续培养4 h后离心, 弃上清, 每孔加入150 μL DMSO, 避光振荡孵育5 min, 用酶标仪检测各孔*D*值。

1.2.2 细胞转染与实验分组 按照Lipofectamine 2000转染试剂说明书分别将si-NC、si-LncRNA RMST、miR-NC、miR-27a-3p mimics、anti-miR-NC与si-LncRNA RMST、anti-miR-27a-3p与si-LncRNA RMST转染H9C2细胞48 h, 然后加入含有200 μmol/L H_2O_2的培养基干预2 h, 分别记为si-NC+200 μmol/L H_2O_2组、si-LncRNA RMST+200 μmol/L H_2O_2组、miR-NC+200 μmol/L H_2O_2组、miR-27a-3p+200 μmol/L H_2O_2组、anti-miR-NC+si-LncRNA RMST+200 μmol/L H_2O_2组、anti-miR-27a-3p+si-LncRNA RMST+200 μmol/L H_2O_2组。同时将未经处理的H9C2细胞记为NC组。

1.2.3 qRT-PCR检测细胞中LncRNA RMST、miR-27a-3p的表达水平 用Trizol试剂提取各组H9C2细胞总RNA, 反转录后得到cDNA, 用荧光定量PCR试剂进行qRT-PCR扩增, 反应体系: SYBR Green Master Mix 10 μL, 正反向引物0.8 μL, cDNA 2 μL, ddH_2O补足体系至20 μL; 反应条件: 95 °C预变性2 min, 95 °C变性30 s, 60 °C退火30 s, 72 °C延伸30 s, 共40次循环。LncRNA RMST以*β-actin*为内参基因, miR-27a-3p以*U6*为内参基因, 用$2^{-\Delta\Delta Ct}$法计算LncRNA RMST、miR-27a-3p相对表达量。

1.2.4 检测氧化应激指标MDA、LDH、SOD的水平 收集各组H9C2细胞培养上清液, 采用2,4-二硝基苯肼显色法检测LDH的水平, 采用反复冻融法裂解各组H9C2细胞, 3 000 r/min转速离心10 min后提取上清液, 用硫代巴比妥酸法检测MDA的水平, 用黄嘌呤氧化酶法检测SOD的水平, 严格按照试剂盒说明书进行操作。

1.2.5 流式细胞术检测细胞凋亡率 收集各组H9C2细胞加入预冷PBS洗涤, 加入500 μL结合缓冲液重悬细胞(4×10^{5}个/mL), 取200 μL悬浮细胞进行实验, 分别加入5 μL Annexin V-FITC与5 μL PI, 室温振荡摇晃孵育10 min, 用FACS Calibur流式细胞仪检测细胞凋亡率。

1.2.6 双荧光素酶报告基因检测LncRNA RMST和miR-27a-3p的靶向关系 将LncRNA RMST和miR-27a-3互补序列及其突变序列分别克隆至psi-CHECKTM-2载体中, 分别构建野生型载体LncRNA RMST-WT与突变型载体LncRNA RMST-MUT, 将miR-NC或miR-27a-3p mimics与载体分别共转染至H9C2细胞, 48 h后收集细胞并取细胞裂解液, 加入用于荧光素酶活性检测的工作液后用生物发光检测仪检测其荧光素酶活性。

1.2.7 Western blot检测Cleaved-caspase-3、Bax蛋白表达 取各组H9C2细胞加入蛋白裂解液, 1 000 r/min转速离心5 min后取上清(即蛋白), 采用Brad-ford法检测蛋白浓度, 10% SDS-PAGE分离蛋白, 半干法转移至PVDF膜, 5%脱脂奶粉封闭2 h, 加入Cleaved-caspase-3(1:1 000)、Bax(1:1 000)一抗与β-actin(1:3 000)抗体稀释液在4°C条件下孵育24 h, 室温条件下加入二抗稀释液(1:5 000)孵育2 h, 滴加ECL显影后用ImageJ软件分析各条带灰度值。

1.3 统计学处理

采用SPSS 21.0统计学软件分析数据, 计量资料以($\bar{x}\pm s$)表示且均符合正态分布, 两组间比较采用独立样本*t*检验, 多组间比较采用单因素方差分析, 以*P*<0.05为差异具有统计学意义。

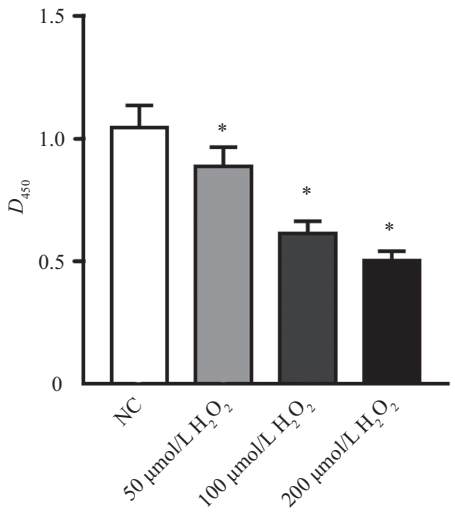
2 结果

2.1 不同浓度H_2O_2对H9C2细胞活力的影响

用不同浓度的H_2O_2处理后H9C2细胞活力降低(*P*<0.05), H_2O_2浓度为200 μmol/L时H9C2细胞存活率约为50%, 因而选用200 μmol/L进行后续实验(图1)。

2.2 H_2O_2诱导H9C2细胞损伤中, LncRNA RMST上调表达, miR-27a-3p下调表达

与NC组比较, 200 μmol/L H_2O_2组LncRNA RMST的表达量升高(*P*<0.05), miR-27a-3p的表达量降低(*P*<0.05)(图2)。

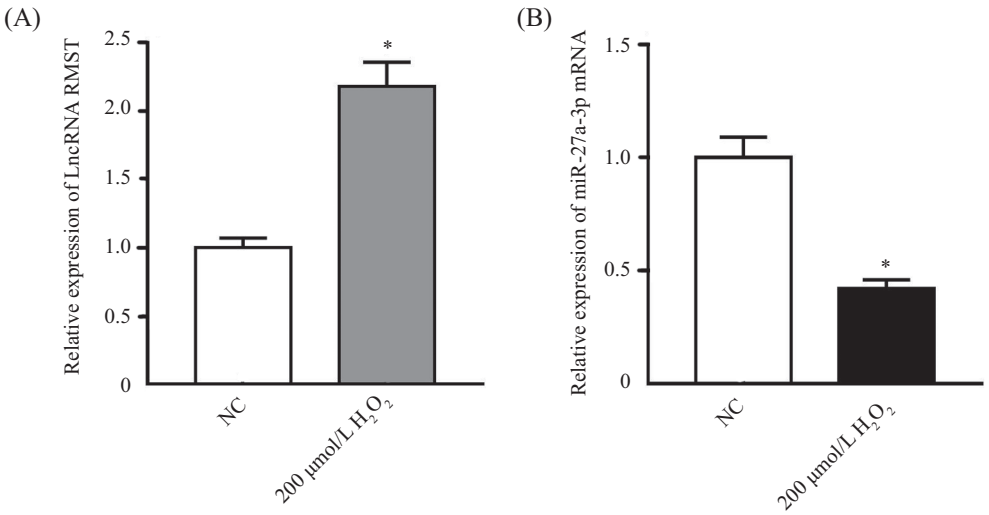


*P<0.05, 与NC组相比。

*P<0.05 compared with NC group.

图1 不同浓度H_2O_2对H9C2细胞活力的影响

Fig.1 The effect of different concentrations of H_2O_2 on the activity of H9C2 cells



A: H_2O_2诱导H9C2细胞损伤中LncRNA RMST表达上调; B: H_2O_2诱导H9C2细胞损伤中miR-27a-3p下调表达。*P<0.05, 与NC组相比。

A: H_2O_2 induced up-regulation of LncRNA RMST expression in H9C2 cell injury; B: H_2O_2 induced down-regulation of miR-27a-3p expression in H9C2 cell injury. *P<0.05 compared with NC group.

图2 H_2O_2对H9C2中LncRNA RMST和miR-27a-3p表达情况的影响

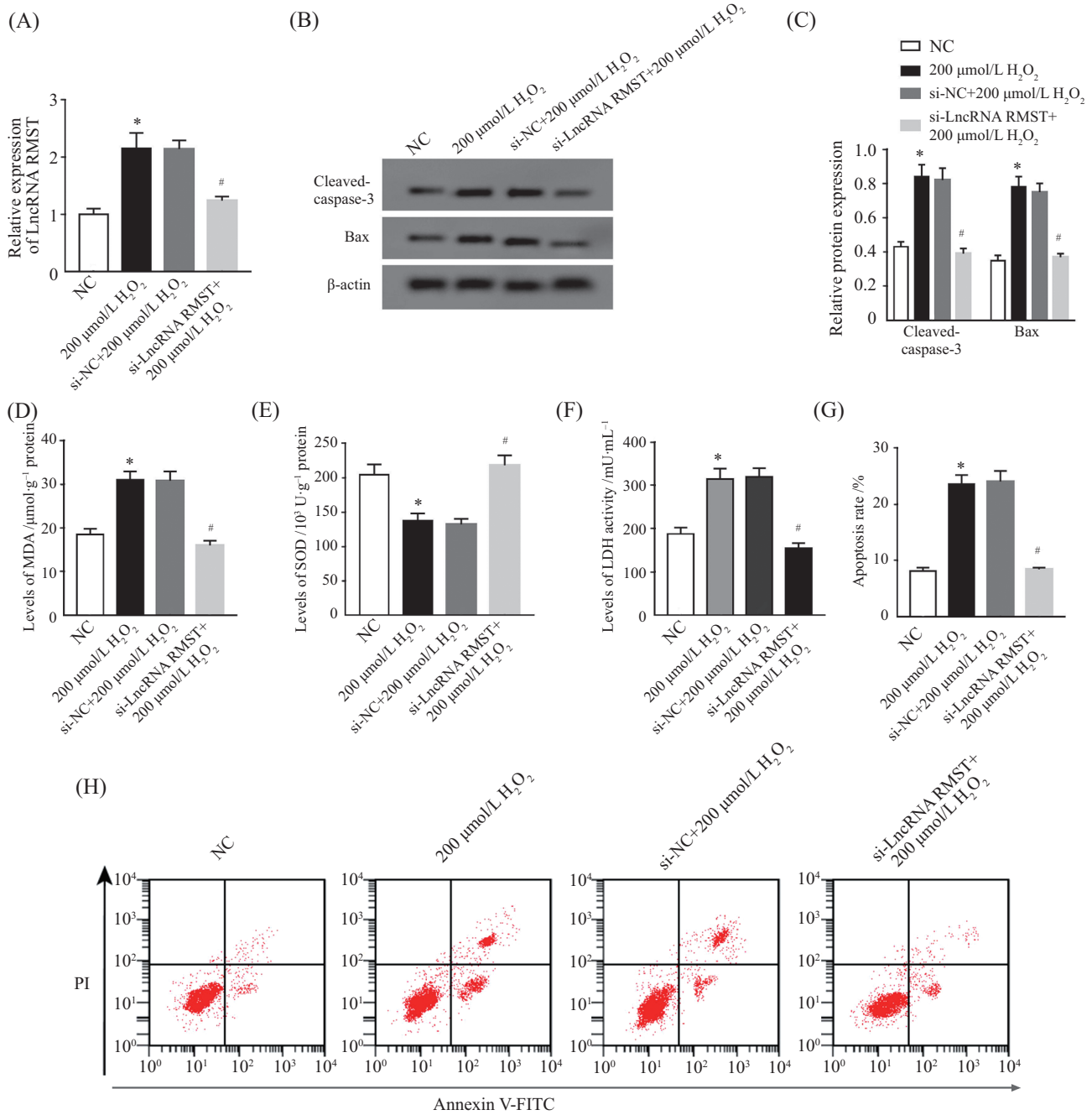
Fig.2 The expression of LncRNA RMST and miR-27a-3p in H9C2 cells induced by H_2O_2

2.3 si-LncRNA RMST抑制H_2O_2诱导的H9C2氧化应激损伤

与NC组比较, 200 μmol/L H_2O_2组MDA、LDH的水平升高(P<0.05), SOD的水平降低(P<0.05), 细胞凋亡率和Cleaved-caspase-3、Bax蛋白水平升高(P<0.05)(图3); 与si-NC+200 μmol/L H_2O_2组比较, si-LncRNA RMST+200 μmol/L H_2O_2组MDA、LDH的水平降低(P<0.05), SOD的水平升高(P<0.05), 细胞凋亡率和Cleaved-caspase-3、Bax蛋白水平降低(P<0.05)(图3)。

2.4 miR-27a-3p抑制H_2O_2诱导的H9C2细胞氧化应激损伤

与miR-NC+200 μmol/L H_2O_2组比较, miR-27a-3p+200 μmol/L H_2O_2组MDA、LDH的水平降低(P<0.05), SOD的水平升高(P<0.05), 细胞凋亡率和Cleaved-caspase-3、Bax蛋白水平降低(P<0.05)(图4)。



A: qRT-PCR检测LncRNA RMST表达水平; B: Western blot检测Cleaved-caspase-3、Bax蛋白的表达; C: Cleaved-caspase-3、Bax蛋白表达的柱状分析图; D: MDA水平柱状分析图; E: SOD水平柱状分析图; F: LDH水平柱状分析图; G: 细胞凋亡率柱状统计图; H: 流式细胞仪检测细胞凋亡。*P<0.05, 与NC组比较; #P<0.05, 与si-NC+200 μmol/L H_2O_2组比较。

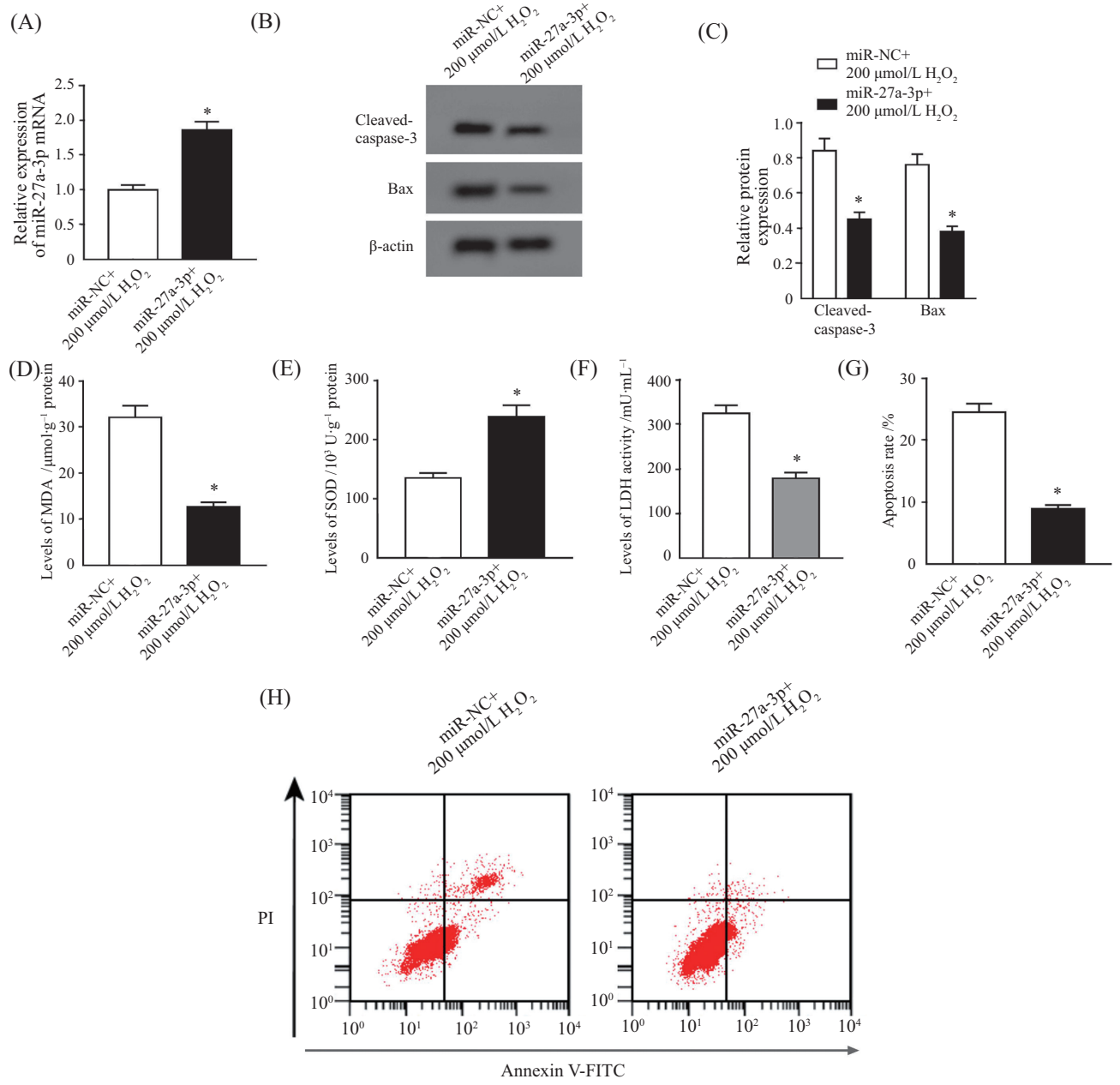
A: qRT-PCR was used to detect the expression level of LncRNA RMST; B: Western blot was used to detect the expression of Cleaved-caspase-3 and Bax protein; C: columnar analysis chart of Cleaved-caspase-3 and Bax protein expression; D: histogram analysis of MDA level; E: histogram analysis of SOD level; F: histogram analysis of LDH level; G: histogram of cell apoptosis rate; H: flow cytometry was used to detect cell apoptosis. *P<0.05 compared with the NC group; #P<0.05 compared with the si-NC+200 μmol/L H_2O_2 group.

图3 si-LncRNA RMST抑制H_2O_2诱导的H9C2细胞氧化应激损伤

Fig.3 si-LncRNA RMST inhibits H_2O_2-induced H9C2 cell oxidative stress damage

2.5 LncRNA RMST靶向miR-27a-3p, 调控miR-27a-3p的表达

Starbase预测LncRNA RMST和miR-27a-3p存在结合位点(图5)。转染miR-27a-3p mimics可降低野生型载体LncRNA RMST-WT的荧光素酶活性(P<0.05), 而对突变型载体LncRNA RMST-MUT的荧光素酶活性无明显影响。与pcDNA组比较, pcDNA-LncRNA RMST组miR-27a-3p的表达量降低(P<0.05); 与si-NC



A: qRT-PCR检测LncRNA RMST表达水平; B: Western blot检测Cleaved-caspase-3、Bax蛋白的表达; C: Cleaved-caspase-3、Bax蛋白表达的柱状分析图; D: MDA水平柱状分析图; E: SOD水平柱状分析图; F: LDH水平柱状分析图; G: 细胞凋亡率柱状统计图; H: 流式细胞仪检测细胞凋亡。*P<0.05, 与miR-NC+200 μmol/L H_2O_2组比较。

A: qRT-PCR was used to detect the expression level of LncRNA RMST; B: Western blot was used to detect the expression of Cleaved-caspase-3 and Bax proteins; C: columnar analysis chart of Cleaved-caspase-3 and Bax protein expression; D: histogram analysis of MDA level; E: histogram analysis of SOD level; F: histogram analysis of LDH level; G: histogram of cell apoptosis rate; H: flow cytometry was used to detect cell apoptosis. *P<0.05 compared with miR-NC+200 μmol/L H_2O_2 group.

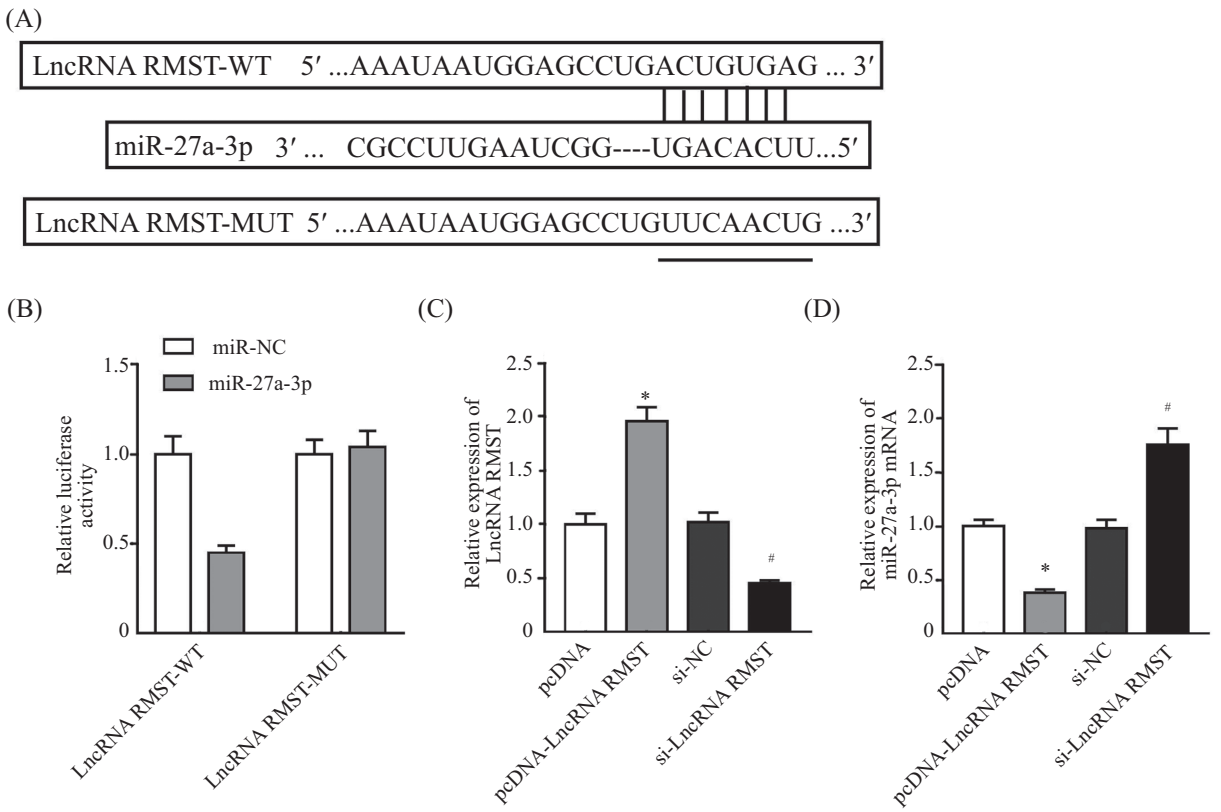
图4 miR-27a-3p抑制H_2O_2诱导的H9C2细胞氧化应激损伤

Fig.4 miR-27a-3p inhibits H_2O_2-induced H9C2 cell oxidative stress damage

组比较, si-LncRNA RMST组miR-27a-3p的表达量升高(P<0.05)(图5)。

2.6 anti-miR-27a-3p可以逆转si-LncRNA RMST对H_2O_2诱导的H9C2氧化应激损伤抑制作用

相比较于anti-miR-NC+si-LncRNA RMST+200 μmol/L H_2O_2组, anti-miR-27a-3p+si-LncRNA RMST+200 μmol/L H_2O_2组中的MDA、LDH的表达水平升高(P<0.05), SOD的表达水平降低(P<0.05), 细胞凋亡率和Cleaved-caspase-3、Bax蛋白水平升高(P<0.05)(图6)。



A: Starbase对miR-27a-3p和LncRNA RMST结合进行预测示意图; B: 荧光素酶活性检测; C: qRT-PCR检测LncRNA RMST的表达水平; D: qRT-PCR检测miR-27a-3p的表达水平。*P<0.05, 与pcDNA组比较; #P<0.05, 与si-NC组比较。

A: Starbase predicted the binding of miR-27a-3p and LncRNA RMST; B: Luciferase activity detection; C: qRT-PCR was used to detect the expression level of LncRNA RMST; D: qRT-PCR was used to detect miR-27a-3p expression level. *P<0.05 compared with pcDNA group; #P<0.05 compared with si-NC group.

图5 LncRNA RMST靶向miR-27a-3p, 且调控miR-27a-3p的表达

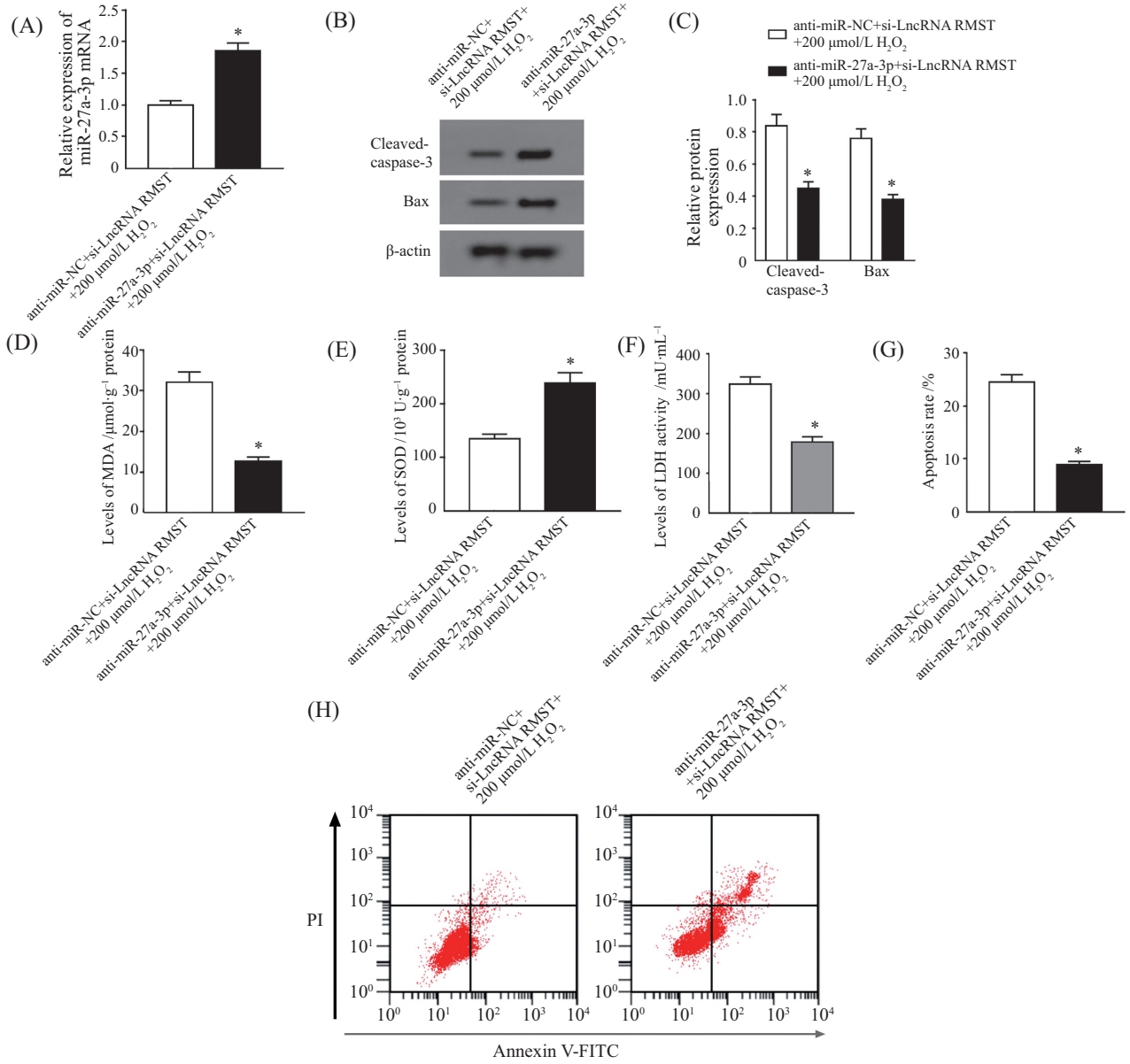
Fig.5 LncRNA RMST targets miR-27a-3p and regulates the expression of miR-27a-3p

3 讨论

氧化应激可诱导细胞凋亡进而引起心肌细胞损伤, H_2O_2能够诱导心肌细胞氧化应激的发生并可用于体外细胞氧化损伤实验。研究表明LncRNA在H_2O_2诱导的心肌细胞损伤中表达上调或下调, 并可充当miRNA的竞争性内源RNA(ceRNA)而调控心肌细胞增殖、凋亡等生物学行为[8-10]。

LncRNA RMST在氧糖剥夺诱导的神经元损伤中表达上调, 抑制其表达可通过调节miR-377/SEMA3A而抑制神经元凋亡及氧化应激[11]。LncRNA RMST可通过靶向结合miR-107进而促进氧糖剥夺诱导的神经元凋亡[12]。氧糖剥夺诱导的脑微血管内皮细胞中LncRNA RMST的表达量升高, 沉默LncRNA RMST可促进细胞增殖及迁移而抑制细胞凋亡[13]。但H_2O_2诱导的心肌细胞中LncRNA RMST的表达趋势尚未可知。本研究用H_2O_2诱导心肌细胞, 结果显示, MDA、LDH的水平升高, SOD的水平降低, 这与既往研究报道结果相似[14], 提示成功建立心肌细胞氧化损伤模型。进一步研究发现, H_2O_2诱导的心肌细胞中LncRNA RMST的表达量升高, 干扰LncRNA RMST表达后H_2O_2诱导心肌细胞内MDA、LDH的水平降低, SOD的水平升高, 提示干扰LncRNA RMST表达可抑制H_2O_2诱导心肌细胞氧化应激反应。本研究结果显示, H_2O_2诱导的心肌细胞凋亡率和Cleaved-caspase-3、Bax蛋白水平升高, 与既往研究报道结果相似[15], 进一步研究发现干扰LncRNA RMST表达后H_2O_2诱导的心肌细胞凋亡率和Cleaved-caspase-3、Bax蛋白水平降低, 提示干扰LncRNA RMST表达可通过抑制氧化应激反应而抑制细胞凋亡进而减轻H_2O_2诱导的心肌细胞损伤。

为进一步探究LncRNA RMST在H_2O_2诱导的心肌细胞损伤中的作用机制, 本研究证实LncRNA



A: qRT-PCR检测LncRNA RMST表达水平; B: Western blot检测Cleaved-caspase-3、Bax蛋白的表达; C: Cleaved-caspase-3、Bax蛋白表达的柱状分析图; D: MDA水平柱状分析图; E: SOD水平柱状分析图; F: LDH水平柱状分析图; G: 细胞凋亡率柱状统计图; H: 流式细胞仪检测细胞凋亡。*P<0.05, 与anti-miR-NC+si-LncRNA RMST+200 μmol/L H_2O_2组比较。

A: qRT-PCR was used to detect the expression level of LncRNA RMST; B: Western blot was used to detect the expression of Cleaved-caspase-3 and Bax proteins; C: columnar analysis chart of Cleaved-caspase-3 and Bax protein expression; D: histogram analysis of MDA level; E: histogram analysis of SOD level; F: histogram analysis of LDH level; G: histogram of cell apoptosis rate; H: flow cytometry was used to detect cell apoptosis. *P<0.05 compared with anti-miR-NC+si-LncRNA RMST+200 μmol/L H_2O_2 group.

图6 anti-miR-27a-3p可以逆转si-LncRNA RMST对H_2O_2诱导的H9C2细胞氧化应激损伤抑制作用

Fig.6 anti-miR-27a-3p reverses the inhibitory effect of si-LncRNA RMST on H_2O_2-induced H9C2 cell oxidative stress damage

RMST可靶向结合miR-27a-3p, 并可负向调控miR-27a-3p的表达。研究表明, miR-27a-3p在脓毒症诱发的急性肾损伤大鼠模型中表达量降低, 并可促进炎症反应的发生[16]。miR-27a-3p在缺氧诱导的心肌细胞中呈低表达, 上调其表达可通过靶向结合TRAF5而减轻缺氧诱导的心肌细胞损伤[17]。缺氧诱导的肾小管上皮细胞中miR-27a-3p的表达量降低, LncRNA NEAT1的表达上调, LncRNA NEAT1可通过下调miR-27a-3p进而促进缺氧诱导的肾小管上皮细胞凋亡[18]。本研究结果显示, H_2O_2诱导的心肌细胞中miR-27a-3p的表达量降低, miR-27a-3p过表达可降低H_2O_2诱导的心肌细胞内MDA、LDH的水平及细胞凋亡率,

而SOD的水平升高, 进一步研究发现抑制miR-27a-3p表达可逆转干扰LncRNA RMST表达对H_2O_2诱导的心肌细胞氧化应激及凋亡的作用。

综上所述, H_2O_2诱导的心肌细胞中LncRNA RMST的表达量升高, miR-27a-3p的表达量降低, 干扰LncRNA RMST表达可通过上调miR-27a-3p进而抑制H_2O_2诱导的心肌细胞氧化应激反应及细胞凋亡进而减轻H_2O_2诱导的心肌细胞损伤, LncRNA RMST/miR-27a-3p分子轴可能是减轻心肌组织损伤的潜在途径, 可为急性心肌梗死等心血管疾病的治疗提供新方向。但关于其具体作用机制仍需进一步探究。

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