中南大学学报(医学版) 2014, 39(3) 232-238 DOI： 10.11817/j.issn.1672-7347.2014.03.002 ISSN: 1672-7347 CN: 43-1427/R

论著

载脂蛋白嵌合模拟肽通过NF-κB途径抑制ox-LDL诱导的巨噬细胞炎症反应

谢琼，李峰，赵水平

1. 湖南省人民医院心内科，长沙 410005；2. 中南大学湘雅二医院心胸外科，长沙 410011；
3. 中南大学湘雅二医院心内科，长沙 410011

摘要：

目的：探讨载脂蛋白嵌合模拟肽Ac-hE-18A-NH2对氧化型低密度脂蛋白(oxidized LDL，ox-LDL)刺激下巨噬细胞肿瘤坏死因子-α(tumor necrosis factor-α，TNF-α)表达的影响及其作用机制。方法：Ox-LDL刺激RAW264.7巨噬细胞，
给予不同浓度的模拟肽Ac-hE-18A-NH2(1~100 μg/mL)干预，收集细胞，测定巨噬细胞TNF-α的分泌和mRNA表达水平。
Western印迹检测ATP结合盒转运蛋白A1(ATP-binding cassette transporter A1，ABCA1)及P-IκB蛋白浓度。EMSA检测核因
子-κB(nuclear factor-κB，NF-κB)活性。结果：Ox-LDL刺激使RAW264.7巨噬细胞TNF-α 分泌和mRNA表达明显增强，细
胞内胆固醇蓄积，促进IκB磷酸化，并激活NF-κB。Ac-hE-18A-NH2浓度依赖性地降低TNF-α 分泌及mRNA表达，上调
ABCA1 mRNA和蛋白的表达，减少细胞内胆固醇含量，抑制NF-κB活化，并抑制IκB磷酸化。相同的实验条件下及作
用浓度，D-4F对于TNF-α 分泌的抑制作用不如Ac-hE-18A-NH2。结论：Ac-hE-18A-NH2能抑制ox-LDL诱导的RAW264.7
巨噬细胞TNF-α分泌和mRNA表达，IκB/NF-κB-TNF-α信号通路是其中作用途径之一。Ac-hE-18A-NH2的抗炎作用优于
apoA-I模拟肽D-4F。

关键词： 载脂蛋白嵌合模拟肽 炎症 肿瘤坏死因子-α 氧化型低密度脂蛋白 巨噬细胞

Ac-hE-18A-NH2 inhibits the inflammatory response induced by ox-LDL via inhibiting NF-κB activation in RAW264.7 macrophages

XIE Qiong, LI Feng, ZHAO Shuiping

1. Department of Cardiology, People’s Hospital of Hunan, Changsha 410005;
2. Department of Cardiothoracic Surgery, Second Xiangya Hospital, Central South University, Changsha 410011;
3. Department of Cardiology, Second Xiangya Hospital, Central South University, Changsha 410011, China

Abstract:

Objective: To evaluate the effect of Ac-hE-18A-NH2 on TNF-α secretion and mRNA expression in ox-LDL-stimulated RAW264.7 macrophages and to elucidate the possible mechanisms.
Methods: Macrophages were incubated in the medium containing various concentrations of Ac-hE18A-NH2 (1-50 μg/mL) with ox-LDL (50 μg/mL) stimulated. The TNF-α level
and intracellular cholesterol content were measured by commercially available quantitation kits following the manufacturer’s instructions. TNF-α and ATP-binding cassette transporter A1 (ABCA1) mRNA expression were detected by real-time PCR. ABCA1 and IκB protein
-expression in the macrophages were determined by Western blot. NF-κB activity was evaluated by electrophoretic mobility shift assay (EMSA).
Results: Ox-LDL stimulation induced a significant increase in TNF-α secretion, mRNA expression, cholesterol accumulation and nuclear factor-κB (NF-κB) activity in RAW264.7 macrophages. Ac-hE-18A-NH2 reduced TNF-α secretion and mRNA expression, up-regulated the ABCA1 mRNA and protein expression, reduced the intracellular cholesterol content, and inhibited NF-κB activation in a dose-dependent manner. Under the same condition and the same concentration, Ac-hE-18A-NH2 was more efficient than D-4F (apoA-I mimetic peptide) in inhibiting the inflammatory response induced by ox-LDL in the macrophages.
Conclusion: Ac-hE-18A-NH2 may suppress TNF-α secretion and mRNA expression in ox-LDLstimulated

RAW264.7 macrophages via IκB-NF-κB signaling pathway. The anti-inflammatory effect of Ac-hE-18A-NH2 is better than that of apoA-I mimic peptide D-4F.

Keywords: apolipoprotein mimetic peptide inflammation tumor necrosis factor-α oxidized low-density lipoprotein macrophage

收稿日期 2013-06-04 修回日期 网络版发布日期

DOI: 10.11817/j.issn.1672-7347.2014.03.002

基金项目:

国家自然科学基金(30770857)。This work was supported by the National Natural Science Foundation of China (30770857).

通讯作者: 赵水平，Email: zhaosp@medmail.com

作者简介: 谢琼，博士，主治医师，主要从事血脂与动脉粥样硬化等研究。

作者Email:

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