

论著

载脂蛋白A I模拟肽对RAW264.7巨噬细胞胆固醇流出的影响

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摘要:

目的: 观察载脂蛋白A I(apoA I)模拟肽D 4F对RAW264.7巨噬细胞胆固醇流出的影响, 并探讨其机制。方法: 巨噬细胞种植于24孔板, 用 $1.85 \times 10^7$  Bq/孔 <sup>3</sup>H 胆固醇和含50  $\mu$ g/mL氧化型低密度脂蛋白(ox LDL)共同孵育 24 h后, 给予不同浓度的D 4F(0~100  $\mu$ g/mL)干预24 h, 收集细胞用液体闪烁计数法检测胆固醇流出。采用酶联免疫吸附试验(ELISA)测定细胞内环磷酸腺苷(cAMP)含量, 采用实时荧光定量PCR及Western印迹检测三磷酸腺苷结合盒转运体A1(ABCA1)的mRNA及蛋白表达。结果: D 4F呈浓度依赖及时间依赖性促进巨噬细胞内胆固醇流出, 增加细胞内cAMP水平, 上调ABCA1 mRNA和蛋白表达。8 Br cAMP显著增加D 4F介导的胆固醇流出和ABCA1表达, 而蛋白激酶A(PKA)抑制剂虽然对基础胆固醇流出及ABCA1表达几乎无作用, 却可以抑制8 Br cAMP对胆固醇流出和ABCA1表达的促进作用。结论: D 4F促进巨噬细胞胆固醇流出, cAMP释放及ABCA1表达, 可能与激活cAMP PKA ABCA1通路有关。

关键词: 载脂蛋白A I模拟肽; 胆固醇流出; 巨噬细胞; 三磷酸腺苷结合盒转运体A1; 环磷酸腺苷

Effect of apolipoprotein A I mimetic peptides on cholesterol efflux in RAW264.7 cells

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Abstract:

Objective To determine the effect and possible mechanism of an apolipoprotein (apo) A I mimetic peptide, D 4F, on cholesterol efflux in RAW264.7 macrophages. Methods RAW264.7 macrophages were incubated in the medium containing 8 bromo cAMP (8 Br cAMP, 0.5 mmol/L) and ox LDL (50  $\mu$ g/mL) for 24 h. Then various concentrations of D 4F (0-100  $\mu$ g/mL) or H89 (20  $\mu$ mol/L, a protein kinase A inhibitor) were added for the purpose of interference. The intracellular cyclic AMP (cAMP) level was determined by enzyme linked immunoabsorbant assay (ELISA). ATP binding cassette transporter A1 (ABCA1) expression in the macrophages was quantitated by real time PCR and Western blot. Results D 4F significantly increased the cholesterol efflux in both concentration and time dependent manner accompanied by the increase in the intracellular cAMP level, ABCA1 mRNA and protein expression. The effect of D 4F on cholesterol efflux ABCA1 expression was enhanced by 8 Br cAMP. Although H89 did not affect the basal cholesterol efflux and ABCA1 expression, it could attenuate the effect of 8 Br cAMP. Conclusion D 4F affects cholesterol efflux, cAMP level, and ABCA1 expression in macrophages, which is likely involved in the pathway of cAMP/PKA/ABCA1.

Keywords: apolipoprotein A I mimetic peptide cholesterol efflux macrophage ATP binding cassette transporter A1 cyclic AMP

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