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论著

三乙烯四胺对*c-myc*启动区转录活性的调节作用

邓小红，殷 菲，刘建辉，郭莉霞

(重庆工商大学药物化学与化学生物学研究中心, 重庆 400067)

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摘要 目的 探讨三乙烯四胺（TETA）如何调节c-myc基因表达。方法 利用圆二色谱分析TETA对c-myc启动区核酸酶超敏元件III$_1$（*c-myc* NHE III$_1$）碱基序列形成的G-四链体DNA(G4-DNA)结构稳定性的影响。同时，分别构建含*c-myc* NHE III1的野生型和突变型的*c-myc*启动区荧光报告质粒，并分别转染HEK293细胞24 h后，再接种到96孔板，TETA以终浓度0，0.1，1.0，10及100 μmol·L^{-1}处理8 h，测定荧光素酶活性，计算TETA对其转录活性抑制率。结果 圆二色谱实验结果表明，TETA 5 μmol·L^{-1}就能够进一步增强*c-myc* NHE III$_1$在240 nm处的负峰和260 nm处的正峰的形成，即增强G4-DNA结构的稳定性。报告基因分析结果表明，TETA能够浓度依赖性地抑制野生型*c-myc*启动区荧光素酶基因的表达，但对突变型*c-myc*启动区荧光素酶基因的抑制能力明显下降。在TETA 1 nmol·L^{-1}作用时，对突变型*c-myc*启动区荧光素酶基因抑制率仅为4.3%，而对野生型的抑制率还高达30.4%。结论 TETA可能通过稳定*c-myc* NHE III$_1$序列形成的G4-DNA结构调节基因的表达。

关键词 三乙烯四胺 基因, c-myc 启动区 核酸酶超敏元件III1

分类号 R966

Regulative effect of triethylene tetramine on transcription of *c-myc* promoter

DENG Xiao-Hong, YIN Fei, LIU Jian-Hui, GUO Li-Xia

(Research Center for Pharmaceutical Chemistry & Chemical Biology, Chongqing Technology and Business University, Chongqing 400067, China)

Abstract

AIM To explore effects of triethylene tetramine (TETA) on the transcription of *c-myc* promoter. **METHODS** Circular dichroism (CD) was collected to identify the influence of TETA on the stability of G-quadruplex formed by *c-myc* promoter region nuclease hypersensitive element III$_1$ (*c-myc* NHE III$_1$) sequence. Furthermore the wild and mutant reporter gene plasmids containing *c-myc* NHE III$_1$ sequence were constructed, the 2 plasmids were transfected into HEK293 cells respectively for 24 h. The transfected cells were replated into 96 wells plate, and treated with different concentrations of TETA (0, 0.1, 1, 10 and 100 μmol·L^{-1}) for about 8 h, the luciferase activity was determined with its substrate BrightGlo. The inhibition rate of TETA on the reporter gene was calculated by the luciferase activity. **RESULTS** TETA 5 μmol·L^{-1} will be able to further enhance absorption at 240 nm (the negative peak) and 260 nm (positive peak). So the TETA maybe assistant the G4-DNA structures formation and increase the stability in the *c-myc* NHE III$_1$ region. Furthermore, from the results of reporter gene analysis, TETA could inhibit the expression of reporter gene in a dose-dependent manner, but for the mutated sequence, the inhibition of TETA on the expression of reporter gene was decreased significantly. With TETA 1 nmol·L^{-1} treated, inhibition rate of mutant-type report gene expression was only 4.3%, while the inhibition rate of wild-type was as high as 30.4%. **CONCLUSION** TETA has negative regulatory effect on *c-myc* promoter through enhancing the stability of G-quadruplex formed by the sequence of nuclease hypersensitive element III$_1$.

Key words triethylene tetramine gene c-myc promoter region nuclease hypersensitive element III 1

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通讯作者 刘建辉 jhliu@ctbu.edu.cn