

## 论文

### 活化T细胞核因子在DEHP调控IL-4表达中作用

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#### 摘要:

目的 通过研究活化T细胞核因子(NFAT)在邻苯二甲酸二(2-乙基己基)酯(DEHP)影响白细胞介素-4(IL-4)表达中的作用,探讨DEHP的免疫毒性机制。方法 以佛波酯(PMA)和离子霉素(Ion)为激活剂,用10、50 $\mu$ mol/L DEHP染毒激活的脾淋巴细胞4 h,同时用0.5 $\mu$ mol/L钙调神经磷酸酶抑制剂他克莫司(FK506)进行干预,最后分别检测IL-4、NFATp、NFATc mRNA表达与NFATp和NFATc蛋白表达。结果 以10 ng/mL PMA+0.5mg/mL Ion为激活剂时,激活组的IL-4 mRNA表达相对值为(2.53 $\pm$ 0.42),50 $\mu$ mol/L DEHP染毒组的相对值为(18.21 $\pm$ 1.67),差异有统计学意义( $P<0.01$ );而FK506干预组的IL-4 mRNA表达相对值为(9.85 $\pm$ 1.24),与50 $\mu$ mol/L DEHP染毒组比较,差异有统计学意义( $P<0.01$ );50 $\mu$ mol/L DEHP染毒组的NFATc mRNA表达相对值为(2.00 $\pm$ 0.32),激活组的相对值为(1.37 $\pm$ 0.10),差异有统计学意义( $P<0.05$ );同时DEHP促进NFATc蛋白在细胞质和细胞核里表达;染毒4 h后,与激活组NFATp mRNA表达相对值(2.51 $\pm$ 0.45)比较,10、50 $\mu$ mol/L DEHP染毒组的相对值分别为(5.14 $\pm$ 0.28)和(5.38 $\pm$ 0.60),差异均有统计学意义( $P<0.01$ );但DEHP降低了细胞质和细胞核里NFATp蛋白表达。结论 NFAT在DEHP调控IL-4表达中具有重要作用。

关键词: 活化T细胞核因子(NFAT) 邻苯二甲酸二(2-乙基己基)酯(DEHP) 白细胞介素-4(IL-4)

### Role of nuclear factor of activated T cells on impact of DEHP on IL-4 expression

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#### Abstract:

Objective To investigate the role of nuclear factor of activated T cells(NFAT)on the impact of phthalate (2-ethylhexyl)ester(DEHP)on interleukin-4(IL-4)expression and to explore the immunotoxicity mechanism of DEHP.Methods Two activating agents of 10 ng/mL phorbol-12-myristate-13-acetate(PMA) +0.5 mg/mL ionomycin(Ion)and 25 ng/mL PMA+1 mg/mL Ion were used to activate spleen lymphocytes.The lymphocytes were exposed to 10 $\mu$ mol/L and 50 $\mu$ mol/L DEHP for 4 hours with or without 0.5 $\mu$ mol/L tacrolimus(FK506).IL-4,NFATp and NFATc mRNA were determined with real time-PCR test.NFATp and NFATc protein were measured with western blotting.Results Under the activating of 10 ng/mL PMA+0.5 mg/mL Ion,the relative value of the expression of IL-4 mRNA was 2.53 $\pm$ 0.42 in activating group and the value was 18.21 $\pm$ 1.6 in 50 $\mu$ mol/L DEHP group,with significant difference between the two groups( $P<0.01$ ).The expression of IL-4 mRNA was 9.85 $\pm$ 1.24 in FK506 group and the expression was obviously reduced compared with 50 $\mu$ mol/L DEHP group( $P<0.01$ ).The relative expression of NFATc mRNA was 2.00 $\pm$ 0.32 in 50 $\mu$ mol/L DEHP group and the expression was 1.37 $\pm$ 0.10 in activating group,with a significant difference between DEHP group and activating group( $P<0.01$ ).On the other hand,DEHP significantly enhanced NFATc protein expression in both cytoplasm and nucleus.The relative expression of NFATp mRNA was 2.51 $\pm$ 0.45 in activating group and the expressions were 5.14 $\pm$ 0.28 and 5.38 $\pm$ 0.60 in 10 $\mu$ mol/L and 50 $\mu$ mol/L DEHP group,with statistically significant differences.But DEHP markedly decreased the expression of NFATp protein in both cytoplasm and nucleus after 4 hours'treatment.Conclusion NFAT plays an important role in the effect of DEHP on IL4 expression.

Keywords: nuclear factor of activated T cells(NFAT) phthalate(2-ethylhexyl)ester(DEHP) interleukin-4 (IL-4)

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