

论文

Nrf 2信号通路在铅致SH-SY5Y细胞氧化应激中作用

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摘要:

目的 研究神经细胞内核因子E 2相关因子2(Nrf 2)信号通路是否对铅暴露所致的氧化应激产生应答及其可能机制。**方法** 用低、中、高剂量(5、25、125 μ mol/L)的醋酸铅溶液对人神经母细胞瘤SH-SY 5 Y细胞染毒,用2',7'-二氯荧光黄双乙酸盐(DCFH-DA)探针检测染毒2 h后细胞活性氧(ROS)水平,染毒24 h后用二巯基双硝基苯甲酸(DTNB)比色法检测还原性谷胱甘肽(GSH)水平,western blot法检测蛋白激酶C- δ (PKC- δ)、酪氨酸激酶2(CK II)以及胞浆和胞核中Nrf 2蛋白的表达水平。结果 随着染毒剂量增加,低、中、高剂量组ROS含量依次为(559.17 \pm 54.56)、(585.50 \pm 36.41)、(621.00 \pm 29.96),与对照组(533.50 \pm 46.47)比较,中、高剂量组含量明显升高($P<0.05$);GSH含量依次为(165.39 \pm 17.37)、(140.92 \pm 14.77)、(84.03 \pm 10.31),与对照组(222.10 \pm 14.91)比较,低、中、高剂量组含量均明显降低($P<0.01$);与对照组比较,低、中、高剂量组胞浆Nrf 2相对灰度值为(0.38 \pm 0.09)、(0.27 \pm 0.09)、(0.25 \pm 0.11),胞浆Nrf 2表达均明显降低($P<0.05$);低、中、高剂量组胞核Nrf 2相对灰度值为(1.38 \pm 0.50)、(1.55 \pm 0.49)、(2.79 \pm 1.56),仅高剂量组胞核Nrf 2蛋白表达明显增高($P<0.05$)。低、中、高剂量组PKC- δ 相对灰度值为(1.84 \pm 0.46)、(2.55 \pm 0.36)、(2.38 \pm 0.77),与对照组比较均明显升高($P<0.05$);低、中、高剂量组CK II相对灰度值为(1.28 \pm 0.32)、(1.34 \pm 0.21)、(1.52 \pm 0.42),与对照组比较仅高剂量组表达明显升高($P<0.05$)。结论 铅致神经细胞氧化损伤的同时激活胞浆中Nrf 2转移入核内,进而发挥氧化应答,PKC- δ 、CK II在铅致Nrf 2激活过程中具有一定作用。

关键词: 铅 人神经母细胞瘤(SH-SY5Y)细胞 活性氧(ROS) 还原性谷胱甘肽(GSH) 核因子E 2相关因子2(Nrf 2) 蛋白激酶C- δ (PKC- δ) 酪氨酸激酶2(CK II)

Role of Nrf 2 signal pathway in lead-induced oxidative stress in SH-SY5Y cells

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Abstract:

Objective To investigate the role of NF-E2-related factor 2(Nrf 2)signal pathway in lead-induced oxidative stress in SH-SY5Y cells as well as the possible mechanism. **Methods** SH-SY5Y cells were exposed to 0,5,25, and 125 μ mol/L lead acetate for 24 hours.After harvesting the cells,the level of reactive oxygen species(ROS)was measured by the method of 2',7'-dichlorofluorescin diacetate(DCFH-DA),and glutathione(GSH)was tested by dithiothymine double-nitrobenzonic acid(DTNB)method.Western blot was used to detect the levels of protein kinase C-theta(PKC- δ),casein kinase 2(CK II)Nrf 2 in the cytoplasm and nucleus. **Results** Compared with the control group,the level of ROS of the moderate and high dose group were obviously increased($P<0.05$),while the level of GSH in all groups obviously decreased($P<0.01$).Compared with the control group,the protein expression level of Nrf 2 in the cytoplasm were significantly decreased($P<0.05$).Meanwhile the protein expression levels of Nrf 2 in the nucleus of the high dose group showed a distinct elevation,which was remarkbly different from that of the control group($P<0.05$). Compared with the control group,the protein expression level of PKC- δ was significantly increased($P<0.05$).The protein expression level of CK II of the high dose group showed a significant elevation($P<0.05$). **Conclusion** The findings demonstrate that lead can induce a nuclear accumulation of the transcription factor Nrf 2,which indicates the mediation of Nrf 2 in the cellular response against the oxidative stress caused by lead.The results also indicate that PKC- δ and CK II play certain role in the Nrf 2 activation through increasing expression levels of two proteins stimulated by lead.

Keywords: lead SH-SY5Y cell ROS GSH Nrf 2 PKC- δ CK II

收稿日期 2011-10-31 修回日期 网络版发布日期

DOI: 10.11847/zgggws-2012-28-07-18

基金项目:

扩展功能

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- 活性氧(ROS)
- 还原性谷胱甘肽(GSH)
- 核因子E 2相关因子2(Nrf 2)
- 蛋白激酶C- δ (PKC- δ)
- 酪氨酸激酶2(CK II)

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