

论著

## 长期低剂量甲醛染毒对永生化人支气管上皮细胞16HBE部分癌症相关基因启动子区甲基化的影响

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**摘要** 目的 探讨低剂量甲醛长期染毒对永生化人支气管上皮细胞16HBE癌症相关基因启动子区甲基化水平的影响。方法 16HBE细胞每周染毒甲醛10 μmol · L<sup>-1</sup> 24 h, 连续24周, 分别于染毒3, 6, 9, 12, 15, 18, 21和24周提取RNA或DNA, 应用DNA甲基化相关酶消化结合荧光定量PCR的方法观察24个癌症相关基因启动子区甲基化水平的变化; 应用荧光定量PCR的方法观察染毒对亚甲基四氢叶酸还原酶基因(*MTHFR*)和成对盒基因(*PAX5*)基因表达的时间-效应关系。结果 与正常对照组16HBE细胞相比, 甲醛染毒细胞4个基因甲基化水平显著改变, 2个基因甲基化程度升高, 2个基因甲基化程度降低; 而在阳性对照人非小细胞癌上皮细胞A549细胞中有9个基因甲基化水平发生显著变化, 其中3个基因甲基化水平升高, 6个基因甲基化水平降低; 甲醛染毒16HBE细胞和A549细胞*MTHFR*基因均发生高甲基化改变, *PAX5*基因均出现低甲基化改变。与正常对照组相比, 甲醛染毒24周的细胞中, *MTHFR*基因启动子区甲基化水平升高, 非甲基化DNA含量降低58.2%, 而*PAX5*基因启动子区甲基化水平降低, 非甲基化DNA含量升高27.1%; 随着甲醛染毒时间延长, *MTHFR*基因表达逐渐降低, 而*PAX5*基因表达逐渐升高。结论 低剂量甲醛长期染毒可以使*MTHFR*基因和*PAX5*基因启动子区甲基化水平异常, 进而引起基因表达水平改变。

**关键词** [甲醛](#) [亚甲基四氢叶酸还原酶基因](#) [成对盒基因](#) [DNA甲基化](#)

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## Effect of long term contamination of low dose formaldehyde on methylation pattern of promoter of cancer related genes in 16HBE cells

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### Abstract

**OBJECTIVE** To explore the effect of long term contamination of low dose formaldehyde on the methylation pattern of the promoter of 24 cancer related genes in 16HBE cells. **METHODS** The 16HBE cells were taken as objects and A549 cells as positive control. The method that combined the digestion of DNA methylation related enzymes and real-time PCR was applied to detect the methylation status of the promoters of the 24 cancer related genes. Real-time PCR was used to observe the expression levels of *MTHFR* and *PAX5* genes. **RESULTS** Compared with normal 16HBE cells, the methylation pattern of 4 out of 24 genes' changed remarkably in formaldehyde treated 16HBE cells, two were hypermethylated and two were hypomethylated. In A549 cells, the methylation pattern of 9 out of 24 genes' changed remarkably, 3 of them were hypermethylated and 6 of them were hypomethylated. *MTHFR* gene was hypermethylated in both formaldehyde treated 16HBE cells and A549 cells, and *PAX5* gene was hypomethylated in both cells. In the formaldehyde treated 16HBE cells, the non-methylated DNA of *MTHFR* gene decreased by 58.2%, while the non-methylated DNA of *PAX5* gene increased by 27.1%. Along with the contamination of low dose formaldehyde the mRNA expression level of *MTHFR* decreased while the mRNA expression level of *PAX5* increased gradually. **CONCLUSION** The long term contamination of low dose formaldehyde could cause aberrant methylation pattern of *MTHFR* and *PAX5* genes and lead to the mRNA expression level change of the two genes.

**Key words** [formaldehyde](#) [methylenetetrahydrofolate reductase gene](#) [paired box 5 gene](#) [DNA methylation](#)

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