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基础研究

烟雾凝聚物对人正常支气管上皮细胞中p16转录的抑制作用及其机制

赵艳红[1,2]|施新革[3]|吴军兵[4]|王春仁[1]

（1. 中国食品药品检定研究院医疗器械检定所生物材料和组织工程室|北京100050；2. 国家食品药品监督管理局 医疗器械技术审评中心|北京100044；3. 新乡医学院第一附属医院骨科|河南 卫辉 453100； 4. 中国科学院生物物理学研究所|北京100101）

摘要：

目的：通过体外模拟吸烟过程来检测抑癌基因p16表达的变化，探讨p16基因在吸烟导致肺癌发生过程中的作用。方法：常规正常支气管上皮细胞（HBE）分为实验组和对照组，分别接受烟雾凝聚物和DMSO处理。利用免疫印迹和Realtime RT-PCR分别检测P16蛋白表达和mRNA的转录水平。构建p16的基因组启动子载体，利用荧光素酶分析烟雾凝聚物对其转录活性的影响。结果：不同浓度（0,10,25,50,100 mg•L^{-1}）的烟雾凝聚物处理HBE后，其p16的mRNA和P16蛋白表达水平明显降低，并且表现出剂量依赖性。大于25 mg•L^{-1}的烟雾凝聚物能明显抑制P16蛋白表达和mRNA的转录水平，与对照组比较差异有统计学意义（P<0.05），其中100 mg•L^{-1}烟雾凝聚物表现出最大的抑制效应。烟雾凝聚物也能以剂量依赖方式抑制p16启动子的转录活性，大于25 mg•L^{-1}的烟雾凝聚物能显著抑制p16启动子的荧光素酶活性，与对照组比较差异有统计学意义（P<0.05），其中100 mg•L^{-1}的烟雾凝聚物表现出最大的抑制效应。结论：烟雾凝聚物能够抑制p16启动子的转录活性，进而抑制P16蛋白的表达；P16蛋白表达水平的降低可能是吸烟导致肺癌发生的一种分子机制。

关键词： 烟雾凝聚物；肺肿瘤；p16基因

Inhibitory effect of |cigarette smoke extracts | on p16 |transcription in human normal bronchial epithelial cells and its mechanism

ZHAO Yan-hong[1,2]|SHI Xin-ge[3]|WU Jun-bing[4]|WANG Chun-ren[1]

（1.Department of Biomaterials and Tissue Engineering, Institute for Medical Devices Control,National Institutes for Food and Drug Control,Beijing 100050,China|2.Center for Medical Device Evaluation/SFDA, Beijing 100044,China|3.Department of Orthopedics,First Affiliated Hospital,Xinxiang Medical University, Weihui 453100,China; 4.Institute of Biophysics,Chinese Academy of Sciences,Beijing 100101,China）

Abstract:

Abstract:Objective
To study the role of p16 in cigarette smoking-induced lung carcinogenesis by detecting the expression of p16 in human normal bronchial epithelial cells（HBE） after exposure to cigarette smoke extracts (CSE) and analyze the underlying mechanism.Methods HBE were treated with various doses of CSE or control DMSO and the protein and mRNA levels of p16 were determined by Western blotting and Realtime RT-PCR respectively.The genomic promoter of p16 was cloned and its transcriptional activity after exposure to CSE was determined by luciferase assay.Results After the treatment of different doses (0,10,25,50,100 mg•L^{-1}) of CSE,the mRNA and protein levels in HBE were significantly inhibited in a dose-dependent manner.More than 25 mg•L^{-1} of CSE conld significantly inhibit the p16 mRNA and protein levels,there was significant difference compared with control group(P<0.05).100 mg•L^{-1} of CSE showed the greatest inhibiory effect. Moreover,the transcriptional activity of the promoter of p16 was significantly suppressed by more than 25 mg•L^{-1} CSE,there was significant difference compared with control group(P<0.05).Conclusion Cigarette smoke extracts can inhibit the expression of p16 by suppressing its transcriptional activity,indicating that p16 might play a key role in cigarette smoking-induced lung carcinogenesis.

Keywords: cigarette smoke extracts; lung neoplasms; p16 gene

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通讯作者: 王春仁

作者简介: 赵艳红（1976—）|女|辽宁省阜新市人|助理研究员|理学博士|主要从事肿瘤分子生物学和细胞生物学研究。

作者Email: （Tel：010-67095687，E-mail：chunrenwang@263.net）

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