

人类与医学遗传学

## RNAi及DNA芯片分析肝癌细胞系中受DNMT3B调控的下游基因

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**摘要** 为揭示DNA甲基转移酶3B (DNMT3B) 在肝癌中是否参与了肿瘤的发生, 应用Western blotting及细胞免疫化学方法分析DNMT3B蛋白在人的正常肝细胞株、肝癌癌旁细胞株及肝癌癌细胞株中的表达。构建了DNMT3B的RNAi稳定表达的重组载体, 并转染入肝癌细胞株SMMC-7721中。以半定量RT-PCR及Western blotting分别鉴定DNMT3B RNAi表达载体对内源性DNMT3B的抑制效率。用高通量的cDNA基因芯片分析了SMMC-7721中DNMT3B抑制后有影响的下游基因谱。结果显示, DNMT3B在肝癌细胞株中的表达水平明显高于肝癌癌旁和正常肝细胞株。DNMT3B的RNAi稳定表达重组载体转染SMMC-7721细胞株2个月后, 观察到DNMT3B明显的受到抑制。cDNA基因芯片分析发现, DNMT3B抑制后诱导了26条基因表达下调, 115条基因表达上调, 包括一些发育相关基因以及肿瘤相关基因, 如SNCG、NOTCH1、MBD3、WNT11、MAOA、FACL4等。提示DNMT3B的高表达可能与肝癌的发生有关, 并以调控其它相关基因的表达而起作用, 包括与发育相关的重要基因。

**关键词** [甲基转移酶; DNA甲基转移酶3B; RNA干扰; 肝癌](#)

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## Identification of potential genes regulated by DNA methyltransferase 3B in a hepatocellular carcinoma cell line by RNA interference and microarray analysis

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### Abstract

Whether DNA methyltransferase 3B (DNMT3B) is deregulated in hepatocellular carcinoma cell lines is still unclear. The expression levels of DNMT3B protein in normal liver cell line, pericarcinoma cell line and hepatocellular carcinoma cell lines were compared by both Western blotting and immunocytochemistry. Long-term downregulated DNMT3B in a hepatocellular carcinoma cell line SMMC-7721 was achieved using a RNAi recombinant plasmid. The suppression of DNMT3B induced by RNA interference was confirmed using semi-quantitative RT-PCR and Western blotting. High throughput cDNA microarray was used to analyze the expression profiling of downstream genes of DNMT3B displayed in the treated cell lines and control. In the result, DNMT3B in hepatocellular carcinoma cell lines was expressed at a significantly higher level compared to those in pericarcinoma cell line and normal liver cell line. A specific DNMT3B siRNA stably expressed from a plasmid vector effectively suppressed the expression of DNMT3B in SMMC-7721 cell line. By microarray analysis, 26 downregulated genes and 115 upregulated genes have been identified in the DNMT3B knockdown cell line, including some important developmental genes and tumor-related genes such as SNCG, NOTCH1, MBD3, WNT11, MAOA and FACL4. The discovery showed DNMT3B was over-expressed in most hepatocellular carcinoma cells lines examined and may be linked to the carcinogenesis of hepatocytes. An array of candidate genes that are involved in the action of DNMT3B have been identified, including those related to development.

**Key words:** methyltransferase; DNMT3B; RNA interference; hepatocellular carcinoma

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