

研究论文

肿瘤抑制因子WT1对人的诱导型一氧化氮合成酶基因的转录调节作用

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摘要 将人的诱导型一氧化氮合成酶(hiNOS)启动子构建在带荧光素酶基因的载体pGL3-basic上, 构建成用荧光素酶为系统的启动子, 以研究载体p8.3iNOS. 结果显示, 肾母细胞肿瘤抑制因子(WT1)能够有效地抑制hiNOS启动子的转录; 且WT1的4个选择性剪接本的抑制效果有所不同, 其中WT1(-/-)在两种肝癌细胞(HepG2和Hep3B)中对hiNOS的表达均具有最强的抑制作用, 并且抑制效果具有剂量依赖性, 用Western blot检测结果进一步证实HepG2细胞中WT1(-/-)过量表达能下调hiNOS表达. 以上结果说明WT1在肝癌细胞中对人的hiNOS具有转录调节作用.

关键词 [肾母细胞肿瘤抑制因子\(WT1\)](#) [人的诱导型一氧化氮合成酶](#) [选择性剪接本](#) [转录调节](#)

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Roles of Wilm's Tumor Suppressor(WT1) in the Regulation of Human Inducible Nitric Oxide Synthase(hiNOS)

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Abstract The Wilm's tumor suppressor gene is one of the important tumor suppressor factors correlated with liver tissue functional abnormalities. The human inducible nitric oxide synthase (hiNOS) has important biological functions *via* catalyzing the production of nitric oxide(NO), which is a signal modulator involved in various immune response, chronic inflammations, as well as carcinogenesis. The roles of Wilm's tumor suppressor(WT1) in the regulation of hiNOS was reported in this paper. We inserted hiNOS promoter to pGL3-basic vector carrying luciferase gene and got the plasmid p8.3iNOS, which was used as a report system for the study of the relationship between WT1 and the hiNOS promoter activity. The results from the luciferase assay demonstrate that WT1 could suppress the transcription of hiNOS gene in two hepatoma derivative cells lines, HepG2 and Hep3B. Moreover, the alternative splicesomes of WT1 had different effects on the inhibition of hiNOS expression among which the alternative splicing form WT1(-/-) had the strongest inhibitory effect on hiNOS in a dose-dependent manner. Western blot assay reveals that over-expressed WT1(-/-) down-regulated the expression of hiNOS protein in HepG2 cell. These results suggest that WT1 could control the expression of hiNOS in transcriptional level.

Key words [Wilm's tumor suppressor\(WT1\)](#) [Human inducible nitric oxide synthase\(hiNOS\)](#) [Alternative spliceosome](#) [Transcriptional regulation](#)

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