lncRNA-uc003uxs在缺氧诱导胃癌侵袭转移中的作用

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Title: The role of lncRNA-uc003uxs in the invasion and metastasis of gastric cancer under hypoxia

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摘要: 目的：探讨长链非编码RNA（long non-coding RNA,lncRNA）-uc003uxs在缺氧诱导胃癌侵袭和转移中的作用。方法：三个胃癌细胞系SGC7901、MKN45、MKN28分别经常氧和缺氧孵育 24 h，提取3例配对的胃癌细胞总RNA，利用高通量lncRNA芯片比较它们之间的表达谱差异，初步筛选与缺氧诱导胃癌侵袭转移相关的关键分子。RT-PCR法检测 lncRNA-uc003uxs在缺氧诱导的胃癌细胞（相对于常氧诱导的胃癌细胞）以及20对胃癌组织（相对于癌旁组织）中的表达水平。通过慢病毒转染，稳定下调SGC7901和MKN28细胞中lncRNA-uc003uxs的表达。通过Transwell迁移和侵袭实验以及裸鼠尾静脉注射内脏转移实验检测lncRNA-uc003uxs下调后对胃癌细胞侵袭和转移能力的影响。结果：高通量芯片分析结果显示：与常氧诱导的胃癌细胞相比，缺氧诱导的胃癌细胞 SGC7901、MKN45和MKN28中有84个共同上调的lncRNA分子以及70个共同下调的lncRNA分子，而多重筛选策略则提示：lncRNA-uc003uxs可能是缺氧诱导胃癌侵袭转移的关键lncRNA分子之一。RT-PCR结果表明：lncRNA-uc003uxs在缺氧诱导的胃癌细胞SGC7901、MKN45和MKN28中显著上调，其在胃癌组织中的表达水平也显著高于癌旁组织。Transwell实验结果显示：缺氧能够显著增加SGC7901和MKN28细胞的迁移和侵袭能力，而下调lncRNA-uc003uxs的表达后，两种细胞的迁移和侵袭能力明显下降。此外，裸鼠尾静脉内脏转移实验也证实lncRNA-uc003uxs的下调抑制了胃癌细胞SGC7901的体内肝肺转移能力。结论：利用高通量芯片筛选，在胃癌细胞中发现了一系列缺氧相关的lncRNA分子。临床标本分析及功能缺失试验证实：lncRNA-uc003uxs是一个缺氧诱导胃癌侵袭转移的关键lncRNA分子。

Abstract: Objective:To investigate the role of lncRNA-uc003uxs in the hypoxia-induced invasion and metastasis of gastric cancer (GC).Methods:High-throughput microarrays were used to compare the lncRNA expression profile difference between normoxia-induced and hypoxia-induced GC cell lines including SGC7901,MKN45 and MKN28 in order to preliminarily screen key molecules related to hypoxia-induced invasion and metastasis of GC.The different expression of lncRNA-uc003uxs was measured in hypoxia-induced GC cells (compared to normoxia-induced GC cells) and 20 pairs of GC tissues (compared to adjacent tissues) using RT-PCR.The expression of lncRNA-uc003uxs in GC cells SGC7901 and MKN28 was down-regulated by lentiviral transfection.Transwell migration and invasion assays and nude mice tail vein injection metastasis assay were employed for investigating the effect of lncRNA-uc003uxs knockdown on the hypoxia-induced invasion and metastasis of GC cells.Results:The results of high-throughput microarrays analysis showed that there were 84 common upregulated lncRNAs and 70 common downregulated lncRNAs in hypoxia-induced GC cells compared with normoxia-induced GC cells.And through multiple screening strategies,we found lncRNA-uc003uxs may be one of key molecules related to hypoxia-induced invasion and metastasis of GC.RT-PCR showed that lncRNA-uc003uxs was significantly increased in hypoxia-induced GC cells SGC7901,MKN45 and MKN28 and compared with

adjacent tissues.The expression of lncRNA-uc003uxs was also upregulated in GC tissues.Transwell migration and invasion assays demonstrated that hypoxia can enhance the abilities of migration and invasion of GC cells SGC7901 and MKN28,however,these two abilities were significantly inhibited after lncRNA-uc003uxs knockdown.In addition,nude mice tail vein injection metastasis assay also verified that lncRNA-uc003uxs knockdown inhibited liver metastasis and lung metastasis of GC cell SGC7901 in vivo.Conclusion:We found a series of hypoxia-related lncRNAs in gastric cancer by means of high-throughput screening microarrays.Clinical specimen analysis and functional loss test confirmed that lncRNA-uc003uxs is a key lncRNA for hypoxia-induced invasion and metastasis of gastric cancer.

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