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miR-107靶向调控Dicer1促进卵巢癌细胞系侵袭转移

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MicroRNA-107 Targeting Dicer1 for Metastasis Control in Ovarian Cancer Cell Lines

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摘要

目的

检测microRNA-107（miR-107）在卵巢癌中的表达水平，探讨其对卵巢癌细胞系侵袭转移的调控作用及分子机制。

方法

qRT-PCR法比较卵巢癌组织、正常卵巢组织、卵巢癌细胞系和正常卵巢上皮细胞中miR-107表达差异，用生物信息学的方法特异预测出miR-107靶基因Dicer1后，通过双荧光素酶报告体系进行验证。上调miR-107表达后，Western blot检测Dicer1的表达变化；划痕实验、Transwell实验观察卵巢癌细胞运动和侵袭能力的改变；qRT-PCR及Confocal观察EMT相关分子E-cadherin、β-Catenin、N-cadherin、Vimentin、Fibronectin、ICAM-1、MMP-9的表达。

结果

miR-107在上皮性卵巢癌组织的表达较正常卵巢组织显著升高（$P<0.05$）；双荧光素酶报告基因系统验证预测结果正确。上调miR-107后，Western blot结果显示Dicer1蛋白质水平被显著抑制，卵巢癌细胞系SKOV3细胞形态发生间质细胞样转变，间质标志分子β-Catenin、N-cadherin及MMP-9表达上升；体外实验表明卵巢癌细胞的运动和侵袭能力得到明显促进。

结论

本研究表明miR-107促进卵巢癌侵袭转移的分子机制是通过下调miRNA加工机器Dicer1，从而介导卵巢癌细胞EMT的发生；抑制miR-107或恢复Dicer1水平可能成为上皮性卵巢癌治疗的有效手段。

关键词： 卵巢癌 微小RNA-107 Dicer1 上皮间质转化

Abstract:

Objective

To explore the expression level of MicroRNA-107 (miR-107) in ovarian cancer, so as to figure out the mechanism involved in invasion and metastasis control of ovarian cancer cell lines for miR-107.

Methods

By comparison miR-107 expression levels in ovarian cancer and normal ovarian tissues, or between normal ovarian surface epithelium and ovarian cancer cell lines by qRT-PCR, we confirmed the differential expression and then predicted Dicer1 as its specific validated target gene with the approach of bioinformatics. Furthermore, the dual luciferase reporter system was adopted to verify the prediction. After elevating miR-107 level, Western blot was performed to detect the protein level of Dicer1; scratch test and transwell assay were employed to check the alteration of movements, invasion and metastasis in ovarian cancer cell line SKOV3; furthermore, qRT-PCR and Confocal were applied to study the level of EMT associated molecular, such as E-cadherin, β-Catenin, N-cadherin, Vimentin，Fibronectin, ICAM-1, and MMP-9 respectively.

Results

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The expression level of miR-107 in epithelial ovarian carcinoma was increased when compared with that of normal tissues (P<0.05). The dual luciferase reporter system validated Dicer1 as a specific target gene of miR-107. Dramatically reduction of Dicer1 was observed with miR-107 overexpression, at the same time, morphological change occured and cell invasion and metastasis ability increased a lot due to the upregulation of mesenchymal molecules，including β-Catenin，N-cadherin, MMP-9 following miR-107 upregulated.

Conclusion

miR-107, acting as an oncogene miRNA, promoted invasion and metastasis via downregulation of miRNA regulatory machinery Dicer1 and mediated EMT process in ovarian cancer. Inhibition of miR-107 or restoration of Dicer1 may represent a new potential therapeutic target for ovarian cancer treatment.

Key words： Ovarian cancer　MiR-107　Dicer1　EMT

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