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MicroRNA-505 functions as a tumor suppressor in endometrial cancer by targeting TGF-α

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Background: Endometrial carcinoma (EC) is one of the most lethal gynecologic cancers. Patients frequently have regional or distant metastasis at diagnosis. MicroRNAs are small non-coding RNAs that participate in numerous biological processes. Recent studies have demonstrated that miR-505 is associated with several types of cancer; however, the expression and function of miR-505 have not been investigated in EC.

Methods: miR-505 expression in normal endometrial tissue, endometrial carcinomas were quantified by Quantitative reverse transcription PCR. The endometrial carcinoma cell lines HEC-1B and Ishikawa were each transfected with miR-505 or scrambled mimics, after which cell phenotype and expression of relevant molecules were assayed. Dual-luciferase reporter assay and a xenograft mouse model were used to examine miR-505 and its target gene TGF-α.

Results: RT-PCR results demonstrated that miR-505 was significantly downregulated in human EC tissues compared to normal endometrial tissues. Besides, miR-505 expression was negatively associated with FIGO stage (stage I-II vs. III-IV), and lymph node metastasis (negative vs. positive). In vitro, overexpression of miR-505 significantly suppressed EC cell proliferation, increased apoptosis and reduced migratory and invasive activity. A miR-505 binding site was identified in the 3′ untranslated region of TGF-α mRNA (TGFA) using miRNA target-detecting software; a dual luciferase reporter assay confirmed that miR-505 directly targets and regulates TGFA. RT-PCR and Western-blotting results indicated that overexpressing miR-505 reduced the expression of TGF-α and the TGF-α-regulated proteins MMP2, MMP9, CDK2, while induced Bax and cleaved-PARP expression in EC cells. In vivo, overexpression of miR-505 reduced the tumorigenicity and inhibited the growth of xenograft tumors in a mouse model of EC.

Conclusions: Taken together, this study demonstrates that miR-505 acts as tumor suppressor in EC by regulating TGF-α.

Biography

Dr. Shuo Chen, now is a associated research of Department of Gynecology, the First Affiliated Hospital of China Medical University. During the past five years, he had published 12 SCI articles as the first author, with the total IF value 45 points. He got the 1st National Woman and Child Health Science and Technology Award in 2015, and Liaoning Provincial Science and Technology Progress Award in 2015. Besides, he was the host of the National Natural Science Foundation of China (No. 81602266).

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