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Suppressive Role of MicroRNA-148a in Cell Proliferation and Invasion in Ovarian Cancer Through Targeting Transforming Growth Factor-β-Induced 2

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Ovarian cancer (OC) is one of the most common gynecological malignancies. MicroRNAs (miRs) play a crucial role in the development and progression of OC, but the underlying mechanism remains largely unclear. Our study investigated the regulatory role of miR-148a in OC cell proliferation and invasion. We found that miR-148a was significantly downregulated in OC tissues compared to their matched adjacent nontumor tissues. In addition, its expression was also reduced in OC cell lines (SKOV3, ES-2, OVCAR, and A2780) compared to normal ovarian epithelial cells. Overexpression of miR-148a caused a significant decrease in OC cell proliferation and invasion, as well as reduced MMP9 protein levels. Transforming growth factor-β-induced 2 (TGFI2) was further identified as a target gene of miR-148a, and its protein expression was downregulated in OC cells after miR-148a overexpression. Restoration of TGFI2 attenuated the suppressive effects of miR-148a on OC cell proliferation and invasion. Moreover, we found that TGFI2 was remarkably upregulated in OC tissues when compared with their matched adjacent nontumor tissues, and observed a reverse correlation between miR-148a and TGFI2 expression in OC tissues. On the basis of these findings, we suggest that miR-148a inhibits OC cell proliferation and invasion partly through inhibition of TGFI2. Therefore, our study highlights the importance of the miR-148a/TGFI2 axis in the malignant progression of OC.

Key words: Ovarian cancer (OC); MicroRNAS (miRs); Transforming growth factor-β-induced 2 (TGFI2); Proliferation; Invasion

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