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Investigating the *In Vitro* and *In Vivo* Effects of RUNX1 on the Proliferation, Migration, Invasion and Apoptosis of Epithelial Ovarian Carcinoma Mediated via TGF-β/Wnt4 Signaling Pathways

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SUMMARY. The main aim of this study was to investigate the effects of RUNX1 (Runt-related transcription factor 1) on proliferation, migration, invasion and apoptosis of epithelial ovarian cancer, and the relationship between RUNX1 and TGF-β signaling pathway and Wnt signaling pathway. RUNX1 siRNA and pcDNA3.1-RUNX1 were transfected into OVCAR-3 and SKOV-3 cells, respectively. Real-time PCR and Western Blot were used to determine the expression of RUNX1. Cell Counting Kit-8, Scratch Assay, Transwell Assay, and Annexin V-FITC/PI Apoptosis Detection Kit were used to detect the cell proliferation, migration, invasion and apoptosis, respectively. RUNX1 siRNA and RUNX1 overexpression attenuated and increased mRNA and protein expression of RUNX1 in OVCAR-3 and SKOV-3 cells, respectively. After RUNX1 silencing, the proliferation, migration and invasion of OVCAR-3 and SKOV-3 cells were both significantly reduced, whereas the apoptosis of the two cell lines were significantly increased. Meanwhile, the expression of TGF-β and Wnt4 were both significantly improved. After RUNX1 overexpression, the results were completely contrary to those of RUNX1 interference. *In vivo* experiment indicated that RUNX1 silencing caused lower tumor volume and slower tumor growth, whereas RUNX1 overexpression caused increased tumor volume and accelerated tumor growth in nude mice. *In vitro* and *in vivo* experiments showed that RUNX1 affected the proliferation, migration, invasion and apoptosis of epithelial ovarian cancer with a mechanism involving TGF-β and Wnt4 signaling pathways.

RESUMEN. El objetivo principal de este estudio fue investigar los efectos de RUNX1 (factor de transcripción relacionado con Runt 1) sobre la proliferación, migración, invasión y apoptosis del cáncer de ovario epitelial, y la relación entre RUNX1 y la vía de señalización de TGF-β y la vía de señalización de Wnt. RUNX1 siRNA y pcDNA3.1-RUNX1 se transfectaron en células OVCAR-3 y SKOV-3, respectivamente. Se utilizaron PCR en tiempo real y Western Blot para determinar la expresión de RUNX1. Se utilizaron el kit de conteo de células-8, el ensayo de rayado, el ensayo Transwell y el kit de detección de apoptosis de anexina V-FITC/PI para detectar la proliferación, migración, invasión y apoptosis celular, respectivamente. La sobreexpresión de ARNip de RUNX1 y RUNX1 atenuó y aumentó la expresión de ARNm y proteína de RUNX1 en células OVCAR-3 y SKOV-3, respectivamente. Después del silenciamiento de RUNX1, la proliferación, migración e invasión de las células OVCAR-3 y SKOV-3 se redujeron significativamente, mientras que la apoptosis de las dos líneas celulares aumentó significativamente. Mientras tanto, la expresión de TGF-β y Wnt4 mejoró significativamente. Después de la sobreexpresión de RUNX1, los resultados fueron completamente contrarios a los de la interferencia de RUNX1. El experimento *in vivo* indicó que el silenciamiento de RUNX1 provocó un menor volumen tumoral y un crecimiento tumoral más lento, mientras que la sobreexpresión de RUNX1 provocó un mayor volumen tumoral y aceleró el crecimiento tumoral en ratones desnudos. Los experimentos *in vitro* e *in vivo* mostraron que RUNX1 afectaba la proliferación, migración, invasión y apoptosis del cáncer de ovario epitelial con un mecanismo que involucra las vías de señalización de TGF-β y Wnt4.

KEY WORDS: epithelial ovarian cancer, overexpression, RUNX1, siRNA, TGF-β, Wnt4.

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