

Knockdown of TROP2 Suppresses Malignant Phenotype and Promotes Platinum Sensitivity in Ovarian Cancer with Involvement of the Lipid Metabolism-Ferroptosis Axis

Dan Yao, Xiaoqing Zhu*

Science and Technology Development Center, Chongqing Medical and Pharmaceutical College, Chongqing, China

Email address:

276572085@qq.com (Dan Yao), 244027226@qq.com (Xiaoqing Zhu)

*Corresponding author

Abstract

Cisplatin resistance is a major cause of treatment failure in advanced ovarian cancer. TROP2 is a transmembrane glycoprotein highly expressed in ovarian cancer and has been implicated in malignant progression and platinum resistance; however, the downstream molecular mechanisms remain incompletely understood. In this study, we established ovarian cancer cell lines with stable TROP2 knockdown and assessed malignant phenotypes and tumorigenic capacity using CCK-8, Transwell, flow cytometry, and a nude mouse xenograft model. Combined with transcriptome sequencing and KEGG enrichment analysis, we identified differentially regulated pathways and validated the expression of key genes. Our results showed that TROP2 knockdown significantly inhibited proliferation, migration, invasion, and in vivo tumour growth, while promoting apoptosis. Notably, cisplatin induced TROP2 expression in a concentration-dependent manner, and this upregulation correlated with reduced drug sensitivity, as TROP2 depletion markedly enhanced cisplatin cytotoxicity in ovarian cancer cells. Transcriptomic analysis and validation revealed that upon TROP2 knockdown, the PI3K-Akt signalling pathway and multiple lipid metabolism pathways were significantly enriched. Specifically, the expression of the elongation of very long chain fatty acids protein 7 (ELOVL7) was markedly downregulated, while the ferroptosis-related genes GPX4 and SLC7A11 were also significantly downregulated, and ACSL4 was significantly upregulated. Collectively, these findings suggest that, TROP2 knockdown suppresses malignant progression and enhances cisplatin sensitivity in ovarian cancer, accompanied by inhibition of the PI3K-Akt pathway, downregulation of ELOVL7-mediated lipid metabolism, and activation of ferroptosis-related gene expression. These findings suggest that TROP2 may regulate a lipid metabolism-ferroptosis axis, providing a novel potential target for reversing platinum resistance and improving therapeutic intervention in ovarian cancer.

Keywords

TROP2, Ovarian Cancer, Cisplatin Resistance, Lipid Metabolism, Ferroptosis