THE DOWNREGULATION OF MIR-509–3P EXPRESSION BY COL11A1-REGULATED HYPERMETHYLATION FACILITATES CANCER PROGRESSION AND CHEMoresistance VIA THE DNMT1/SUMO-3 AXIS IN OVARIAN CANCER CELLS

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Introduction It has been revealed that miR-509–3p is a strong tumor suppressor that attenuates migration and disrupts multicellular spheroids in multiple ovarian cancer cell lines, sensitizes to cisplatin, and remarkably downregulates in recurrent and metastatic ovarian cancer. In this study, we hypothesize that miR-509–3p downregulated by promoter hypermethylation through COL11A1 leads to ovarian cancer progression.

Methods The A2780CP70 and OVCAR-8 cells transfected with miR-509–3p mimic, while the A2780 and OVCAR-3 cells transfected with miR-509–3p inhibitor. The A2780CP70 cells transfected with a small interference RNA of COL11A1, and the A2780 cells transfected with a COL11A1 expression plasmid. The mRNA of COL11A1 and miR-509–3p and miR-509–3p hypermethylation of 137 ovarian tumors were determined by real-time reverse transcription-polymerase chain reaction and sequencing.

Results We found that miR-509–3p is aberrantly downregulated in ovarian cancer tissues and correlated with disease progression, survival, and COL11A1 expressions. The invasive EOC cells phenotypes are regulated by miR-509–3p. The miR-509–3p promoter region (p278) hypermethylation is an extremely important mechanism by which miR-509–3p transcription is regulated. The frequency of hypermethylation was significantly higher in EOC tumors with miR-509–3p downregulation than in those with high miR-509–3p expression. Additionally, Kaplan-Meier curve, stratified by the hypermethylation site of miR-509–3p, showed patients with hypermethylation had significantly shorter OS than those without hypermethylation. Mechanistic studies indicated that miR-509–3p transcription downregulated by COL11A1 through increased DNMT1 stability was achieved by combined DNMT1 and miR-509–3p promoter. Moreover, miR-509–3p targets SUMO-3 in ovarian cancer cells.

Conclusion/Implications We propose that the miR-509–3p/SUMO-3 axis potentially uncovers new targets for drug resistant metastatic ovarian cancer treatment.


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Abstract EP238/#102 Figure 1 Diagnostic performance of ADNEX, two-step strategy, O-RADS 2019 and O-RADS 2022. Above, ROC curves for the four models, Below, AUC, sensitivity, specificity, accuracy, positive and negative predictive values with 95% confidence intervals. Abbreviations: AUC, area under the curve; ROC, receiver operating curve; PPV, positive predictive value; NPV, negative predictive value