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.
Introduction It is unclear whether ultrasound risk stratification models for adnexal lesions perform well when used by novice providers. We aim to compare the performance of four commonly used models to detect ovarian cancer, when the operator has only basic experience.

Methods Women with adnexal masses treated in 2019 were identified retrospectively. Patients were included if they underwent surgery within 3 months of diagnosis or had at least 12 ±2 months of follow-up. A non-expert operator (European Federation of Societies for Ultrasound in Medicine and Biology level I) classified each lesion using ADNEX, two-step strategy (benign descriptors followed by ADNEX), O-RADS 2019, and O-RADS 2022. The primary outcome measure was AUC [95% confidence interval], compared across the four models.

Results A total of 556 women were included in the analyses: 452 benign and 104 malignant. The AUCs of ADNEX, the two-step strategy, O-RADS 2019, and O-RADS 2022 were 0.90 [0.87–0.94], 0.91 [0.88–0.94], 0.88 [0.85–0.91], and 0.88 [0.84–0.91], respectively (figure 1). The two-step strategy performed significantly better than the O-RADS algorithms (both p=0.01). With all the algorithms, the observed malignancy rate was 1.91–2.17% among lesions categorized as ‘almost certainly benign’, two-fold higher than the expected <1% (table 1). Out of the four methods, lesions wrongly classified as ‘almost certainly benign’ were borderline tumors (n=4) and metastases (n=3).

Conclusion/Implications In the hands of a novice provider, all algorithms performed well, and were able to distinguish benign from malignant lesions. ADNEX misclassified only one malignant patient as ‘almost certainly benign’, compared to 5–6 patients by the other models.

Abstract EP238/#102 Table 1 The calibration (i.e., the observed malignancy rate compared to the expected rate) is shown in Table 1A. Data are reported as number of malignant cases per cell/total number of patients in the cell (cell%). Table 1B describes the clinical and radiological characteristics of malignant cases misclassified as ‘almost certainly benign’ by at least one of the models. Abbreviations: BC, benign descriptor; EC, endometrial cancer; GI, gastro-intestinal; na, not available; N, number; US, ultrasound.