Methods Medroxyprogesterone acetate (MPA)-resistant endometrial cancer cells were established through continuous treatment of endometrial cancer cells (RL95–2 and Ishikawa) with gradually escalating doses of MPA. RNA-seq was performed on both original and MPA-resistant EC cells to evaluate DEGs. Gene-set enrichment analysis (GSEA) was also performed to find biologic processes or pathways in relation to MPA resistance. Further validation was undertaken by real-time polymerase chain reaction (RT-PCR) on selected genes.

Results The profiles of DEGs were substantially different between RL95–2 and Ishikawa cells. In MPA-resistant RL95–2 cells, the enriched hallmark gene sets include KRAS signaling, down, myogenesis, and late estrogen response. In MPA-resistant Ishikawa, hallmark gene sets of TNFα signaling via NFκB, hypoxia, and late estrogen response were significantly enriched. Common hallmark gene sets in both MPA-resistant RL95–2 and Ishikawa include late estrogen response and myogenesis. In addition, common gene ontology biological processes include cellular response to corticosteroid stimulus and epithelial cell differentiation.

Conclusions We identified DEGs and several pathways enriched in MPA-resistant endometrial cancer cells as potential therapeutic targets of progesterone resistance, which need further validation.

Conclusions

Methods Endometrial cancer organoids were cultured using endometrial cancer surgical specimens. After establishment of the organoids, we performed whole genome sequencing (WGS) on original tumor tissues and the paired organoids to identify driver mutations, mutational signatures, and structural variations. We also classified the organoids based on the TCGA molecular classifications.

Results Endometrial cancer organoids were successfully established in 7 of 34 cases (20%) and 11 cases (32%) are ongoing. Among them, we performed WGS analysis on 5 pairs of original endometrial cancer tissue and organoid. Although numerous passenger mutations were accumulated during organoid culture, all the established organoids retained the driver mutations of the tumors and showed similar mutational signatures. The organoids comprised the 4 TCGA molecular classifications, including 1 POLE ultramutated, 1 MSI (MMRd mutation), 1 TP53 mutated, and 2 copy-number low groups.

Conclusions We developed endometrial cancer organoids representing the 4 TCGA molecular classifications, which will provide useful experimental models for translational research.

Abstracts

EP012/#891 EXPRESSION OF CHEMOKINE RECEPTOR AND SUPPRESSION OF INHIBITORY RECEPTORS OF CD8 T CELL ERADICATED EFFECTIVELY CERVICOVAGINAL TUMOR IN MOUSE

Sung-Jong Lee, Taek Sang Lee*, School of Medicine, Yonsei University, Department of Obstetrics and Gynecology, Seoul, Korea, Republic of

Objectives Activation of exhausted CD8 T cell and migration of immune cells into tumor site is an important for overcoming resistance to cancer therapy. We evaluated the role of suppression of inhibitory receptors and chemokine axis in cervicovaginal tumor bearing mouse.

Methods C57BL/6 mice were categorized into four groups according to treatment modality. Mice were challenged with 1×10⁶ TC-1 cells on cervix and vagina. HPV DNA therapeutic vaccine was injected intramuscularly and intratumoral injection of GMCSF was performed. The mice were harvested on day 21 and immune cells were investigated by flow cytometry. We checked the expression of inhibitory receptors of CD8 T cells, including PD1, TIM3 and LAG3. Chemokine axis such as CXCL9, CXCL10, and CXCX3 were evaluated to know migration mechanism.

Results Combination of HPV DNA vaccine and GMCSF resulted in significantly lower expression of TIM3 inhibitory receptors of CD8+ T cells in tumor (p<0.05). However, expression level of PD1 and LAG3 was not changed after combination therapy. They significantly induced accumulation of tumor specific CD8 T cell in tumor site and increased expression of CXCX3 on tumor infiltration CD8 T cell (p<0.05). CXCL9, chemokine, was overexpressed in cervicovaginal tumor after combination therapy (p<0.05). However, expression level of CXCL10 was not changed after combination therapy. Finally, mice treated with combination therapy survived significantly longer than other groups with single therapy (p<0.05).

Conclusions In conclusion, we overcame T cell exhaustion and identified chemokine axis during migration of CD8 T cell into cervicovaginal tumor using HPV DNA vaccine and GMCSF.

EP013/#933 TESTING FOR MISMATCH REPAIR PROTEIN DEFICIENCY, MICROSATELLITE INSTABILITY, AND Lynch syndrome in ovarian cancer: a systematic review and meta-analysis

Cristina Mitric*, Lina Salman, Soyun Rachel Kim, Sarah Ferguson, University Health Network, University of Toronto, Gynecologic Oncology, Toronto, Canada; Sunnybrook Odette Cancer Centre, Division of Gynecologic Oncology, Toronto, Canada; Princess Margaret Cancer Centre/University Health Network/Sinai Health Systems, Gynecologic Oncology, Toronto, Canada; Sunnybrook Odette Cancer Centre, Division of Gynecologic Oncology, Toronto, Canada; Princess Margaret Cancer Centre/University Health Network/Sinai Health Systems, Gynecologic Oncology, Toronto, Canada

Objectives Identifying Lynch syndrome (LS) in endometrial cancer through reflex tumour testing for mismatch repair protein deficiency (MMRd) and microsatellite instability (MSI) is widely accepted, but knowledge is limited about its value in ovarian cancer. The current systematic review and meta-