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## OBJECTIVE

- To evaluate ovarian clear cell carcinoma (OCCC) and endometrial clear cell carcinoma (ECCC) using multiplatform profiling technology and compare their molecular profiles to clear cell renal cell carcinoma (ccRCC).

## BACKGROUND

- Ovarian clear cell carcinoma is rare, accounting for approximately 5-25% of epithelial ovarian cancers (EOC) with a higher prevalence in Asian women (1).
- These tumors are high-grade, and women with advanced stage disease have a poorer prognosis than those with high grade serous EOC (2). Advanced clear cell gynecologic malignancies remain amongst the most challenging diseases to manage.
- OCCCs have a high frequency of common genetic mutations including ARID1A and PIK3CA and higher expression of HNF1β compared to high grade serous EOC.
- OCCCs have similar gene expression profiles compared to endometrial and renal CCCs (3).
- Molecular profiling of clear cell ovarian cancer may help to identify new targeted therapy as well as predictive biomarkers.

## METHODS

- OCCC, ECCC, and ccRCC tumor samples were evaluated from 2015 to 2018 by Caris Life Science for multiplatform analysis (Caris Life Science, Phoenix, AZ).
- Mutation analysis was performed using fragment analysis (FA), gene amplification with chromogenic in situ hybridization (CISH), and/or next-generation sequencing (NGS) with the NextSeq platform (Illumina, Inc., San Diego, CA).
- Chi-square testes were used to determine molecular differences between subtypes.

**Table 1:** Study Sample Characteristics

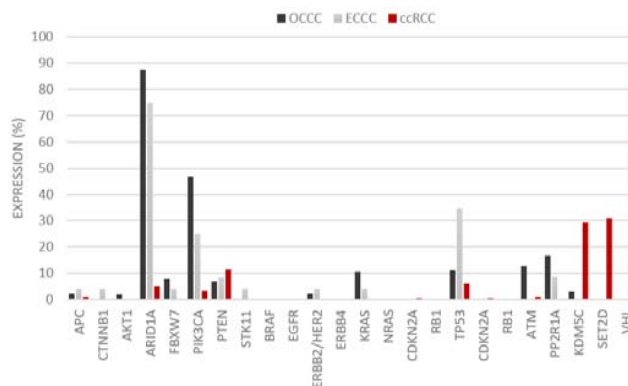
	OCCC	ECCC	ccRCC
Specimens (N)	164	75	234
Median age (years, range)	57.5 (26-80)	67 (44-83)	-

## RESULTS

**Table 2:** Molecular portraits of clear cell ovarian and endometrial carcinoma with comparison to clear cell renal cell carcinoma.

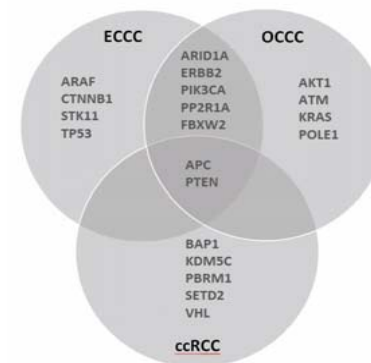
Pathway	Marker	Method	OCCC (%)	ECCC (%)	ccRCC (%)
Tumor Mutational Burden	-	-	7.0	-	0.6
Transcription/translation	<i>PBRM1</i>	NGS	0.0	-	43.9
	<i>SETD2</i>	NGS	0.0	0.0	31.1
	<i>VHL</i>	NGS	0.0	-	80.3
Wnt	<i>APC</i>	NGS	2.3	4.2	1.1
	<i>CTNNB1</i>	NGS	0.0	4.2	0.0
PIK3CA Akt mTOR	<i>AKT1</i>	NGS	2.1	0.0	0.0
	<i>ARID1A</i>	NGS	87.5	75.0	5.1
	<i>FBXW7</i>	NGS	7.7	4.2	0.0
	<i>PIK3CA</i>	NGS	46.8	25.0	3.3
	<i>PTEN</i>	NGS	7.1	8.3	11.4
MAPK	<i>STK11</i>	NGS	0.0	4.2	0.0
	<i>BRAF</i>	NGS	0.0	0.0	0.0
	<i>EGFR</i>	NGS	0.0	0.0	0.0
	<i>ERBB2/HER2</i>	CISH	5.8	9.4	-
	<i>ERBB2/HER2</i>	NGS	2.2	4.2	0.0
	<i>ERBB4</i>	NGS	0.0	0.0	0.0
	<i>KRAS</i>	NGS	10.6	4.2	0.0
Cell cycle	<i>NRAS</i>	NGS	0.0	0.0	0.0
	<i>CDKN2A</i>	NGS	0.0	0.0	0.6
	MSH-high	NGS/FA	6.4	11.5	-
	<i>MSH6</i>	NGS	4.7	1.3	0.0
	<i>PP2R1A</i>	NGS	16.7	8.7	0.0
	<i>RBI</i>	NGS	0.0	0.0	0.0
	<i>TP53</i>	NGS	11.1	34.8	6.3

**Figure 1:** Molecular portraits of clear cell ovarian and endometrial carcinoma with comparison to clear cell renal cell carcinoma.



## CCC MUTATION PROFILES

**Figure 2:** Comparisons between ECCC, OCCC, and ccRCC. Individual differences between groups with p-value <0.05. Similarities with p-value >0.05



## CONCLUSIONS

- OCCC and ECCC are similar diseases requiring novel approaches to treatment.
- ccRCC, although pathologically similar, has differential mutation expression patterns than OCCC and ECCC.
- ccRCC and OCCC/ECCC have common mutations in *APC* and *PTEN*.
- Prospective clinical trials are needed to examine targeted therapies as well as checkpoint inhibition in these gynecologic disease subtypes.

## REFERENCES

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