SGO ANNUAL MEETING ON WOMEN'S CANCER San Diego, CA • 2024

THE POWER OF SHARED PURPOSE: Transforming Gynecologic Cancer Care

Molecular Characterization of Squamous Cell Ovarian Cancers for Identification of Therapeutic Targets

CARIS LIFE SCIENCES

Jessie Hollingsworth[1], Sharon Wu[2], Anusha Adkoli[1], Alex Farrell[2], Kurt Hodges[2], Matthew J Oberley[2], Anthony N Karnezis[3], Premal H Thaker[4], Eugenia Girda[1]

1. Rutgers, New Jersey, 2. Caris Life Sciences, 3. UC Davis, California, 4. Washington University, St Louis, Missouri

Background:

- Squamous cell carcinoma (SCC) represents <1% of all Ovarian cancers (OC) and is associated with worse prognosis compared to High-Grade Serous OC (HGSOC)
- It is thought to arise predominantly from malignant transformation of mature cystic teratomas (MCT) but can also arise from Brenner's tumors (BT) and endometriosis
- **This study seeks to identify prognostic factors and molecular markers associated with OSCC**

Methods:

- 15 BT, 32 OSCC and 11,968 HGSOC tumors were analyzed using NGS of DNA (NextSeq, 592 genes and NovaSeq, WES) and RNA (NovaSeq, WTS) (Caris Life Sciences)
- Microsatellite instability (MSI) was tested by IHC and NGS
- Tumor mutational burden (TMB) measured by totaling all nonsynonymous mutations per tumor (TMB-H: ≥ 10 mutations/MB)
- PD-L1 IHC positivity was determined by a cut-off of >2|5% (SP142)
- Real-world overall survival (OS) was obtained from insurance claims and calculated from tissue collection to last contact
- Statistical significance determined by chi-square and Mann-Whitney U test and adjusted for multiple comparisons (q-value <0.05)

Results:

Table 1. Demographics

Characteristics	Brenner	Squamous	HGSOC
N	15	32	11968
Age, median (range)	63 (52-87)	55.5 (33-76)	65 (15-90)
TMB, median (range)	4 (1-16)	7 (1-54)	3 (0-344)
Biopsy Site			
Primary, N (%)	10 (66.7)	12 (37.5)	5525 (46.1)
Metastatic, N (%)	5 (33.3)	20 (62.5)	6303 (52.6)
Unclear, N (%)	0 (0)	0 (0)	146 (1.22)

Fig 1. Mutational landscape

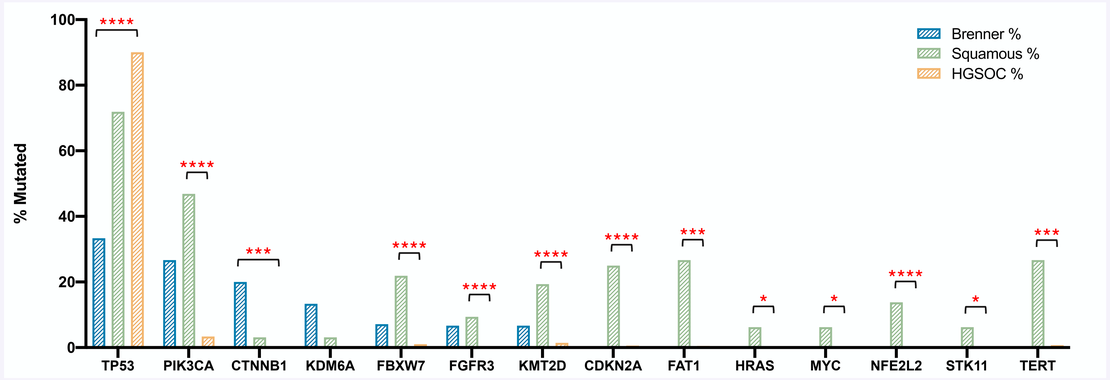


Fig 2. ER and PR staining

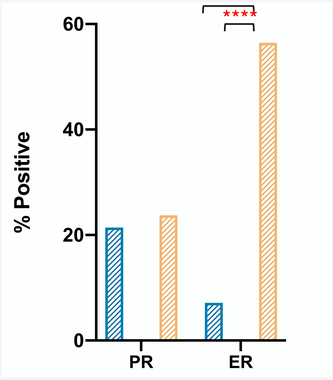


Fig 3. Immune Microenvironment of BT vs Squam OC vs HGSOC

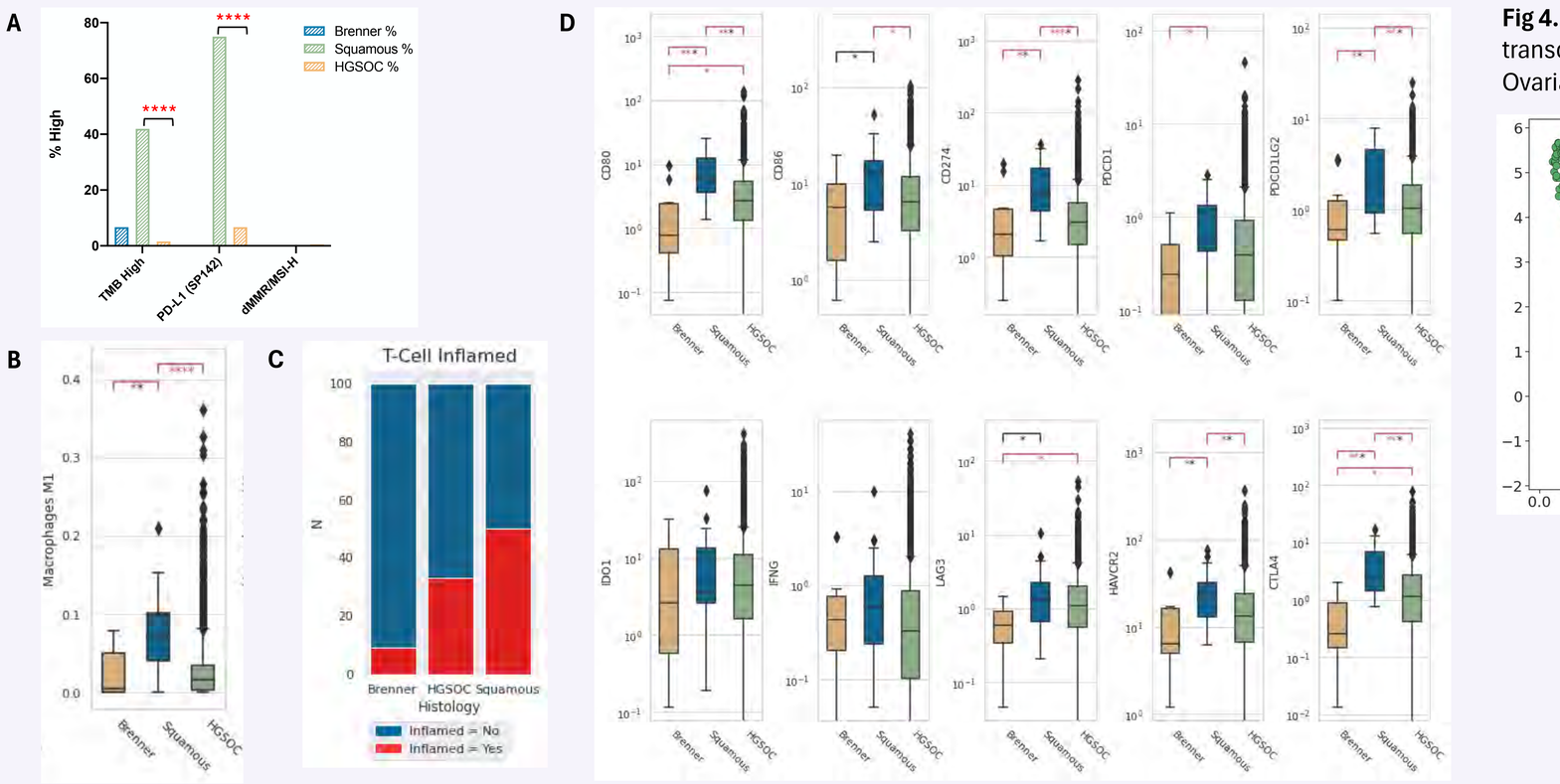
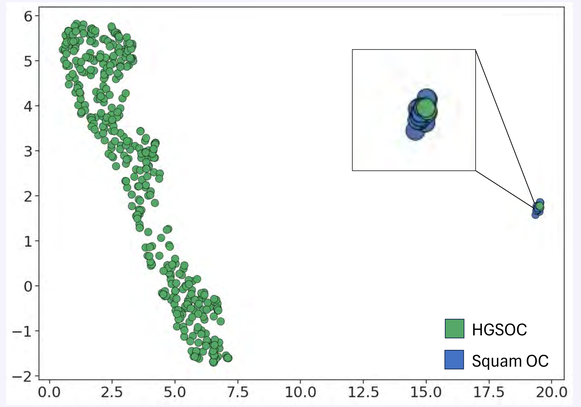


Fig 4. UMAP using K-means clustering to visualize transcriptomic differences in HGSOC vs Squamous Ovarian tumors



Conclusion:

- OSCC tumors were more likely to be TMB-H compared to BT and HGSOC, with increased mutational prevalence in multiple genes like PIK3CA, FBXW7, CDKN2A, FAT1, pTERT but no ER or PR positivity
- Additionally, OSCC tumors also had increased expression of many IC genes, infiltration of M1 Macrophages and higher T-cell inflamed frequency. UMAP analysis showed OSCC and HGSOC have distinct transcriptomic profiles
- One limitation of this study is the small sample size of OSCC compared to HGSOC, but further characterization of this rare histological subtype with a poor prognosis may lead to identification of therapeutic targets.

Poster ID: 222