INTRODUCTION

- Ovarian cancer is the 10th most common cancer among women and the 5th most lethal in the US. Epithelial ovarian cancer (EOC), is the most common type of ovarian cancer (>85%) with a 5-year survival rate below 50%, owing to late diagnosis and lack of effective therapy.[1]
- EOC mostly spreads into the peritoneal cavity leading to the formation of ascites.[2]
- Ovarian cancer (<85%) with a 5-year survival rate below 50%, owing to late diagnosis and lack of effective therapy.[3]
- In EOC, both DTCs and CTCs, in ascites and blood respectively, exist as single cells and clusters. CTC clusters are believed to be extremely rare, but have a ≈ 50x higher metastatic potential than single cells.[4] Their capture and characterization would allow for better understanding of the mechanisms driving dissemination and help to monitor disease in EOC.
- Targeting fragile clusters is challenging and high shear stress can lead to their dissociation, leading to a poor assessment of the cluster population.

FACILE CAPTURE OF CTC CLUSTERS

- We introduce a gentle gravity-flow filtration system for the capture of large clusters from blood and revealed their widespread presence in EOC patients.

2 CTC CLUSTERS FROM OVARIAN ORTHOTOPIC TRANSPLANTS IN MICE

- Capture of OV90 clusters from mice blood
- Clusters were captured in all mice
c-Clusters size varied between 2 and >100 cells

3 CTC CLUSTERS FROM EPITHELIAL OVARIAN CANCER PATIENTS

- Cluster capture from patient blood
- Clusters were captured in 12/12 EOC patients
- Cluster size varied between 2 and >100 cells

Molecular characterization of CTC clusters
- Most clusters express both EpCAM and c-MET
- Strong heterogeneity within clusters
- Decrease of the number of CTC clusters in patients receiving chemotherapy
- CTC and cluster counts continued dropping while CA125 already plateaued, suggesting that they could be more sensitive than CA125 in monitoring therapy.

REFERENCES


CONCLUSION

- We developed a gravity-flow filtration method that offers low shear stress and found CTC clusters in the blood and ascites of every mouse in our study. Staining for EMT markers revealed distinct phenotypes between CTC clusters from blood and ascites, suggesting the involvement of different mechanisms in their dissemination.
- CTC single cells and clusters were found in the blood of every EOC patient, and cluster size distribution was strikingly similar between mice and patients. To the best of our knowledge, this is the first study identifying clusters in all patients, and thus it highlights their prevalence among EOC patients.
- In a time course study of one EOC patient, a correlation between the decrease of CA125 concentration and the number of single cells and clusters was observed. After therapy, increase in CTC count than in CA125 level suggest that CTCs could provide a more sensitive readout, along with additional information about the disease via CTC and cluster counts, and, protein expression patterns.
- In the future, CTCs and clusters might be used to better understand and manage the disease, including identifying subtypes, selecting precision therapies, and predicting and tracking recurrence.