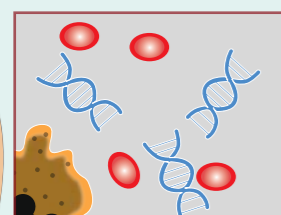


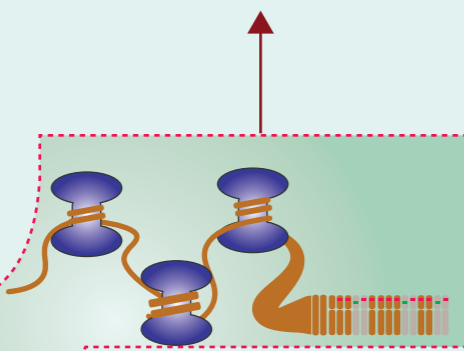
Predicting Therapeutic Outcome in High-Grade Serous Ovarian Cancer by Circulating DNA Analysis



Cell-Free DNA (cf-DNA)
 - freely circulating molecules in blood
 - contain DNA of tumor origin

Liquid Biopsy

- can analyze *BRCA1/2* mutations in cf-DNA samples
- can predict treatment outcome if successful



BRCA1/2 mutations & reversions

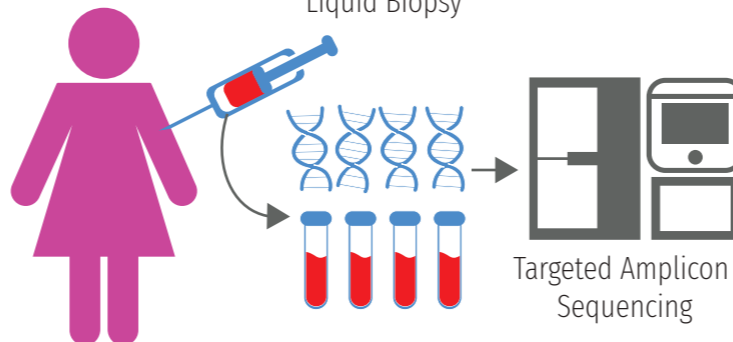
- mutations favor response to chemotherapy
- reversions could result in chemoresistance

HGSC = High-Grade Serous Ovarian Cancer



30 patients with HGSC with *BRCA1/2* mutations

Liquid Biopsy



Patients with *BRCA1/2* reversions in tumor samples

		Positive	Negative
Patients with <i>BRCA1/2</i> reversions in plasma samples	Positive	4 True positive	0 False positive
	Negative	2 False negative	24 True negative

Positive predictive value = 1
 Negative predictive value = 0.9



Patients with *BRCA1/2* reversions

Chemotherapy



Emergence of drug resistance and relapse

Background

- 30 plasma (blood) and tumor samples obtained
- Group I:** Patients with history of malignancy before diagnosis of HGSC
- Group II:** Patients with recurrent HGSC

Methodology

Targeted Amplicon Sequencing

- performed using primers flanking *BRCA1/2* mutations
- primer design not based on prior knowledge of reversion sequences
- reversions analyzed in both tumor and plasma samples
- results subsequently matched to understand significance of cf-DNA liquid biopsy in identifying *BRCA1/2* mutations and reversions

Results

- *BRCA1/2* mutations found in all analyzed tumor samples
- reversions found in only 4 tumor samples from group II

Outcome

Chemotherapy with platins and poly-ADP ribose polymerase inhibitor-based drugs is ineffective in patients with *BRCA1/2* reversion mutations

Chemotherapy response in patients with HGSC can be predicted using a noninvasive liquid biopsy