Tumor Sequencing and Next-Generation Sequencing

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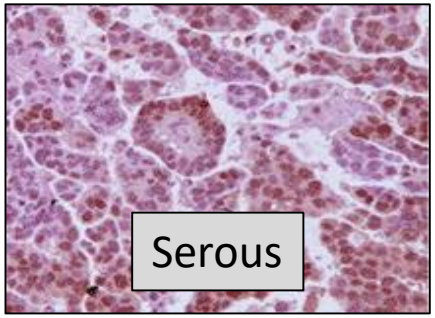
No Disclosures

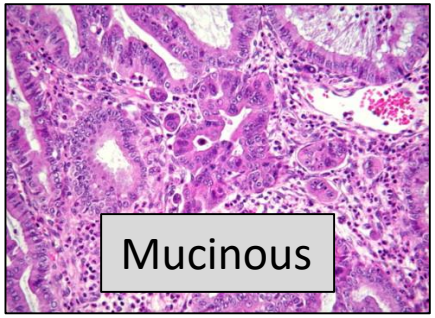
Objectives

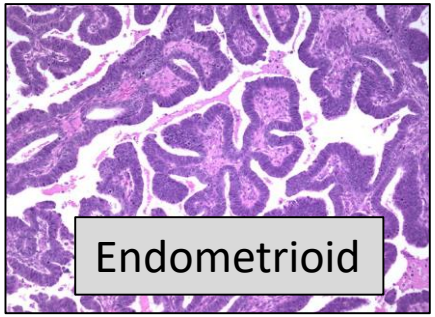
- Review the role of tumor genomics in ovarian cancer

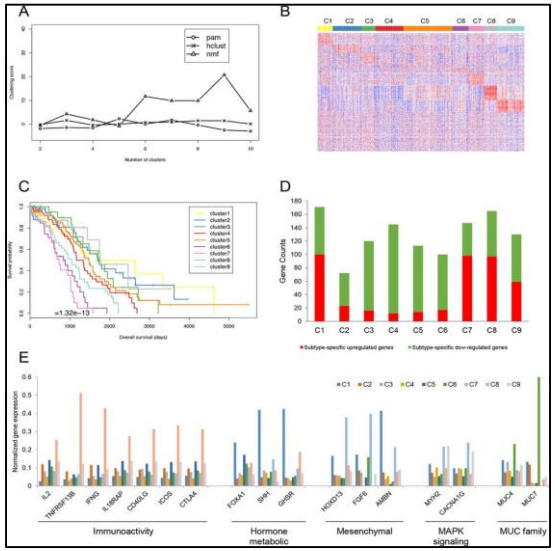
- Discuss the potential uses of next-generation sequencing for ovarian cancer

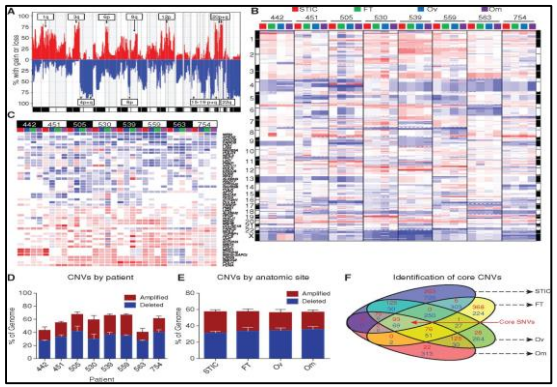
Classifying Ovarian Cancer











Precision Medicine

- Tailor treatments to genetic changes in each patient's cancer

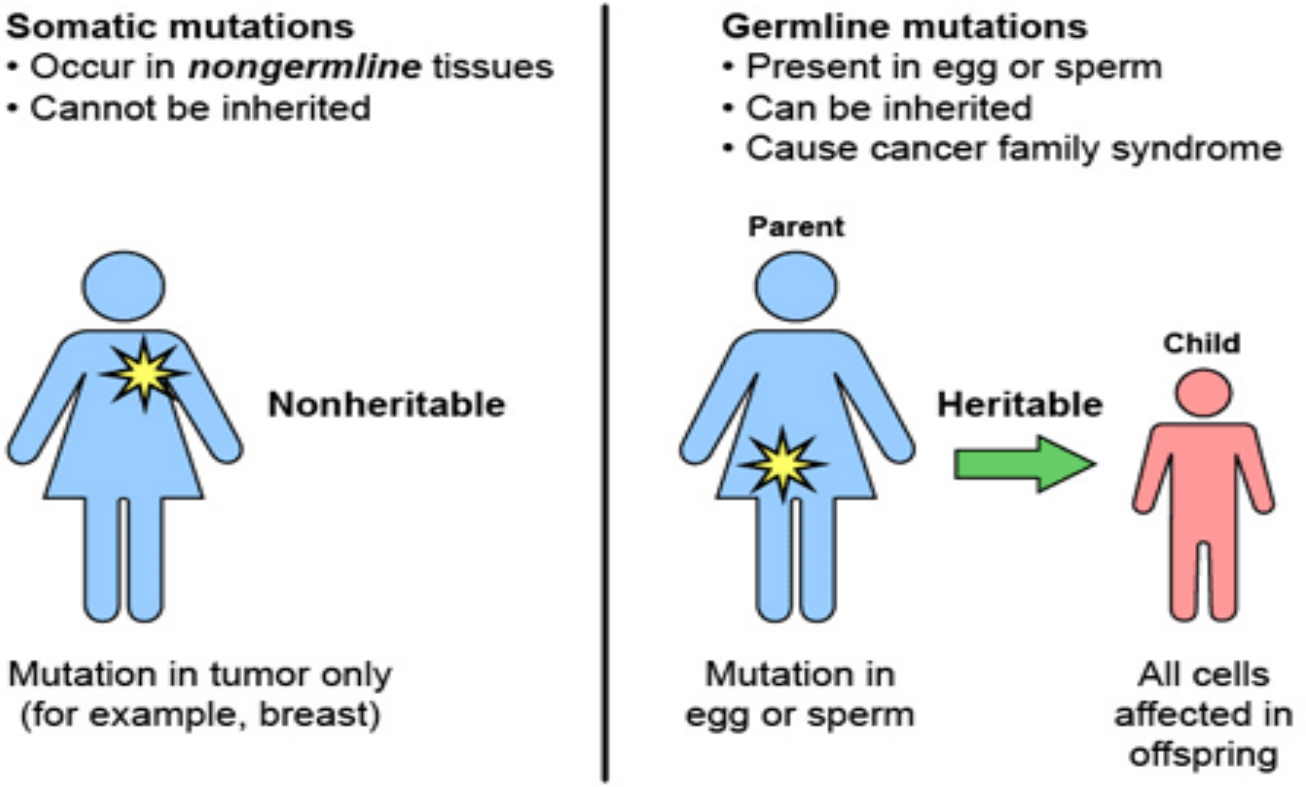
- The promise:
  - Find new/unexpected treatments
  - Avoid ineffective and toxic treatments

- A work in progress…

What can vary between tumors?

- Germline mutations: inherited mutations (ex. BRCA)
- Somatic mutations: mutations found in tumor but not in other cells
- Functional changes: more complex but can include epigenetic changes

Germline versus Somatic



Adapted from the National Cancer Institute and the American Society of Clinical Oncology

Note: blood tests will *generally* not pick up somatic mutations

Germline Testing

- Usually a blood or saliva test
- Inherited mutations
  - BRCA mutations
  - Lynch syndrome
  - Other rare conditions
- Useful for counseling about other cancers but also for some therapeutic options:
  - BRCA: PARP inhibitors
  - Lynch syndrome: immunotherapies

Somatic Mutation Testing:
Next Generation Sequencing (NGS)

- Must test the tumor
  - Direct tumor biopsy
  - Tumor cells in blood stream

- How to obtain tumor:
  - Use material already available (i.e. from prior surgery)
  - Obtain a new biopsy (unclear benefit to obtaining new material rather than using old)

Somatic Mutation Testing:
Next Generation Sequencing (NGS)

- Several commercial tests available
- General testing concept:
  - Assess DNA of tumors
  - Assess RNA of tumors
  - Compare to normal tissues
- Generally covered by insurance

FOUNDATION MEDICINE

CARIS LIFE SCIENCES

TEMPUS

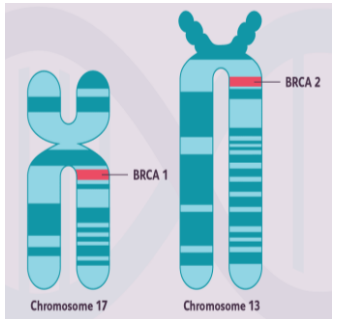
And many more…
No specific endorsements

How is this useful?

- Not useful for all patients (yet)
- Several classes of treatments:
  - BRCA-like mutations: PARP inhibitors
  - Immunogenic tumors: immunotherapies
  - Chemotherapy sensitivity: response to standard agents
  - Response to non-ovarian regimens
  - Clinical trial enrollment

BRCA-like mutations

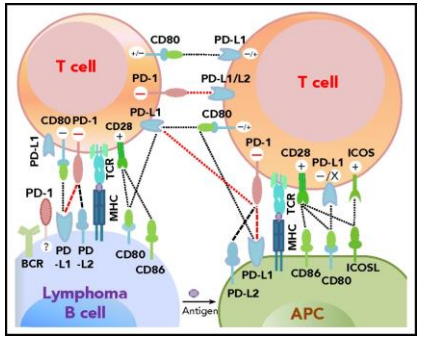
- Somatic mutations in BRCA or other similar genes/homologous recombination deficiency (HRD)



- Treatments: PARP inhibitors
  - After primary chemotherapy (maintenance)
  - After chemotherapy for first recurrence
  - As a single agent for recurrent disease

Immunogenic tumors

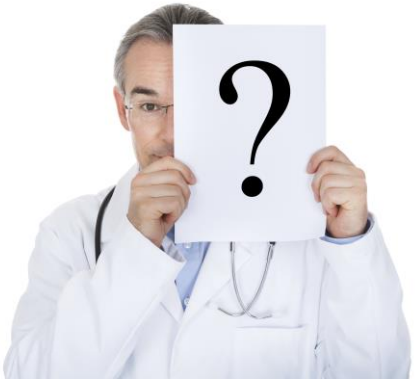
- Several types:
  - Lynch genes (MLH1, MSH2, MSH6, PMS2)
  - High PD-1 expression
  - High tumor burden



- Treatments: pembrolizumab
  - Checkpoint inhibitor (more by Dr. Matei)
  - FDA approved ***independent of tumor type***

Chemotherapy sensitivity

- Specific genes correlate with chemotherapy response (maybe)
- Treatments:
  - ERCC1: cisplatin/carboplatin
  - Topo I: topotecan
  - ARID1: PARP inhibitors
  - VEGF: bevacizumab
  - Hormone receptors: aromatase inhibitors
- Guide sequence of therapy, not options



Response to non-ovarian regimens (some off label uses)

- Identify genes correlating with therapy response to non-ovarian cancer specific drugs or drugs generally inactive in ovarian cancer
- Treatments:
  - NTRK: entrectinib (NTRK inhibitor, FDA approved)
  - ARID1A: HDAC inhibitors
  - Her-2: trastuzumab (Herceptin)
- Other examples: treatments for colon, lung or breast cancers

Clinical Trials

- May find mutations that qualify for a trial
  - Ovarian cancer specific trials (rare)
  - Non-disease specific trials (more common)
  - Often early phase trials

- NGS reports often list available trials

NGS: Not Perfect

- Most patients do not *yet* have actionable mutations
- Insurance usually covers testing but this is not guaranteed
- Must have tissue available for testing
- Speak to your oncologist about it!

THANK YOU