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Molecular Classification of Endometrial Cancer

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Survive and Thrive 2022

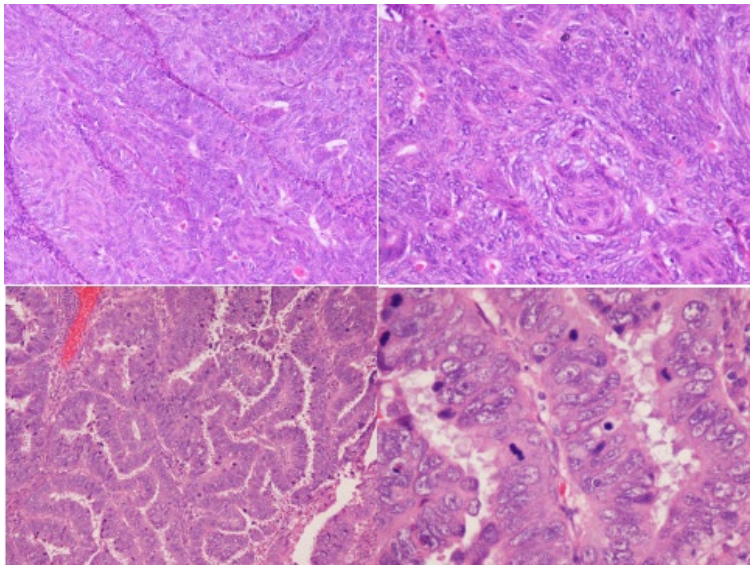
Disclosures

None

What is cancer classification?

- Classification – grouping cancers together that act similarly
  - Allows for better decision-making regarding the best treatment options

- Many different approaches to grouping cancer
  - Pathology
  - Grade
  - Stage
  - Molecular features



Endometrial Cancer: Type I vs Type II

- Traditionally, endometrial cancer was classified into two pathologic groups using a combination of these features

Characteristic	Type I	Type II

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Stage	Often early	Often advanced
Etiology	Unopposed estrogen	Sporadic

Endometrial Cancer: Type I vs Type II

- This classification system:
  - Grade and histopathology is not always reproducible
    - This can lead to heterogeneity in not only classification, but also research and clinical trials
  - Somewhat more limited ability to risk stratify patients

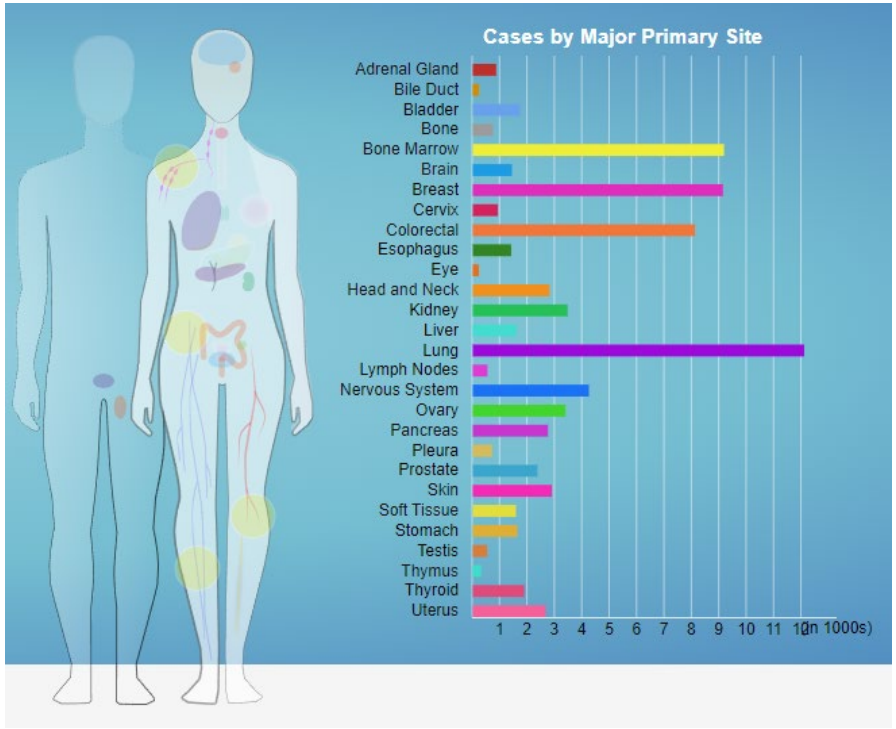
Can we do better?

Molecular Classification

The Cancer Genome Atlas (TCGA)

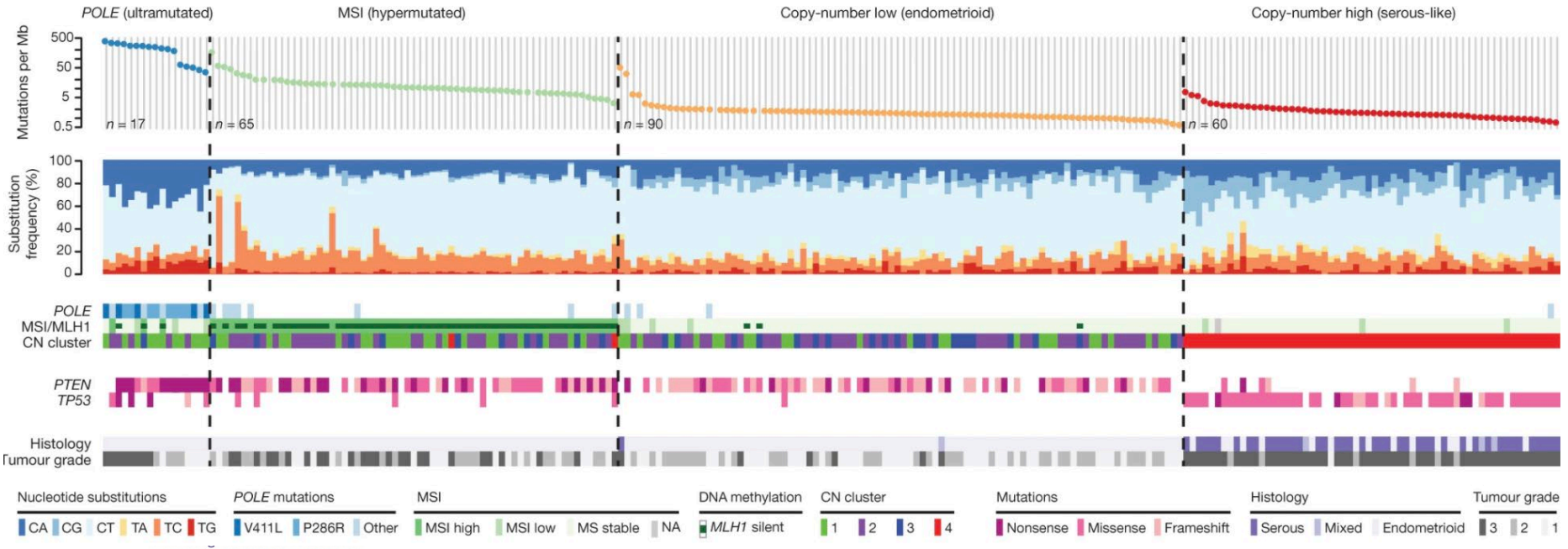
- Landmark cancer genomics program
  - National Cancer Institute
  - National Human Genome Research Institute

- Molecularly characterized multiple cancer types with matched normal samples
  - 2664 cases of uterine cancer
  - Multiple histologies

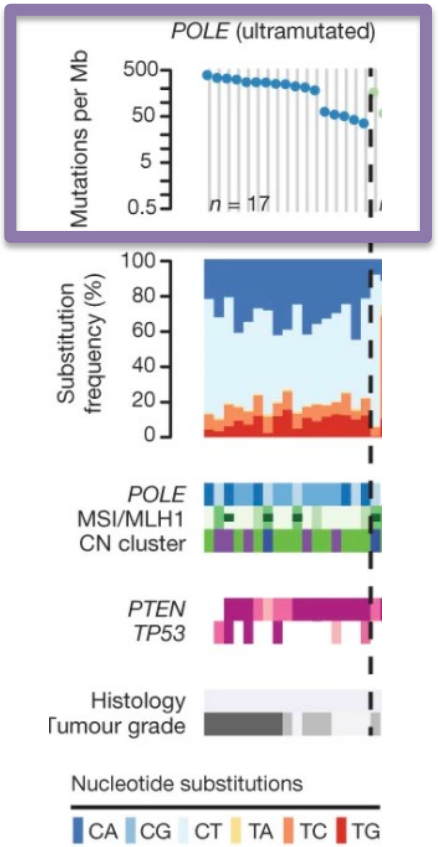


TCGA Molecular Classification

- Grouping endometrial cancer based on molecular characteristics rather than pathologic characteristics

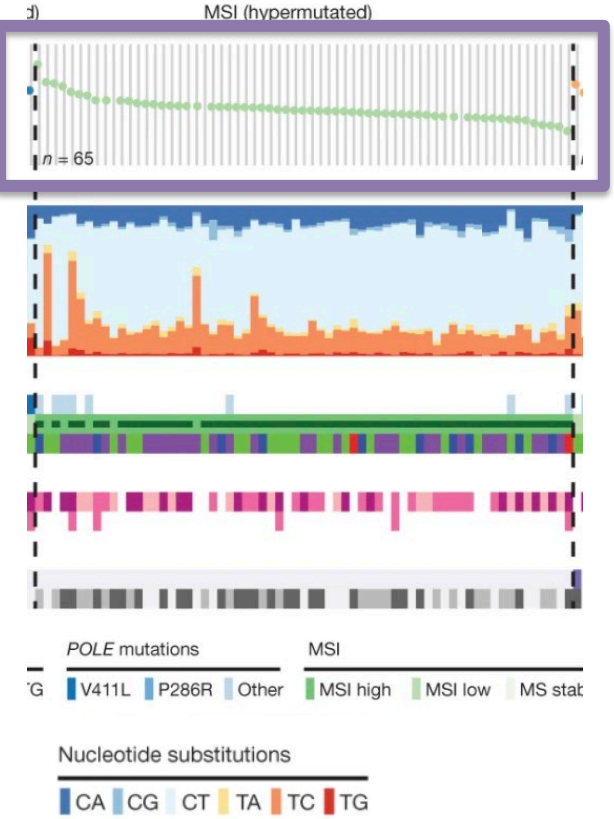


TCGA Molecular Classification: POLE



- POLE Mutation
  - 4-8% of endometrial cancers
  - Very high mutational burden
  - Excellent prognosis
    - Decreased recurrence risk

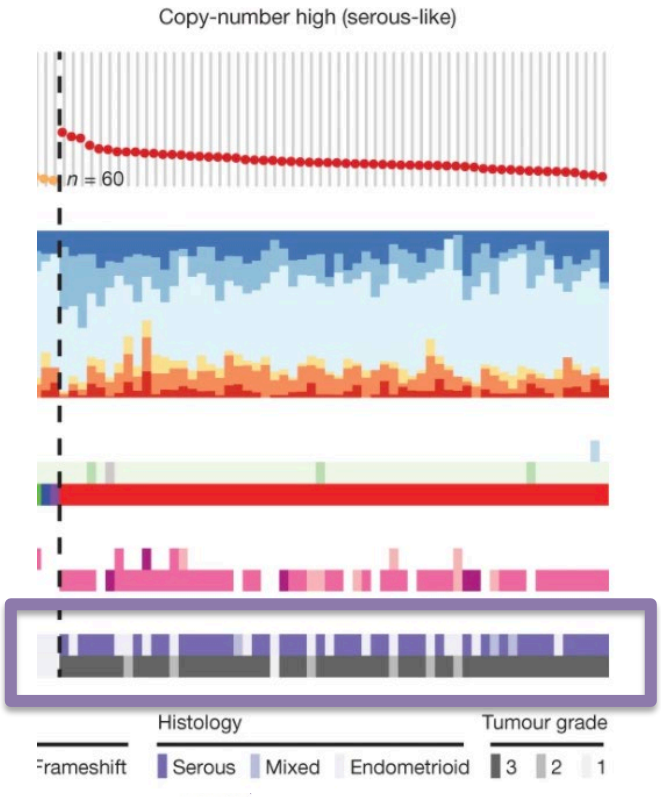
TCGA Molecular Classification: MSI or dMMR



- MSI = microsatellite instability
- dMMR = deficient mismatch repair

- 20-40% of endometrial cancer
- Intermediate prognosis group
  - Predictive of response to immunotherapy

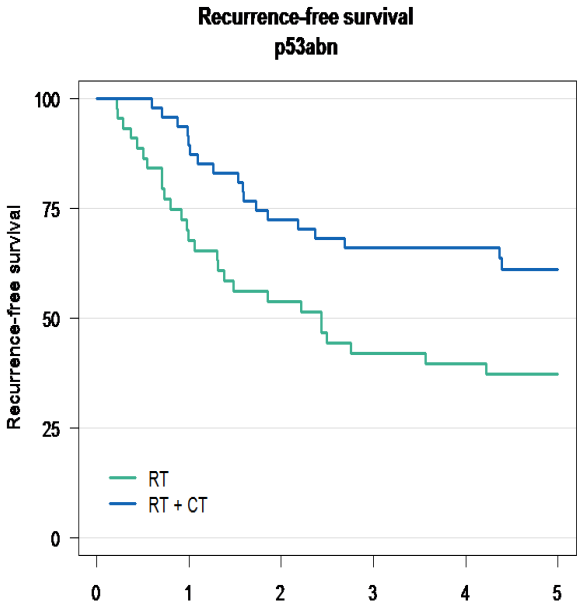
TCGA Molecular Classification: Copy number high



- “Serous-like” (73% in this group are serous histology)

- Aggressive, poor prognosis
- P53 mutated

TCGA Molecular Classification: Copy number high

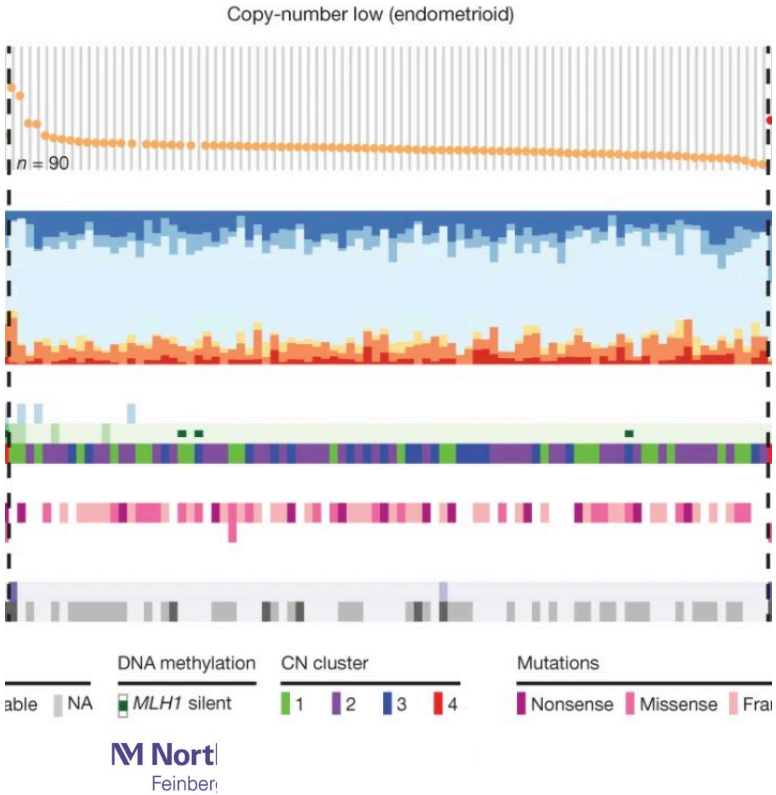


p=0.015, HR 0.50 (95%CI 0,28-0,88)

- "Serous-like" (73% in this group are serous histology)

- Aggressive, poor prognosis
- P53 mutated
  - Chemotherapy may have greater benefit for these patients than others in the adjuvant setting

TCGA Molecular Classification: Copy number low

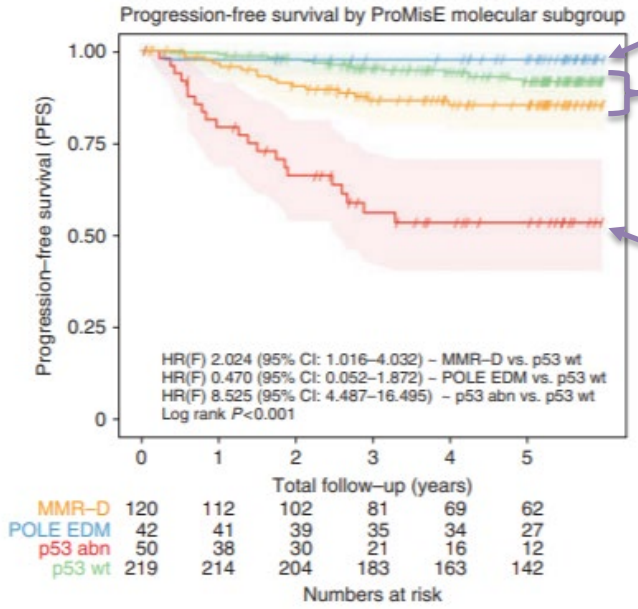


- Also known as “no specific molecular profile” (NSMP)

- 40-50% of endometrial cancer
- Intermediate prognosis group
- Hormone receptors
- Further molecular characterization in order to stratify
  - CTNNB1
  - L1CAM

So what does that all mean, and why should you care?

Proactive Molecular Risk Classification for Endometrial cancer (ProMisE)



- Using these categories has excellent prognostic ability
- Potential to drive therapy!
  - Use of immunotherapy
  - Use of chemotherapy
- Ongoing current trial: PORTEC – 4A

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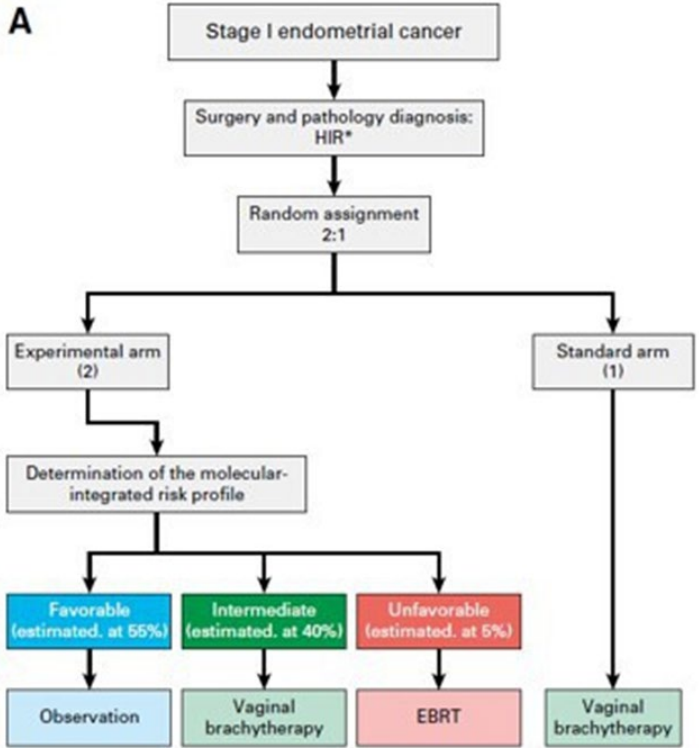

- Prognostic ability
- Potential to drive therapy!

- Ongoing current trial: PORTEC – 4A
  - Randomized trial of molecular profile-based versus standard recommendations for adjuvant radiotherapy for women with early stage endometrial cancer

In summary…

- We are learning more and more about how endometrial cancer acts and responds to treatment

- Molecular classification represents a new way of grouping these cancers, and gives a more nuanced view
  - This will hopefully allow us to better tailor treatment to each woman's specific tumor

Thank You!

Any questions?