**DNA Repair Deficiencies Are Common in Gynecologic Cancers and Can Be Targeted by Therapies to Kill Cancer Cells**

- **Deficient mismatch repair (dMMR)** causes mutations and microsatellite instability (MSI)

- **Double-strand breaks are repaired by:**
  - Homologous recombination
  - Nonhomologous end joining

- **DNA DAMAGE**

- **Damaged bases or single-strand breaks are repaired by:**
  - Base excision repair
  - Nucleotide excision repair
  - Mismatch repair

- **~33%** of endometrial cancers have dMMR/MSI

- **~50%** of ovarian cancers have HRD

### dMMR/MSI Is a Biomarker for Response to Checkpoint Inhibitors

**dMMR/MSI tumors:**
- Have high mutation rates
- Accumulate neoantigens
- Are immunogenic

**dMMR/MSI can be identified by immunohistochemistry or polymerase chain reaction analysis**

### HRD May Predict Magnitude of Sensitivity to PARPi

- **BRCA1/2 mutation** is an important cause of HRD, although HRD can also result from many other causes

- **Platinum sensitivity** is a biomarker for PARPi sensitivity in some settings

**Current genetic tests (e.g., BRCA mutation analysis, HRD testing) cannot identify all patients who may benefit from PARPi therapy**

### References:

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