

# Endometrial Cancer



Erika Li, Tomas Manea, Nathan Yoon  
QBIO 490

# **Review Paper: Endometrial cancer - Crosbie et al., 2022**

# Endometrial Cancer: A Review

- **Most common** gynecological cancer in high-income countries
- Incidence is rising globally (up 132% in last 30 years)
- **6th most common** cancer among women
- 2020 - 417,000 diagnoses

3% - lifetime risk

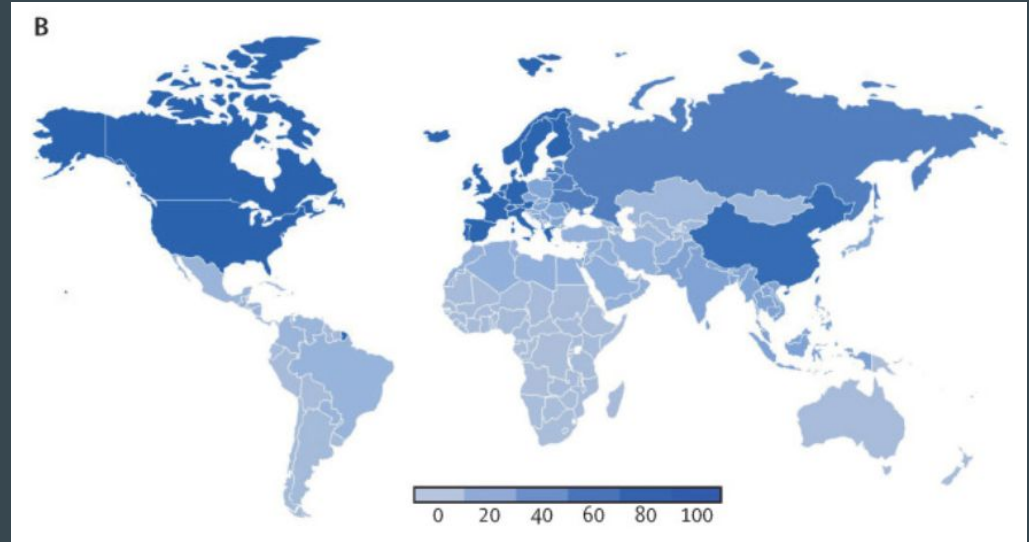


Figure 1B. Age-standardized incidence rate of endometrial cancer 2019 (100 000 population) per GBD region. Crosbie et al., 2022.

# How do we spot endometrial cancer?

- “It’s complicated”
- Postmenopausal bleeding - probability of cancer increases with age
- Diagnosis requires tissue exam
- EM thickness  $\geq 5$  mm indicates potential for cancer

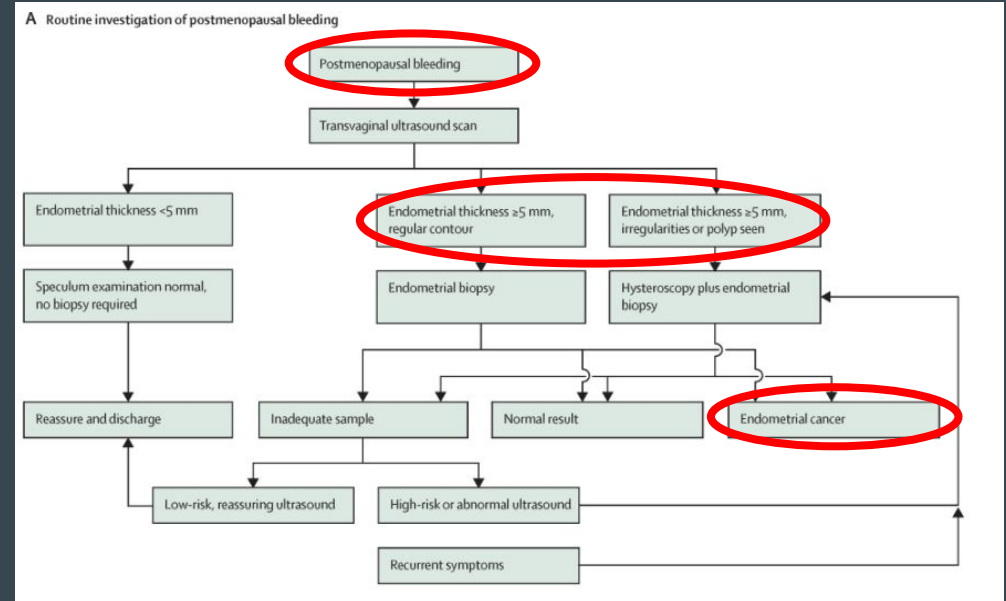


Figure 2A. Current diagnostic pathways for endometrial cancer. Crosbie et al., 2022.

# Risk Factors

- Risk increases with **AGE** and **BMI** - cancer with the **strongest** link with obesity
  - BMI > 40: 10-15% chance of cancer ~ lung cancer in smokers
- Obesity -> high CRP, IL-6, TNF-alpha -> endometrial formation +
- Estrogen - EM growth, progesterone - EM in check
  - Post-menopause - progesterone deficiency

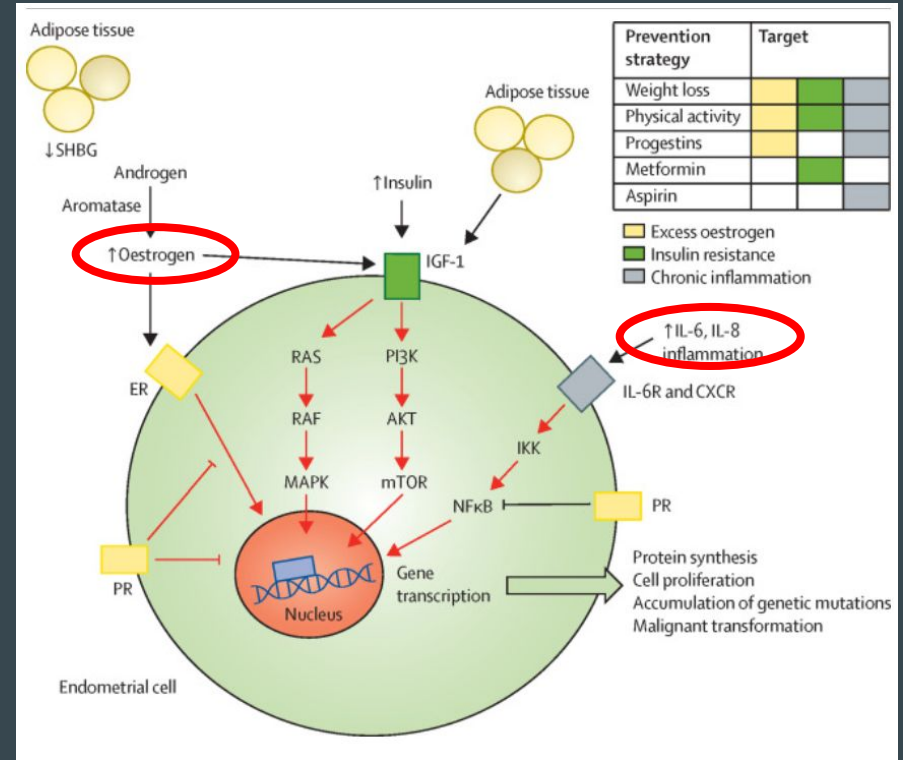


Figure 3. Obesity-associated endometrial cancer: pathways to carcinogenesis and targets for prevention. Crosbie et al., 2022.

# Surgery and Treatment

- Current mainstay of treatment: **total hysterectomy + bilateral salpingo-oophorectomy**
- Minimally invasive surgery shown to have non-inferior outcomes. Preferred whenever possible
- Fertility-sparing treatment? Currently *not very great*
  - Oncological recurrence ~35% after treatment
  - Pregnancy prospects ~27%
- **Weight loss leads to both less cardiovascular disease and increased endometrial cancer survival rate**

**Research Paper:**  
**Analysis of endometrial carcinoma TCGA reveals  
differences in DNA methylation in tumors from  
Black and White women - Asif et al., 2023**

# Introduction

- Racial disparities
  - Tumor subtypes
  - Mortality rates
- Social determinants of health
  - Impacts on epigenetic alterations, such as **DNA methylation**
- Epigenetic modifications contribute to endometrial carcinogenesis
  - Global hypomethylation
  - Hypermethylation at CpGs in promoter regions
  - Result: **oncogene activation, tumor suppressor inhibition, genomic instability**



# Gap in knowledge

Given that there are significant **racial disparities** in endometrial carcinoma, and the relationship between social determinants of health and epigenetic alterations, could there be *epigenetic* differences in endometrial cancer between Black and White women?

# Methods

- Downloaded endometrial carcinoma methylation and clinical data from TCGA
    - 46 normal tissues and 439 tumor samples
  - Parsed by race, leaving 393 samples
    - 294 White samples, 99 Black samples
- 
1. Differentially methylated CpGs were identified using Limma package in R
  2. Differentially methylated regions were identified with DMRcate
  3. Survival analysis generated with survival R package
  4. Correlation analysis between changes in methylation and gene expression
  5. Enrichment analysis

# Results

## 1. DMC's Analysis -

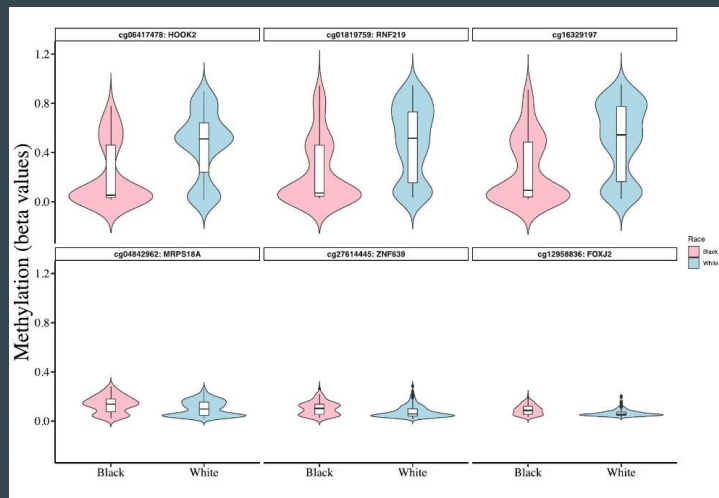


Fig 1A. Volcano plot for differentially methylated CpGs (DMCs) in tumors from White vs Black patients. *Crosbie et al., 2022*

## 2. DMC's Analysis -

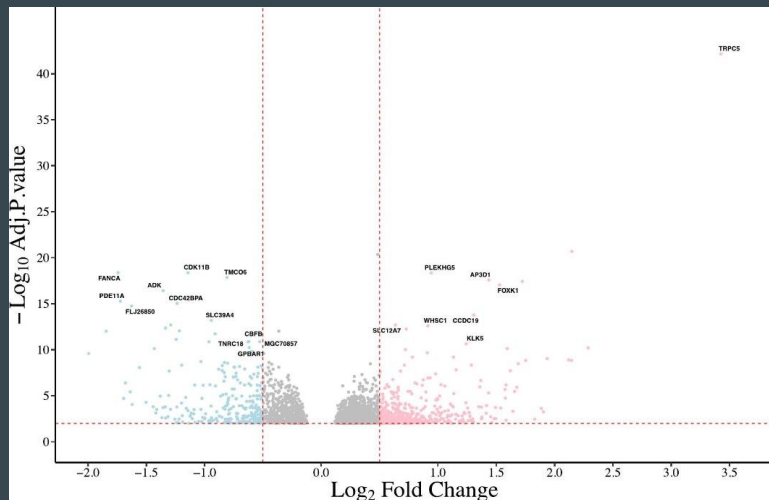


Fig 1B. Volcano plot of six significant differentially methylated CpGs (DMCs) between White and Black tumors. *Crosbie et al., 2022*

# Results Contin.

## 3. Visualization of DMR using UCSC Genome Browser

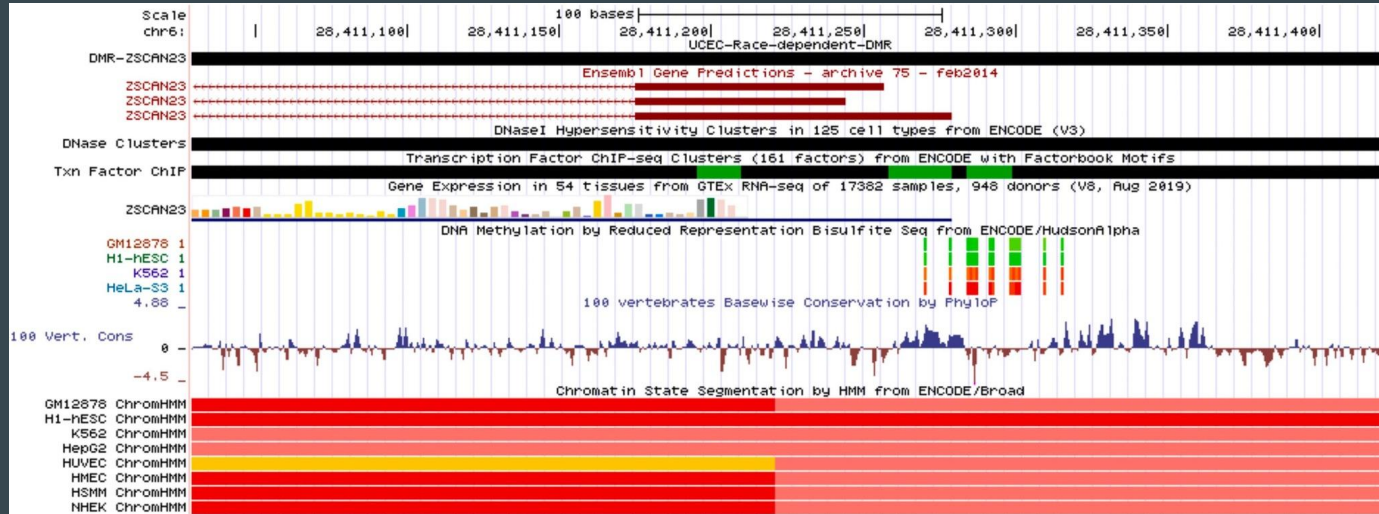


Fig 2. Visualization of DMR using UCSC Genome Browser. *Crosbie et al., 2022*

# Discussion

1. Gene promoter hyper/hypomethylation is key in cancer studies
2. Linked with racial disparities in cancer incidence and mortality rounds out the epigenetic regulation of cancer-associated genes
3. Selected Genes—in insulin signaling pathway—demonstrated twice as hypervariable in Black than White tumor samples

# Works Cited

- Asif, H., Foley, G., Simon, M., Roque, D., & Kim, J. J. (2023). Analysis of endometrial carcinoma TCGA reveals differences in DNA methylation in tumors from Black and White women. *Gynecologic Oncology*, 170, 1-10.  
<https://doi.org/10.1016/j.ygyno.2022.12.011>.
- Crosbie, E. J., Kitson, S. J., McAlpine, J. N., Mukhopadhyay, A., Powell, M. E., & Singh, N. (2022). Endometrial cancer. *The Lancet*, 399(10333), 1412-1428.