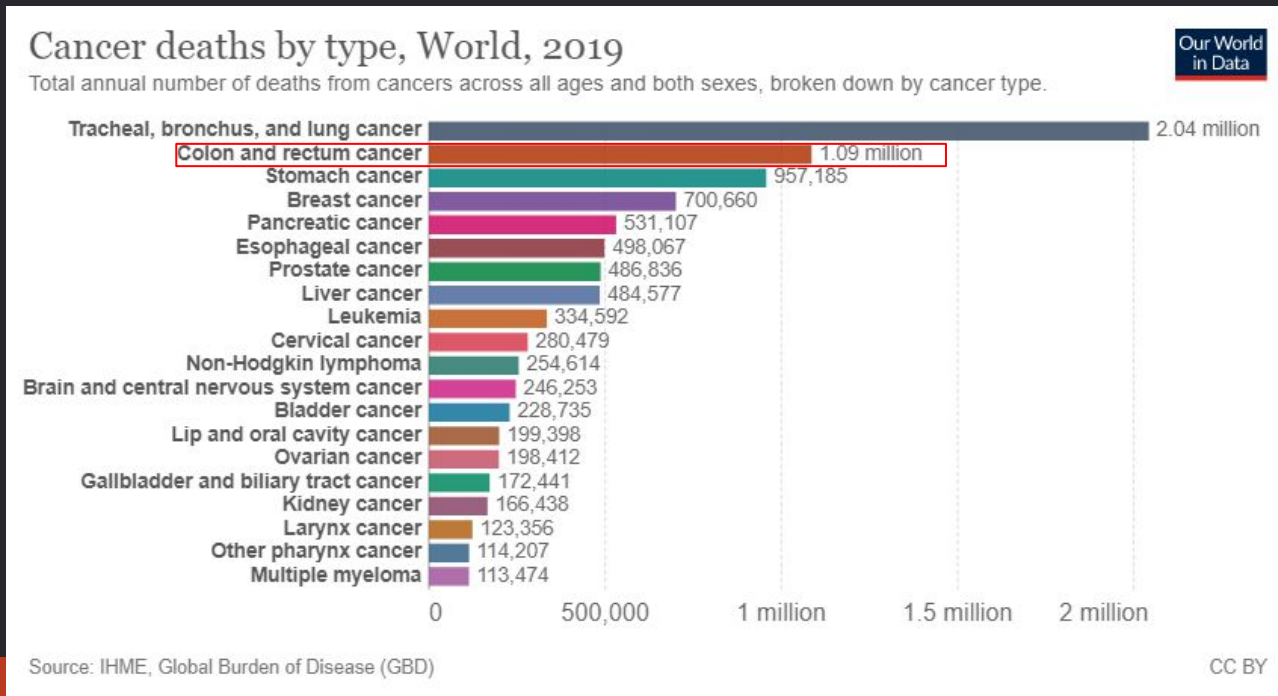# Characterizing Molecular Differences Between Male and Female Colorectal Cancer Patients

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Introduction

- Colorectal cancer (CRC) is the second most common cause of cancer death

Cancer deaths by type, World, 2019
Total annual number of deaths from cancers across all ages and both sexes, broken down by cancer type.

Cancer type	Deaths
Tracheal, bronchus, and lung cancer	2.04 million
Colon and rectum cancer	1.09 million
Stomach cancer	957,185
Breast cancer	700,660
Pancreatic cancer	531,107
Esophageal cancer	498,067
Prostate cancer	486,836
Liver cancer	484,577
Leukemia	334,592
Cervical cancer	280,479
Non-Hodgkin lymphoma	254,614
Brain and central nervous system cancer	246,253
Bladder cancer	228,735
Lip and oral cavity cancer	199,398
Ovarian cancer	198,412
Gallbladder and biliary tract cancer	172,441
Kidney cancer	166,438
Larynx cancer	123,356
Other pharynx cancer	114,207
Multiple myeloma	113,474

Source: IHME, Global Burden of Disease (GBD)

Our World in Data

CC BY

Introduction

- Female CRC patients: significantly better overall survival rates than male patients

- Sex-based differences in gene and protein expression → differences in disease progression and survival

- Identifying sex-based biomarkers and drug targets would significantly improve patient outcomes

Our Goal

- Utilize publicly available datasets to identify molecular differences between male and female CRC patients at a multi-omic level
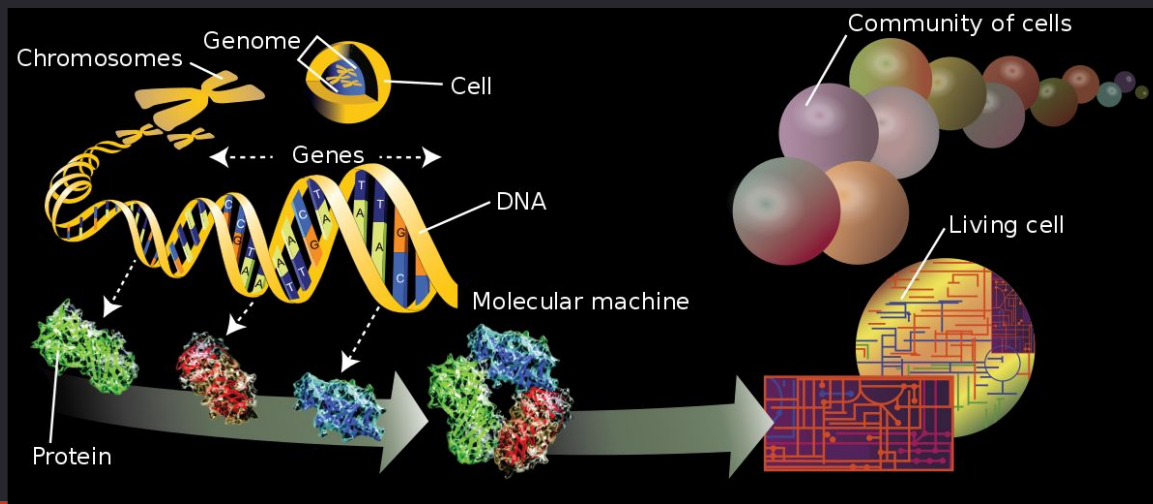
Methods

- Data from The Cancer Genome Atlas (TCGA) & Clinical Proteomic Tumor Analysis Consortium (CPTAC)

- TCGA: genomics, transcriptomic, and clinical data
  - Over 20,000 primary cancer datasets
  - 33 different cancer types

- CPTAC: large-scale proteomic data in relation to TCGA clinical data

Methods

- MAF analysis via R package 'maftools'
  - Determine if mutation type & frequency are sex-differentiated

- Transcriptomic analysis via R package 'DESeq2'
  - Determine if there is differential expression between sexes

- Quantify relationship between gene and protein expression levels via Python packages 'Matplotlib' and 'seaborn'

Dataset Overview - TCGA

	Female	Male
# of patients	244	280
Avg. age (years)	66	68
White	115	122
Black	32	29
Asian	3	8
Native American	0	1
No race info	94	120

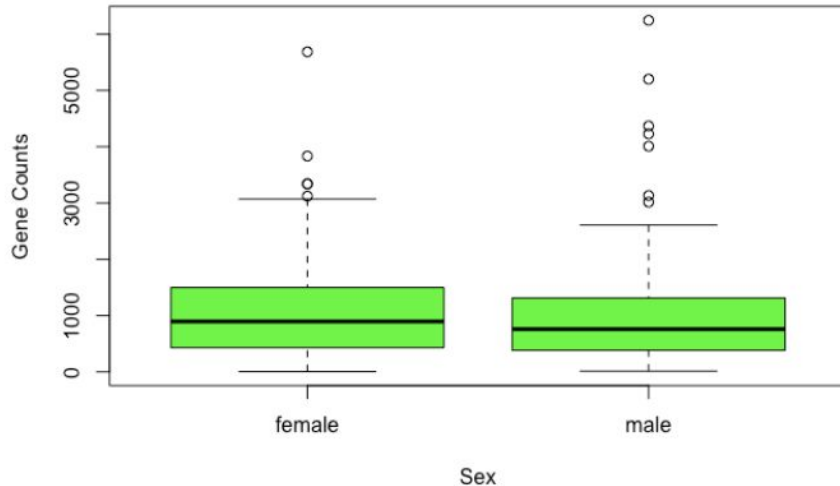# Female Patients Show Better Overall Survival Than Male Patients
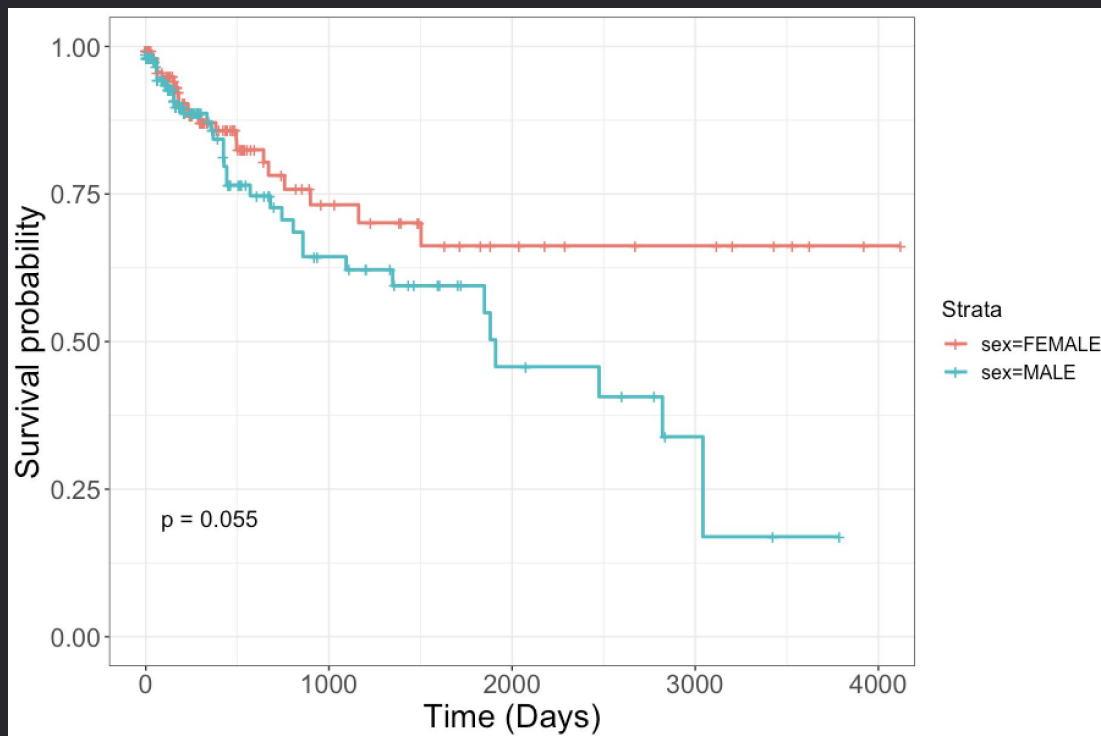
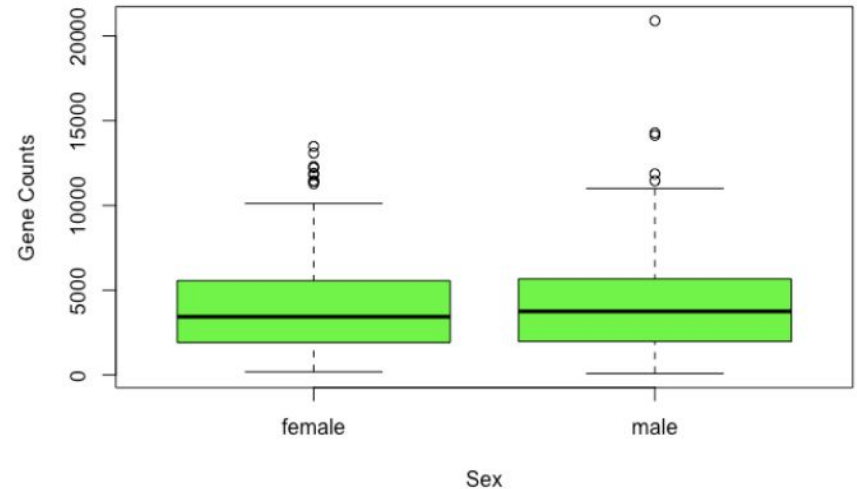# Mutation types & percentages are quite similar between sexes
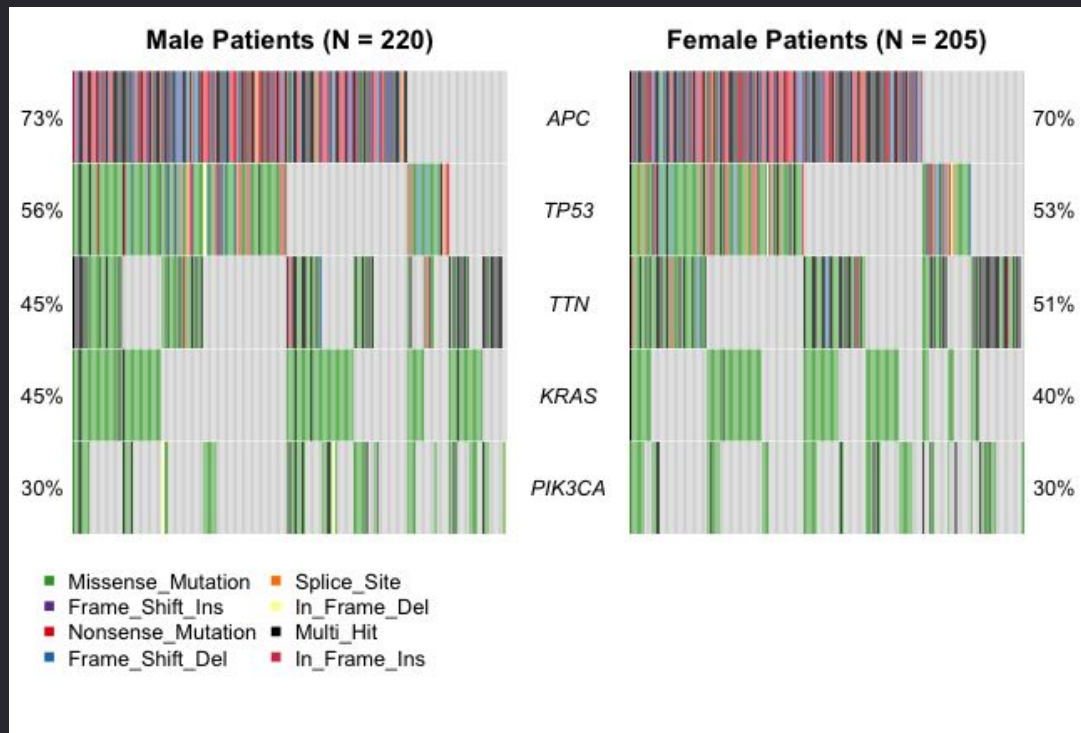
Gene expression of the top 5 most mutated genes does not differ between sexes
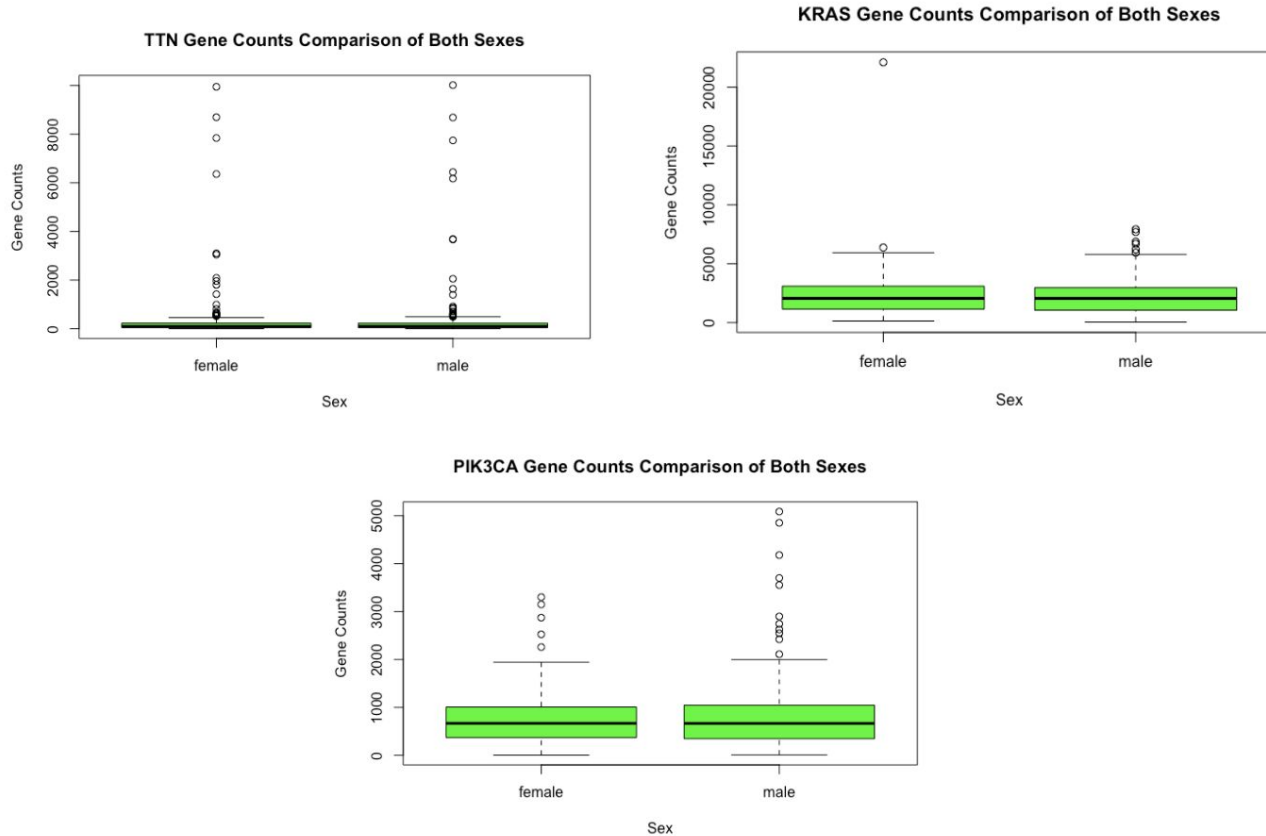
Gene expression of the top 5 most mutated genes does not differ between sexes cont.

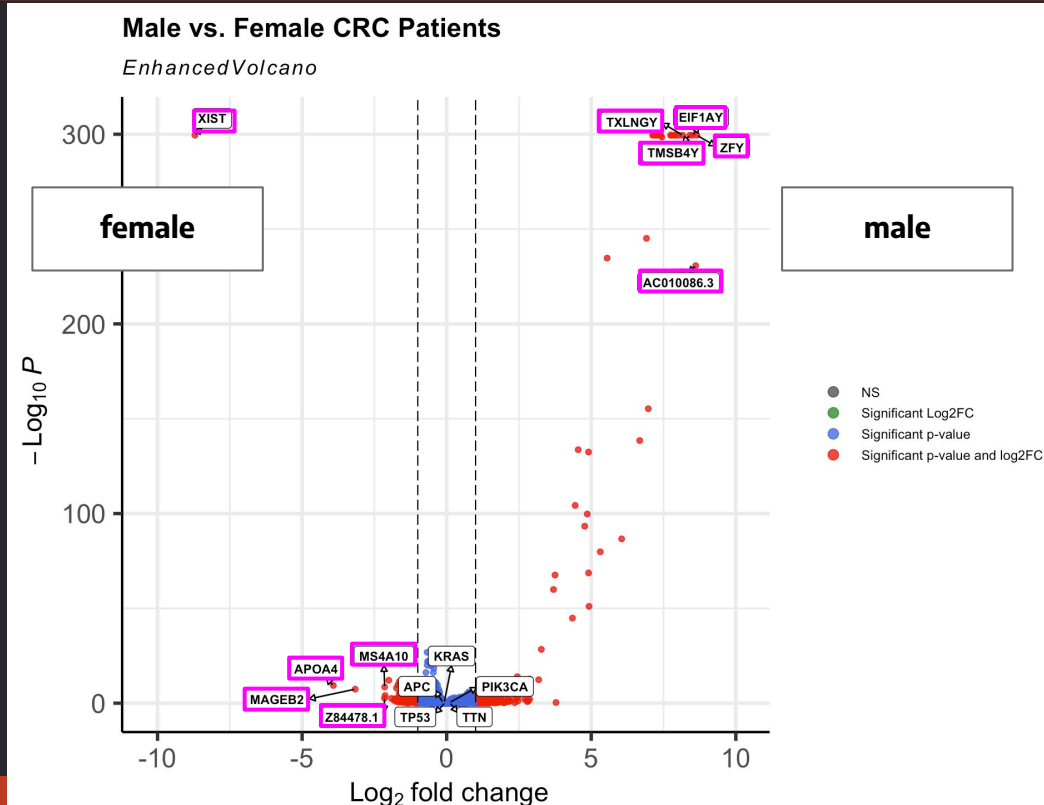# Differential gene expression of the top 5 most mutated genes does not differ between sexes

Gene	log2FoldChange	padj
APC	-0.136	0.364
TP53	-0.063	0.747
TTN	0.119	0.663
KRAS	-0.086	0.463
PIK3CA	0.103	0.449

- Positive log2FoldChange = overexpressed in male patients
- Negative log2FoldChange = overexpressed in female patients
- Significant log2FoldChange are values > 1 or < -1

Differentially expressed genes between male and female patients

Top 5 most overexpressed genes for each sex are highlighted in purple

Differential Gene Expression Analysis

- Initial analysis mainly identified noncancer-related sex-linked genes as the most differentially expressed genes between male and female patients

- We then conducted a differential gene expression analysis between normal and cancer tissue in male and female CRC patients

Differentially expressed genes between normal and cancer tissue in male CRC patients
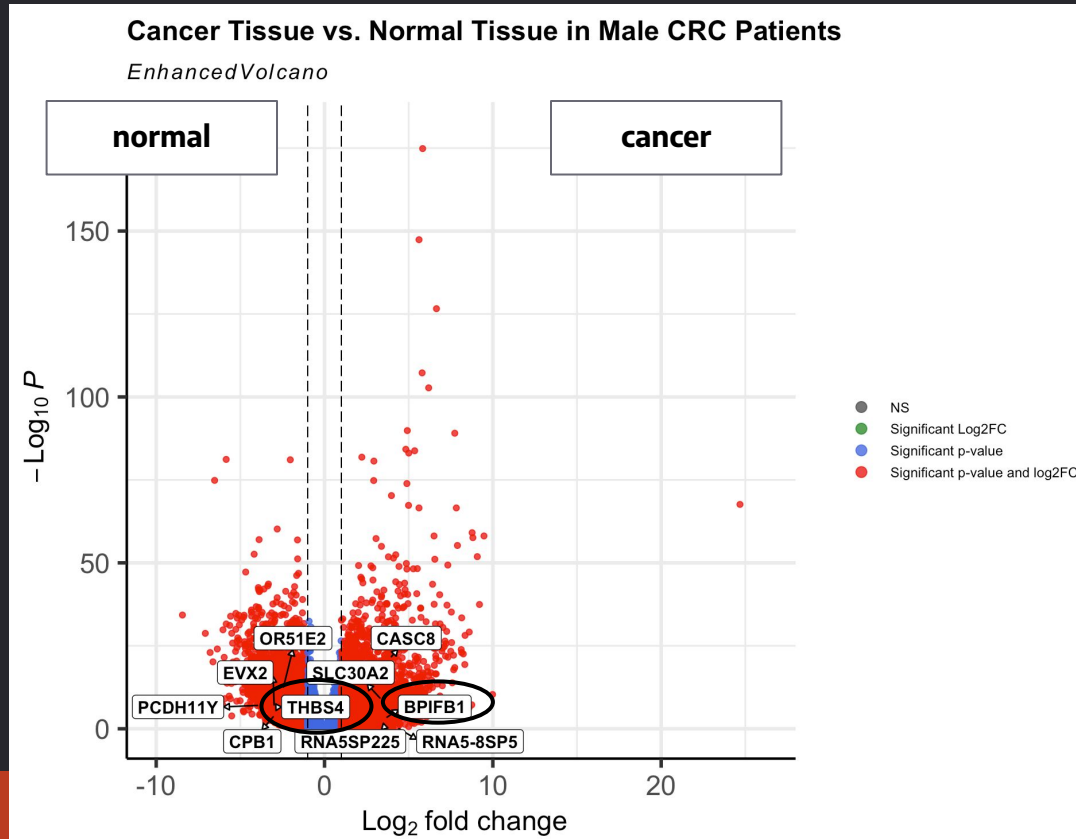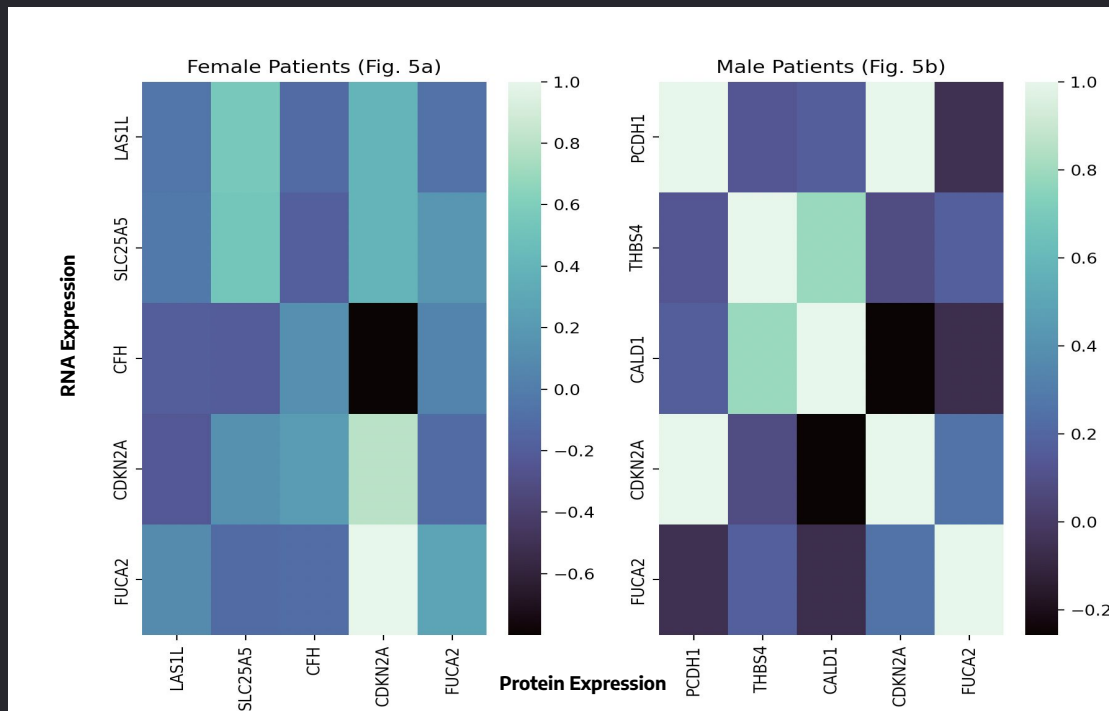

Top 5 most overexpressed genes for each tissue type that are unique to male patients are labeled

Differentially expressed genes between normal and cancer tissue in female CRC patients
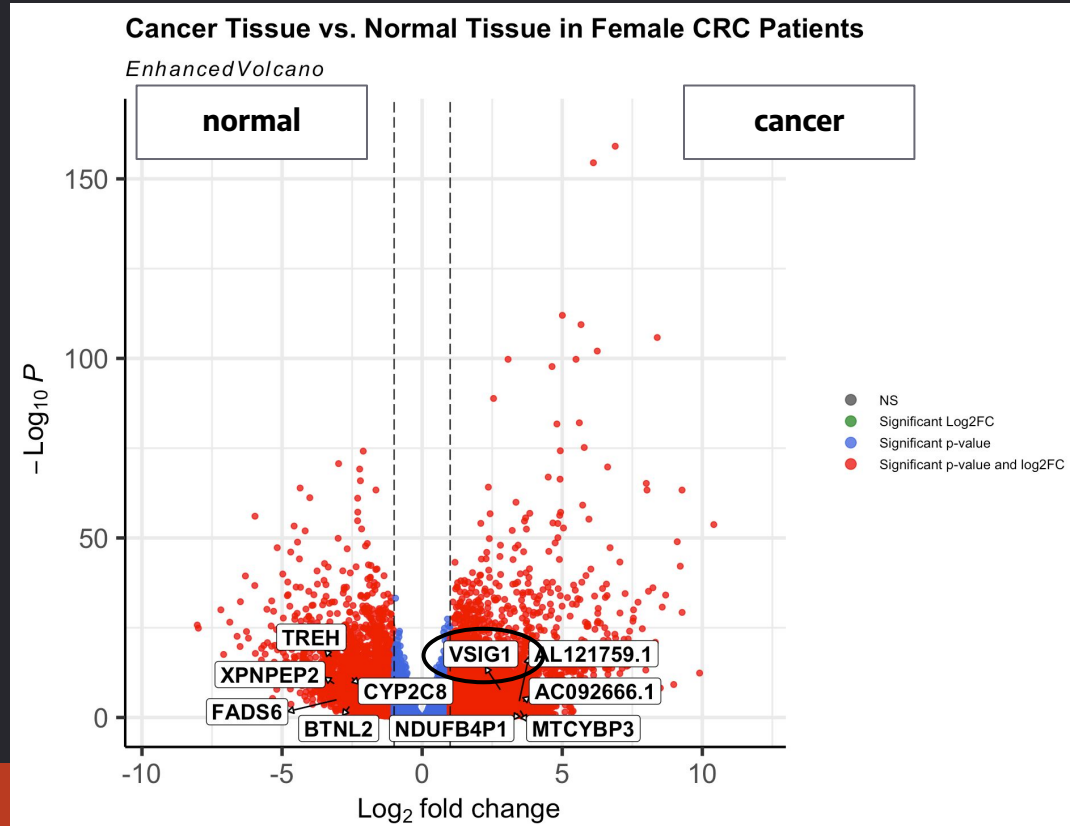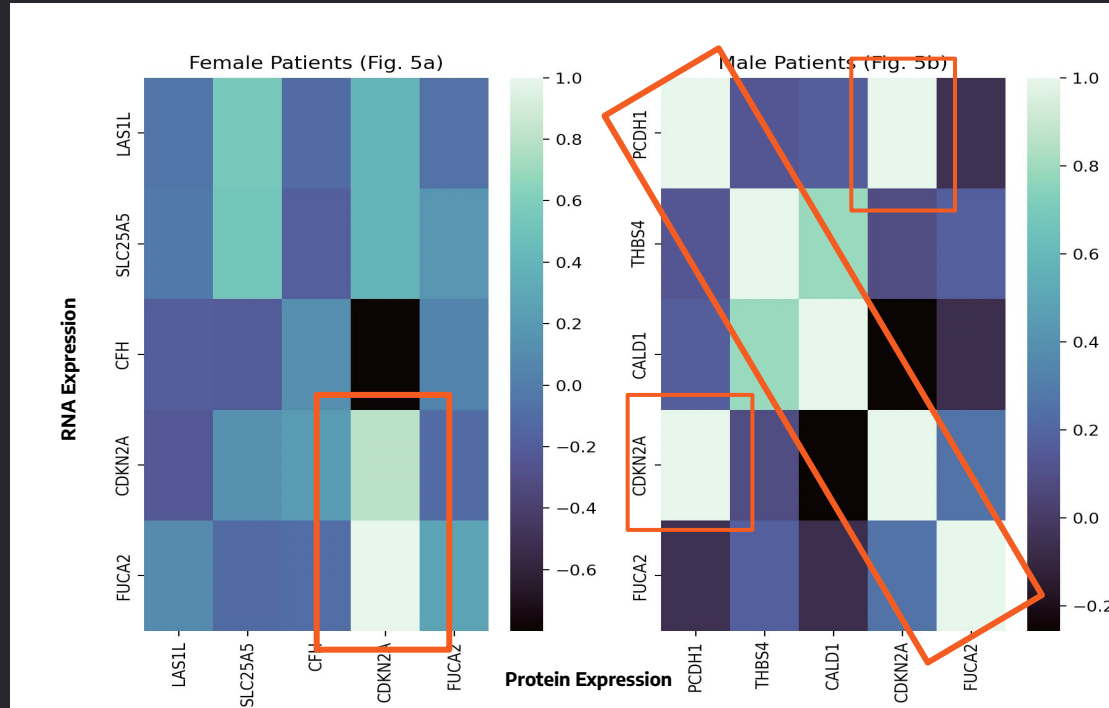

Top 5 most overexpressed genes for each tissue type that are unique to female patients are labeled

RNA & protein expression correlations are sexually differentiated

RNA & protein expression correlations are sexually differentiated

Discussion

- Evidence of sex-differentiated survival

- No significant mutation differences

- Identification of differentially expressed genes in male and female patients

  - *VSIG1, BPIFB1, CDKN2A, THBS4*

Genes of Interest for Female Patients

- *VSIG1* - cell to cell recognition
  - Overexpressed in female cancer tissue
  - Reduction in metastasis in multiple cancers → better survival rates

- *CDKN2A* correlated with *FUCA2*
  - Both involved in immune response

Genes of Interest for Male Patients

- *BPIFB1* - inflammatory gene
  - Overexpressed in male cancer tissue
  - Associated with tumor growth in gastric cancer

- *THBS4* - cell adhesion and migration
  - Underexpressed in male cancer tissue
  - Shown to act as a tumor suppressor gene in CRC

Future Directions

- Conduct further research on these genes of interest to potentially identify differences in clinical progression and survival

- Explore potential therapeutic options to target these genes and improve patient outcomes

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Thank You!
Questions?