



# Demographic, Health History, and Lifestyle Factors in Association with Biomarkers of Prognosis in **Colorectal Tumours**

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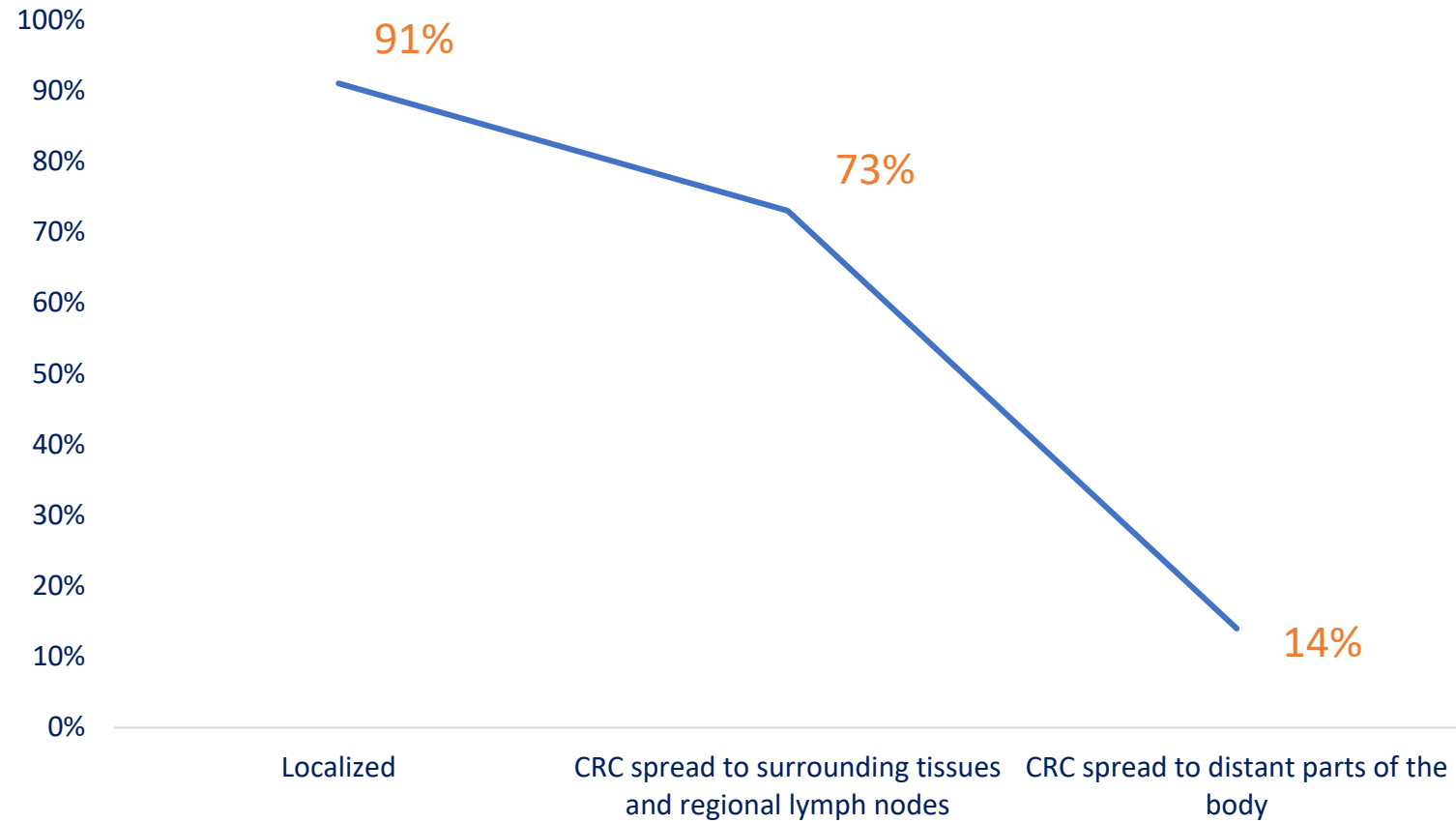




### Land Acknowledgement

I would like to begin by acknowledging that the land on which we gather is the unceded territory of the Coast Salish Peoples, including the territories of the xwməθkwəyəm (Musqueam), Skwxwú7mesh (Squamish), Stó:lō and Səlílwətaʔ/Selilwítulh (Tseil- Waututh) Nations.

# Colorectal Cancer (CRC) Survival



# Colorectal Cancer (CRC) Prognosis

- Demographic Factors
- Health History Factors
- Lifestyle Factors

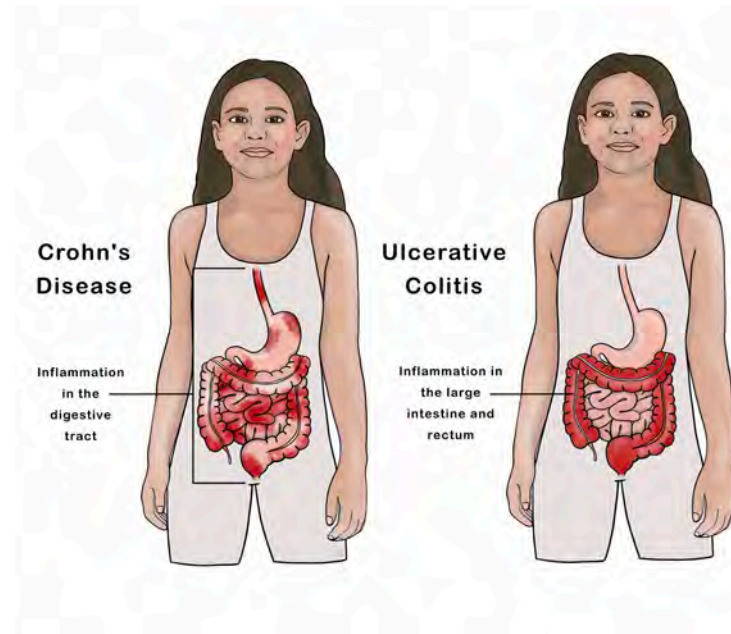
# Colorectal Cancer (CRC) Prognosis

## Demographic Factors

- Biological Sex
  - Mortality higher in men than women
- Age
  - Mortality higher in older than younger patients
- Race
  - African Americans have highest CRC mortality rates in the U.S.

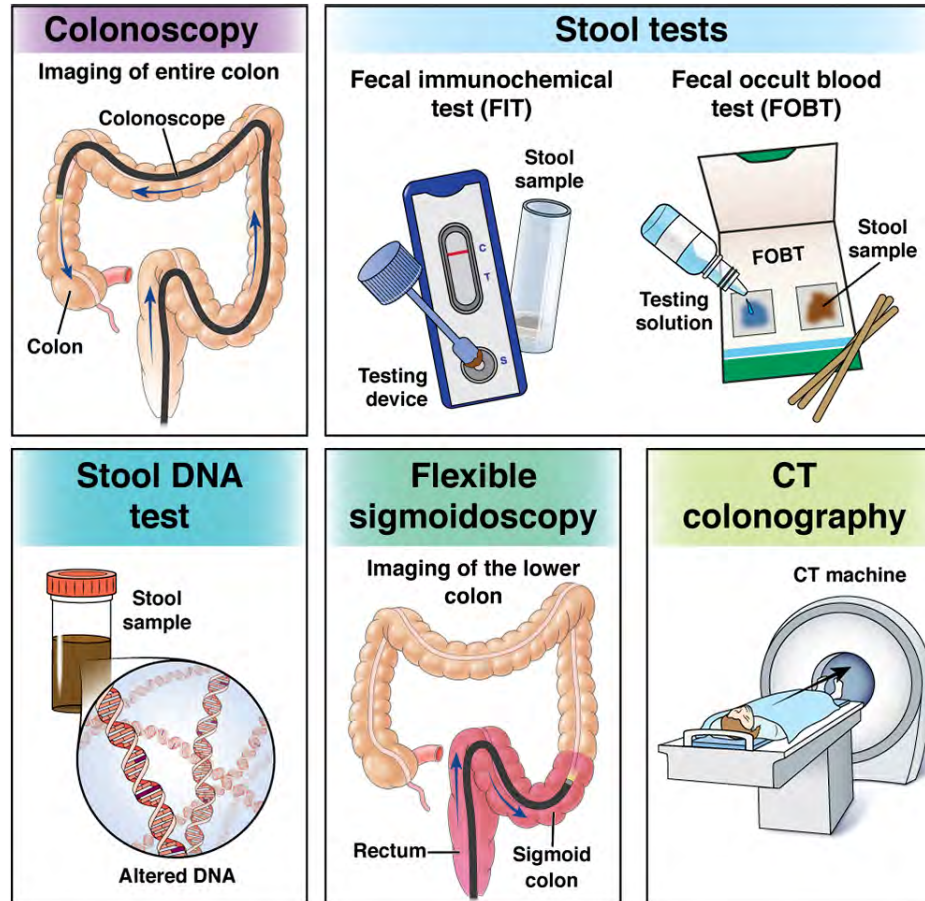
# Colorectal Cancer (CRC) Prognosis

## Health History Factors



# Colorectal Cancer (CRC) Prognosis

## Health History Factors



# Colorectal Cancer (CRC) Prognosis

## Lifestyle Factors



**No smoking**



**Moderate  
Alcohol  
consumption**



**Healthy  
Body mass  
index (BMI)**



**Good  
Physical  
Activity**



**Healthy Diet**



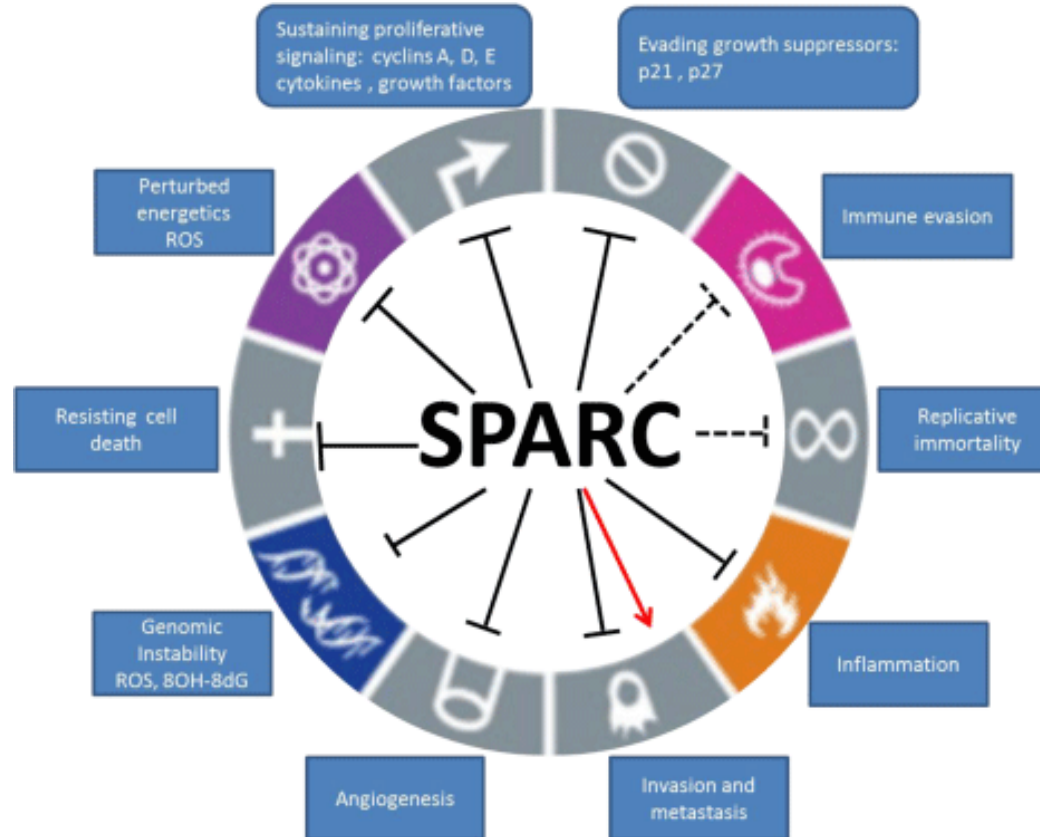
# Mechanisms Underlying Associations with Prognosis

- Biological Sex
  - Sex hormone impact on immune system
- Physical activity
  - Decreases in insulin and insulin-like growth factor

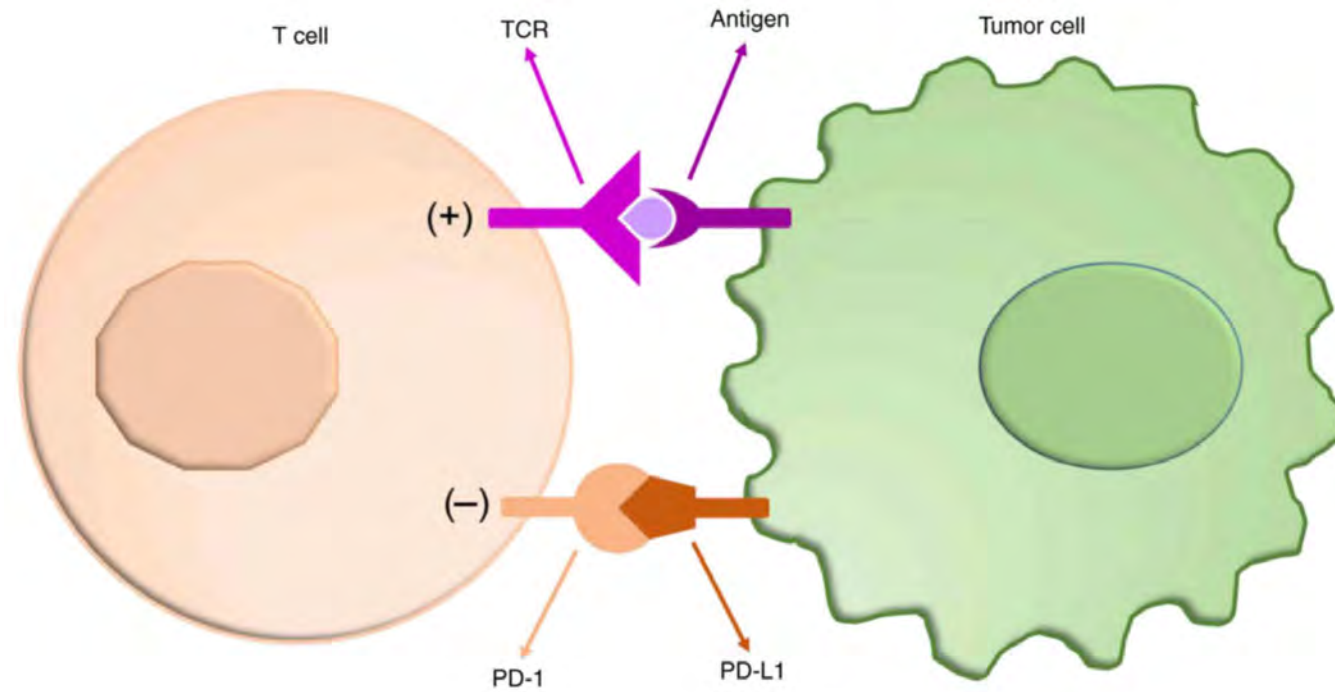
# Mechanisms Underlying Associations with Prognosis

- Biological Sex
  - Sex hormone impact on immune system
- Physical activity
  - Decreases in insulin and insulin-like growth factor
- Differences in expression of tumour markers may underlie multiple associations with prognosis

# Colorectal Cancer (CRC) and SPARC



# Colorectal Cancer (CRC) and PD-L1



# Study Objectives

To explore the association of factors with expression of two biomarkers of prognosis in CRC tumours, **SPARC** and **PD-L1**

# Study Methods


















## BC Generations Project

- 29,796 British Columbians
  - 2009 - 2016
  - 35 – 69 years of age
  - Completed baseline demographic, health, and lifestyle questionnaire



# BCGP Virtual Tumour Biorepository

## The BC Generations Project as a Tumor Tissue Resource for Cancer Research

by  Umaimah Zanif <sup>1</sup>  ,  Jessica Chu <sup>1</sup> ,  Jonathan Simkin <sup>1,2</sup>  ,  Trevor Dummer <sup>2</sup> ,  
 Ryan Woods <sup>1,3</sup> ,  Eric Belanger <sup>4</sup>   and  Parveen Bhatti <sup>1,2,\*</sup> 

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# Cases for Inclusion

115 incident CRC cases diagnosed in BCGP

University Health Network  
LABORATORY MEDICINE PROGRAM  
DEPARTMENT OF PATHOLOGY  
308 Spadina Street  
Toronto, Ontario, M5S 2C4  
Tel: 416-464-5500  
FAX: 416-464-5801

**Surgical Pathology Consultation Report**  
"Adapted"

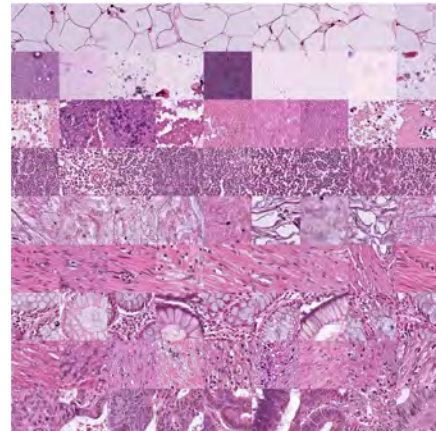
Requester: Pathway, MRCGP  
Specimen: 12248797C4  
Date: 12/24/2014  
Time: 10:24 AM  
Requester: Dr. Peter Watson  
Specimen: 12248797C4  
Date: 12/24/2014  
Time: 10:24 AM  
Requester: Dr. Peter Watson  
Specimen: 12248797C4  
Date: 12/24/2014  
Time: 10:24 AM

**Requested:**  
1. Colonoscopy, 12/24/14  
2. H&E slides  
3. IHC for CK20, CK7, CDX2, p53  
4. IHC for Ki-67  
5. IHC for p16  
6. IHC for p53  
7. IHC for p16  
8. IHC for p53

**Consolidated Therapeutic Report**

**Observations**  
Please refer to the attached slides for details. The slides are available for review at the University Health Network, 308 Spadina Street, Toronto, Ontario, M5S 2C4. The slides are available for review at the University Health Network, 308 Spadina Street, Toronto, Ontario, M5S 2C4. The slides are available for review at the University Health Network, 308 Spadina Street, Toronto, Ontario, M5S 2C4.

**Diagnosis**  
1. Colonoscopy, 12/24/14  
2. H&E slides  
3. IHC for CK20, CK7, CDX2, p53  
4. IHC for Ki-67  
5. IHC for p16  
6. IHC for p53  
7. IHC for p16  
8. IHC for p53



Resection reports for 69/115 located via BCGP Virtual Tumour Biorepository

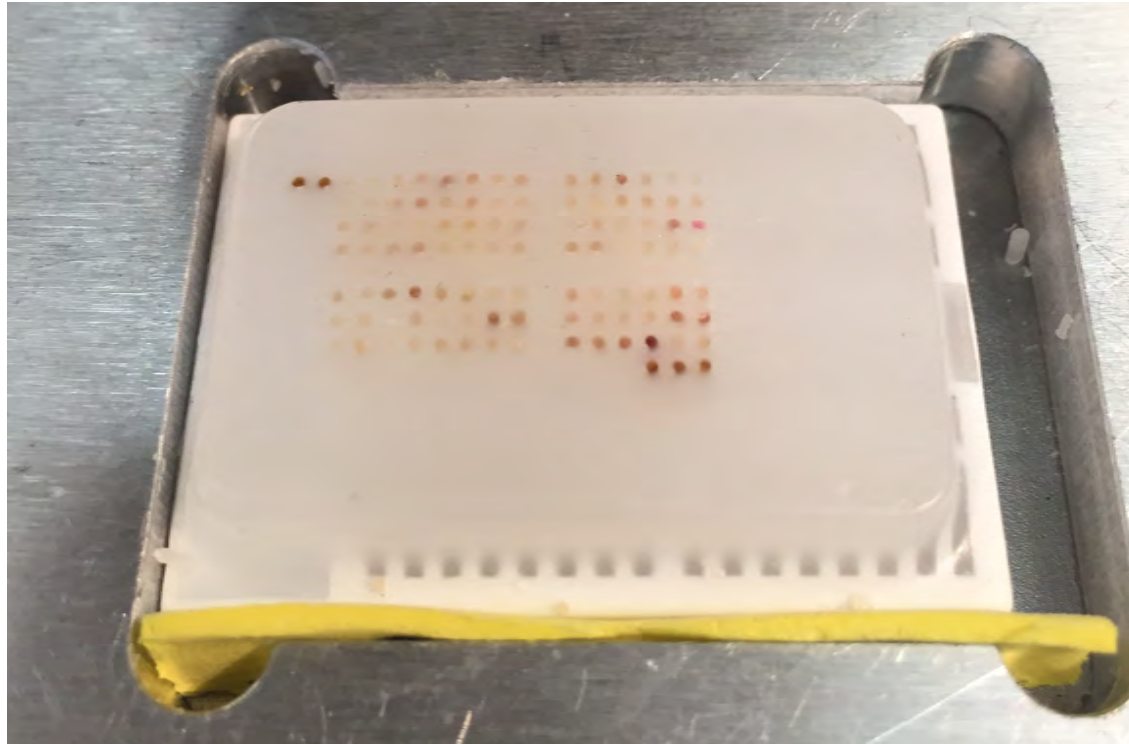
H&E slides requested for 61 cases from Provincial pathology labs

54 cases sent to Dr. Peter Watson at DRC to identify specific blocks for core extraction

FFPE Blocks for 54 cases requested and received

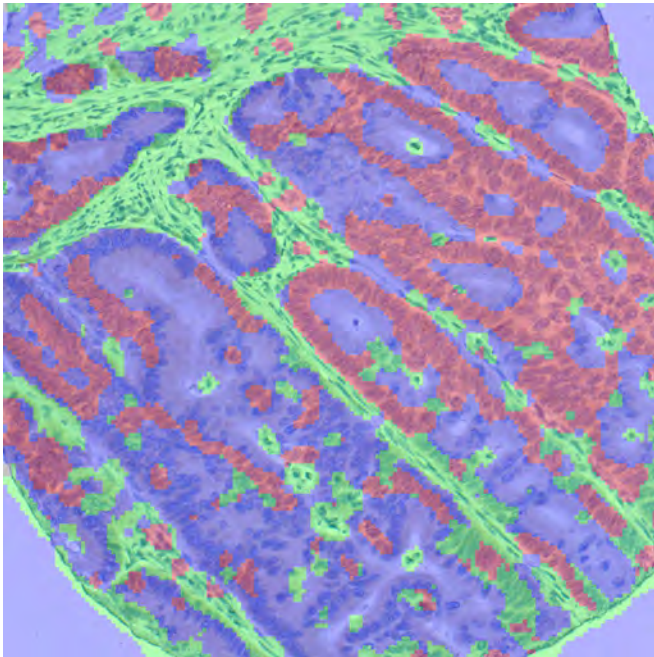


# Tissue Microarray (TMA) Creation

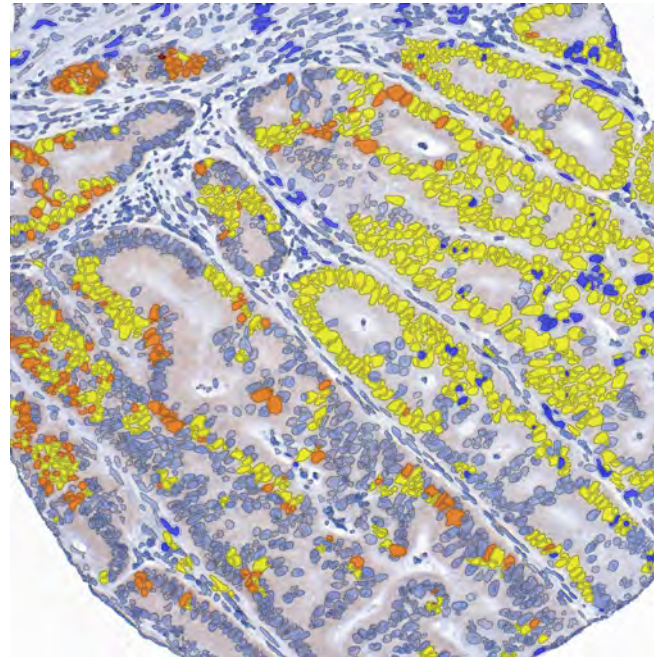


# IHC Staining SPARC

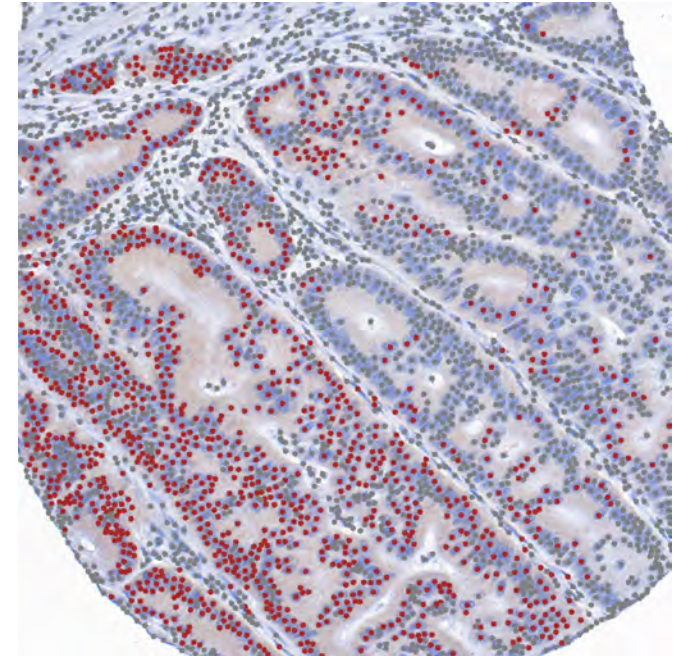
Tissue Segmentation Map



Score Map



Phenotype Map



# Data Analysis

- Linear regression analyses to evaluate associations of demographic, health history, and lifestyle factors (dependent variables) with ln-transformed SPARC and PD-L1 H-scores in epithelial and non-epithelial tumour tissues

# Study Results

Variable	N (%)
<b>BMI (kg/m2)</b>	
<25	15 (30.6%)
≥25	34 (69.4%)
<b>Sex</b>	
Female	26(53.1%)
Male	23(46.9%)
<b>Age at Dx</b>	
≤64	27 (55.1%)
>64	22 (44.9%)
<b>Ethnicity</b>	
White	46 (93.9%)
Non-White	3 (6.1%)
<b>Household Income</b>	
≤\$74 999/year	25 (51%)
>\$74 999/year	24 (49%)
<b>Education Level</b>	
Lower than bachelor's degree	25 (51%)
At Least bachelor's degree	24 (49%)

# Study Results

Variable	N (%)
<b>Colorectal Cancer Screening History</b>	
Ever	33 (67.3%)
Never	16 (32.7%)
<b>Hours slept per night</b>	
≥7 hours	34 (69.4%)
<7 hours	15 (30.6%)
<b>Fruit Consumption</b>	
≤2 servings/day	34(69.4%)
>2 servings/day	15(30.6%)
<b>Vegetable Consumption</b>	
<3 servings/day	22 (44.9%)
≥3 servings/day	27 (55.1%)
<b>Frequency of Alcohol Consumption</b>	
Once a week or less	22 (44.9%)
More than once a week	27 (55.1%)
<b>Ever Smoked at least 100 cigarettes</b>	
No	22 (44.9%)
Yes	27 (55.1%)
<b>Total physical activity MET-minutes/week</b>	
<median	22 (44.9%)
≥median	27 (55.1%)

# Study Results

## H-Score Distribution

Marker	H-Score				
	Mean	SD	Median	Minimum	Maximum
<b>SPARC</b>					
Tumor, epithelium	10.1	12.5	4.5	0.5	62.5
Tumor, non-epithelium	13.2	6.0	13.2	3.5	27.3
<b>PD-L1</b>					
Tumor, epithelium	3.2	6.1	1	0	39.5
Tumor, non-epithelium	5.9	8.2	2.7	0.3	39.8

# Study Results

Linear Regressions - SPARC

Variable	SPARC Epithelial Tissue			SPARC Non-epithelial Tissue		
	Ratio	95% CI	p-value	Ratio	95% CI	p-value
<b>Household Income</b>						
≤\$74 999/year		Ref.			Ref.	
>\$74 999/year	1.09	0.56, 2.12	0.79	1.33	1.02, 1.73	0.04
<b>Ever Smoked at least 100 cigarettes</b>						
No		Ref.			Ref.	
Yes	0.53	0.28, 1.00	0.05	0.88	0.67, 1.16	0.38

# Study Results

Linear Regressions – PD-L1

Variable	PD-L1 Epithelial Tissue			PD-L1 Non-epithelial Tissue		
	Ratio	95% CI	p-value	Ratio	95% CI	p-value
<b>Sex</b>						
Female	2.84	1.41, 5.74	0.005	1.66	0.86, 3.20	0.13
Male		Ref.			Ref.	
<b>Colorectal Cancer Screening History</b>						
Ever	2.18	1.00, 4.77	0.05	2.02	1.02, 4.01	0.05
Never		Ref.			Ref.	



# Study Strengths

- Detailed pre-diagnostic data on a variety of demographic, health history and lifestyle factors

## Study Limitations

- Small sample size
- 57% of cases excluded
- Tumour stage information limited

## Study Conclusions

Larger-scale studies with prognostic data are needed to confirm our findings, but our results suggest that differences in expression of SPARC and PD-L1 may contribute to the previously observed impacts of some demographic, health history, and lifestyle factors on CRC prognosis

# Acknowledgements

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Laura Game

Peter Watson

Jessica Chu



**BC Generations Project**

Your time today builds a healthier tomorrow.

Sindy Babinszky

Treena McDonald

Katy Milne

Jaclyn Parks

Talen Oostenbroek



**CanPath**

Canadian Partnership  
for Tomorrow's Health

**BC  
CAN  
CER**

CANCER CONTROL  
RESEARCH

Provincial Health Services Authority