









# THE ROLE OF THE VAGINAL MICROBIOME IN RACIAL DISPARITIES IN PRECANCEROUS CERVICAL LESIONS

Kathy Tossas, PhD, MS, Assistant Professor, HBP, Epidemiology Director, Office of Catchment Area Data Access & Alignment, Massey Cancer Center

## Disclosures

I have the following relevant financial relationships to disclose:

- Virginia Commonwealth University Employee
- Consultant for Flatiron Health Equity Scientific Advisory Board
- Pfizer Speaker's Bureau
- Grant/Research support from: ACS, Pfizer, NIH
- Stockholder in: Abbott



### Microbiome & Cancer PubMed, 2000 - 2023





#### HPV → Cervical Cancer: More than meets the eye





# The vaginal microbiome differs by R/E and is susceptible to our experiences



Images source: Chacra, et.al. (2021) *Microbial Pathogenesis* 



## Vaginal Microbiome Consortium





#### VAGINAL MICROBIOME CONSORTIUM

## Methods: Firth logistic regression

Research Question:	What is the role of the VMB in HPV-CIN and does it differ by Race?	CIN Risk = Race + Microbiome + HPV + Confounders
Main outcome:	Cervical Intraepithelial neoplasia, grade 3 (CIN3), dx anytime AFTER smp collection. Avg. f/u $\rightarrow$ 3.6 yrs	Race/Ethnicity
Main effect:	**VMB from (v1-v3) 16S rRNA taxonomic profiles of ~3,000 women collected at routine gyne visits, trichotomized based on <i>a priori</i> knowledge, by taxonomic abundance	
Secondary effect:	Self-reported race	Microbiome
Adjustments:	HPV, age, smoking, and pregnancy status	HPV CIN
Model:	Multivariable Firth Logistic Regression	

#### \*\*VMB:

- 1. "Lactobacillus crispatus"  $\rightarrow$  L. crispatus, L. gasseri and L. jensenii (all generally associated with gynecologic health)
- 2. *"L. iners"* (considered a transitional state)
- 3. "Other" → including taxa, such as Gardenerella vaginalis, Atopibium vaginae, Lachnocurva vaginae and others (often a/w adverse gynecologic outcom

## Results – Descriptive (3,020 women, 93 CIN3)

By race	AI (N=3,0	 )20)	Blacks (n=2,112; 70%)	Whites (n=908, 30%)	By CIN	Al (N=3,	l 020)	CIN3 (n=93)	<cin3 (n=2,927)</cin3 
Mean Age	34		33	36	<b>Mean Age</b> (p=0.14)	34	ŀ	32	34
HPV self-report (ever)					HPV status (ever)				
Positive	343	12	9	20	Positive	343	12	18	12
CIN3 status					Race				
<cin3< td=""><td>2927</td><td>97</td><td>96</td><td>98</td><td>Non-Latinx Blacks</td><td>2112</td><td>70</td><td>84</td><td>69</td></cin3<>	2927	97	96	98	Non-Latinx Blacks	2112	70	84	69
CIN3	93	3	4	2	Non-Latinx Whites	908	30	16	31
Vaginal Microbiome					Vaginal Microbiome				
Optimal	556	18	12	33	Optimal	556	18	8	19
L. iners	904	30	30	29	L. iners	904	30	28	30
Sub-optimal	1560	52	58	38	Sub-optimal	1650	51	63	50

\*All vars significant at p<0.05 unless otherwise noted



## Results – Associative (3,020 women, 93 CIN3)





#### The interaction suggest perhaps adaptive immunity?



# Re-do with actual HPV+ @ sampling (N=530, CIN3=54) HPV+ @ MPV+ @ MPV+ Women with

Table 1: Imputed Data Model Results (10 datasets, kNN imputation, k-5)

	<u>Transitory vs. Low-Risk</u>			<u>High-Risk vs. Low-Risk</u>			
Model	OR	95% CI	p-value	OR	95% CI	p-value	
Unadjusted	1.9	0.8, 5.4	0.17	3.1	1.4, 8.2	0.01	
*Race-Adjusted	1.7	0.7, 4.5	0.27	2.7	1.1, 6.5	0.03	
<b>Race-Interaction</b>	No Significant Interaction Terms						



\*Other variables considered but not included based on BIC criteria: age, marital, income, edu, etc.

suboptimal VMB

have  $\sim$ 2X the risk of

CIN3 vs. those with

optimal VMB

# The lack of interaction suggest perhaps HPV evasion



## How important is the VMB in Race $\rightarrow$ CIN3?



Paths to HSIL					
N=1,168	Coefficients	pct			
B₩→HSIL	0.021	65%			
BW→GBU→HSIL	0.012	36%			
BW→HPV→GBU→HSIL	2.4864E-07	0%			
B₩→HPV→HSIL	-0.0002627	-1%			
SUM	0.032257549				
The following paths were statistically significant at					

The following paths were statistically significant at p<0.05: BW $\rightarrow$ GBU; GBU $\rightarrow$ HSIL

\*adj for BW, GBU

Non-trivial! 36% of the race  $\rightarrow$  HSIL association mediated through VMB. Mechanistic, prophylactic, therapeutic implications... (VMB amenable to pre and probiotics).

na man says PA increased his meds, made him think he wa / for pointing out flag

Tyree & Kaicey Baylor | Thursday, July 16th 2020



called his doctor Pamela C/Dell through video chat Friday afternoon and when he pointed d by David Wilson)

GRETNA, Va. (WSET) -- A Gretna man says his Danville physician assistant increased his medication dosage after he noticed a confederate flag on the PA's wall.

Donald Wilson is diagnosed with anxiety and PTSD, causing him to seek psychiatric care.

What he thought would be a regular follow-up appointment, Wilson said turned into a traumatic experience.

Wilson called his healthcare professional, Pamela O'Dell, through video chat Friday afternoon. When he noticed O'Dell, sitting by a confederate flag, he said it caught him off guard.



## What is the VMB "channeling"?



Next: K01 - How would race "work through" the VMB to promote HSIL?



# Other Funded Projects

Acknowledge/redistribute institutional power → shift from equity to justice needs power/privilege redistribution via allyship, sponsorship

#### Does the VMB play a role in HPV carcinogenicity? (HPV L1 genetic heterogeneity)



Race

![](_page_17_Picture_2.jpeg)

### **Community Projects**

Chickahominy TRUTH Project Funder: Jeffress Trust

![](_page_18_Figure_2.jpeg)

Chickahominy TRUTH Project Funder: RWJF

![](_page_18_Picture_4.jpeg)

![](_page_18_Picture_5.jpeg)

Project COALESCE Funder: Pfizer

Signs prohibited on

state roads: VDOT

code (33.2-1204)

Community Health Center 🔶

### My work at the Massey Cancer Center

Virginia Commonwealth University Massey Cancer Center Data Portal

Powered by SAS

![](_page_19_Picture_3.jpeg)

![](_page_19_Picture_4.jpeg)

### The Coquí lab – Cancer Outcome Queries to Understand Inequities

![](_page_20_Picture_1.jpeg)

Savannah Reitzel, 2<sup>nd</sup> yr PhD AACR Scholar-in-training award Hot Topics Talk!

![](_page_20_Picture_3.jpeg)

Bianca Owens, PhD candidate AACR Minority Scholar Award Poster

![](_page_20_Picture_5.jpeg)

Josly Pierre-Louis, 2<sup>nd</sup> yr PhD GMaP Travel Award Poster

![](_page_20_Picture_7.jpeg)

Shreya Raman, M3 AACR Scholar-in-training award Poster

#### Newly arrived advisees:

- Paula Tatiana Rivera Mejia 1<sup>st</sup> yr, PhD. Fulbright scholar
- Kira Randolph, 2<sup>nd</sup> yr MPH
- Yazmin Woodard, 1<sup>st</sup> yr MPH
- Kimberly Borrero, BS→Med school

![](_page_20_Picture_14.jpeg)

![](_page_20_Picture_15.jpeg)

#### Gretna man says PA increased his meds, made him think he was crazy for pointing out flag

AA

by Elizabeth Tyree & Kaicey Baylor | Thursday, July 16th 2020

![](_page_21_Picture_2.jpeg)

nfederate flag in the background, he said that Dr. O'Dell in

f 

GRETNA, Va. (WSET) -- A Gretna man says his Danville physician assistant increased his medication dosage after he noticed a confederate flag on the PA's wall.

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**Differences in Race-Related Stress Experiences between** members of community organizations (19% White, 71% Black) and FQHC staff (75% White, 20% Black)

![](_page_21_Figure_10.jpeg)

## **Acknowledging & Redistributing Power**

![](_page_21_Picture_12.jpeg)

#### **Policy - The Alberta Clinic Sign**

![](_page_22_Picture_1.jpeg)

![](_page_22_Figure_2.jpeg)

![](_page_22_Picture_3.jpeg)

![](_page_22_Picture_4.jpeg)

Signs prohibited on state roads: VDOT code (33.2-1204) Map of State-Owned Roads, Total and Affected Federally Qualified Health Centers in Virginia

![](_page_22_Picture_7.jpeg)

123 clinics, ~239,000 pt

![](_page_22_Picture_9.jpeg)

## Chickahominy TRUTH Project

Trust, Research, Understand, Tell, Heal

![](_page_23_Picture_2.jpeg)

![](_page_23_Figure_3.jpeg)

![](_page_23_Picture_4.jpeg)

![](_page_23_Figure_5.jpeg)

![](_page_24_Figure_0.jpeg)

![](_page_24_Figure_1.jpeg)

#### Current Map: 60 cancers

#### Original Map: ~15 cancers

#### Cancer Distribution

Туре	Count	Pct	Endocrine- related?	Associated with water pollution	Occupational/air	all
bladder	1	2%		1		1
brain	3	5%		1		1
Breast	19	32%	1			1
Colon	8	13%		1		1
Kidney	2	3%		1		1
Leukemia	3	5%				0
liver	3	5%				0
lung	7	12%			1	1
Lymphoma	2	3%				0
ovarian	1	2%	1			1
prostate	4	7%	1			1
rectal	1	2%		1		1
stomach	2	3%		1		1
stomach/perineum	1	2%		1		1
testicular	1	2%	1			1
Unsure/Unknown	2	3%				0
Grand Total	60	100%	4	7	1	12

#### The Chickahominy TRUTH Project

Jeffress Trust

EnviroTestKit

sale

is as easy as 000

![](_page_26_Picture_2.jpeg)

- <u>R</u>esearch Identify knowledge gaps | Collect hx prioritizing affected families (engaging survivors as T-to-T to disseminate tools) | Test well water | research policies, etc.
- <u>U</u>nderstand summarize data, jointly discuss to understand
- <u>T</u>ell Disseminate results using mixed media (video, print) and Traditional Knowledge practices (orally, etc.)
- <u>H</u>eal Collectively give and receive healing through information, respect, as a form of (health or data) reparations

#### Draft Budget – 2 years, \$150 K

- \$63,097 VCU staff
- \$89,903 Chickahominy Tribe
  - \$32,000 well water testing kits
  - \$10,000 Chickahominy Health District
  - \$6,000 community dissemination (townhalls, videos, infographics, Traditional Knowledge)

## **Specific Aims**

1. Identify structural factors and barriers associated with perceived cancer risk, and cancer care

2. Assess cancer knowledge and access to care gaps as well as perceived risks, including testing individual (wells) and community (creeks) water sources using EPA-certified testing

3. Develop and deploy culturally-tailored cancer education and resource navigation, including groundwater safety education, policies and remediation.

![](_page_28_Picture_0.jpeg)

#### This kit provides testing for 200 contaminants:

(Bacteria) – Total Coliform & E. Coli,

 (32 Metals) – Aluminum, Antimony, Arsenic, Barium, Beryllium, Boron, Cadmium, Calcium, Chromium, Cobalt, Copper, Hexavalent-Chrome, Iron, Lead, Lithium, Magnesium, Manganese, Molybdenum, Nickel, Phosphorus, Potassium, Selenium, Silica, Silicon, Silver, Sodium, Strontium, Thallium, Tin, Vanadium, Zinc.

• (12 Physical Properties) – Alkalinity, Hardness, Tannin/Lignin, pH, Total Dissolved Solids, Turbidity, Bicarbonate, Carbonate, Conductivity, Langelier Saturation Index, Ryznar Stability Index, Aggressive Index.

• (7 In-organics) – Chloride, Fluoride, Bromide, Nitrate-N, Nitrite-N, Sulfate, Orthophosphate.

• (**Pesticides**): Aldrin, Chlordane, Dieldrin, Endrin, Heptachlor, Heptachlor Epoxide, Hexachlorobenzene, Hexachlorocyclopentadiene, Lindane, Methoxychlor.

• (Herbicides): Alachlor, Atrazine, Butachlor, Metolachlor, Metribuzin, Propachlor, Simazine

- (Plasticizers): Di(2-ethylhexyl)adipate, Di(2-ethylhexyl)phthalate
- (Mutagenic and Highly Carcinogenic): Benzo(a)pyrene-(PAH)

• **(TTHM's Package) – Volatile Organics:** Chloroform, Bromoform, Chlorodibromomethane, Bromodichloromethane, Total THM's

- 78 Volatile Organic Compounds)
- (47 VOC TIC's): Tentative Identifiable Compounds

![](_page_29_Picture_0.jpeg)

![](_page_30_Picture_0.jpeg)

![](_page_30_Picture_1.jpeg)

![](_page_31_Picture_0.jpeg)

#### Results, part 1 – Associative (3,020 women, 93 CIN3)

Adjusted	Stratified (race*VMB, p=0.04)			
(BW, VMB, HPV, age, pregnt, smoke)	by VMB (within race)	by race (within VMB groups)		
2.0 (1.1, 3.9)	7.8 (1.7, 74.5)	6.0 (1.3, 56.9)		

![](_page_32_Figure_2.jpeg)

#### **The Natural History of HPV Infection**

![](_page_33_Figure_1.jpeg)

![](_page_34_Figure_0.jpeg)

t-SNE plots of beta diversity (Bray-Curtis distance) and composition of the vaginal microbiome associated with race and CIN3. (a) Beta diversity quantified by Bray-Curtis distance and visualized by the t-distributed stochastic neighbor embedding plot in participants with different races and CIN3 states is shown. The association between beta diversity of the vaginal microbiome and CIN3 was measured by the Adonis test. (b) db-RDA analysis to show the composition of the microbiomes and the relative abundance of taxa associated with two factors, i.e., race and CIN3 state. Microbiomes with CIN3 negative and positive are color-coded by red and green, respectively. Each blue dot represents a taxon.