



University for the Common Good



# Ryan Kean Anaerobe 2024

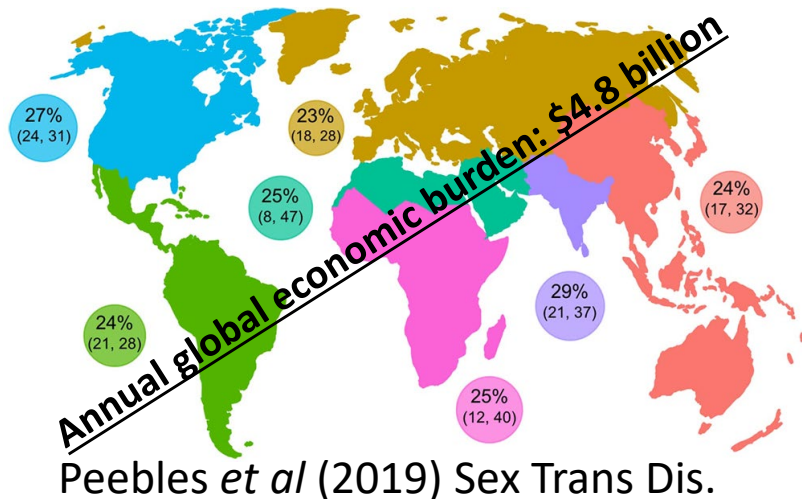
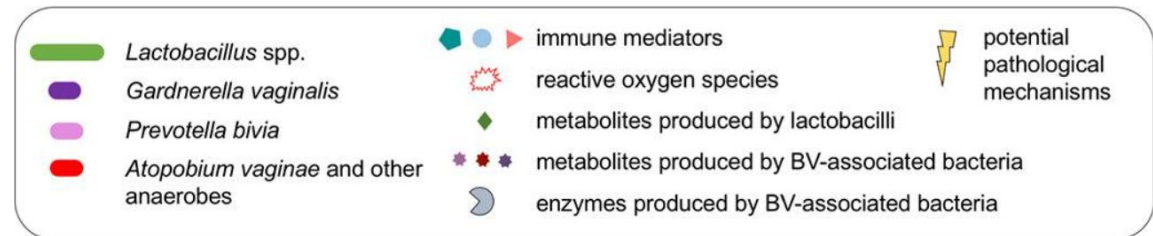
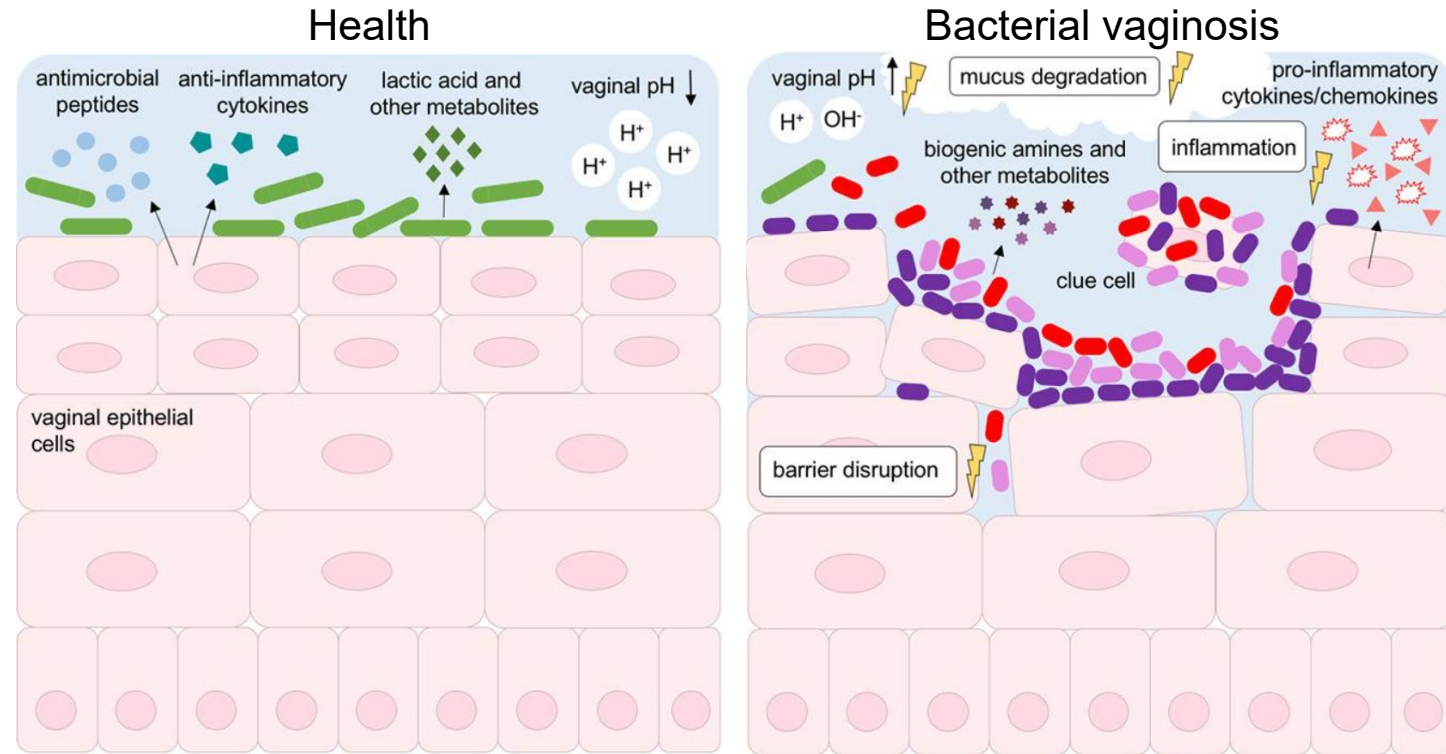
## Application of endolysins as novel antimicrobials against bacterial vaginosis



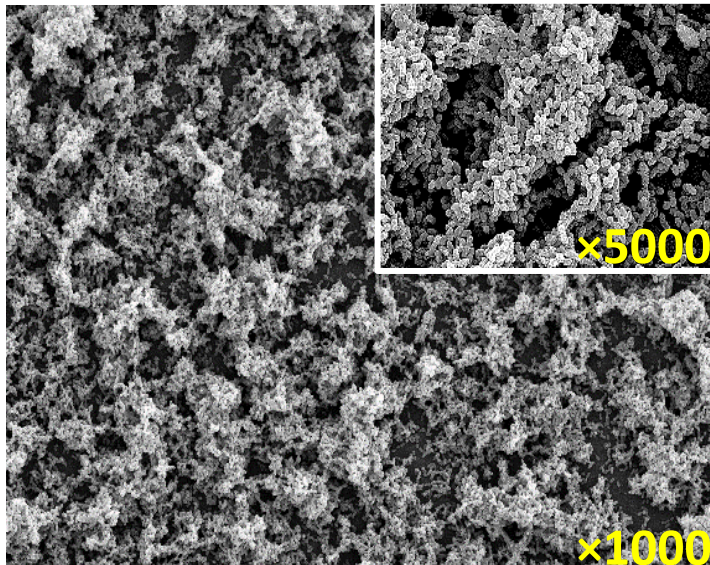
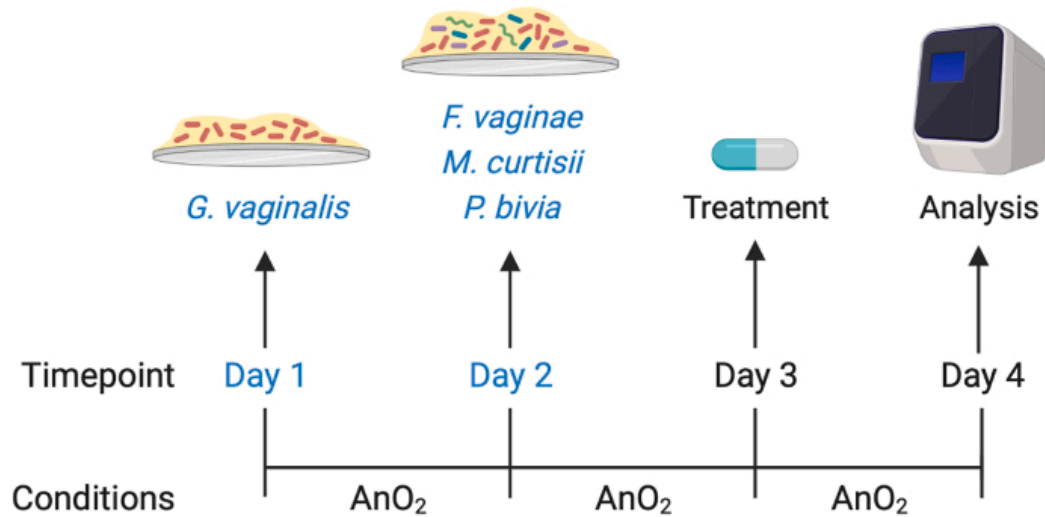
@ryankean29

# Biofilms in Bacterial Vaginosis

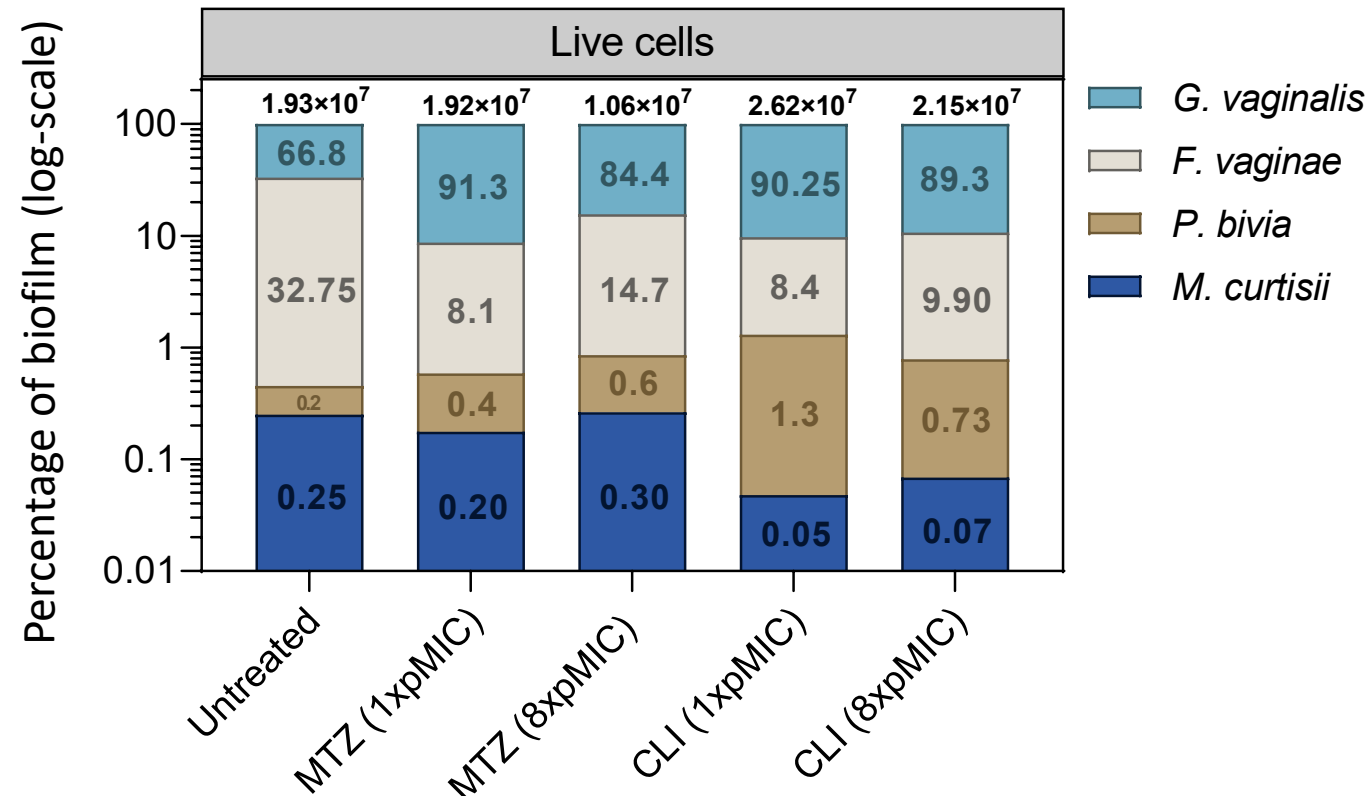
- BV is caused by a dysbiosis of the healthy microbiome (primarily lactobacilli)
- Currently, it is believed that *Gardnerella vaginalis* acts as the initial binding organism in BV, elevating the pH and allowing other anaerobes to grow



# Novel BV Biofilm Model

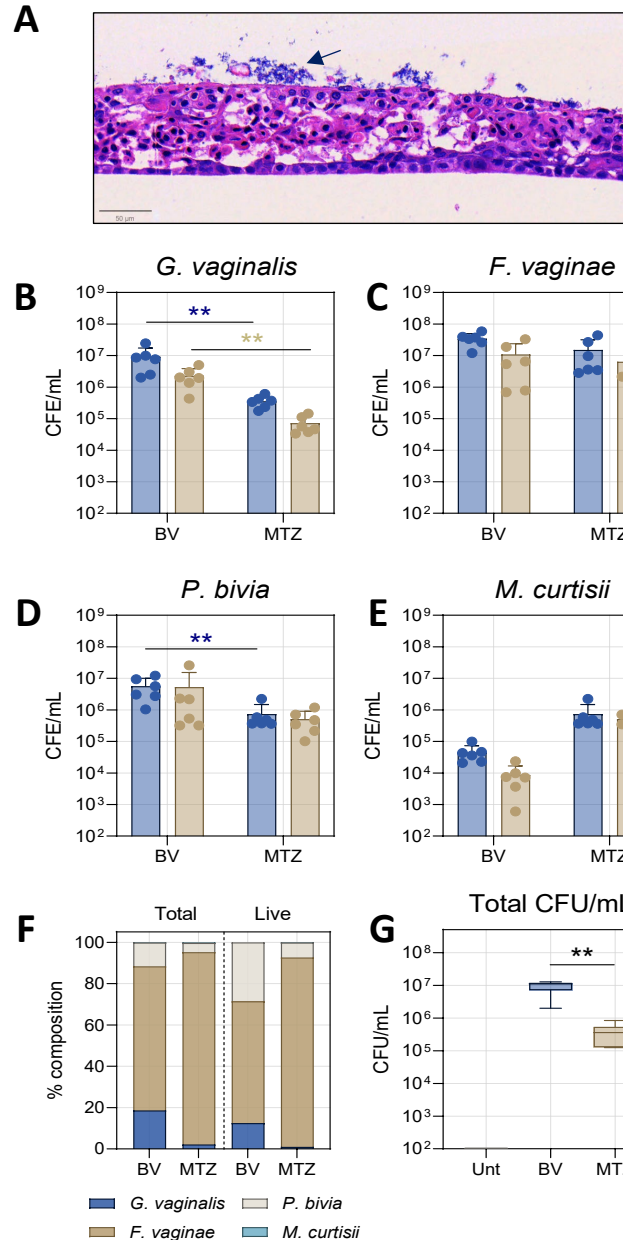


- Compositionally representative of BV
- High(ish) throughput
- Tolerate clinically relevant concentrations of antimicrobials

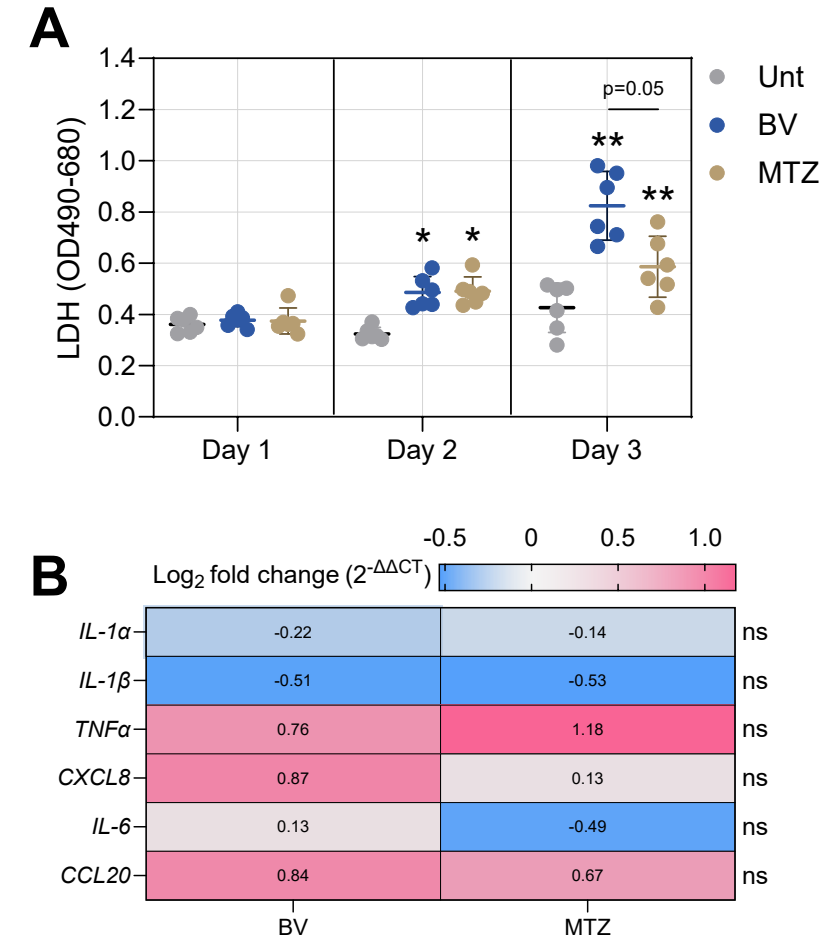


# BV Biofilm co-culture system

- Organotypic model is compositionally different from other model
- High MTZ treatment reduces *G. vaginalis* load but not accessory pathogens.
- Small reduction in cytotoxicity and inflammatory profile with MTZ treatment – accessory pathogens potentially driving recurrence.



EPISKIN



Johnston *et al* Unpublished.



# Research areas of interest

## Live Biotherapeutic Products

- Anti-biofilm activity
- Mechanism(s) of action
- Engraftment potential

## Antimicrobial potential of endolysins

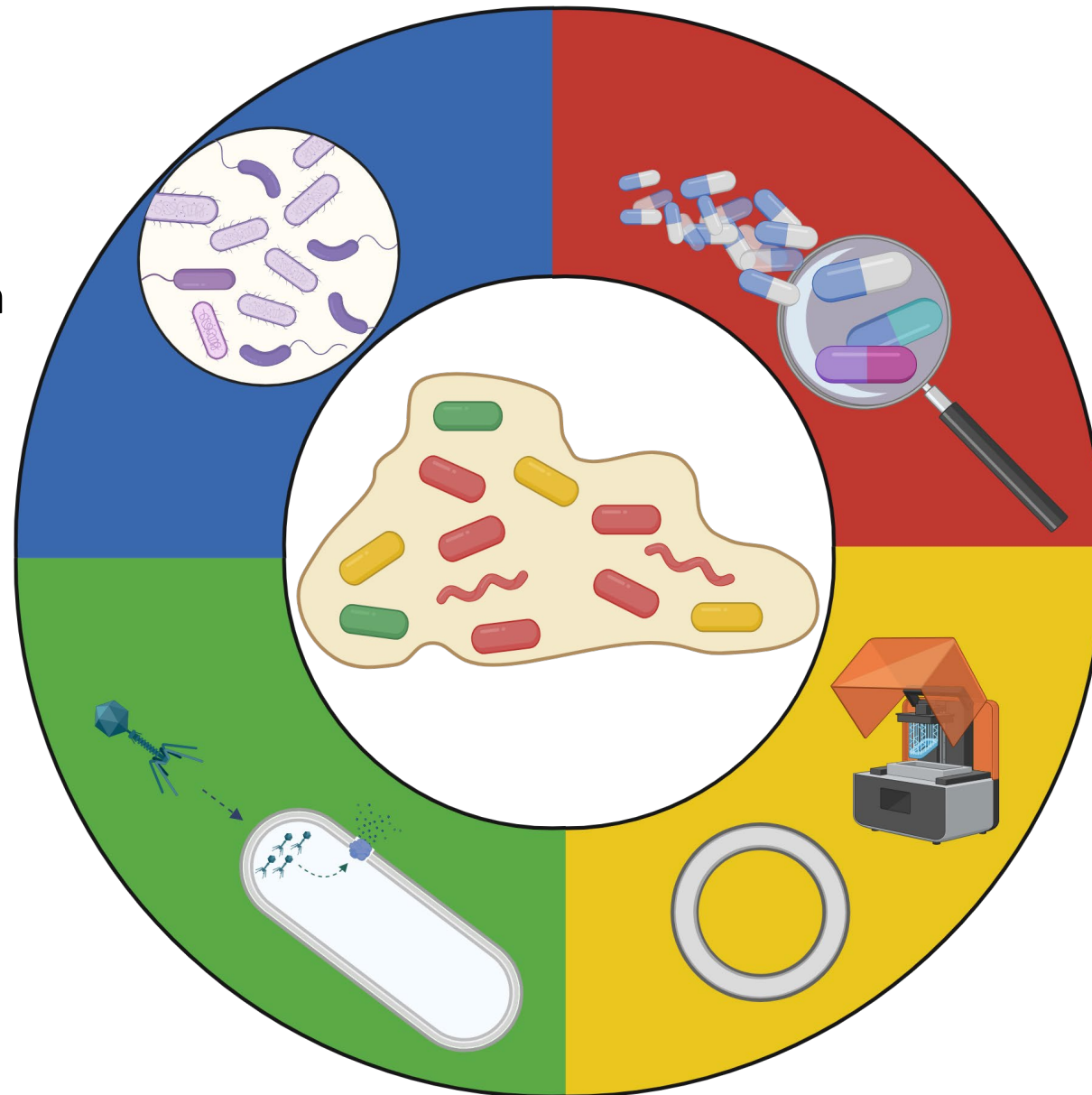
- Species-specificity and antibiofilm potential
- Payload delivery using LBPs

## Drug repurposing

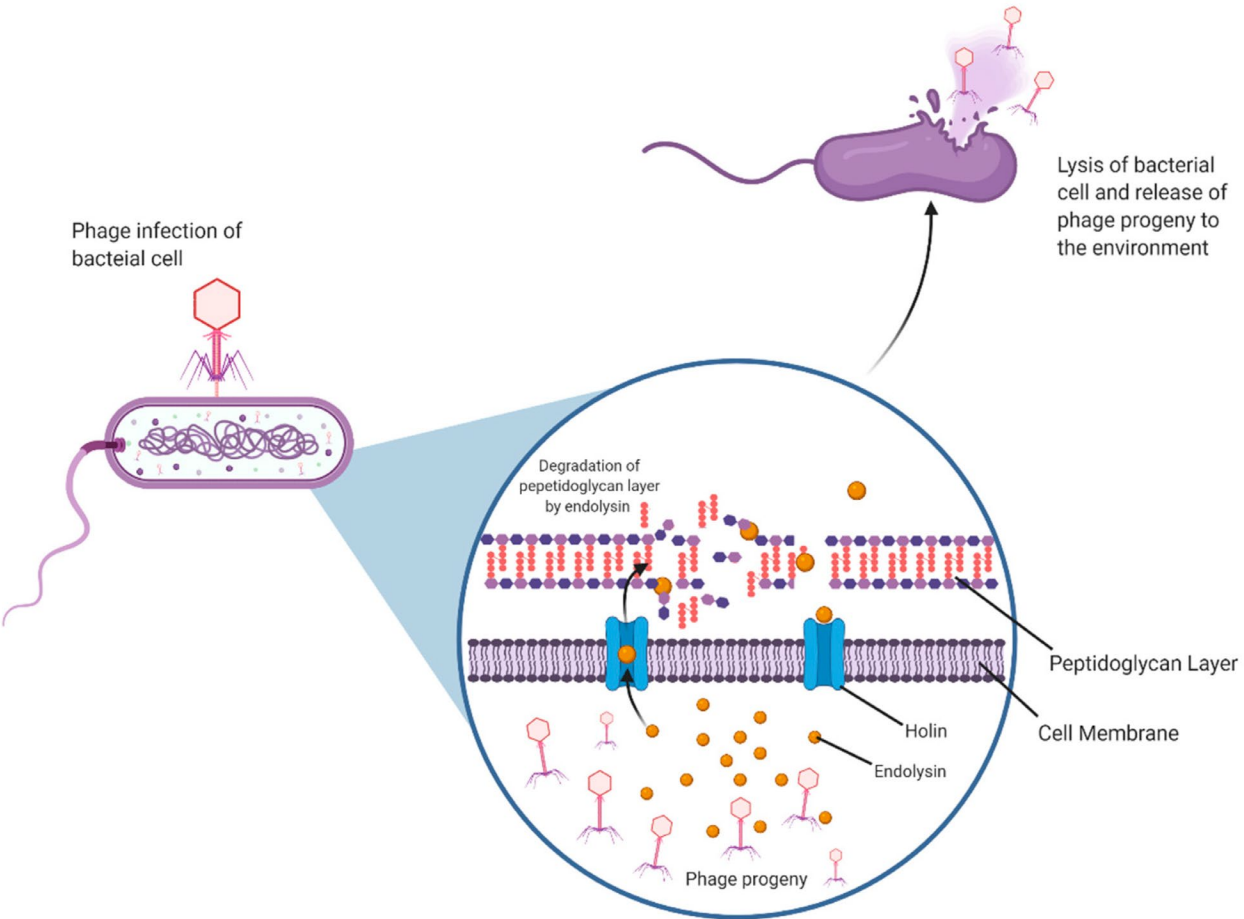
- Screened >2100 compounds to date
- Selectivity for pathogens
- Cross-kingdom activity

## Antifouling medical devices

- 3-D printing & additive manufacturing to increase biocompatibility
- pH responsive coatings for drug release

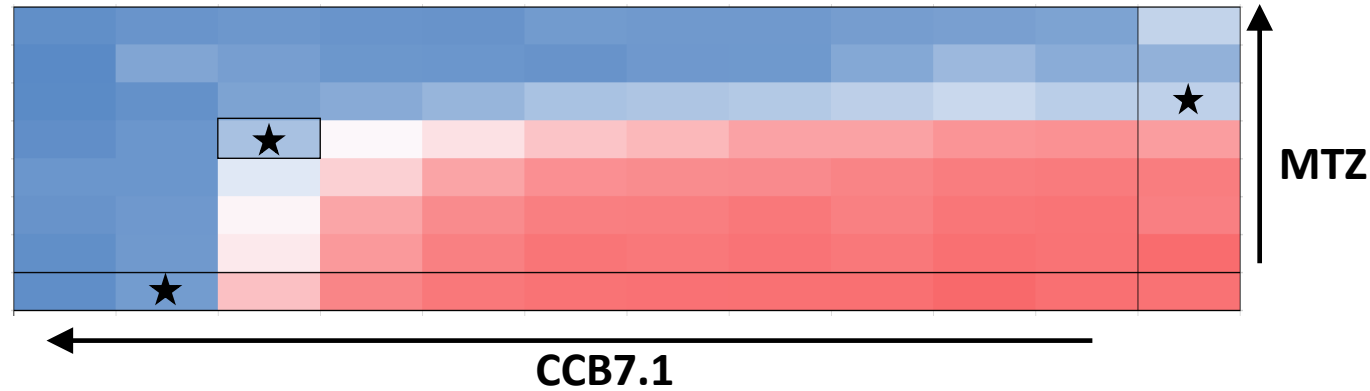
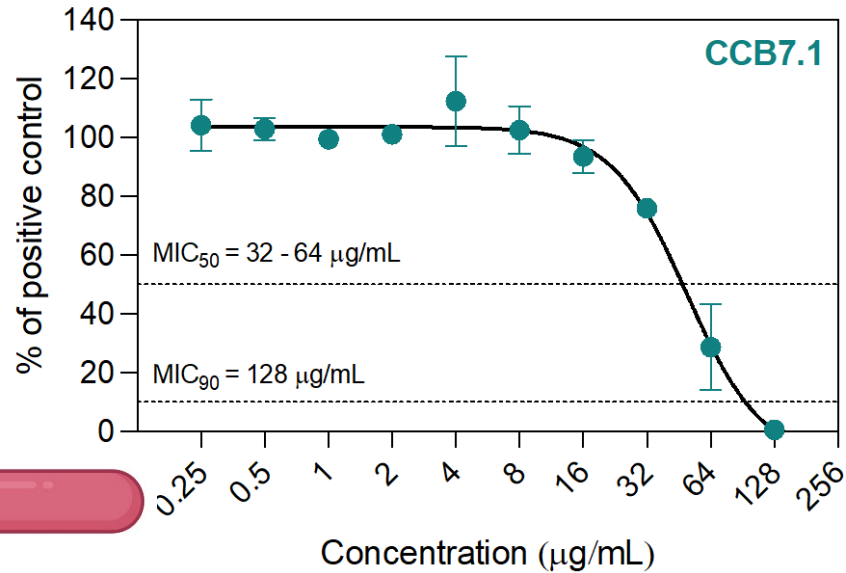


# Endolysins – Targeted Proteins



Murray *et al* (2021) *Viruses*.

# Endolysins – Planktonic activity



Additive activity with metronidazole FIC = 0.5

Dose dependent activity against *G. vaginalis*

<i>Lactobacillus jensenii</i> DSMZ 20557	>256	>256	0.12
<i>Lactobacillus crispatus</i> DSMZ 20584	>256	>256	0.06
<i>Gardnerella swidsinskii</i> CCUG 72429T	32	≥256	>32
<i>Gardnerella piotii</i> CCUG 72425T	64	≥256	0.5
<i>Gardnerella vaginalis</i> ATCC 14018	128	8	0.06
	CCB7.1	MTZ	CLI

Genus level activity against *Gardnerella spp.* No activity against lactobacilli

Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

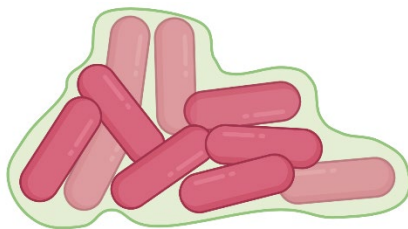
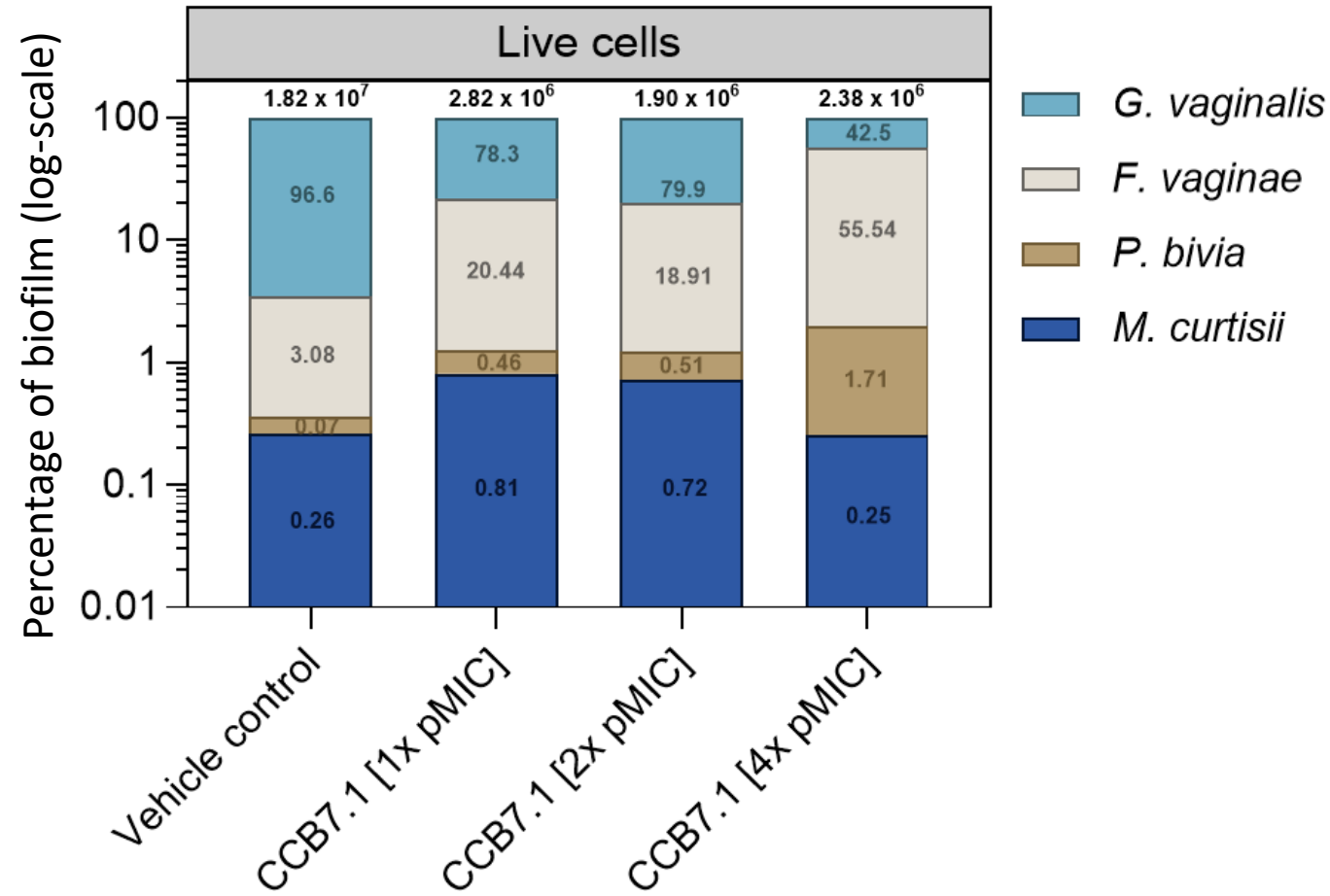
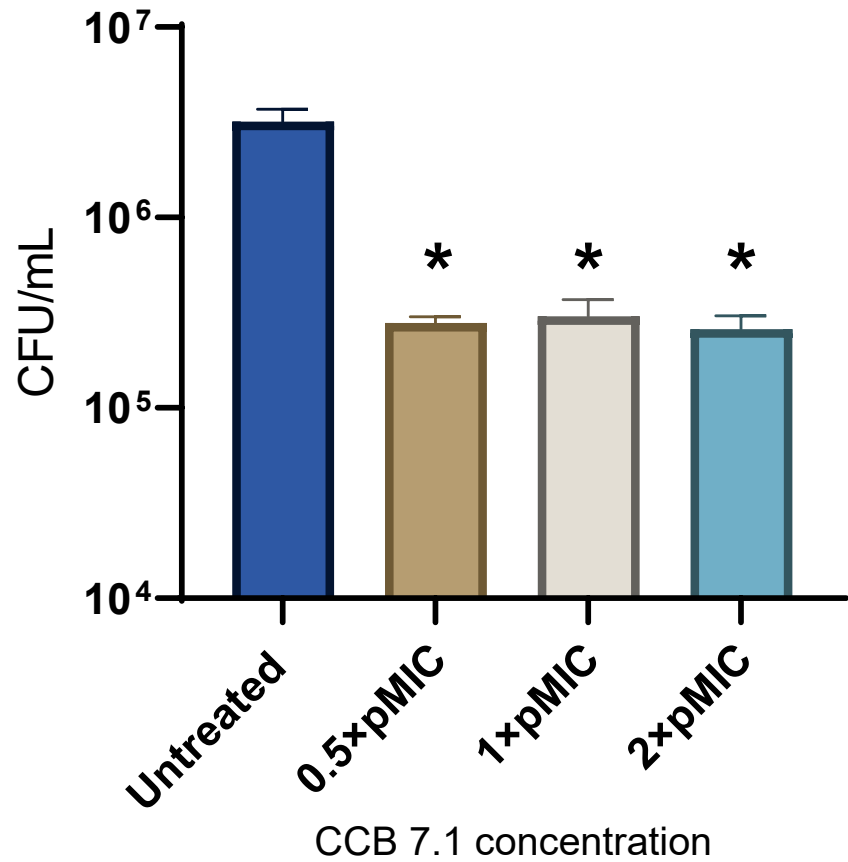
**Biofilm**

ELSEVIER journal homepage: [www.sciencedirect.com/journal/biofilm](http://www.sciencedirect.com/journal/biofilm)

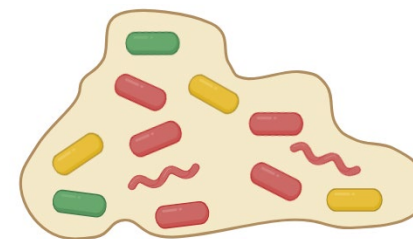
*In vitro* bacterial vaginosis biofilm community manipulation using endolysin therapy

William Johnston<sup>a,b</sup>, Alicia Ware<sup>a,b</sup>, Willemijn Frederique Kuiters<sup>a</sup>, Christopher Delaney<sup>b,c</sup>, Jason Lee Brown<sup>b,c</sup>, Suzanne Hagen<sup>d</sup>, David Corcoran<sup>e</sup>, Matthew Cummings<sup>e</sup>, Gordon Ramage<sup>b,c</sup>, Ryan Kean<sup>a,b,\*</sup>

# Endolysins – Biofilm activity



Johnston *et al* (2023) Biofilm.





# Acknowledgments



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David Corcoran  
Madeline Butler  
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