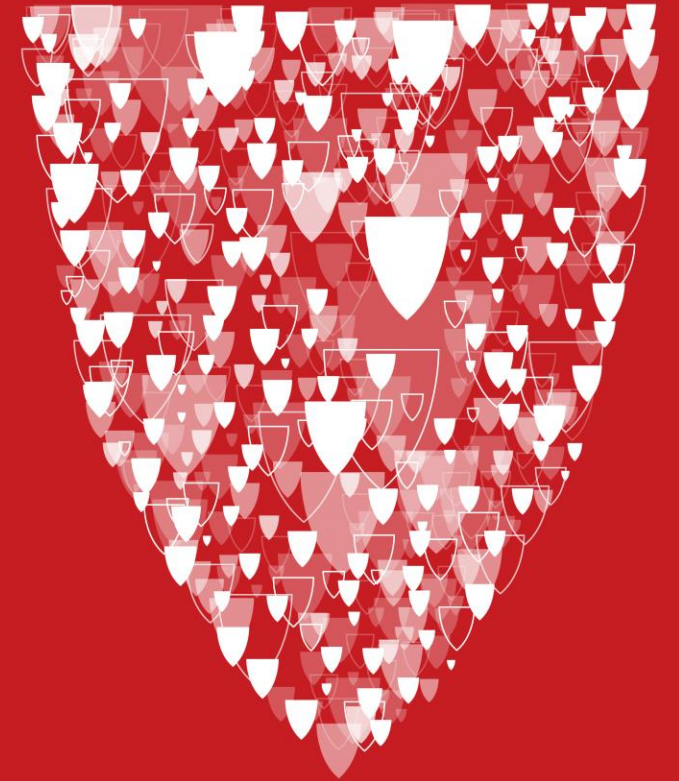


Deep Learning & Microbiome Pharmacology

- UH Research Day
- Douglas Brubaker



Disclosures

- **Patent: U.S. Application No. 63/747,418**
- **Scientific Advisory Board, Treasure Biosciences**
- **Unpublished Data – Please No Photos or Sharing**

Understanding Microbiome Influences on Host Cellular Biology



Damilola Lawore, MS
Vaginal Microbiome
Cancer Therapeutics
Immune Cell Engineering



Xia-Ying (Rachel) Liu
Gut Microbiome
Colorectal Cancer
Therapeutics &
Prognosis



**Smrutiti Jena PhD
(Alumni)**
Vaginal Microbiome
Antibiotic Resistance
Metabolism & Biofilm



Raymond Krajci, MBA
Database management
Algorithm standards
Project coordination



Alexis Heath
Vaginal Microbiome
Infertility & IVF
Endometriosis



**Javier Muñoz PhD
(Alumni)**
Gut Microbiome
IBD
Multi-omics



Alex Bergendorf
Gut Microbiome
AI and Deep Learning
IBD, Psoriasis

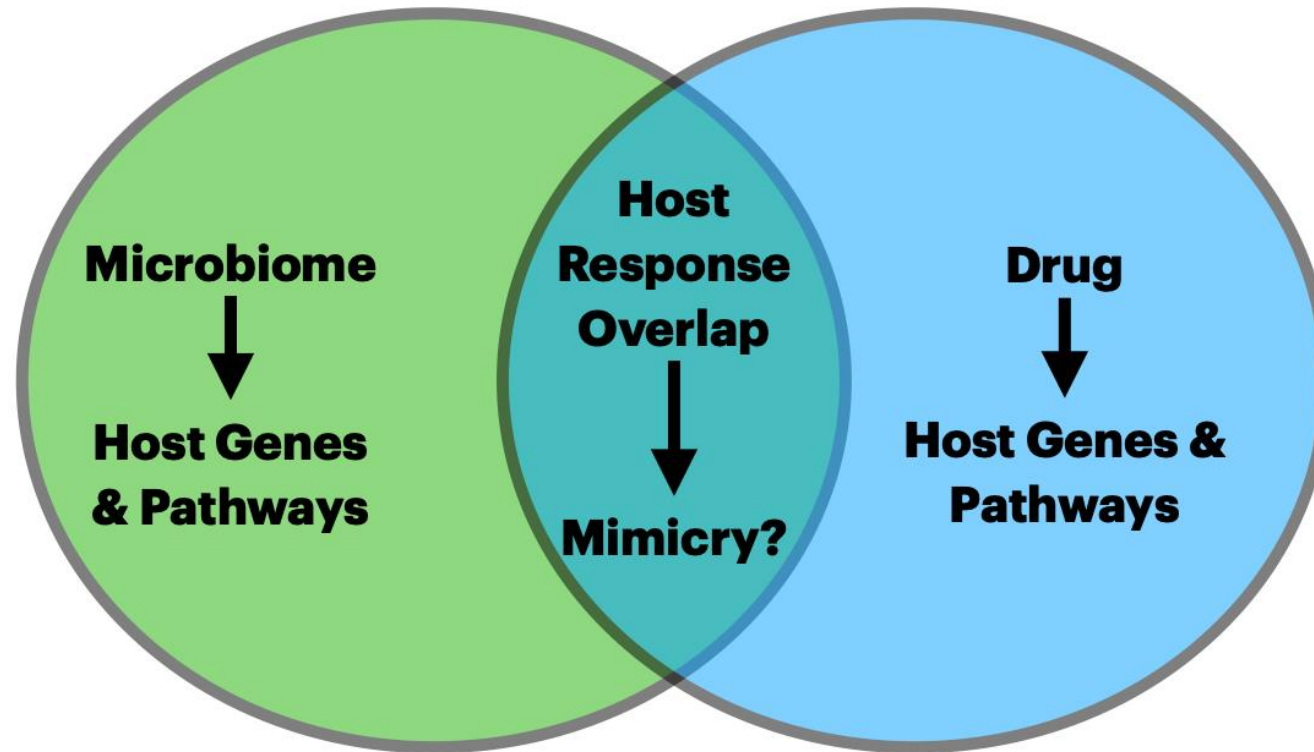


Dali Nemecio
Gut/Vaginal Microbiome
Endometriosis
Drug Metabolism



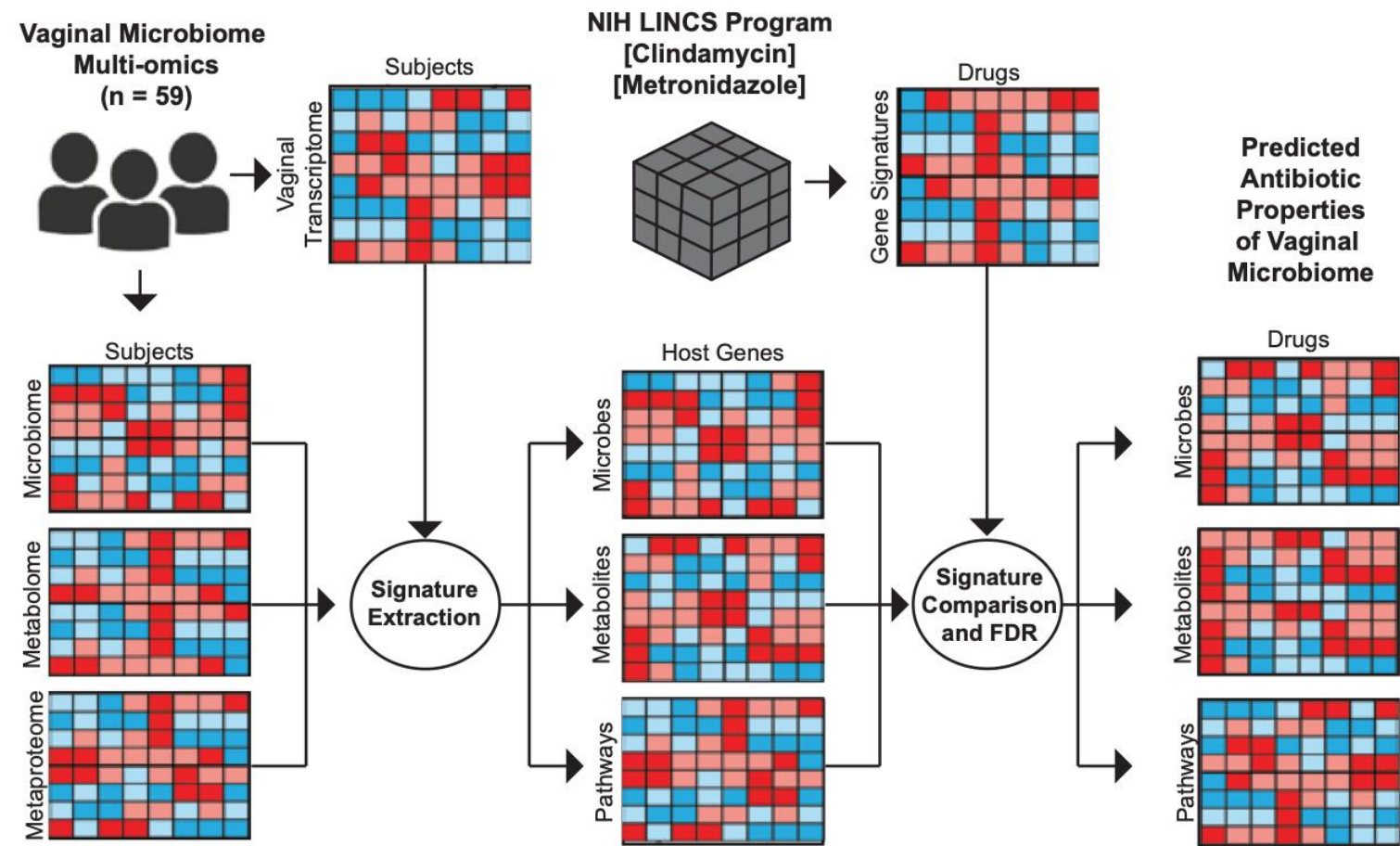
**Nina Render
(Alumni)**
Vaginal Microbiome
Endometriosis
Progesterone

Leveraging Perturbation Biology Concepts in Host-Microbiome Interactions



Goal: To Classify the Effects of Microbiome Factors on the Host In Terms of the Actions of Known Pharmacologic Compounds

Building Similarity Scores for Host Responses to Drug and Microbiome Perturbations



Scaling Up to Custom, Proprietary Microbiome Pharmacology Databases

Vaginal Microbiome

52,000 perturbations
1000+ cell types

100 metabolites
165 taxa
125 bacterial peptides

**2+ Billion Training
Data Points**

Gut Microbiome

52,000 perturbations
1,000+ cell types

609 metabolites
574 taxa

**6+ Billion Training
Data Points**

Pending Databases

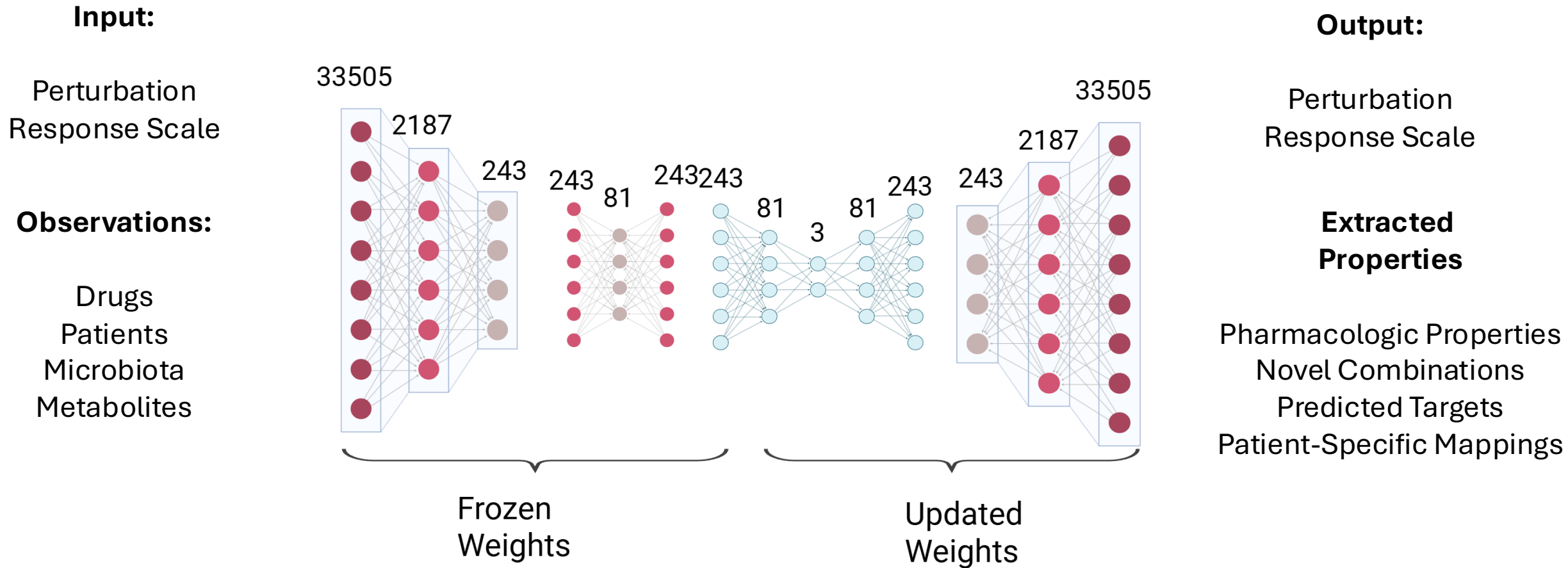
Skin Microbiome
Oral Microbiome

Pending Modalities

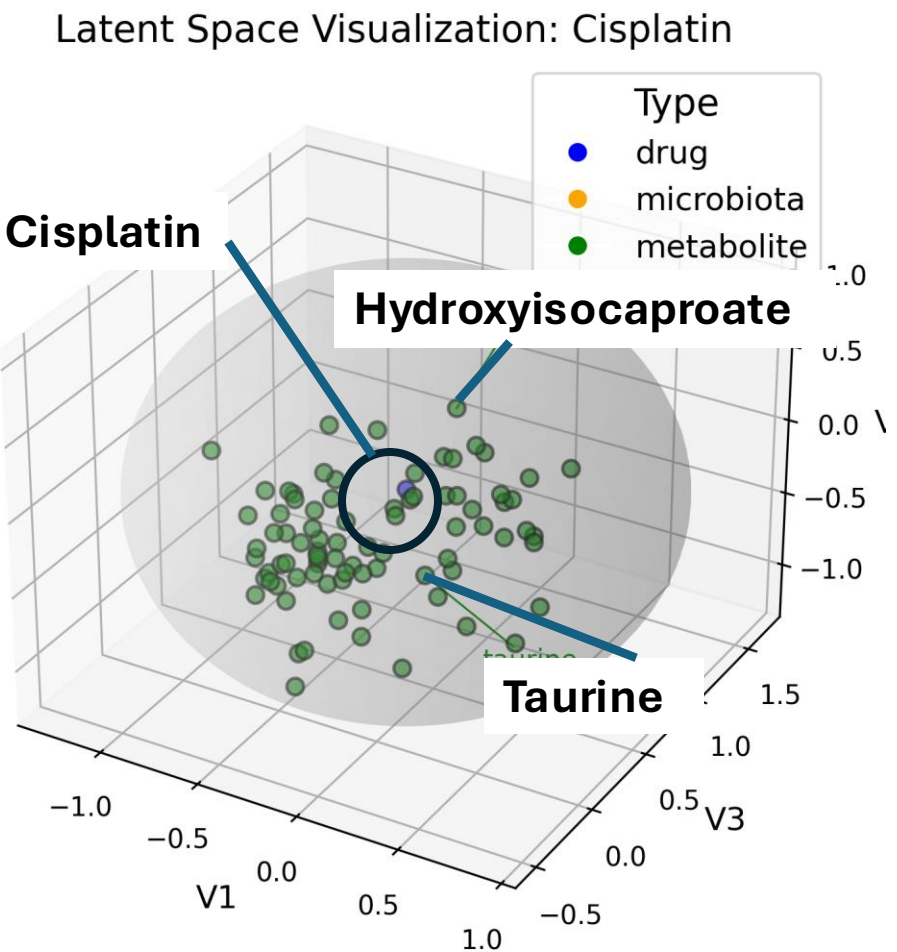
Perturb-Seq
CRISPR Screens
siRNA Screens

Deep Learning for Inference, Simulation, and Design of Microbiome Combinations

– Microbiome Pharmacology Neural Network



Test Case 1: Identifying Vaginal Metabolites for Endometrial Cancer Treatment



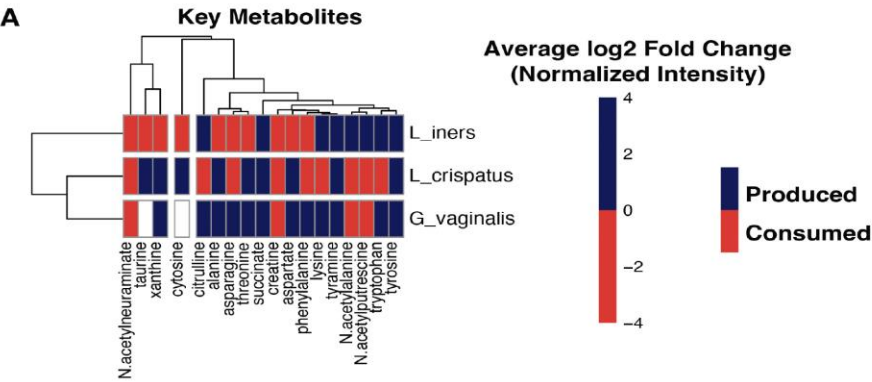
Vaginal microbiome composition is associated with cancer prognosis.

Production and consumption of metabolites by vaginal taxa can impact tumor viability

- (1) Highlight radius of compounds around anti-cancer agent in latent space (e.g. cisplatin).
- (2) Rank-based selection of metabolites based on proximity to the desired drug to mimic

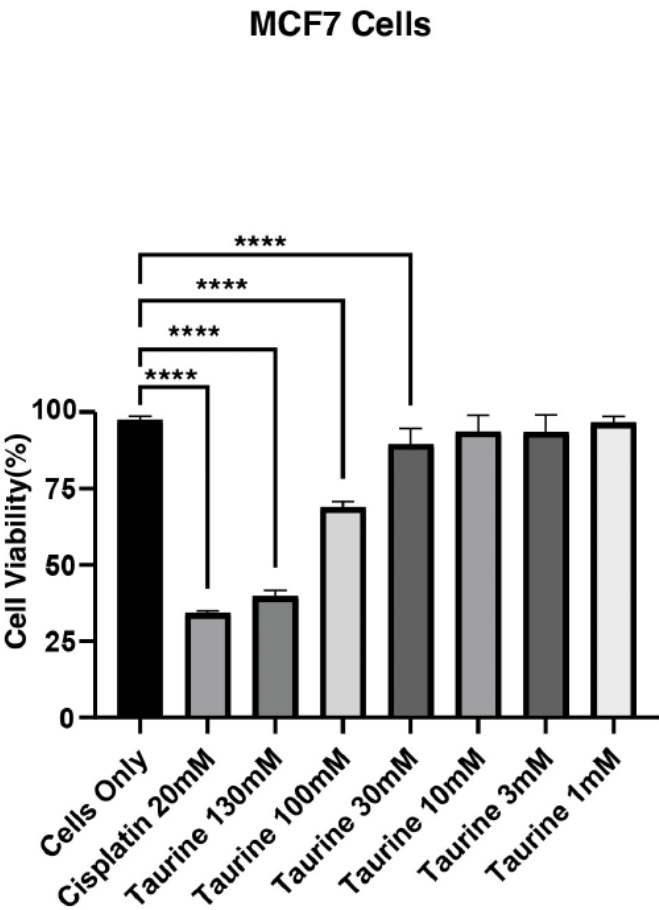
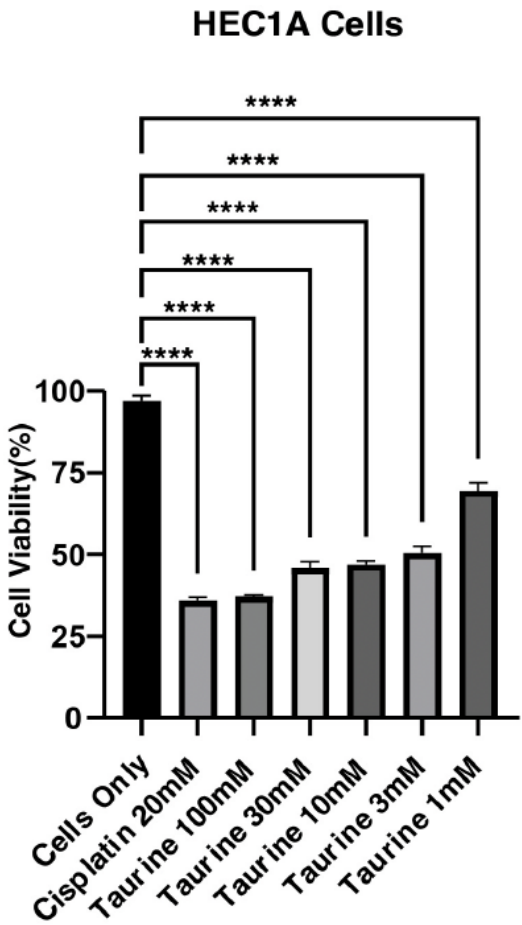


Lactobacillus crispatus-produced Taurine inhibits endometrial cancer viability - predicted and experimentally confirmed from vaginal microbiome pharmacology database

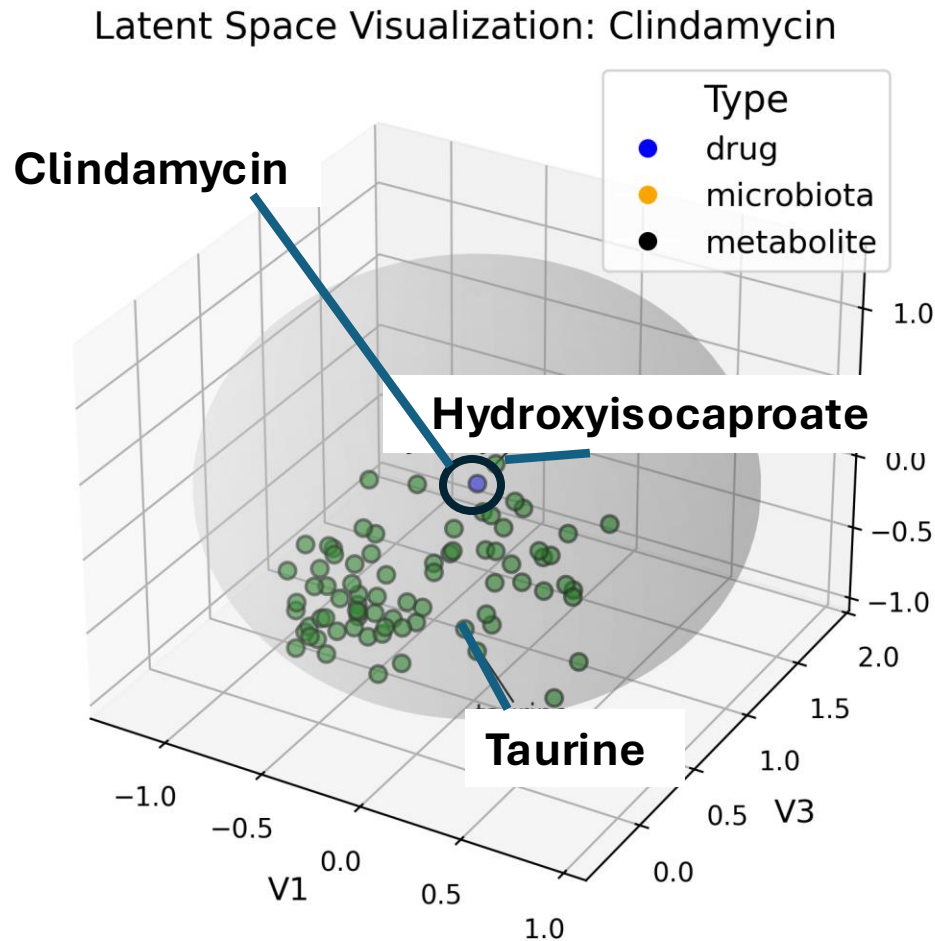


Computational microbiome pharmacology analysis elucidates the anti-cancer potential of vaginal microbes and metabolites

Damilola C. Lawore¹, Smrutiti Jena¹, Alicia R. Berard^{2,3}, Kenzie Birse^{2,3}, Alana Lamont², Romel D. Mackelprang⁴, Laura Noel-Romas^{2,3}, Michelle Perner⁵, Xuanlin Hou⁴, Elizabeth Irungu⁶, Nelly Mugo^{4,6}, Samantha Knodel^{2,3}, Timothy R. Muwonge⁷, Elly Katabira⁷, Sean M. Hughes⁸, Claire Levy⁹, Fernanda L. Calienes⁹, Florian Hladik^{8,9,10}, Jairam R. Lingappa^{4,10,11}, Adam D. Burgener^{2,3,12}, Leopold N. Green¹ and Douglas K. Brubaker^{3,13*}



Test Case 2 – Identifying vaginal metabolites with antibiotic potential



Loss of vaginal homeostasis and overgrowth of anaerobes is called **bacterial vaginosis**

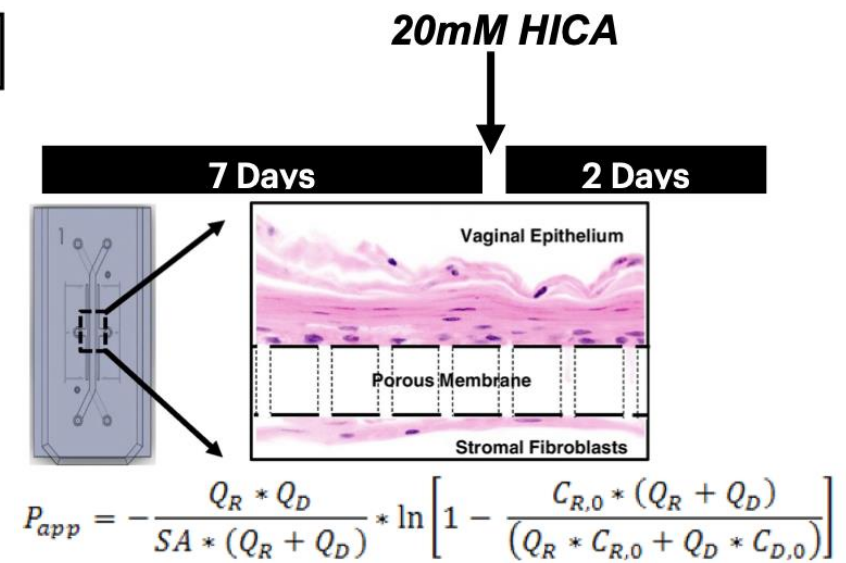
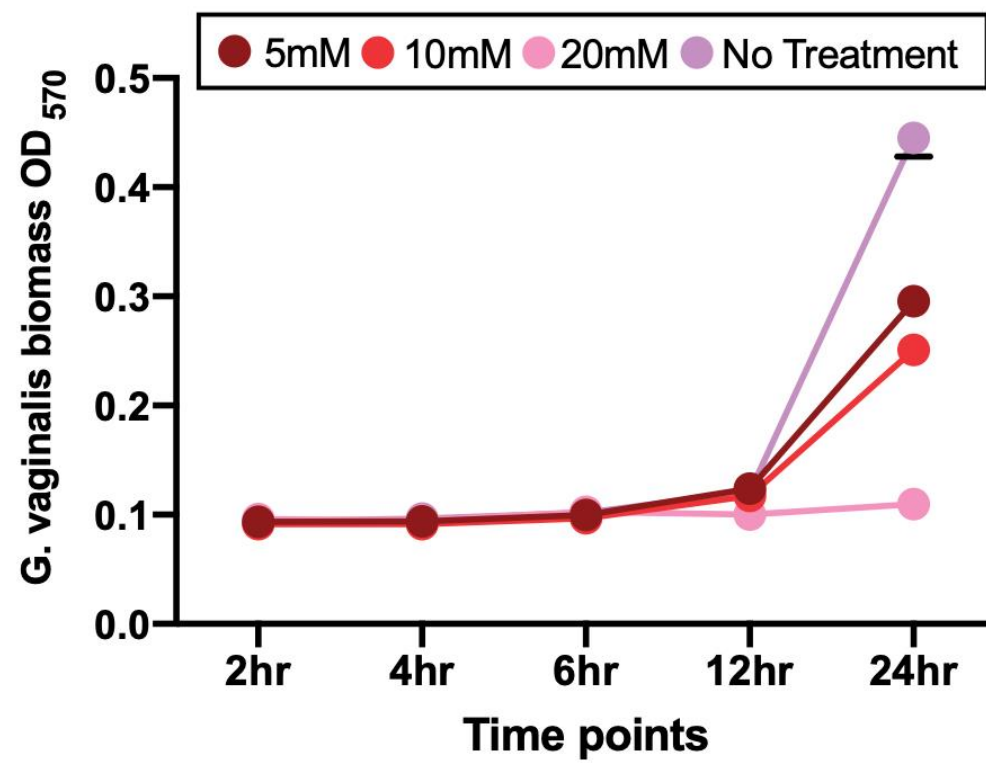
50% of cases are recurrent and many plagued by **antibiotic resistance**

- (1) Highlight radius of compounds around antibiotic agent in latent space (e.g. cisplatin).
- (2) Rank-based selection of metabolites based on proximity to the desired drug to mimic



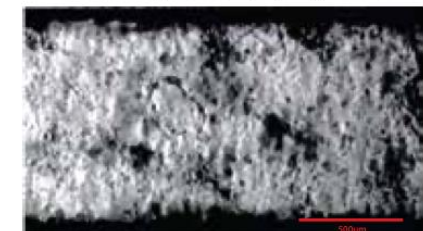
bioRxiv
THE PREPRINT SERVER FOR BIOLOGY

Lactobacillus crispatus-produced Hydroxyisocaproate selectively kills bacterial vaginosis bacteria and improves vaginal barrier integrity.



**Emulate Human
Vagina-on-a-Chip
Microfluidics Model**

Emulate Vagina-Chip (Brightfield 4X)



7 days post-seeding
(pre-treatment)



Media Control
48hr



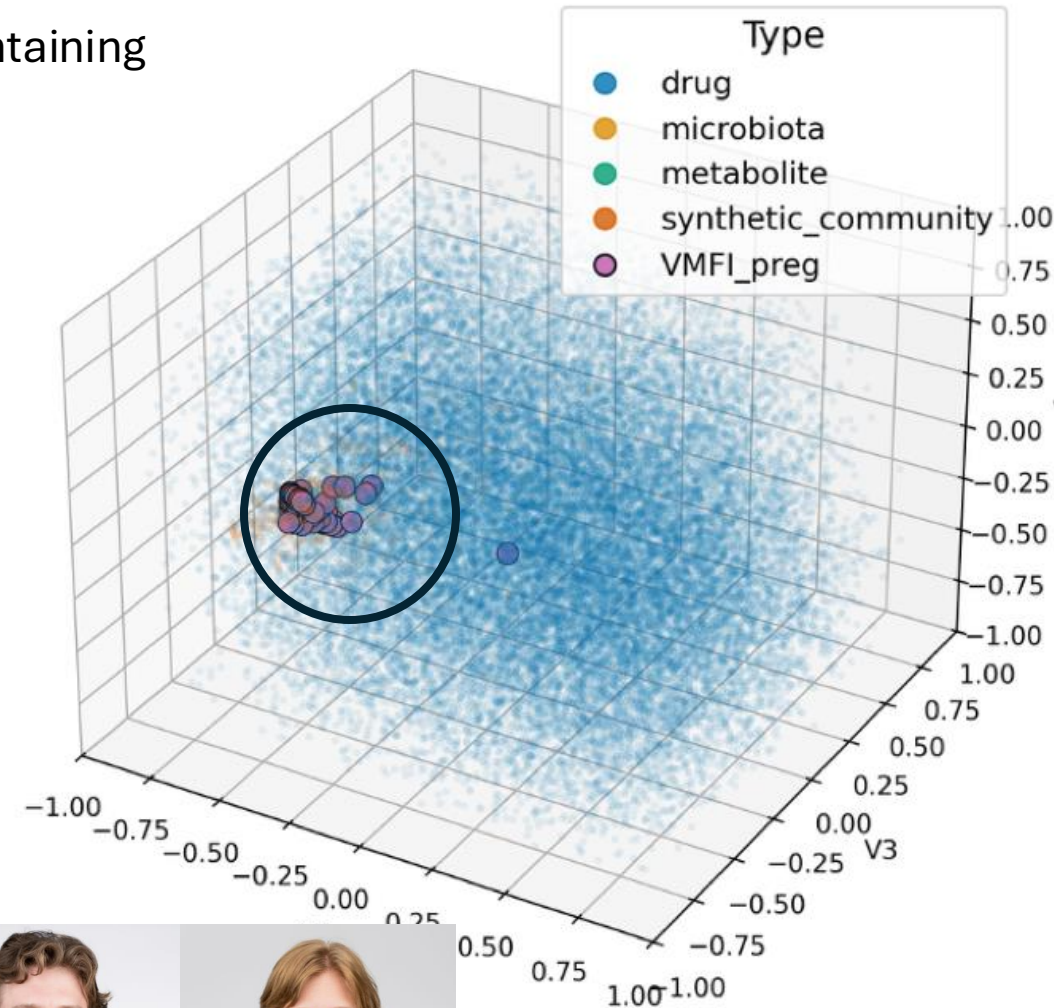
20mM HICA
48hr

The Next Frontier – Mechanism-Based Design of *Eubiotics*

- **Eubiotics** – formulations of supplements and therapies containing
- **probiotics, prebiotics, and postbiotics**

- (1) Map patients with desired phenotype into MiPNN
- **(microbiome, RNA-seq, metabolomics.....)**
- (2) Identify factors in **radius of target phenotype** in latent space
- (3) Simulate and extract combinations of factors that **map formulation to phenotype**

- ***Recently Awarded Funding – Designing Eubiotics for***
- ***Optimizing successful pregnancy after IVF***

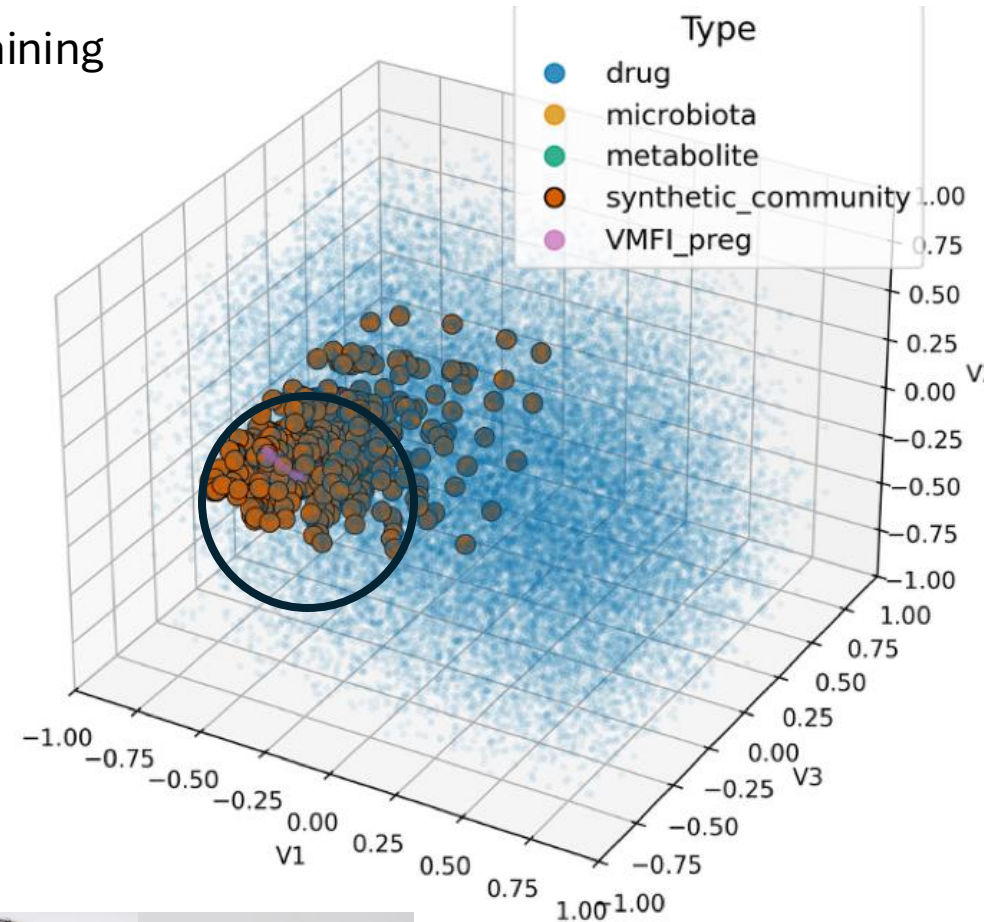


The Next Frontier – Mechanism-Based Design of *Eubiotics*

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- **map formulation to phenotype**

- ***Recently Awarded Funding – Designing Eubiotics for***
- ***Optimizing successful pregnancy after IVF***



Questions?

