Integrating Vaginal Microbiome and Immune Profiles with Machine Learning to Predict IVF success

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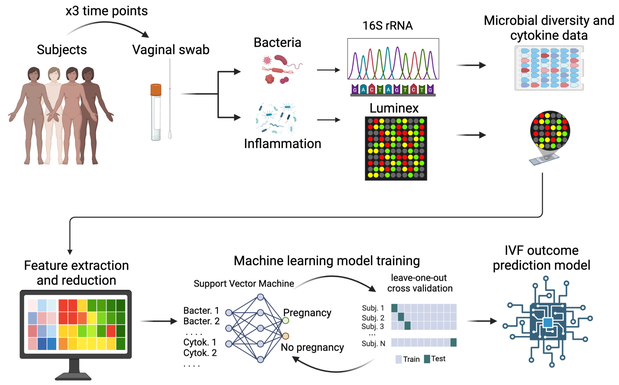
Introduction

Low-diversity, *Lactobacillus*-dominant vaginal microbiome communities are associated with favorable reproductive outcomes.
Host inflammatory responses and microbial composition are tightly linked, yet their combined impact on fertility remains unclear.
IVF success rates remain limited, particularly in unexplained infertility.

We hypothesized that **vaginal microbiome composition and mucosal inflammation jointly influence IVF outcomes** .

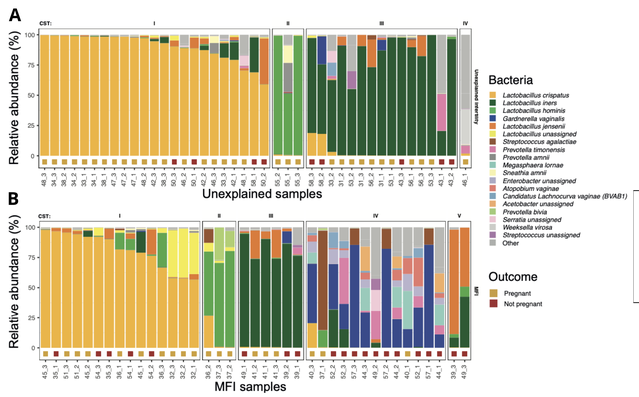
Methods and Cohort



	No Clinical Pregnancy (n=10)	Clinical Pregnancy (n=18)	p-value
Age, median (IQR)	35.7 (32.6, 36.5)	35.6 (33.7, 37.4)	0.581
Type of infertility, n (%)			
MFI	3 (30.0%)	11 (61.1%)	0.115
Unexplained	7 (70.0%)	7 (38.9%)	
Race, n (%)			
White	8 (80.0%)	18 (100.0%)	0.119
Asian	2 (20.0%)	0	

Vaginal Microbiome

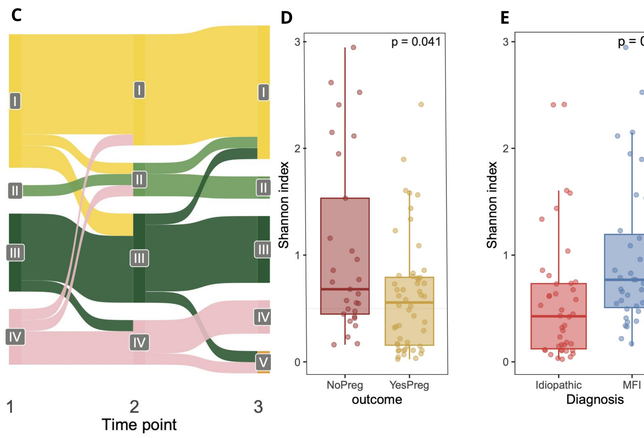
Presence of CST I was associated with a clinical pregnancy in Unexplained (A) and MFI (B).



Most participants had the same CST assignment across all three time points (C).

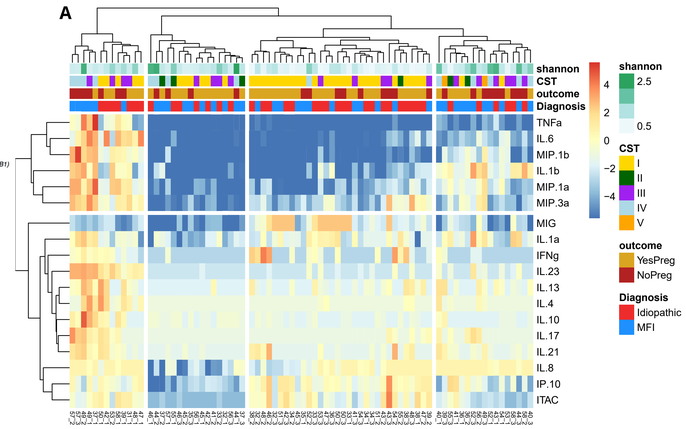
Participants who conceived had **significantly lower microbial diversity** (D).

Participants with MFI had higher diversity than those with unexplained infertility (E).



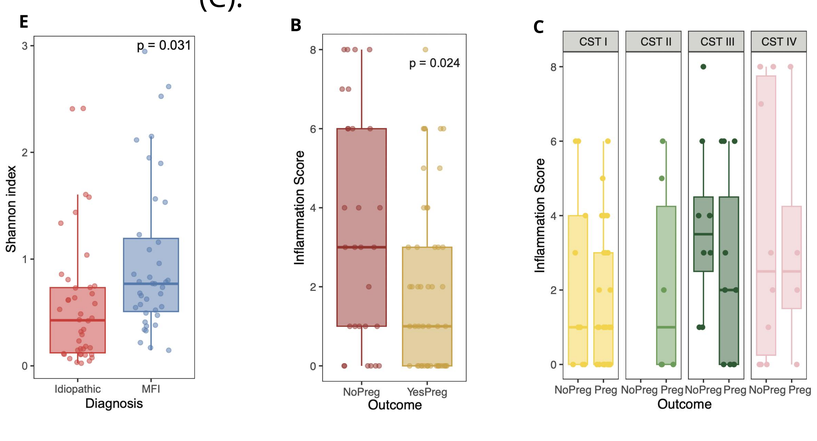
Vaginal Inflammation

18 vaginal analytes were analyzed across samples. There were no notable differences in immune markers between infertility diagnosis or pregnancy outcomes (A).



Inflammation score was calculated as the number of cytokines in the **top quartile** per sample and included key pro-inflammatory markers.

Lower vaginal inflammation was associated with clinical pregnancy (B) & CST III was associated with higher inflammation in participants who did not become pregnant (C).

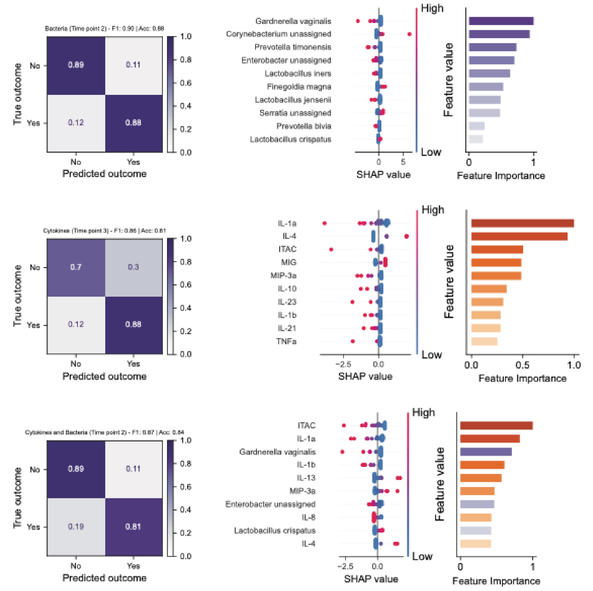


Machine learning model predicts pregnancy

Microbiome-based model achieved highest performance at oocyte retrieval (timepoint 2, F1 score = 0.90)

Inflammation-based model performed best at embryo transfer (timepoint 3, F1 score = 0.86)

Combined models also demonstrated strong predictive performance



Negative predictors (associated with non-pregnancy): *Gardnerella vaginalis*
Pro-inflammatory cytokines (IL-1α, ITAC)

Positive predictors (associated with pregnancy): *Lactobacillus crispatus*

Acknowledgments

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