

# **Microbiome and cervical cancer**

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# Microbiome

# Human microbiome

- Various microbes colonize on human body.
- 1.3 x a greater number of cell than human cells (30 trillion).
- Gene contents are 100 x more than human (23,000).
- Different composition of microbes inhabit in different body site.
- The composition of microbes in each body site change during our lifetime.
- Individual differences of microbiomes

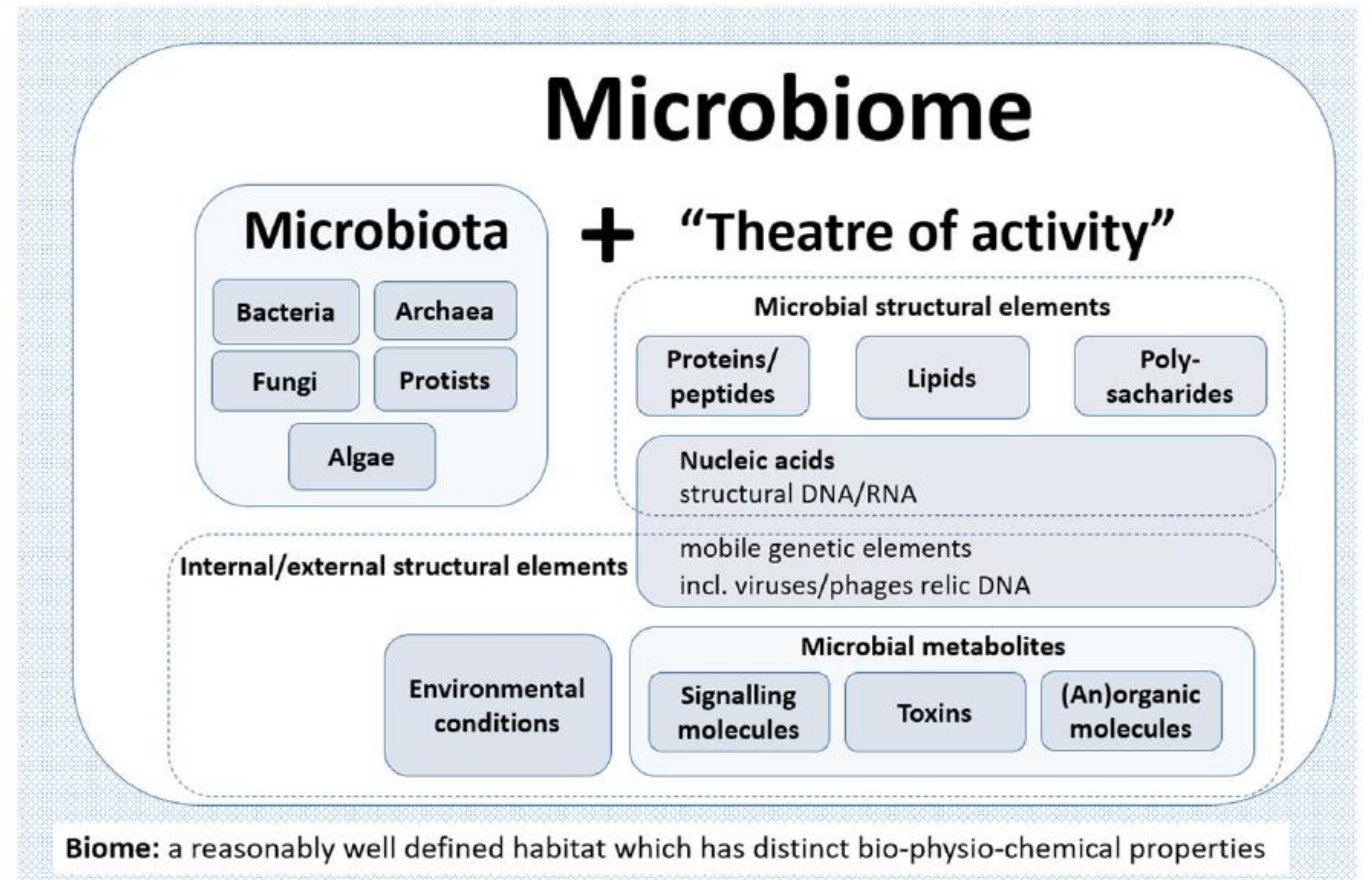
# Microbiome

- **Microbiome**

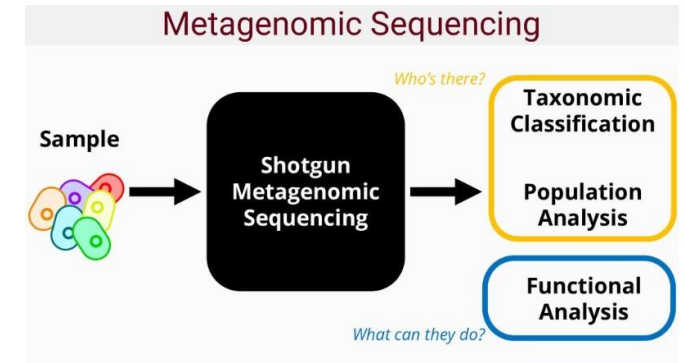
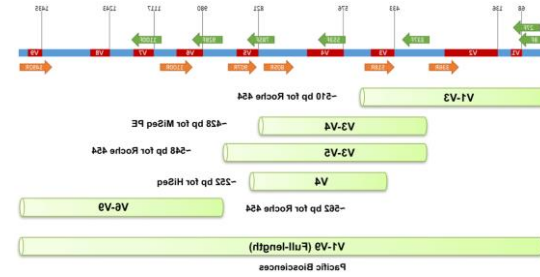
- Microbiota + genome → Micro + biome
- Total microbe and their activity resulting in the formation of specific ecological niche
- To understand their interactions with their ecological niche

- **Micobiota**

- The assembly of microorganisms



- **16s rRNA Amplicon vs. Shotgun Metagenome**



Aspect	16S rRNA Amplicon Sequencing	Shotgun Metagenomics
Target	Bacterial 16s rRNA gene (specific regions like V3-V4)	Entire metagenome (bacteria, viruses, fungi, archaea)
Taxonomic Resolution	Genus level (limited species resolution)	Species to strain level
Functional Profiling	Limited	Comprehensive (genes, pathways, resistance gene)
Microbial Diversity	Limited bacterial only	Includes bacteria, fungi, viruses and archaea
Data Complexity	Lower data volume, simpler analysis	Higher data volume, requires complex bioinformatics
Cost and Time	Lower cost, fast turnaround	Higher cost, longer data processing time
Clinical Applications	General microbial community profiling	Detail microbial ecosystem, functional and strain-level analysis

# Microbiome study

Who is there?

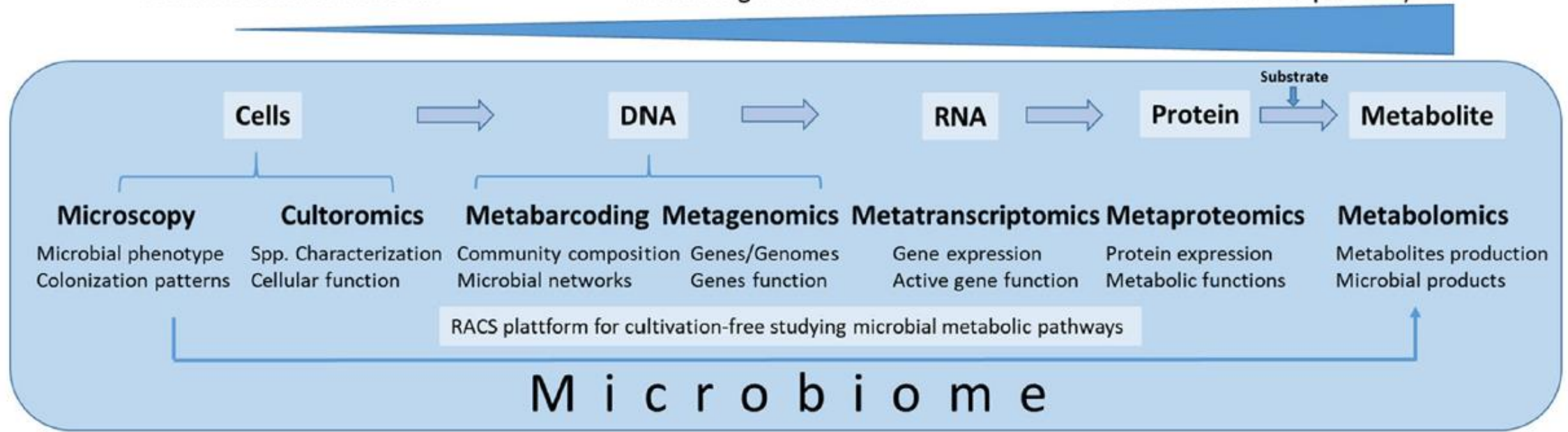
**Microbial potential:**  
available cellular material

What can they do?

**Metabolic potential:**  
available genetic material

What are they doing?

**Microbial function:**  
active metabolic pathways



# **Female urogenital microbiome**

# Female urogenital microbiota

- 9% of the body's total microbial population
- Lower track having a bacterial burden 100-10,000 fold more than the upper track

*Lactobacillus*

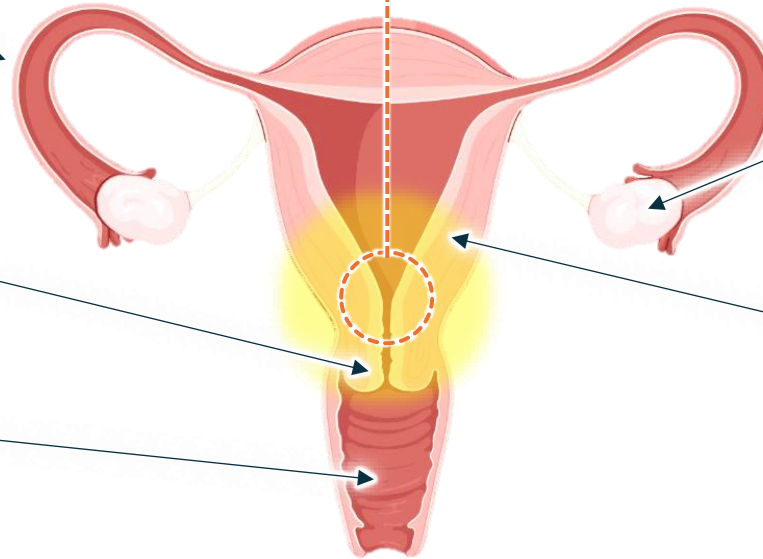
Dysbiosis

Variability

Heritability

- *Staphylococcus*
- *Enterococcus*
- *Lactobacillus*
- *Ropionibacterium*
- *Prevotella*
- *Pseudomonads*

Uterine tube



Ovary

- *Lactobacillus*
- *Actinomyces*
- *Prevotella*
- *Staphylococcus*

Cervix

- *Lactobacillus*
- *Prevotella*
- *Gardnerella*
- *Veilonella*

Endometrium

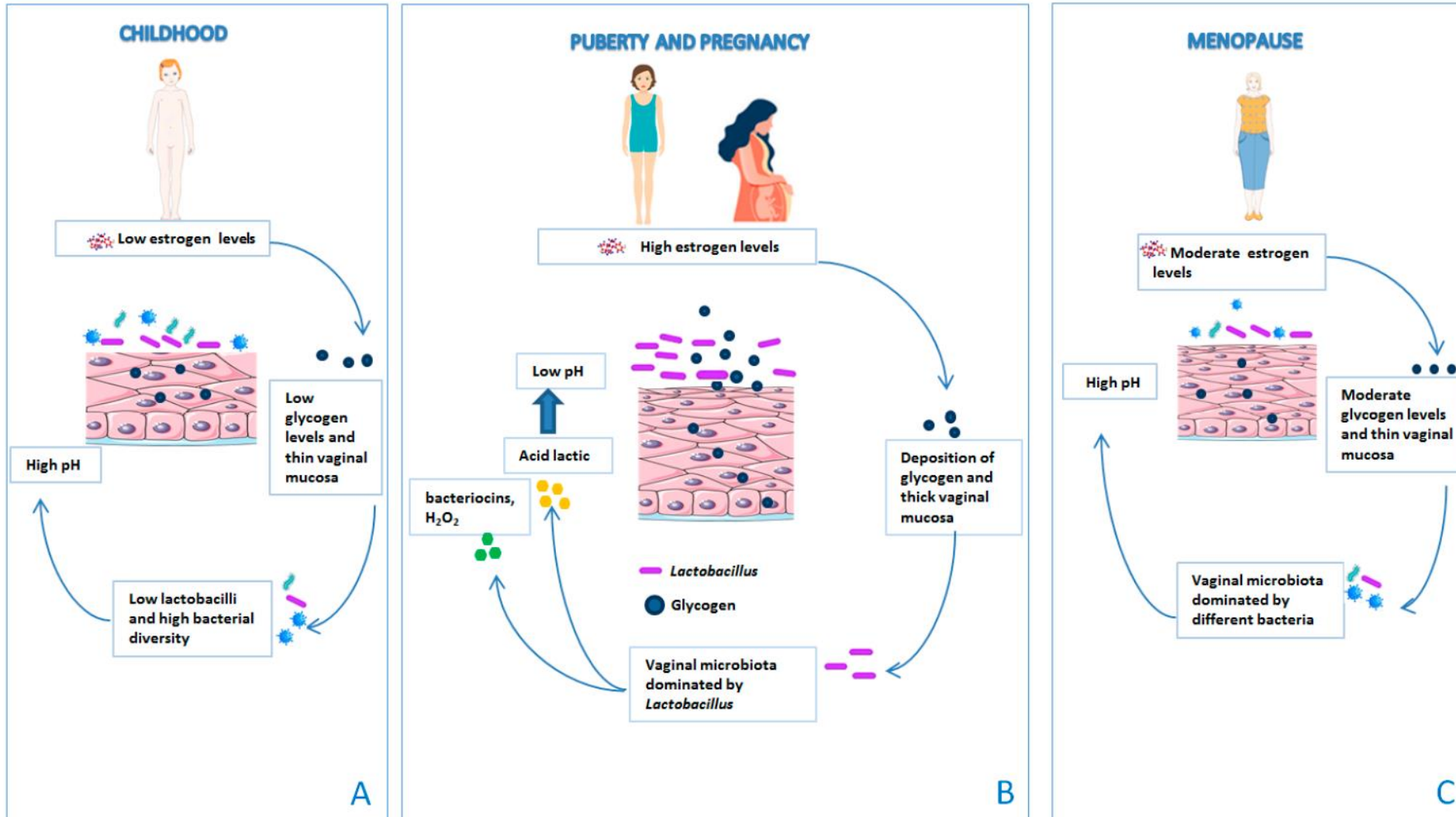
- *Lactobacillus*
- *Prevotella*
- *Flacobacterium*
- *Bifidobacterium*
- *Streptococcus*

Vagina

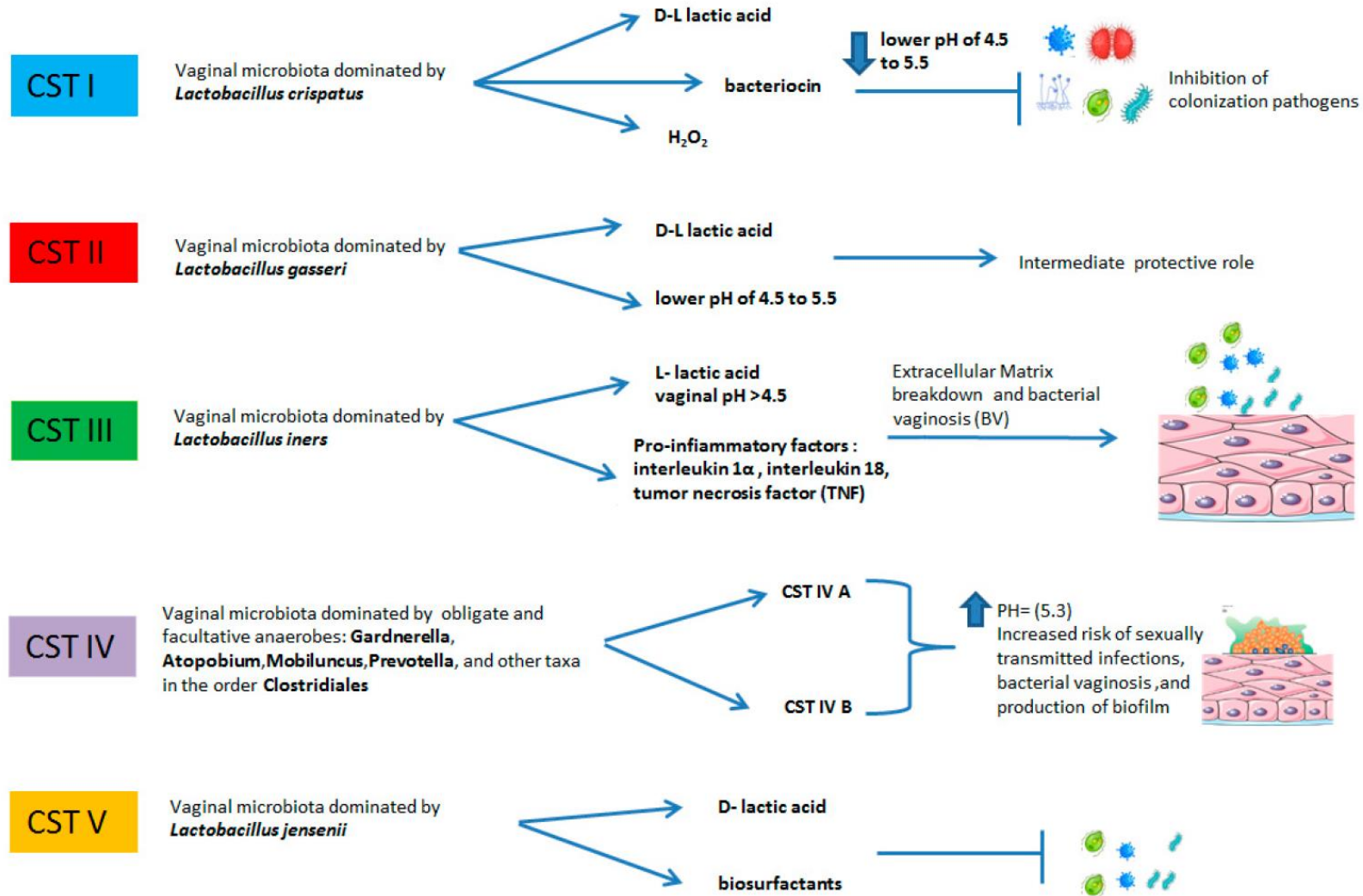
- *Lactobacillus*
- *Prevotella*
- *Gardnerella*
- *Atopobium*
- *Dialister*
- *Sneathia*
- *Candida* (yeast form)

Associated with various gynecologic diseases and QOL

# Vaginal microbiota changes throughout a woman's life

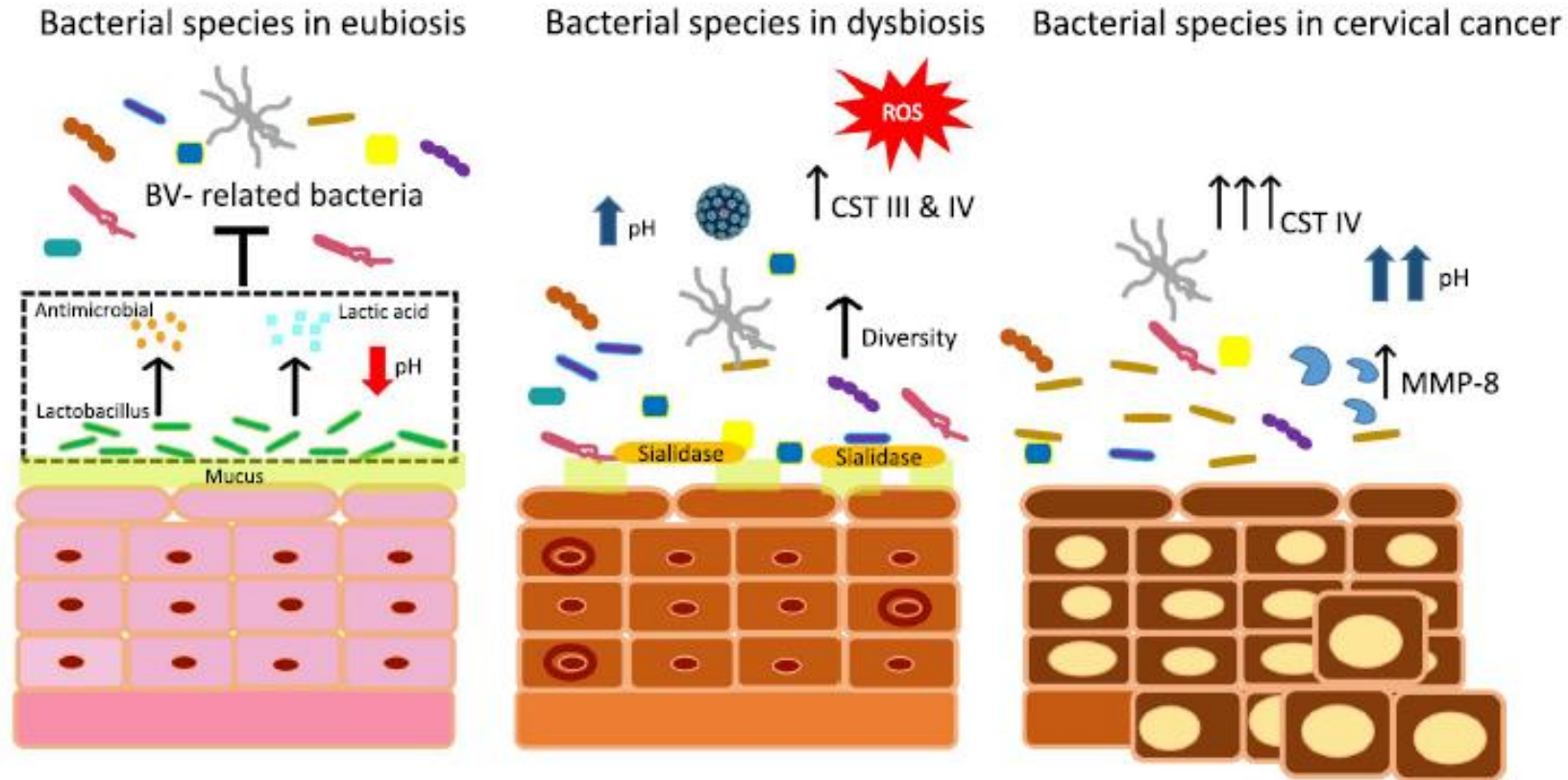


# The Community State Types (CSTs)

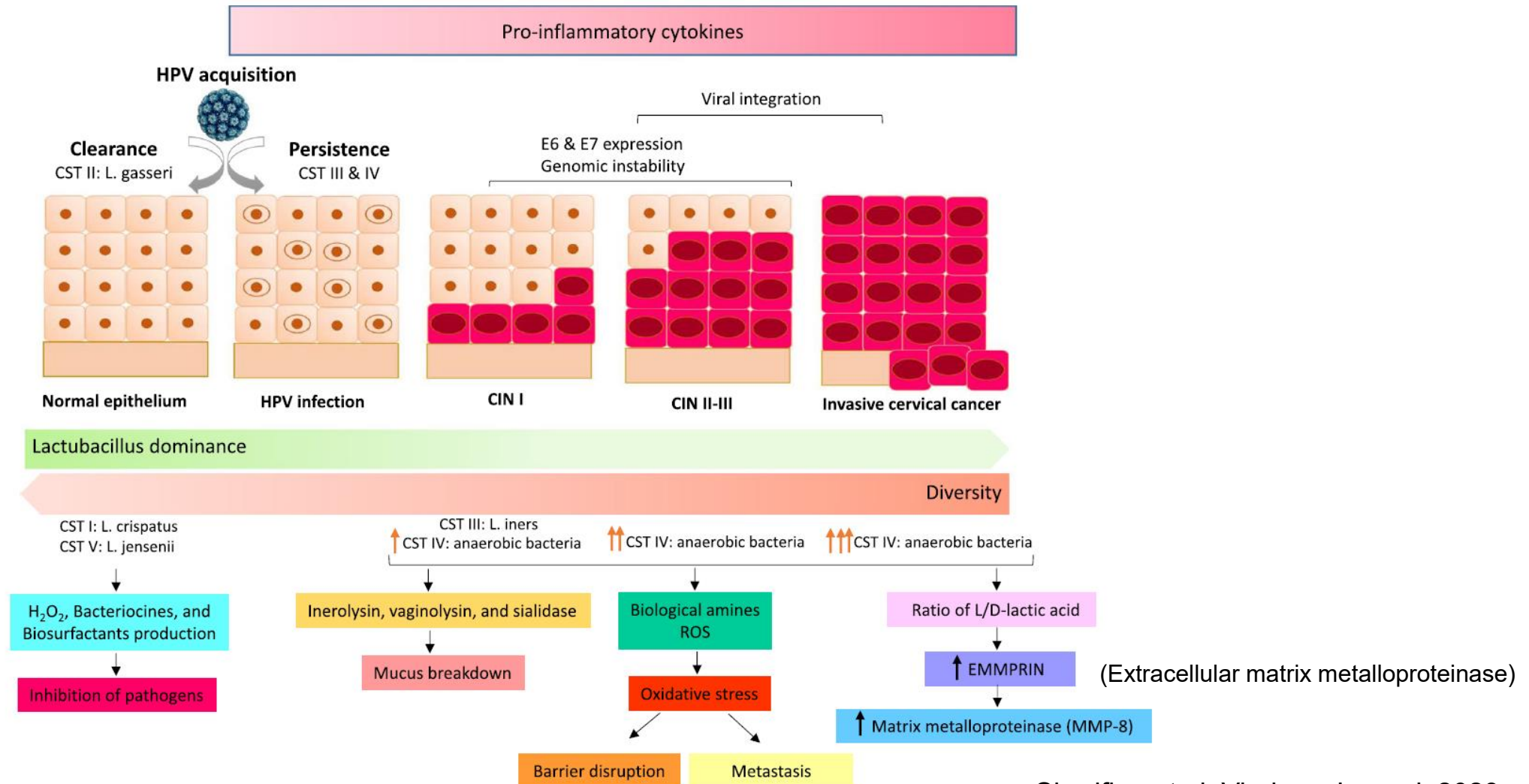


# **Vaginal microbiome and cervical cancer**

# Dysbiosis, HPV infection and cervical cancer

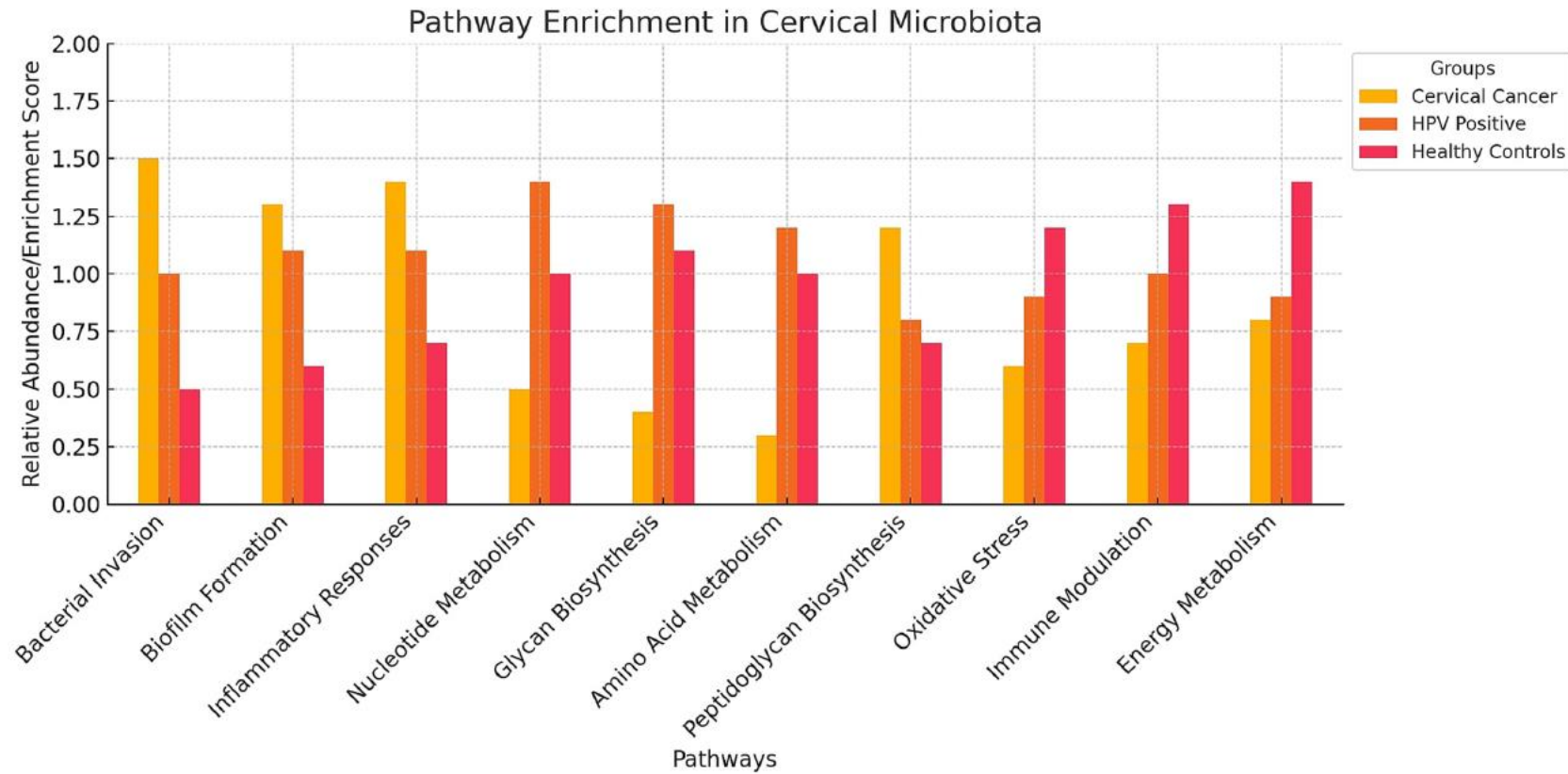


# Dysbiosis, HPV infection and cervical cancer





# Cervical microbiota and metagenomics: Development and progression of cervical cancer

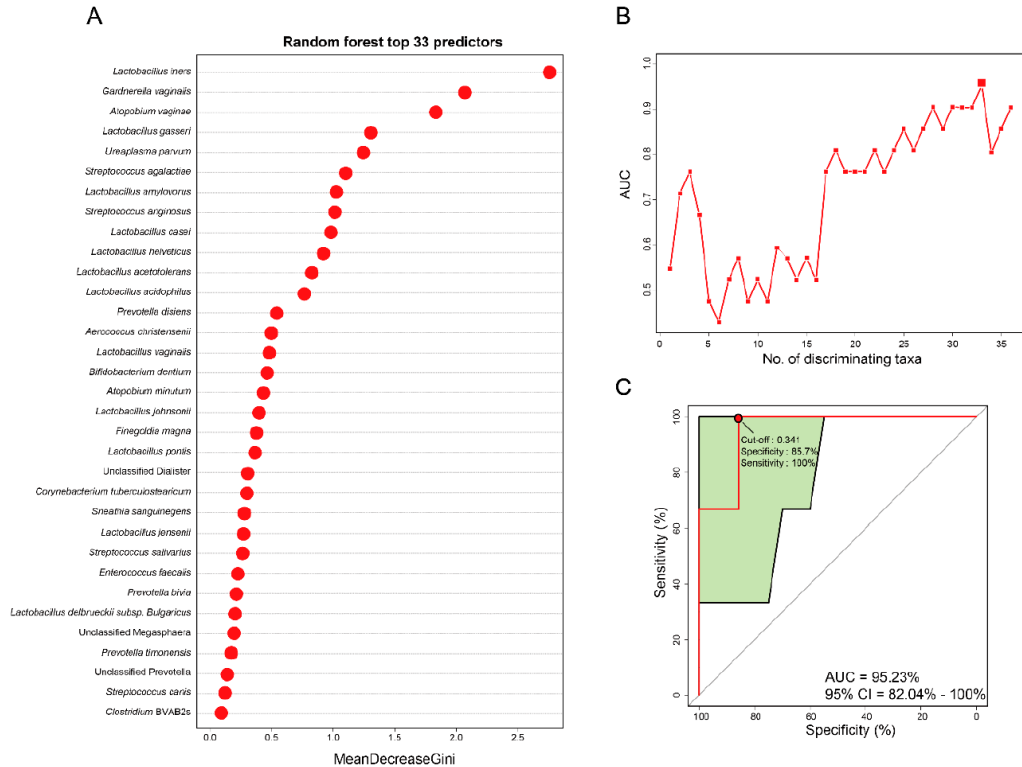


**Previous, present and future our study for microbiome**

# Vaginal Microbiome-Based Bacterial Signatures for Predicting the Severity of Cervical Intraepithelial Neoplasia



Lee et al. 2020

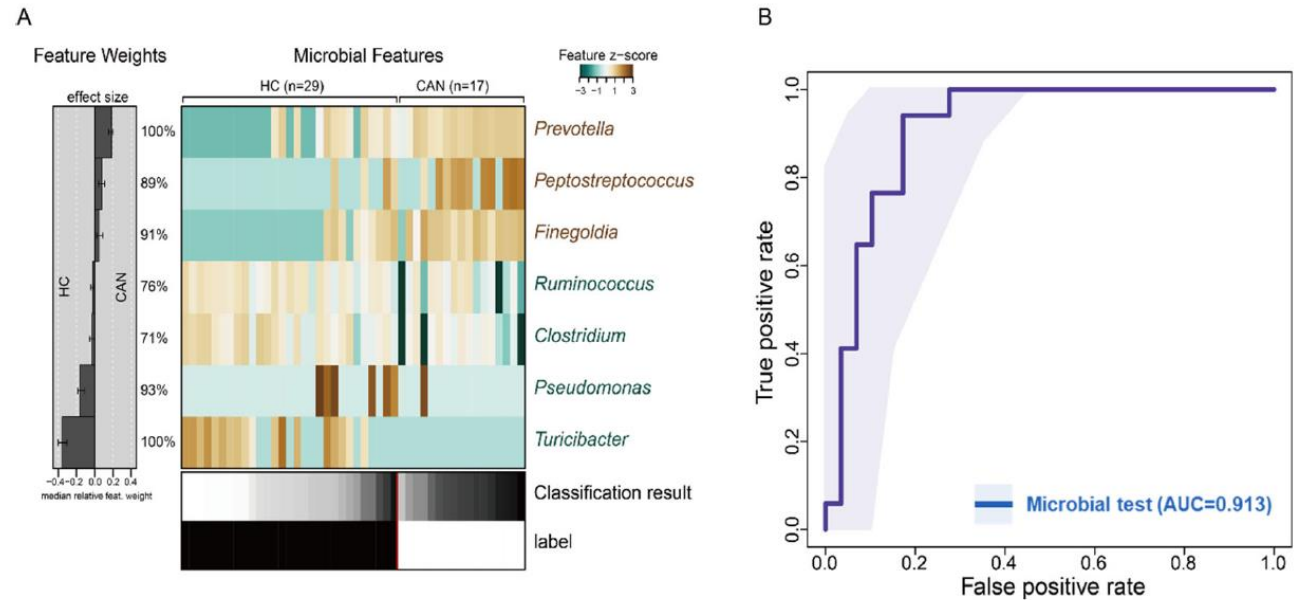


Random forest classifier model to predict HSIL using bacterial signatures (33 bacterial species)

# Dynamics of Fecal Microbiota with and without Invasive Cervical Cancer and Its Application in Early Diagnosis



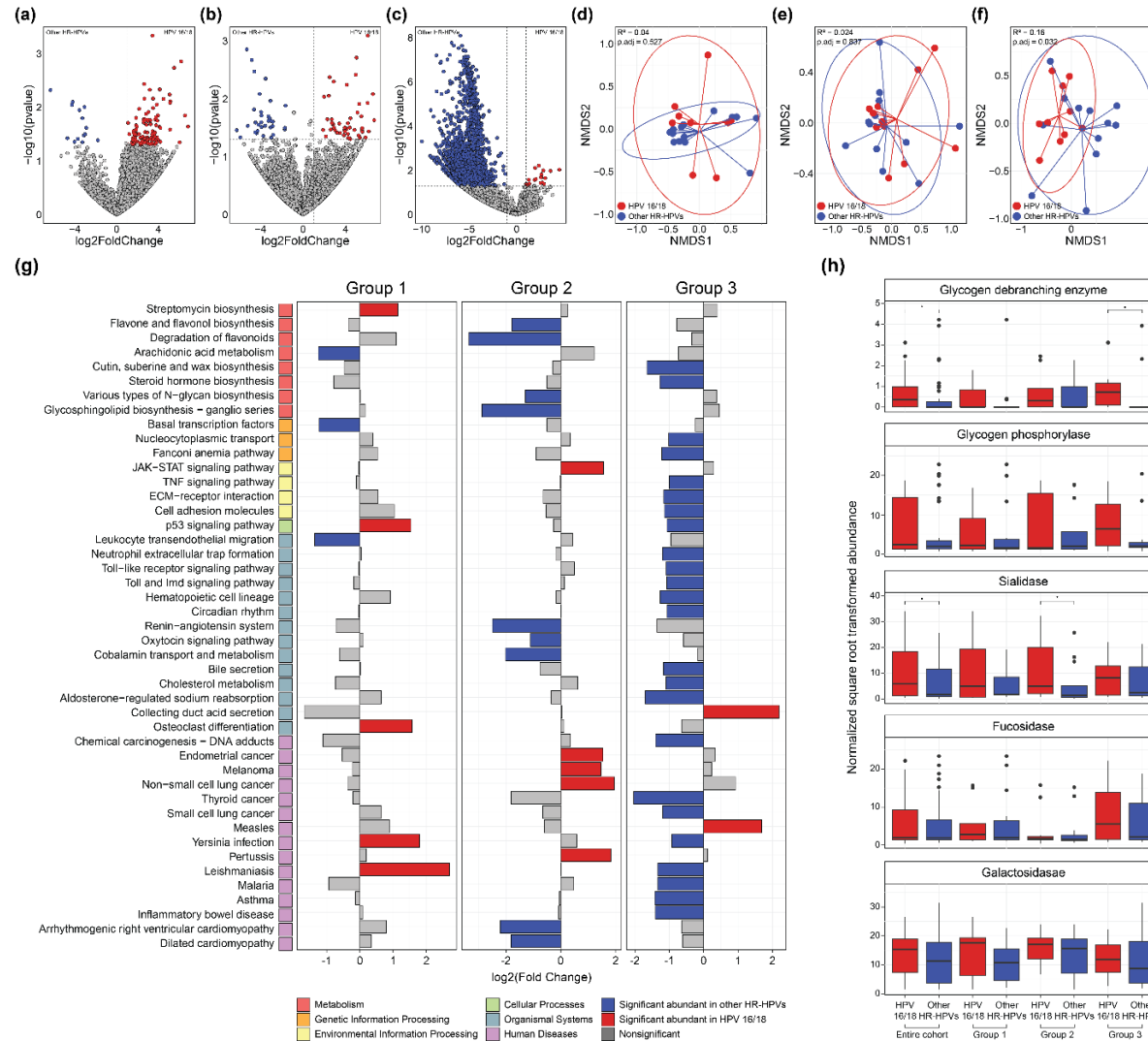
Kang et al. 2020



Dynamics of fecal microbiota (Healthy vs. cervical cancer)

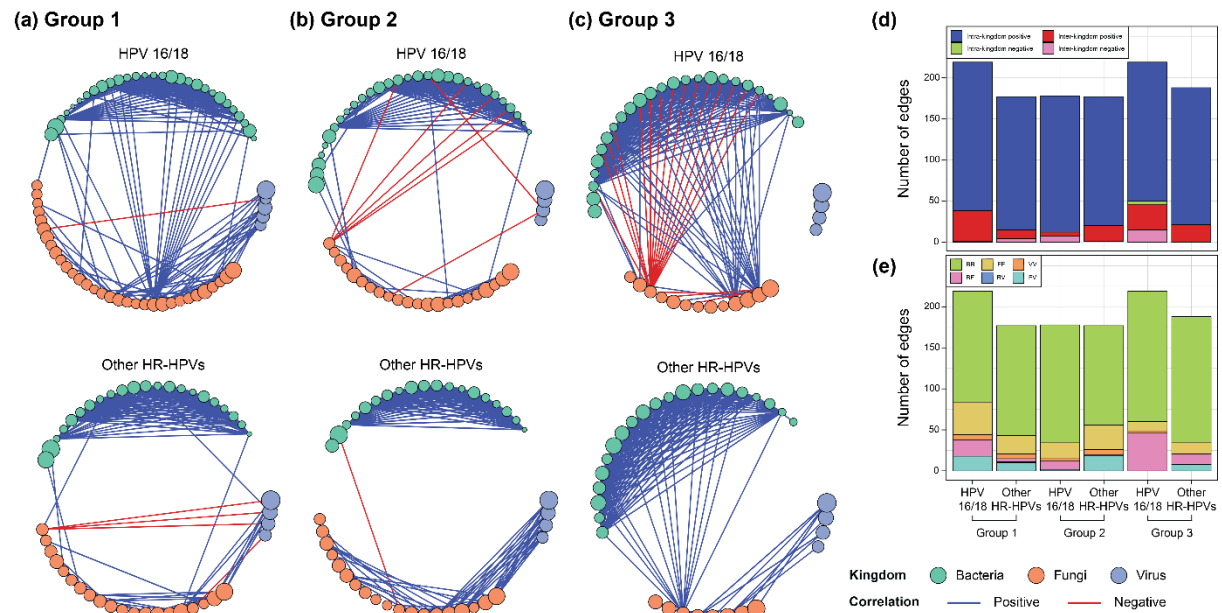
# Metagenomic Insights into Vaginal microbiome in Women Infected with HPV 16 and 18

npj | biofilms and microbiomes Jung et al. 2025, accepted



- HPV 16 and 18 vs other high-risk HPV
- **Functional pathway analysis**
  - HPV 16/18 are enriched in immune response and inflammation pathways
  - Other HR-HPV are linked to pathways affecting cellular metabolism and hormonal signaling

# Metagenomic Insights into Vaginal microbiome in Women Infected with HPV 16 and 18

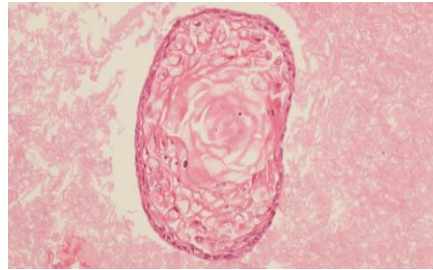


- Bacterial-fungal correlations increased in the HPV 16/18 infected group.
- Suggesting complex synergistic interaction

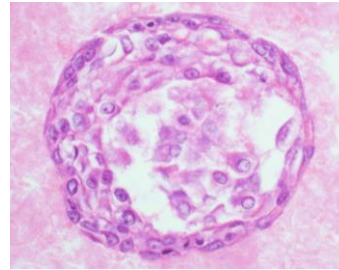
# Microbial metabolites control self-renewal and precancerous progression of human cervical stem cells

nature communications

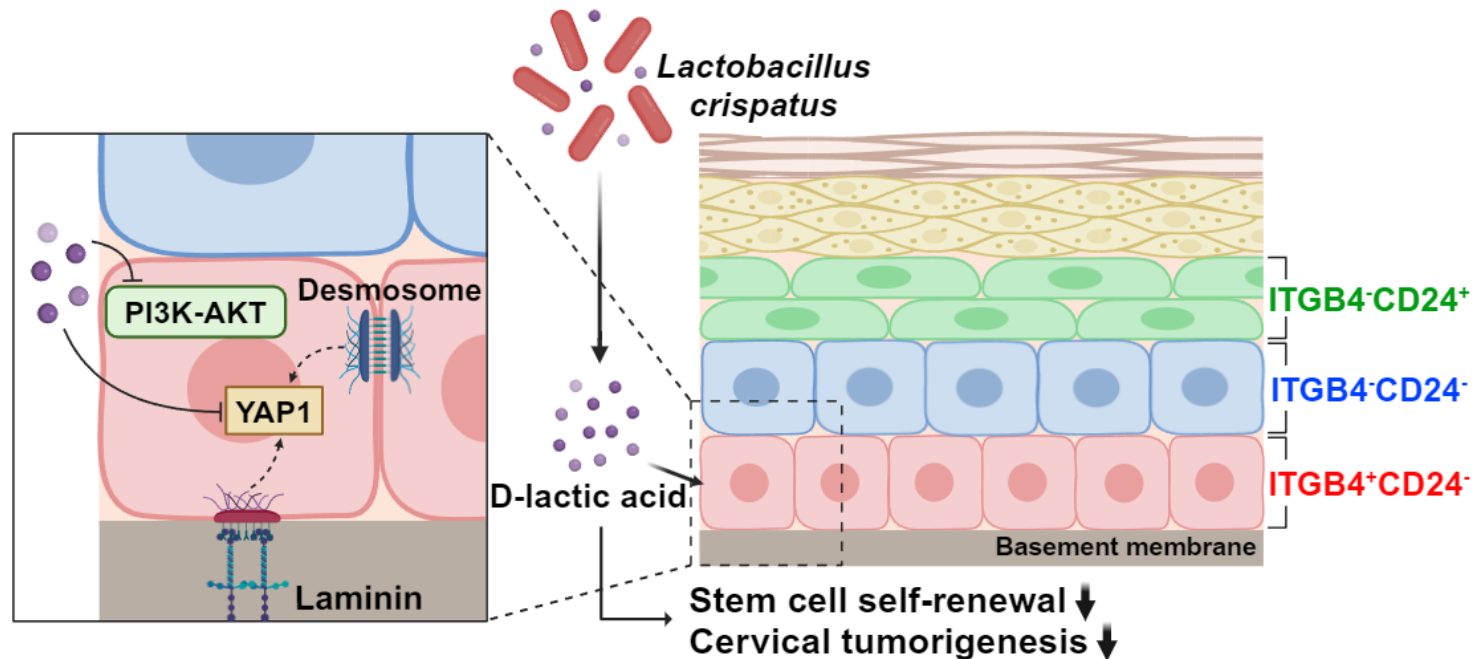
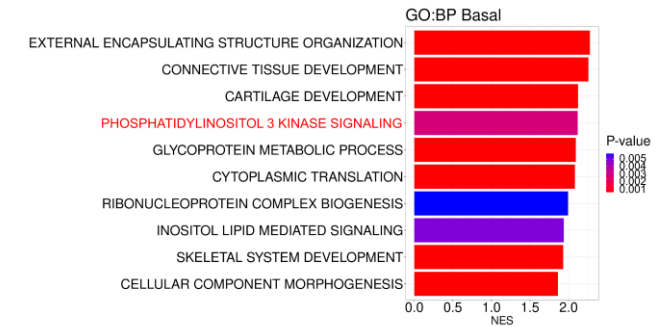
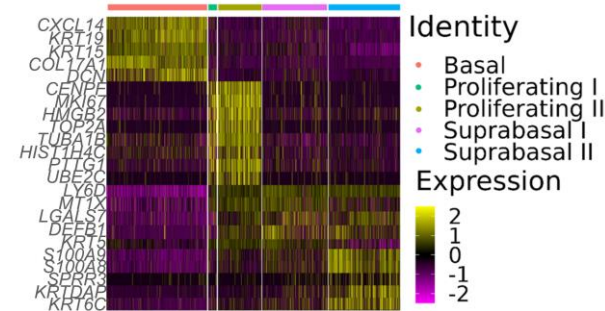
Myeong et al. 2025



normal



HSIL

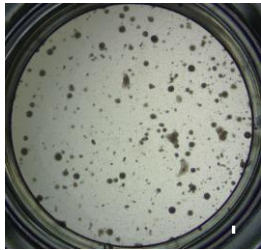
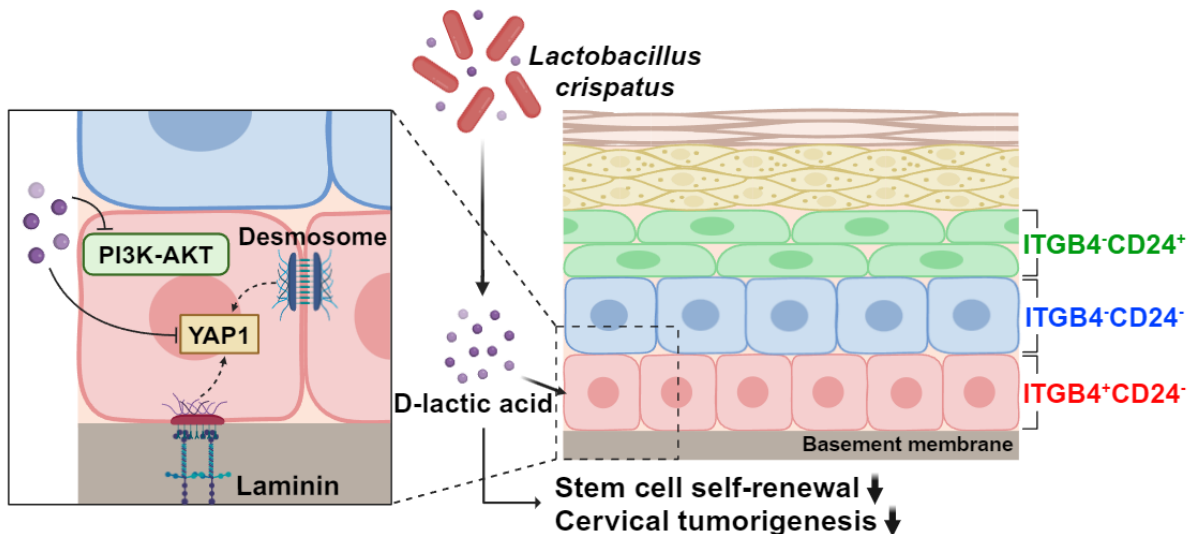
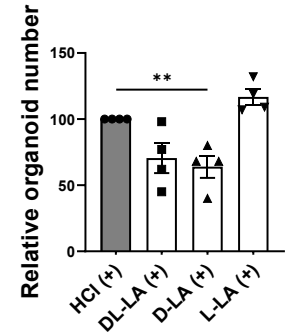
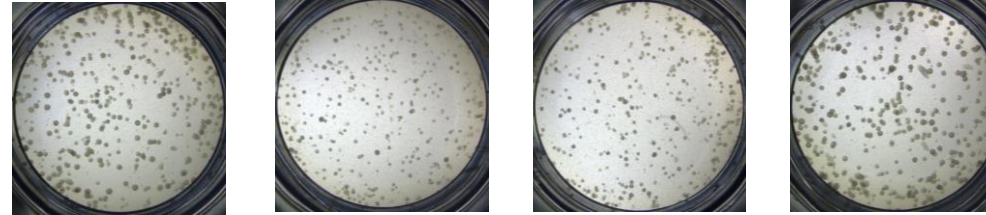
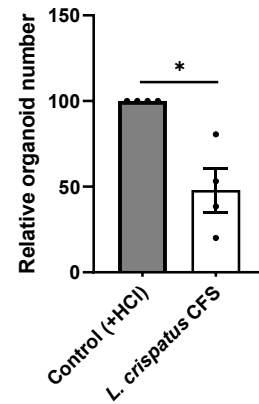
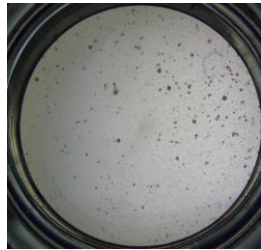


- Using single-cell RNA sequencing, we characterize the cellular heterogeneity of the human ectocervix and identify cluster-specific cell surface markers.
- PI3K-AKT** pathway and **YAP1** regulates self-renewal and differentiation of human cervical stem cells.

# Microbial metabolites control self-renewal and precancerous progression of human cervical stem cells

Myeong et al. 2025

Control CFS (+HCl)

*L. crispatus* CFS

- **Lactobacilli-derived lactic acid** regulates cervical stem cells' self-renewal and early tumorigenesis through PI3K-AKT pathway and YAP1.
- **D-lactic acid** suppresses growth of normal and precancerous organoids, while L-lactic acid does not.

# Female Urogenital Track

## Establishment of Female Urogenital Microbiome Data Platform and Comparative Clinical Research

Funded by the Ministry of Health & Welfare, Republic of Korea  
(RS-2023-KH135444)

- **Health group : 1000 cases**
- **Disease group : 1000 cases**
  - CIN, cervical cancer : 300 cases
  - Endometrial cancer : 100 cases
  - Ovary cancer : 50 cases
  - Breast cancer : 50 case
  - Infectious disease : 300 cases
  - Endometriosis : 100 cases
  - Preterm birth : 100 case
- **Vaginal swab**
  - 16s rRNA Amplicon sequencing (full length)
  - Shotgun metagenome sequencing (10GB)
- **Clinical information**
- **Multionics study**

# Take home message

- The vagina microbiota play an important role in the acquisition, persistence, and clearance of HPV in the human vagina.
- Increased diversity of vaginal microbiota and reduced abundance of *Lactobacillus spp.* contribute to development of cervical cancer.
- Because microbiome is influenced by various lifestyle factors such as dietary pattern, international joint research is essential for microbiome research.
- I am looking forward to conducting various microbiome studies with ASGO and AOGIN.

**Thank you for listening !**