Microbiome as a trigger from LSIL to HSIL: Is it the clue?

Sergio Serrano

INSTITUTO RAMÓN Y CAJAL DE INVESTIGACIÓN SANITARIA IRYCIS

SaludMadrid Hospital Universitario Ramón y Cajal

ENFERMEDADES INFECCIOSAS H.U RAMÓN Y CAJAL

Outline

1 Microbiome – HPV Interactions

2 Diagnostic Applications

3 Therapeutic Implications

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1 Microbiome – HPV Interactions

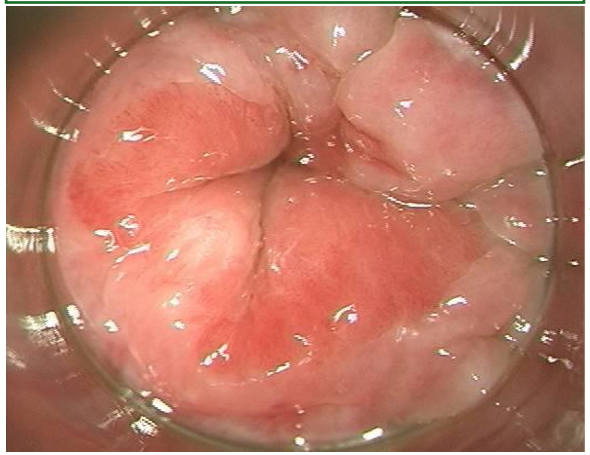
2 Diagnostic Applications

3 Therapeutic Implications

Anal cancer is markedly increased in people with HIV

But The Mechanisms Are Unclear

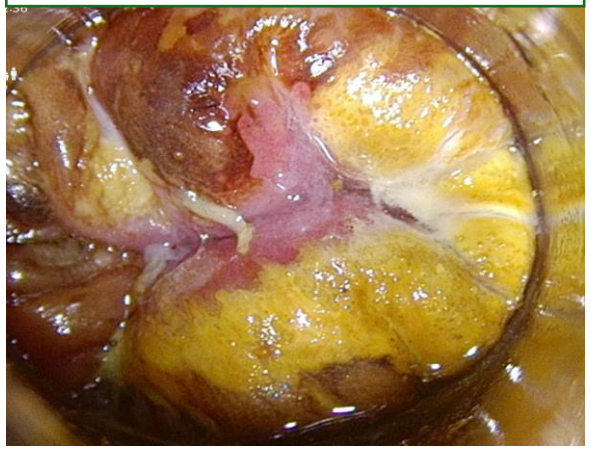
Normal / LSIL



40%

After 1y: 22-30%

HSIL



- **MSM, HIV-**:
  - 1/4196 per y (0.02%/y)
- **MSM, HIV+:**
  - 1/263 per y (1.72%/y)
  - 2.3% over 3 y

Cancer

Tong W, *et al.* Progression to and spontaneous regression of high-grade anal squamous intraepithelial lesions in HIV-infected and uninfected men. AIDS 2013

Mathews WC, *et al.* Natural History of Anal Dysplasia in an HIV-Infected Clinical Care Cohort: Estimates Using Multi-State Markov Modeling. PLoS ONE. 2014. 9(8):e104116

Jongen VW et al. Anal Squamous Intraepithelial Lesions (SILs) in Human Immunodeficiency Virus-Positive Men Who Have Sex With Men: Incidence and Risk Factors of SIL and of Progression and Clearance of Low-Grade SILs. J Infect Dis. 2020;222(1):62.

Machalek DA, *et al.* Lancet Oncol. 2012;13(5):487.

Goldstone S, *et al*. Five-year cumulative incidence of invasive anal cancer among HIV-infected patients according to baseline anal cytology results: an inception cohort analysis. HIV Med 2015; 16:191–5.

Fazendin EA, *et al*. Condyloma acuminatum, anal intraepithelial neoplasia, and anal cancer in the setting of HIV: do we really understand the risk? Dis Colon Rectum 2017; 60:1078–82

Mette T. Faber *et a*l. Risk of Anal Cancer Following Benign Anal Disease and Anal Cancer Precursor Lesions: A Danish Nationwide Cohort Study, Cancer Epidemiol Biomarkers Prev 2020

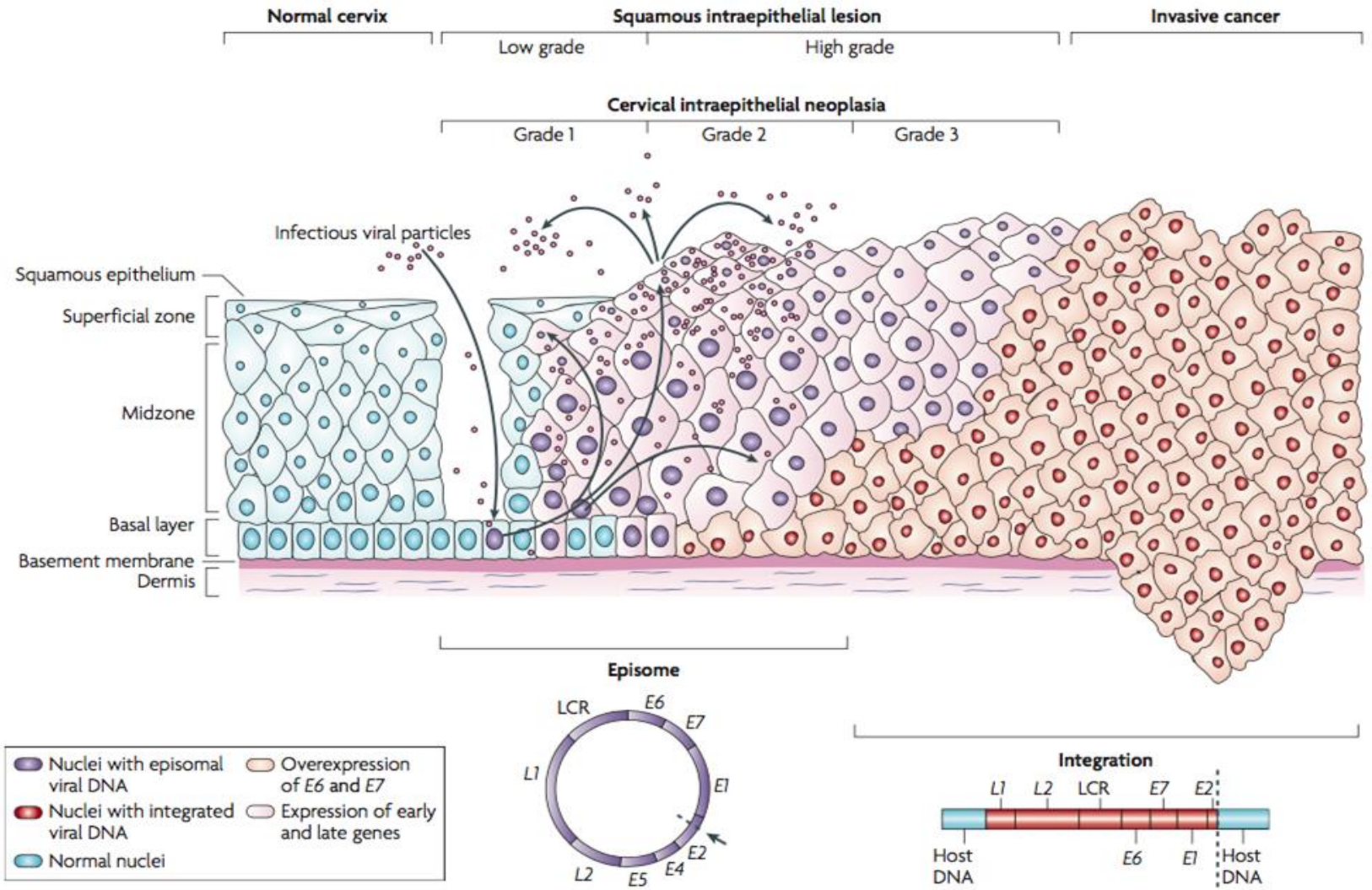
Poynten *et al*. The Natural History of Anal High-grade Squamous Intraepithelial Lesions in Gay and Bisexual Men. Clin Infect Dis. 2021 Mar 1;72(5):853-861.

Clinical discordance between stable sexually active couples: Why?

Patient 1: MSM with HIV on ART, CD4 >500, HPV 16+

Patient 2 (his partner): MSM with HIV on ART, CD4 >500, HPV 16+

HPV infection is exclusively intraepithelial

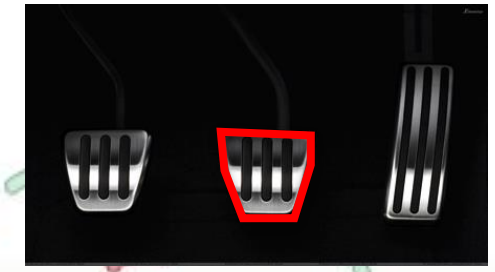


Woodman CB, et al. The natural history of cervical HPV infection: unresolved issues. Nat Rev Cancer. 2007 Jan;7(1):11-22

Microbiota-mediated induction of Th17 cells and autoimmunity

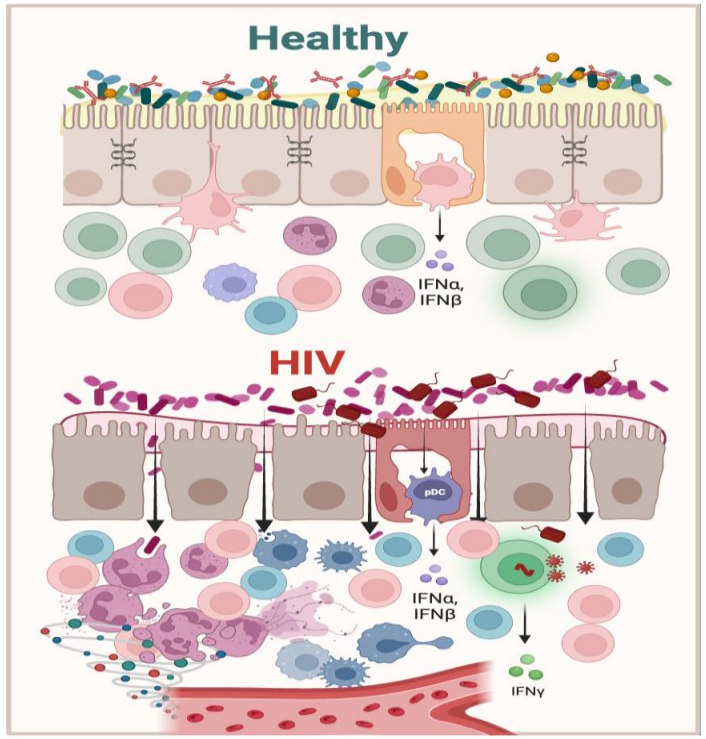
Honda & Litmman. Nature 2016

Influence of the microbiota and diet on subsets of regulatory T cells in the epithelium

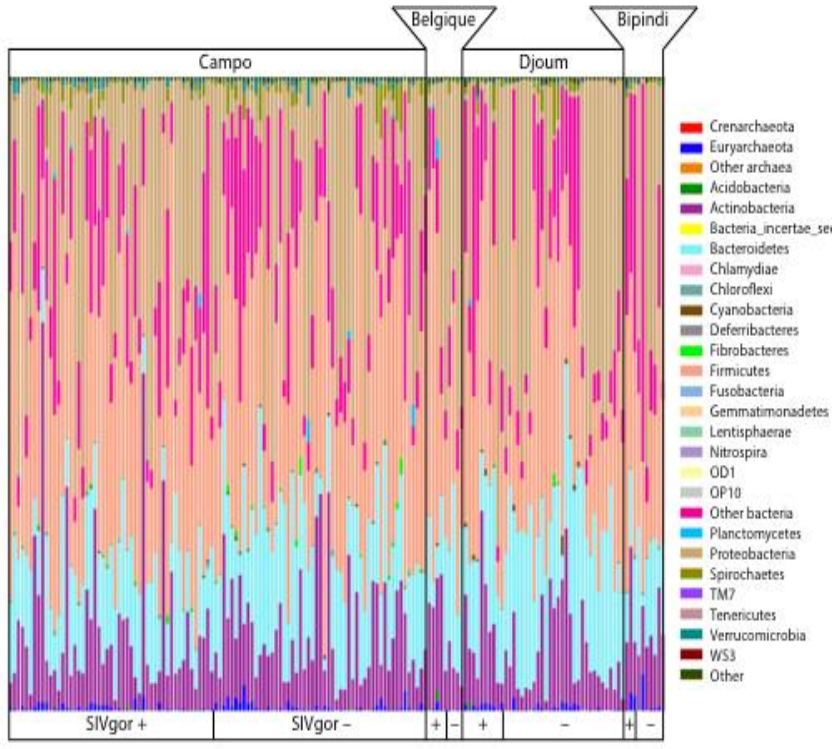


Honda & Litmman. Nature 2016

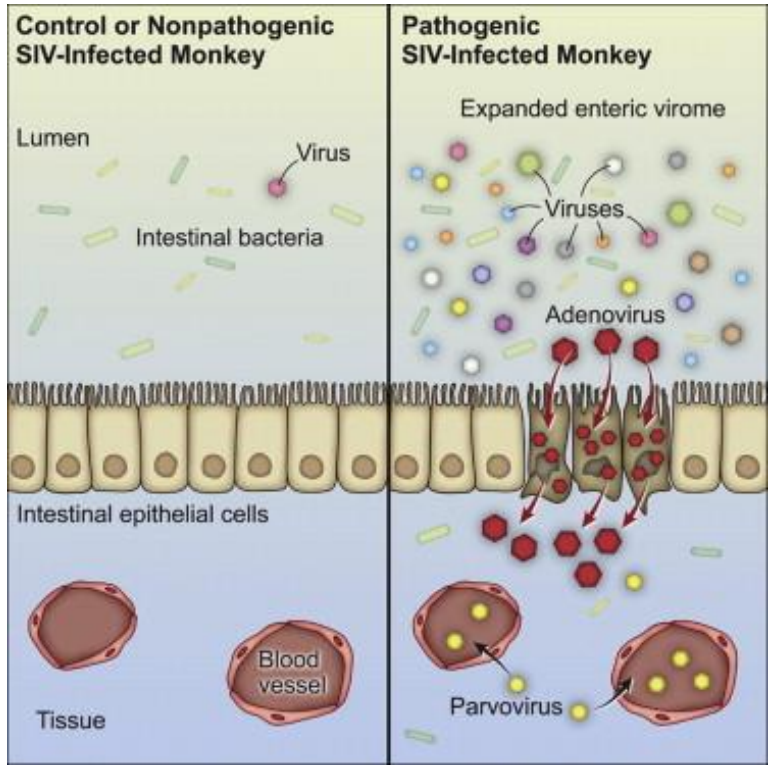
Is there an HIV-Associated Dysbiosis?



Brechley & Serrano-Villar. Microbiome 2024

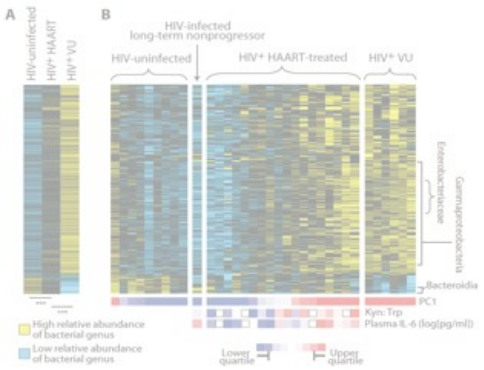


Moeller. Molecular Ecology 2015

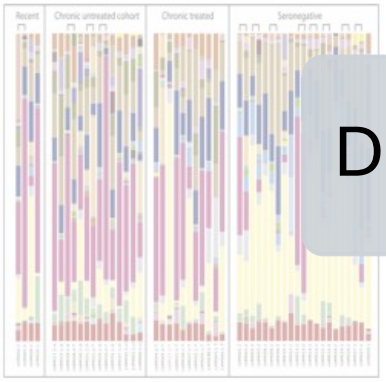


Handley. Cell 2012

Is there an HIV-Associated Dysbiosis?



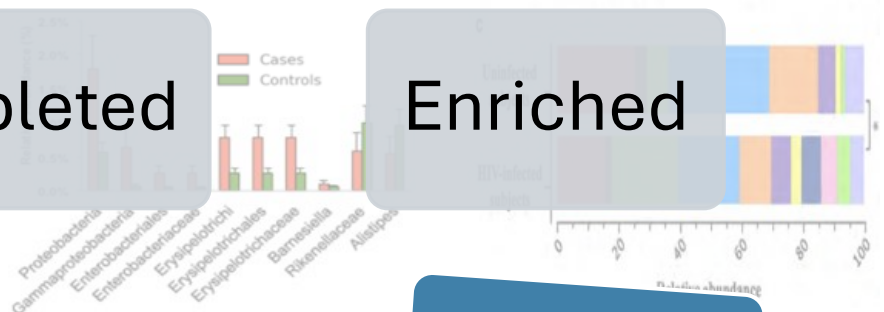
Vujkovic-Cvijin. Sci Trasl Med 2013



Lozupone. Cell Host Microbe 2013

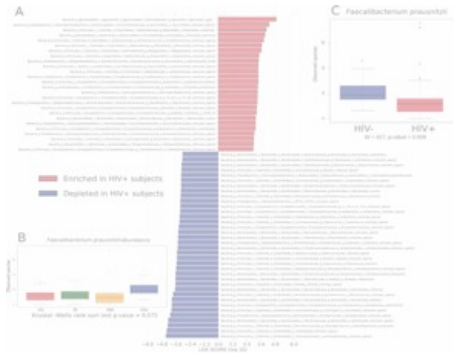
Depleted

Enriched

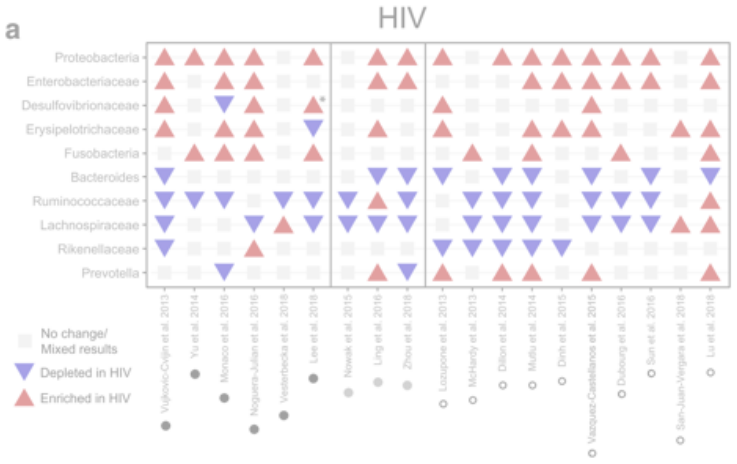


Mutlu. JID 2014

munol. 2014



Vázquez. Mucosal Imm 2015

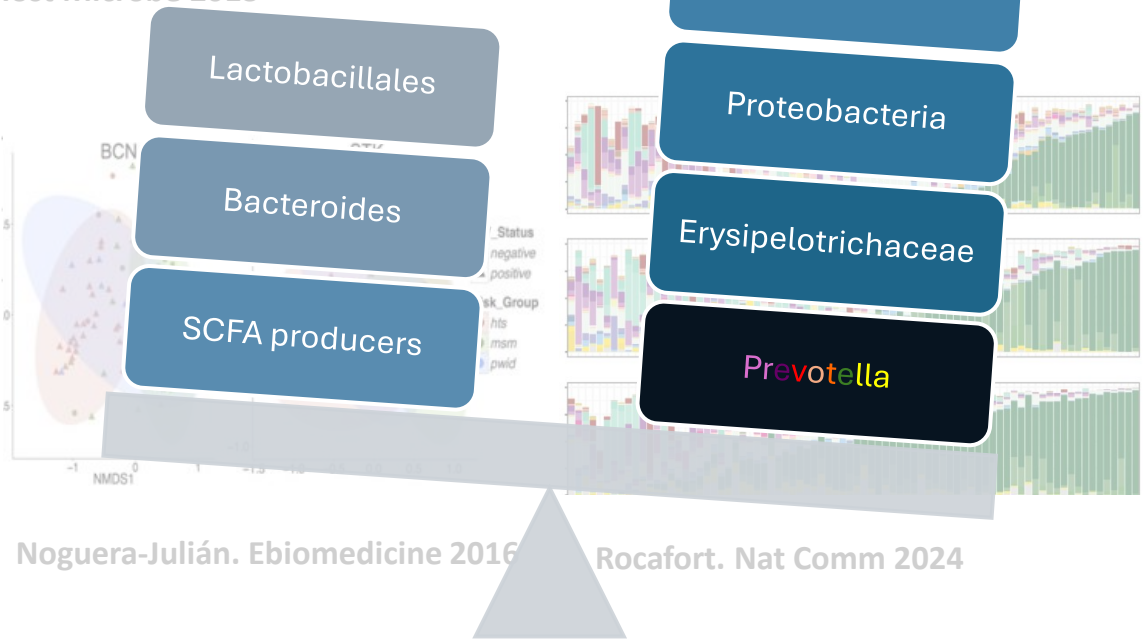


Vujkovic-Cvijin et al., Curr HIV/AIDS Rep 2019

Lactobacillales

Bacteroides

SCFA producers



Noguera-Julián. Ebiomedicine 2016

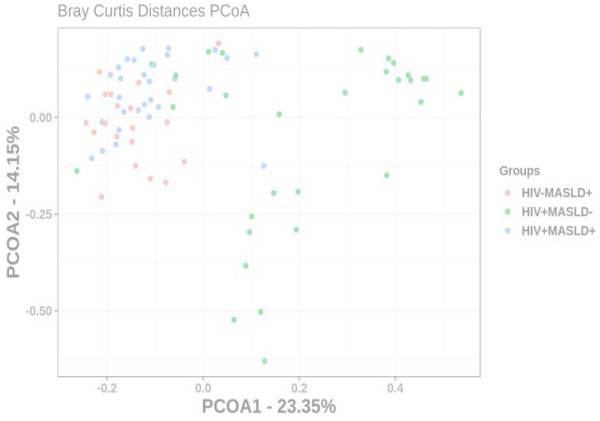
Pathobionts

Proteobacteria

Erysipelotrichaceae

Prevotella

Rocafort. Nat Comm 2024

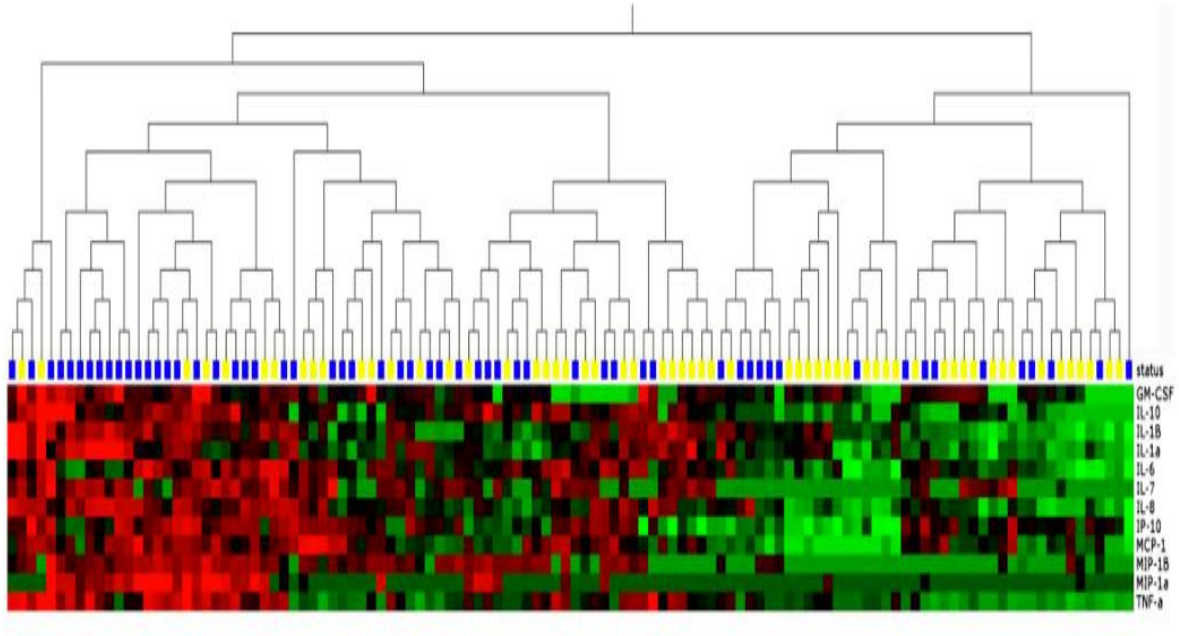


Martínez-Sanz. Front Immunol 2023

Microbiome's Effects on HIV. *Passive mechanisms*

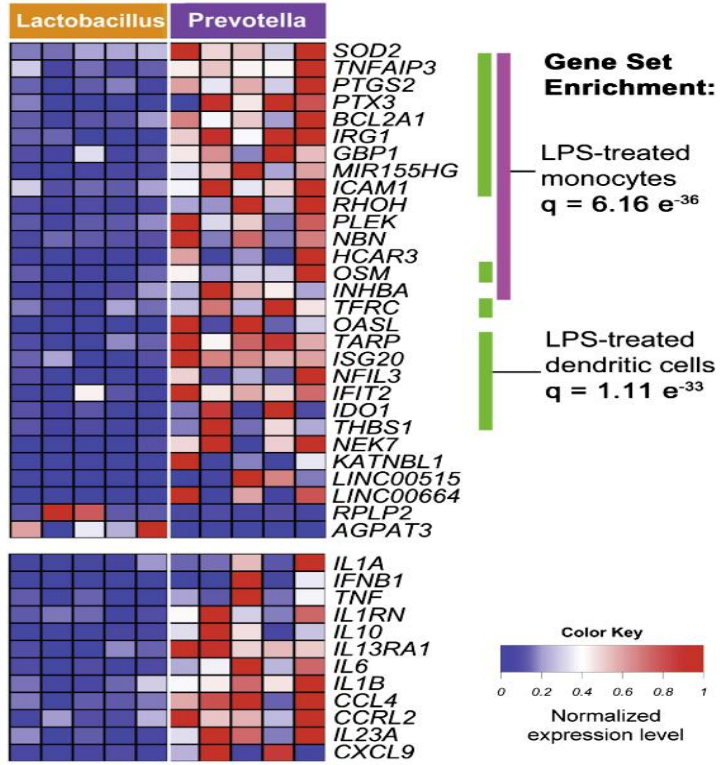
The Cervicovaginal Microbiota Influences the Risk of HIV Acquisition in Women

Women who later became HIV–infected had up-regulated preinfection cervicovaginal cytokine concentrations (risk x3)



Masson et al. JID 2015

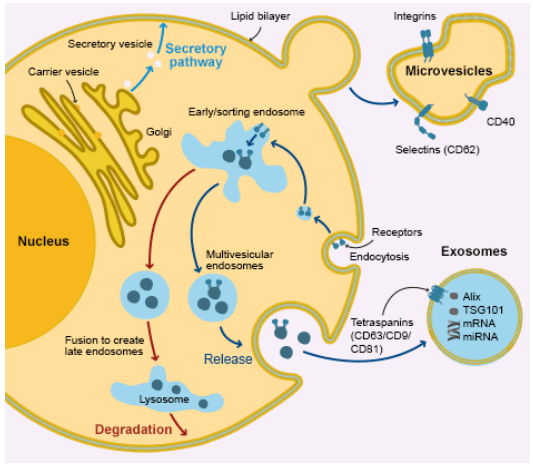
Bacterial vaginosis determines local inflammation via TLR-4 signaling



Anahtar et al. Immunity 2015

Microbiome's effects on HIV replication. *Active mechanisms*

Extracellular vesicles from lactobacilli inhibit HIV replication



Lactobacilli cultures

Ultracentrifugation

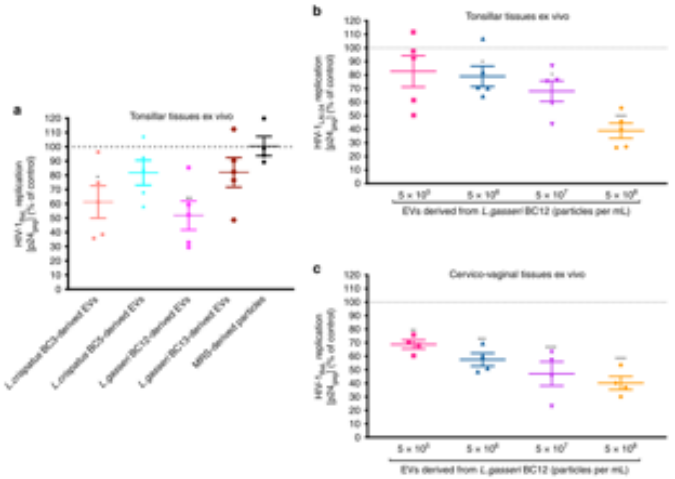


Table 1 Protein cargo of EVs derived from *L. gasseri* BC12 and *L. crispatus* BC5.

Lactobacillus-derived EV-associated proteins	Accession number
1. ATP synthase subunit beta	ATPB_LACGA
2. ATP synthase subunit alpha	ATPA_LACGA (+1)
3. Phosphonates import ATP-binding protein PhnC	PHNC_LACGA
4. ATP synthase subunit b	ATPF_LACGA
5. Enolase 2[a]	ENO2_LACGA
6. 60 kDa chaperonin[a]	CH60_LACGA (+1)
7. Enolase 1	ENO1_LACGA (+1)
8. Elongation factor Tu[a]	EFTU_LACGA
9. ATP synthase gamma chain[a]	ATPG_LACGA
10. Foldase protein PrsA 1[a]	PRSA1_LACJO
11. ATP synthase subunit beta	ATPB_LACAC
12. ATP synthase subunit delta[a]	ATPD_LACGA
13. 50S ribosomal protein L4[b]	RL4_LACAC
14. Pyruvate kinase[a]	KPYK_LACDE
15. 30S ribosomal protein S4	RS4_LACGA (+1)
16. Triosephosphate isomerase[a]	TPIS_LACGA (+1)
17. 50S ribosomal protein L21[b]	RL21_LACAC (+1)
18. 50S ribosomal protein L2[b]	RL2_LACGA (+2)

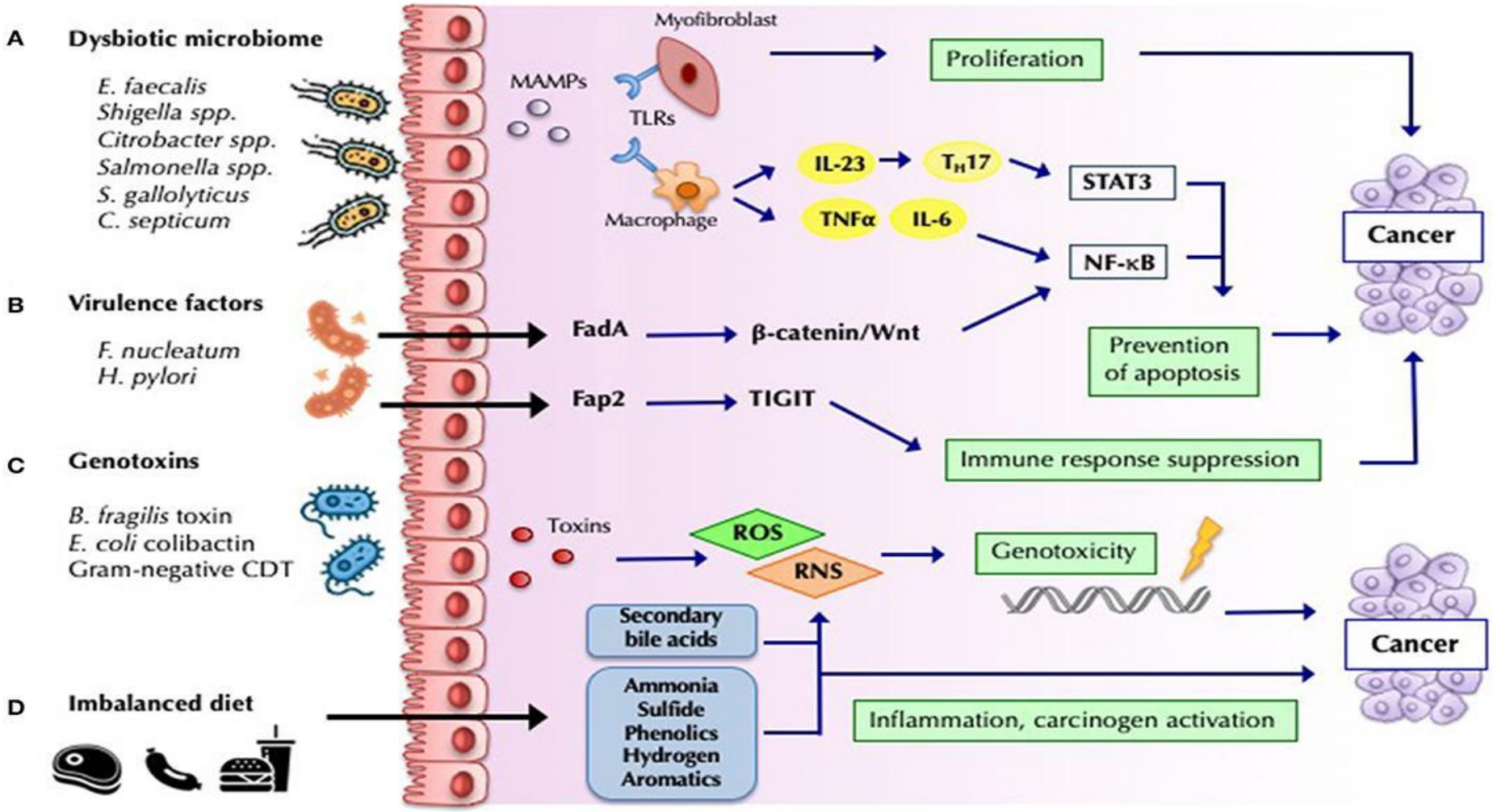
[a]Protein identified only in *L. gasseri* BC12-derived EVs
[b]Protein identified only in *L. crispatus* BC5-derived EVs

EVs released by lactobacilli into culture medium protect human T cells as well as human cervico-vaginal and tonsillar tissues ex vivo from HIV-1 infection, through the inhibition of viral attachment and entry in the target cells.

Ñahui-Palomino. Nature Comm 2019

The microbiome affects cancer pathogenesis and treatment outcomes

Consistent with the Previous Links Between the Microbiome and Cancer Pathogenesis

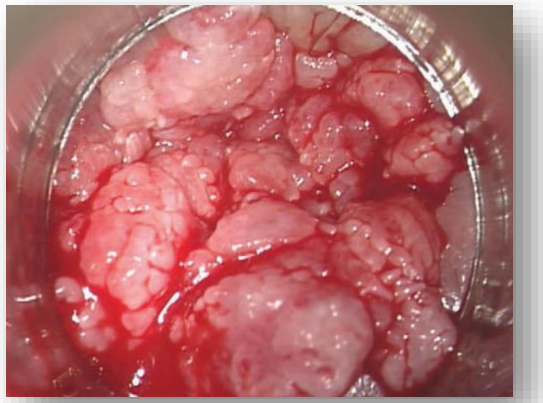


Herrera, Martínez-Sanz, Serrano-Villar.
Frontiers in Immunology 2018

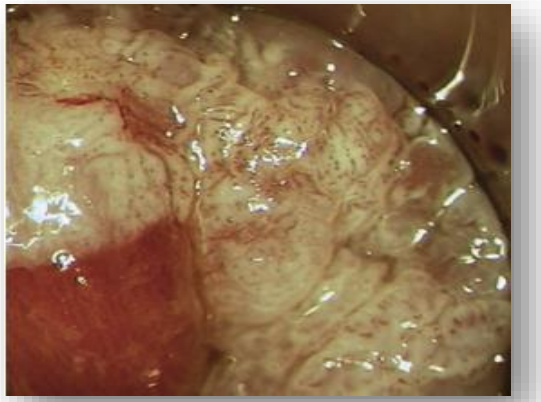
HPV-Associated disease risk are increased in PWH

Does the Microbiome Influence HPV disease?

Anal condyloma



Anal HSIL

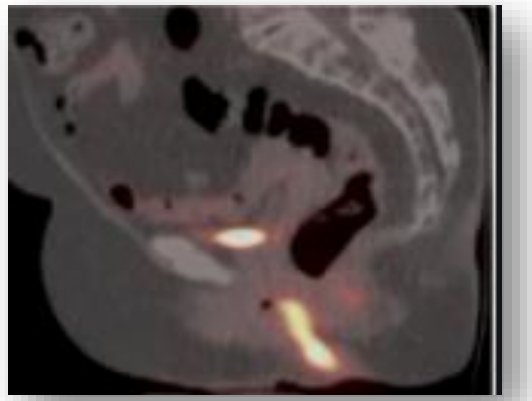


Cervical HSIL

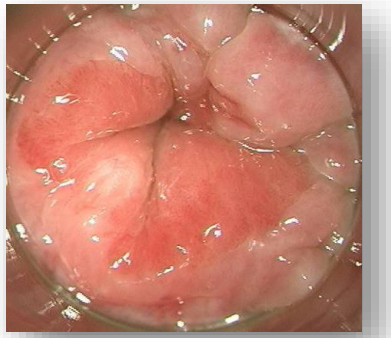
Anal cancer

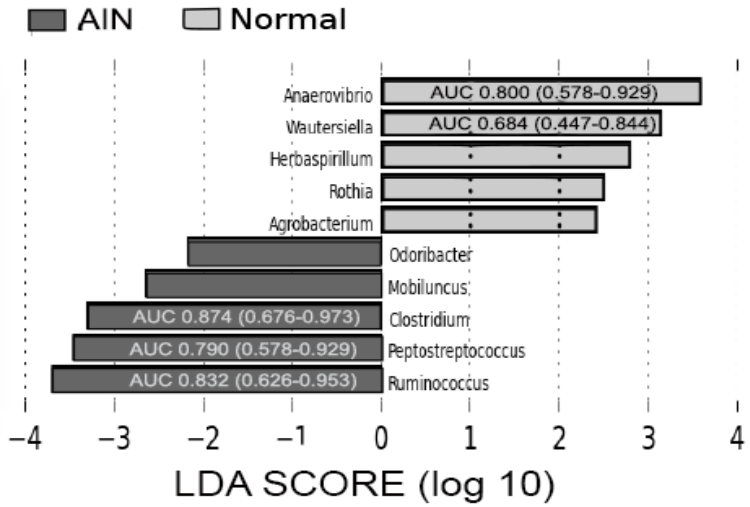
Oral cancer

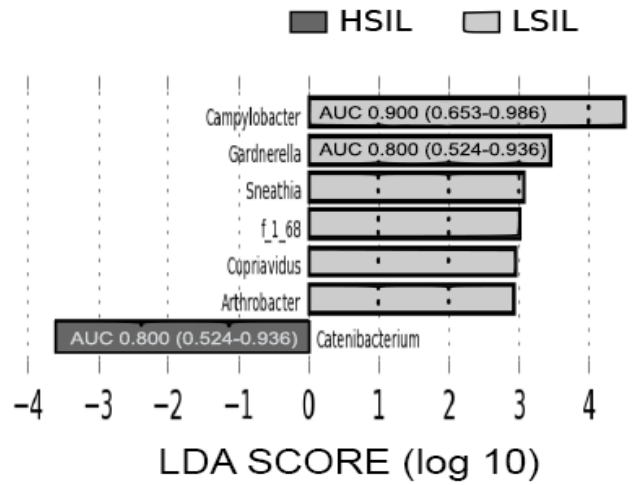
Vulvar cancer

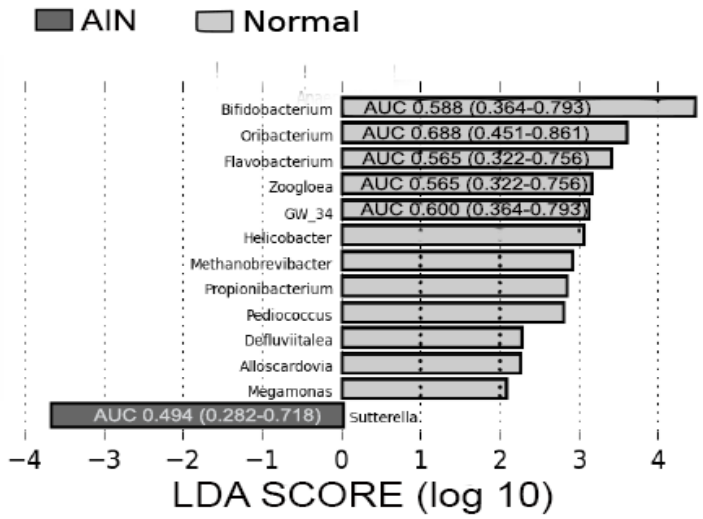


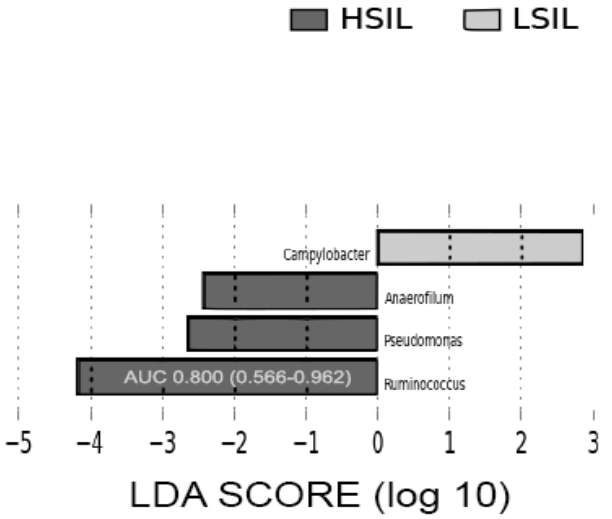
Bacterial Signatures Associated with Anal Dysplasia Differ in Anal Biopsies vs. Stools







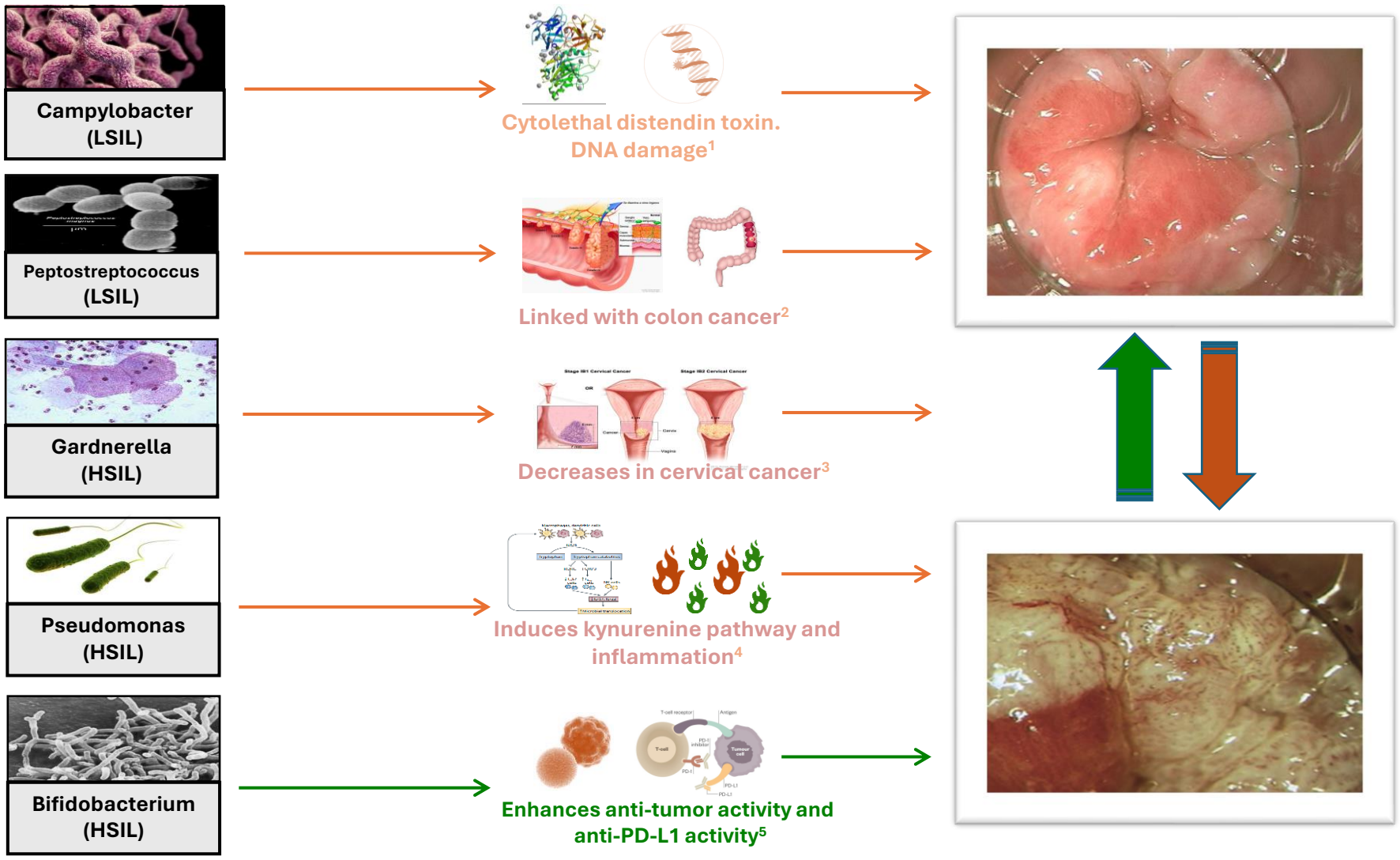




Serrano-Villar S... Moreno S, AIDS 2017

Bacterial Signatures Associated with Anal Dysplasia

Consistent with Reported Links Between the Microbiome and Cancer Pathogenesis



Serrano-Villar S... Moreno S, AIDS 2017

1 Martínez. Int J Med Microbiol 2006. 2 Candela. World J Gastroenterol 2014. 3 Audirac-Chaulifor. Plos One 2014 4 Favre. Sci Transl Med 2010. 4 Sivan. Science 2014.

Is there an HPV-Associated Dysbiosis?

Mixed Results

Increased:
- *Gardnerella*
- *Atopobium*
- *Sneathia*
- *Prevotella*
- *Megasphaera*

Decreased:
- *Lactobacillus* species

Ref.	Study population	Outcome	Microbiome analysis	Main results
Shen *et al.* [25]	156 women with HR-HPV (divided in 3 groups: No lesion, LSIL and HSIL)	Changes in the microflora and its metabolites to mine for potential biomarkers that can be used to predict the risk of cervical cancer	16S rRNA sequencing	Women with HPV infection: ↑ Gardnerella Women with HSIL: ↑ Atopobium ↑ Sneathia ↓ Streptococcus decreased
Serrano-Villar *et al.* [10]	42 MSM HIV-infected individuals undergoing screening for anal HPV-associated lesions	To identify mechanisms by which HIV infection facilitates persistence of HPV in the mucosa and increases the risk of AIN and progression from low-grade to high-grade intraepithelial lesions	16S rRNA sequencing	In mucosa, individuals with AIN: ↑ Peptostrepcoccus, ↑ Anerovibrio, Subjects with LSIL: ↑ Campylobacter Subjects with HSIL: ↑ Gardnerella ↑ Catenibacterium In feces, individuals with AIN: ↓ Bifidobacterium ↓ Peptostreptococcus. Subjects with LSIL: ↑ Campylobacter Subjects with HSIL: ↑ Ruminococcus ↑ Pseudomonas
Di Paola *et al.* [18]	28 women with persistent HPV, 27 women with HPV clearance, and 17 controls (1-year follow-up)	To identify the microbial profiles associated with viral clearance or persistence.	16S rRNA sequencing	HPV persistence group: ↓ Lactobacillus dominance ↑ Anaerobes species (Gardnerella, Prevotella, Atopobium, Megasphoera)
Audirac-Chalifour *et al.* [21]	Samples from a biological bank (2008–2011): 268 SIL 205 women with HPV negative as controls 171 CSCC	HPV infection and the development of SIL and CC are associated with changes in microbiota diversity.	16S rRNA sequencing	HPV persistence or SIL: ↑ Atopobium vaginae Women with CC: ↑ Fusobacterium Women with CIN: ↑ Sneathia
Mitra *et al.* [20]	169 premenopausal women attending colposcopy clinic; 20 normal, 52 LSIL, 92 HSIL, 5 ICC.	To correlate the structure of the vaginal microbiome with the presence of CIN.	16S rRNA sequencing	Vaginal HSIL: ↑ Sneathia, ↑ Peptostreptococcus anaerobius ↑ Anaerococcus tetradius ↓ L. jensenii
Nowak *et al.* [6]	130 Nigerian MSM	To define anal microbial patterns for MSM and their correlations with HR-HPV, HIV, and other biological and behavioral characteristics.	16S rRNA sequencing	Anal HPV16 infection: ↑ Sneathia
Shannon *et al.* [30]	65 African/ Caribbean women 23 HPV- and 36 HPV+	Examined differences in cervico-vaginal levels of pro-inflammatory and chemoattractant cytokines and the associated composition and structure of the vaginal microbiota	16S rRNA sequencing	HPV presence: ↑ Lactobacillus iners ↓ Lactobacillus spp. ↓ Fusobacterium

Table 1 (*Continued*)

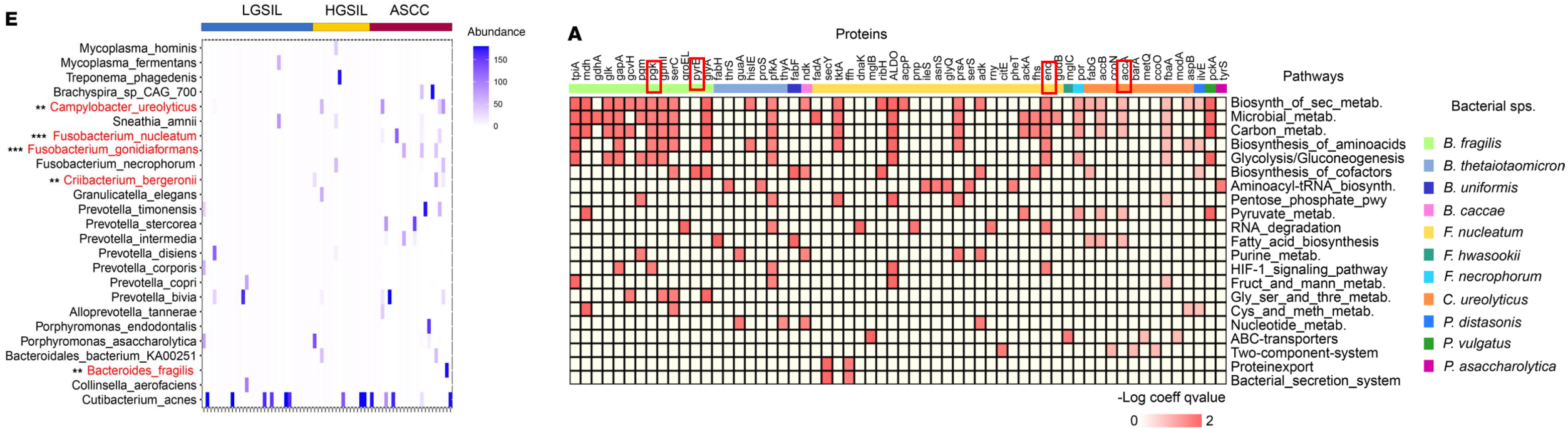
Ref.	Study population	Outcome	Microbiome analysis	Main results
Onywera, *et al.* [16]	87 South African women.	Characterized the composition of cervical microbiota in Black South African women and its associations with HPV infections	16S rRNA sequencing	HPV-HR: ↑ Gardnerella ↑ Sneathia ↑ Atopobium ↑ Aerococcus ↑ Pseudomonas
Piyathilake *et al.* [31]	430 women diagnosed with abnormal cervical cells.	Explored the association between the cervicovaginal microbiome and CIN	16S rRNA sequencing	Persistent cervicovaginal HPV: ↑ Gardnerella ↑ Prevotella ↑ Megasphaera ↑ Atopobium Women with CIN 2+: ↑ L.iners and unclassified Lactobacillus species
Gressel *et al.* [22]	55 Postmenopausal women	Characterized the endometrial, cervicovaginal, and anorectal microbiota of postmenopausal women	16S rRNA sequencing	Uterine serous cancers: ↓ Pseudomonas ↑ L. iners
Elnaggar *et al.* [27▪]	60 patients with high-grade lower genital tract dysplasia and 21 patients with SCCA	To identify differences in anal microbiome composition in the settings of HPV infection, anal dysplasia, and anal cancer	16S rRNA sequencing	Individuals with anal cancer: ↑ Peptoniphilus ↑ Prevotella ↑ Porphyromonas ↑ Fusobacterium (significantly enriched in anal cancer cases compared to high-risk normal samples).
Ron *et al.* [7]	99 HIV-infected and 29 HIV-uninfected MSM; all underwent anal cytology and HRA	Identifying the association between anal HSIL lesions and specific changes in the microbiota	16S rRNA sequencing	Individuals with HSIL: ↑ Aloprevotella spp. ↑ Treponema succinifaciens ↓ Prevotella ↓ Sneathia, and ↓ Ruminococcaceae
Serrano *et al.* [26▪▪]	213 individuals with HIV who had completed all of the cytologic and histologic evaluations (HSIL and anal cancer screening)	Characterized the composition and functions of the anal microbiome associated with HSIL in MSM with HIV.	16S rRNA sequencing	Individuals with HSIL: ↑ Prevotella copri* ↓ Streptococcus periodonticum, ↓ Dialister succinatiphilus ↓ Prevotella stercorea ↓ Sneathia sanguinegens ↓ Fusobacterium* goniadiaformans ↓ Anaerovibrio lipolyticus *Produced succinyl-CoA and cobalamin at higher concentrations.
Oh *et al.* [19]	120 women: 70 CIN cases. 50 Controls:normal cytology or ASCUS.	Identifying the cervical microbiota of Korean women and the association between the cervical microbiota and CIN	16S rRNA sequencing	Higher risk of CIN: ↑ *A. vaginae, G. vaginalis, L. iners* ↓ *L. crispatus*
Lee *et al.* [32]	68 female twins with HPV infection-discordant in Korea	Characterized the association between the vaginal microbiota and HPV infection using a twin cohort	16S rRNA gene sequencing	HPV positivity: ↓ Lactobacillus spp. ↑ L. iners ↑ Sneathia spp. ↑ Megasphaera

Ron R, Moreno E, Rosas M, Serrano-Villar S. The microbiome as a biomarker of anal precancerous lesions in people with HIV. Curr Opin Infect DIs 2023.

Is the Microbiome Contributing to HPV Progression Through Its Metabolism?

The "Active" Microbiota: Insights from Metatranscriptomics

70 anal biopsies: 31 LGSIL, 16 HGSIL, and 23 ASCC



Specific species (*Fusobacterium nucleatum, Bacteroides fragilis*) were more prevalent in ASCC than precancerous lesions.

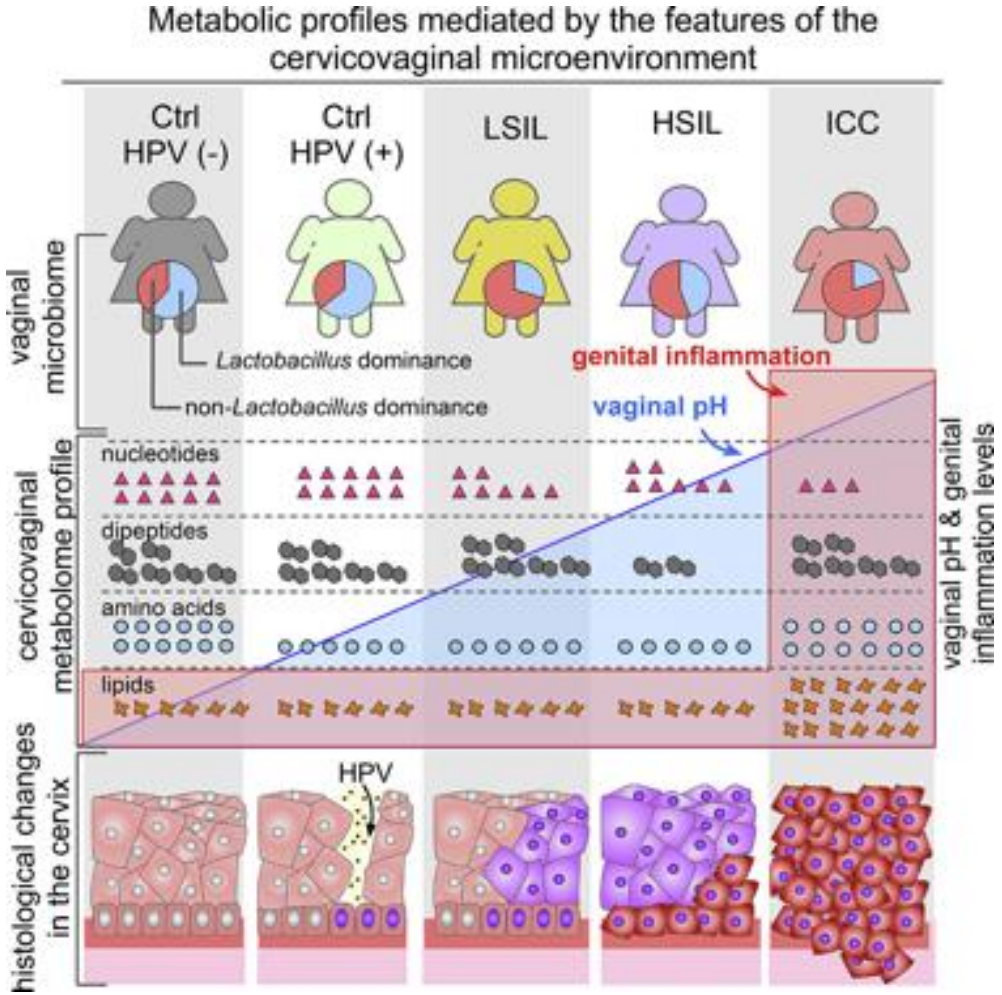
These species correlated with:

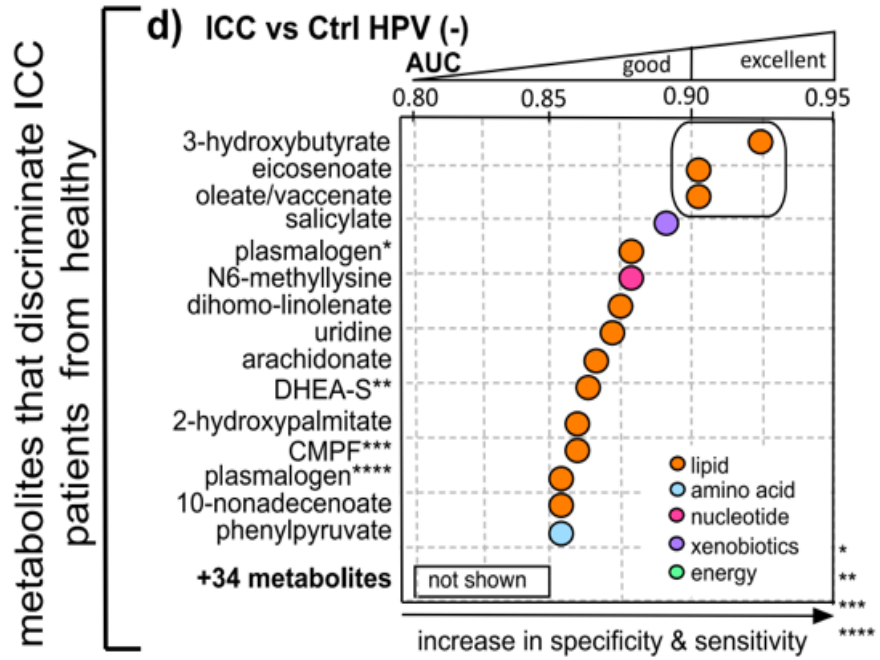
- gene-encoding enzymes (Acca, glyQ, eno, pgk, por)
- oncoproteins (FadA, dnaK)

Lacunza E,..., MC. Abba. Transcriptome and microbiome-immune changes across preinvasive and invasive anal cancer lesions. JCI Insight 2024

Is the Microbiome Contributing to HPV Progression Through Its Metabolism?

The "Active" Microbiota: Insights from Metabolomics





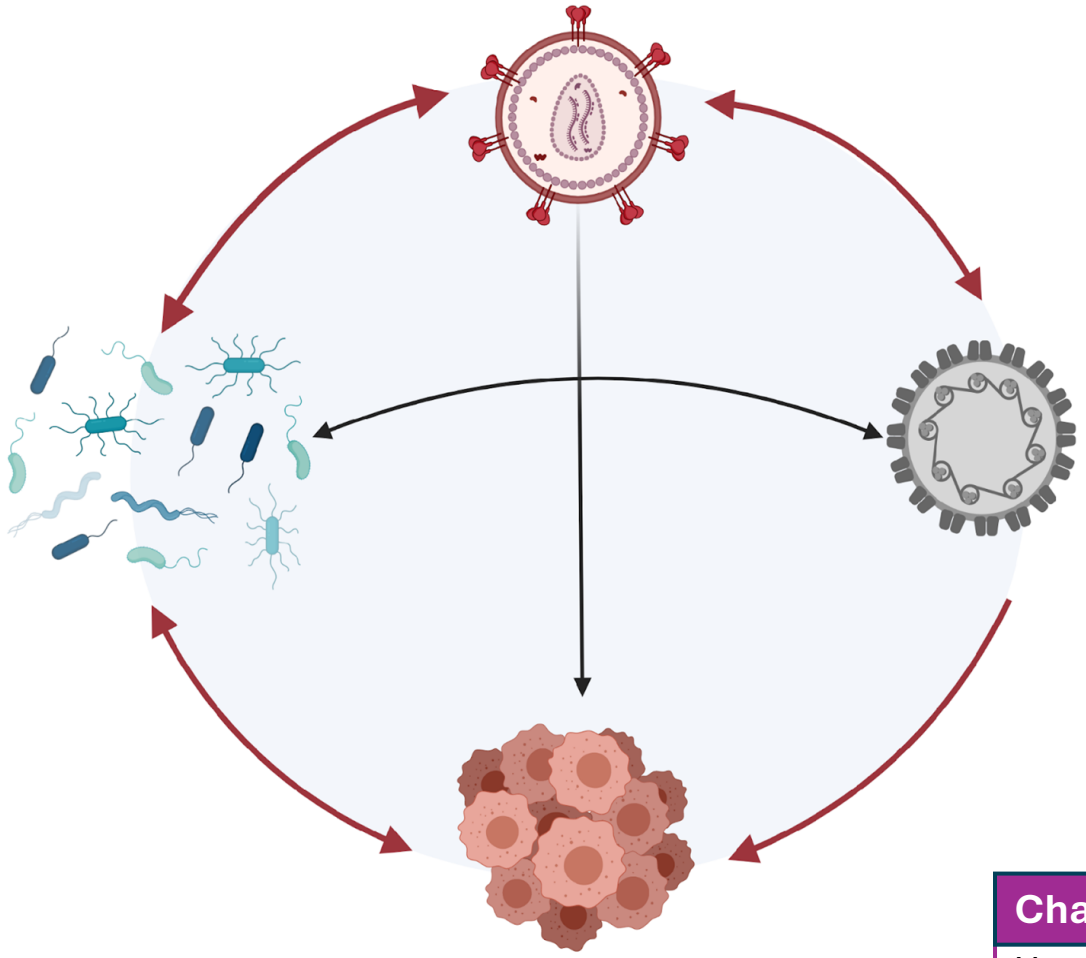
Potential links between 3-hidroxybutyrate and HPV oncogenesis

1. **Immune Suppression**: Inhibits NLRP3, reducing immune response, allowing HPV persistence.
2. **Epigenetic Changes**: Acts as HDAC inhibitor, promoting oncogene expression (E6/E7).
3. **Metabolic Shifts**: Alters the vaginal microenvironment, supporting viral survival.
4. **Cell Proliferation**: Influences cellular proliferation, increasing risk of malignant transformation.

Ilham. Ebiomedicine 2019

Challenges to address relationships

Association or causation?



Vaginal Microbiome and HPV Persistence

- Metabolites like biogenic amines, glutathione, and lipids, linked to HPV persistence.
  - HPV persistence and dysplasia.
  - Dominance of non-Lactobacilli facilitates HPV
- *L. iners* and *L. crispatus* associated with lower risk.
- Sneathia or Gardnerella linked to HPV-induced carcinogenesis.

Microbiome and Inflammation in HPV

- Lactobacillus-depletion increases inflammation and promotes HPV oncogene expression and malignant cell growth.
- Promotes coinfections, e.g., Chlamydia trachomatis.
- HPV down-regulates innate molecules, affecting Lactobacillus growth.

Proinflammatory Cytokines and HPV Carcinogenesis

- Specific inflammation markers related to progression to carcinogenic status, potential clinical markers for preventing high-grade lesions.
- Specific metabolic profiles associated with HPV progression.

Challenges ahead

Most studies are cross-sectional, making it difficult to determine causality between microbiota and HPV infection

Moreno E, Ron R, Serrano-Villar S. The microbiota as a modulator of mucosal inflammation and HIV/HPV pathogenesis: From association to causation. Front Immunol. 2023 Jan 23:14:1072655

Outline

1 Microbiome – HPV Interactions

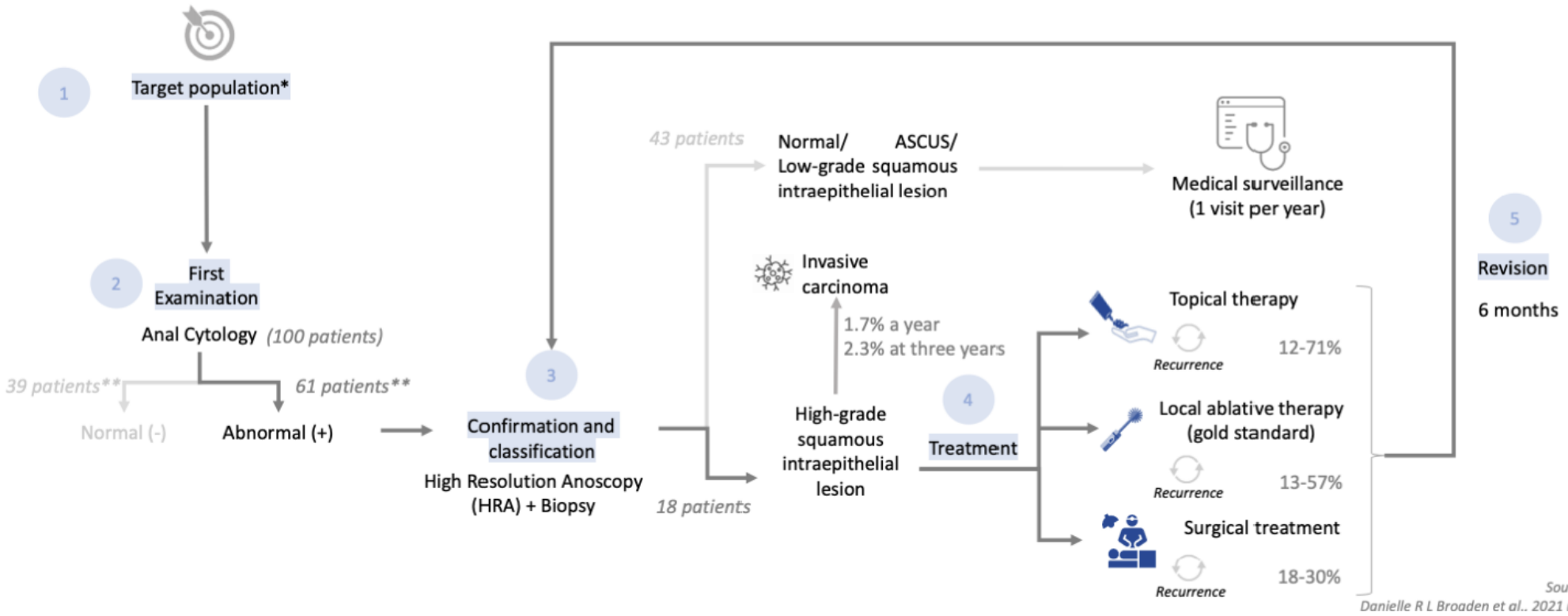
2 Diagnostic Applications

3 Therapeutic Implications

Anal cancer is markedly increased in people with HIV

But the specificity of anal cytology is poor

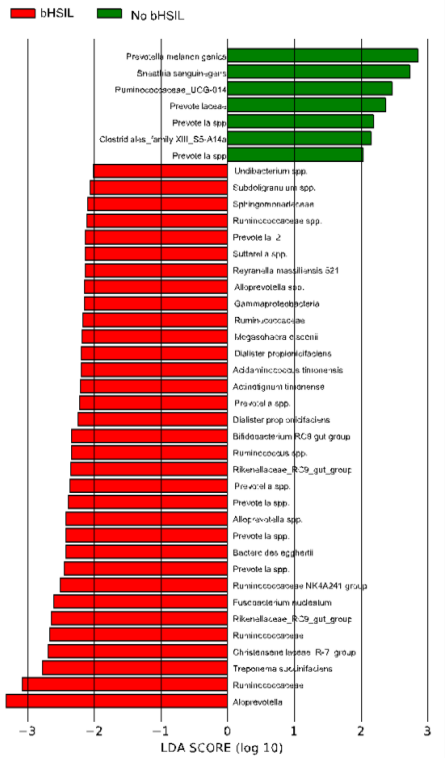
- MSM with HIV exhibit a disproportionately high (85 to 300-fold) risk of anal cancer[1,2].
- Screening and treating high-grade squamous intraepithelial lesions (HSIL), the cancer precursor, decreases the risk of anal cancer. The prevalence of HSIL is high (~40%)[3].
- The specificity of the current screening test, anal cytology, is poor (46% - 65%) [4, 5], but its negative predictive value is high (~95%) [5].



1. Clifford GM. et al. A meta-analysis of anal cancer incidence by risk group: Toward a unified anal cancer risk scale. Int J Cancer 148, 1–11 (2020). 2. Koroukian SM. et al. Excess cancer prevalence in men with HIV: A nationwide analysis of Medicaid data. Cancer 128, 1987–1995 (2022).
3. Palefsky JM. et al. Treatment of Anal High-Grade Squamous Intraepithelial Lesions to Prevent Anal Cancer. New England Journal of Medicine 386, 2273–2282 (2022).
4. Clarke MA, Wentzensen N. Strategies for screening and early detection of anal cancers: A narrative and systematic review and meta-analysis of cytology, HPV testing, and other biomarkers. Cancer Cytopathol 126(7):447-460 (2018)
5. Serrano-Villar et al. Screening for Precancerous Anal Lesions with P16/Ki67 Immunostaining in HIV-Infected MSM. Plos One 2017

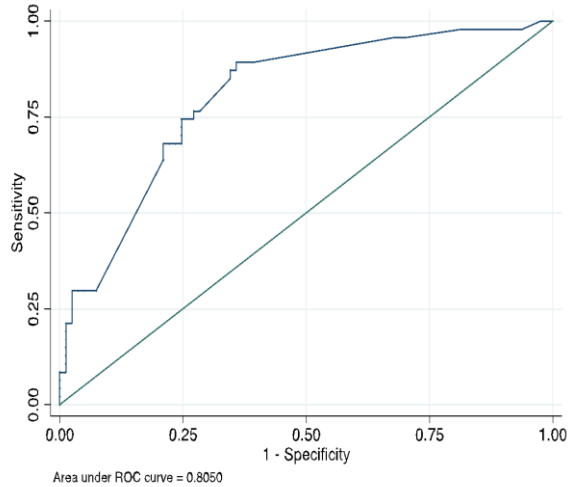
Exploring the Microbiota as a Diagnostic Tool for Anal Precancer

Anal cytologies from 128 individuals: 47 (36.7%) with bHSIL and 81 (63.3%) without HSIL



Diagnostic test	Sensitivity (%)	Specificity (%)	AUC ROC	P value
Anal citology[1]	72 (59-85)	57 (46-68)	-	0.002
Bacterial biomarkers[2]	37 (23-51)	90 (84-96)	0.737	0.002
Bacterial biomarkers[2] + anal citology	65 (51-79)	83 (74-90)	0.805	0.0006

[1]High or low intraepithelial squamous lesions = positive
[2]Abundance of Ruminococcaceae NK4A214 and Alloprevotella, absence of Prevotella melanonigenica and Ruminococcaceae UCG-014

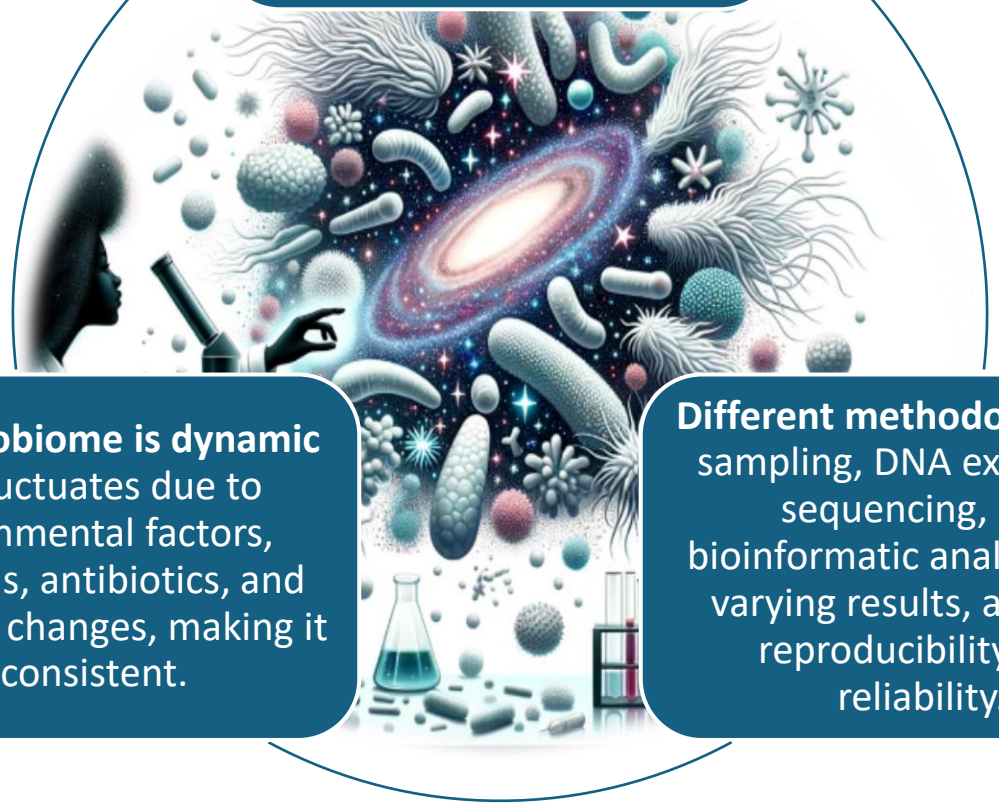


From 35 (94%) of false positive cytologic results, the combination of these four biomarkers reclassified to true negative 33 (94%), significantly improving the predictive performance of anal cytology alone to AUC 0.805.

Ron R... Serrano-Villar. Exploiting the Microbiota for the Diagnosis of Anal Precancerous Lesions in Men Who Have Sex With Men. JID 2021

Challenges to leverage the microbiome as a diagnostic tool

Microbiomes differ between individuals due to genetics, lifestyle, diet, geography, etc., making it hard to establish a baseline for diagnosis.



The microbiome is dynamic and fluctuates due to environmental factors, infections, antibiotics, and hormonal changes, making it inconsistent.

Different methodologies for sampling, DNA extraction, sequencing, and bioinformatic analysis yield varying results, affecting reproducibility and reliability.

Microbiome-based SCReening of Anal Cancer in PWH (SCRATCH)

Using Multiomics To Guide Biomarker Discovery

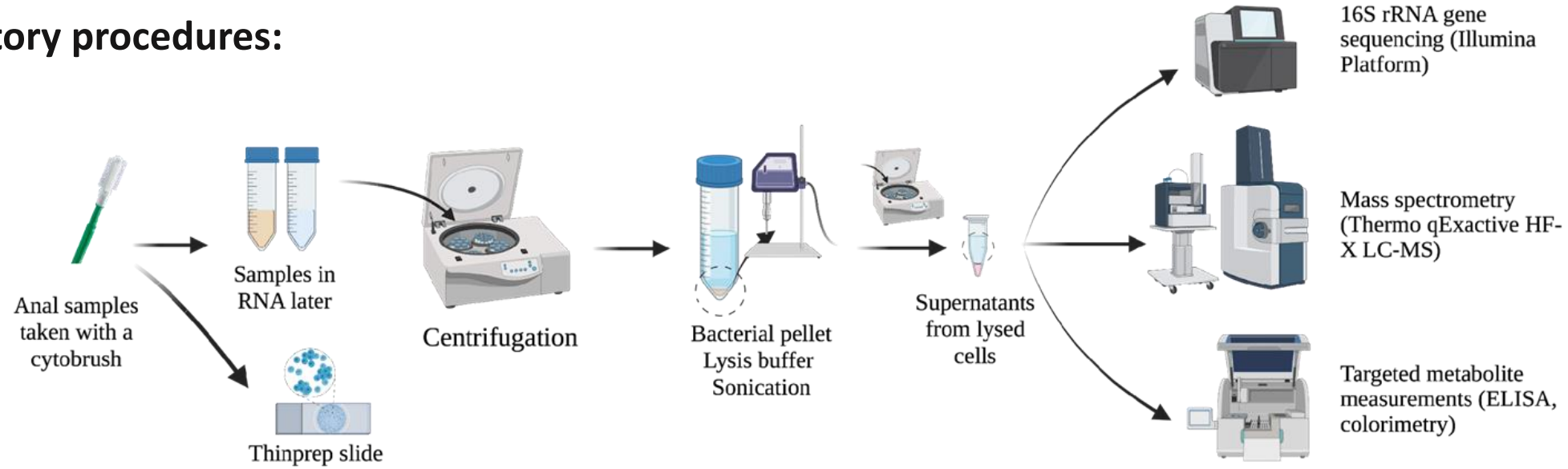
SCRATCH

Objectives: Identify anal bacterial biomarkers to improve the accuracy of anal cytology for HSIL diagnosis.

Study population: 213 PWH undergoing HSIL screening with concomitant anal cytology + HRA in 4 clinical sites in Spain and Italy.

- Discovery cohort: 167 (70 [42%] with confirmed HSIL)
- Validation cohort: 46 (25 [54%]with confirmed HSIL)

Laboratory procedures:



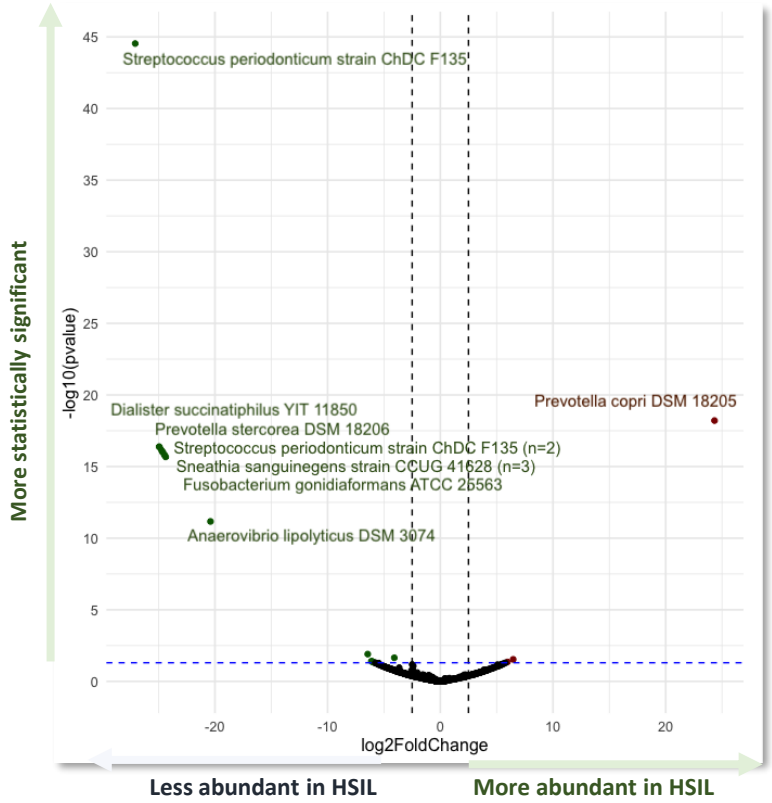
Microbiome-based SCReening of Anal Cancer in PWH (SCRATCH)

Using Multiomics To Guide Biomarker Discovery

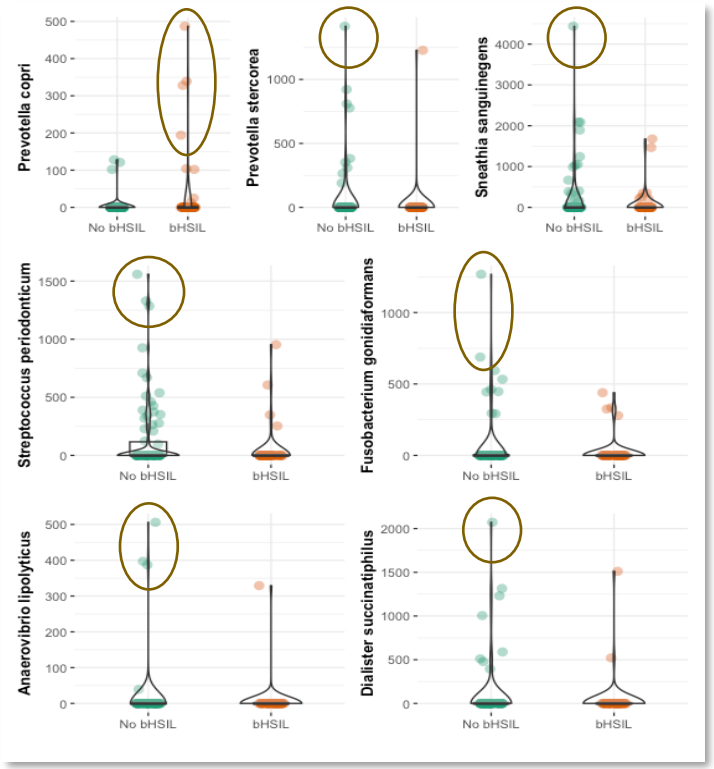
SCRATCH

Anal microbiota composition did not consistently predict HSIL

Differentially abundant bacteria

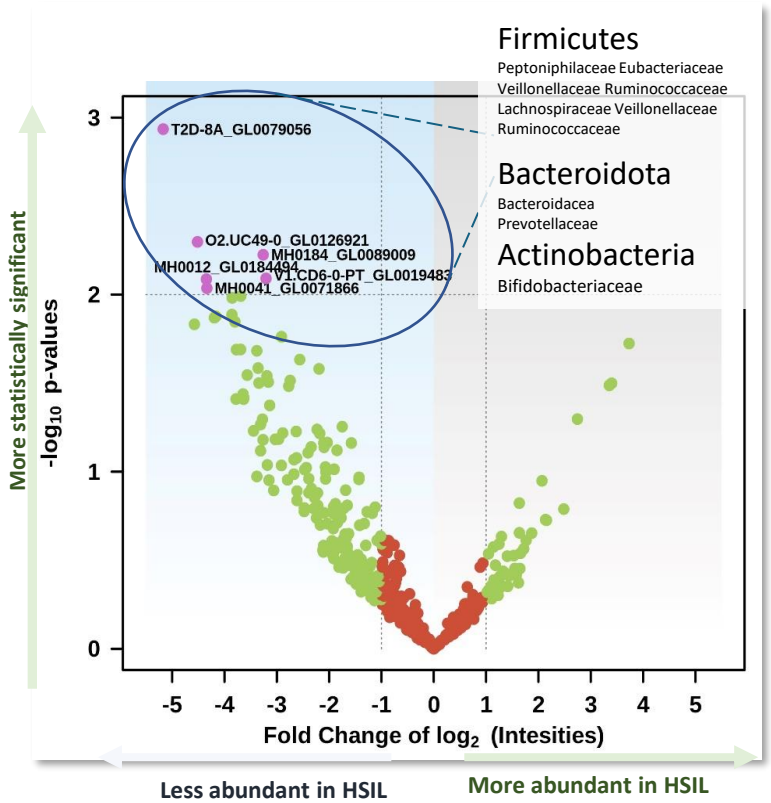


Significantly differential bacteria



Relevant differences in bacterial proteins and HSIL

Differentially expressed proteins



Serrano-Villar... Ferrer. *Microbiome-Derived Cobalamin and Succinyl-CoA as Biomarkers for Improved Screening of Anal Cancer*. Nature Medicine 2023 Jul;29(7):1738-1749. **Link for free access: https://rdcu.be/dg9g9**

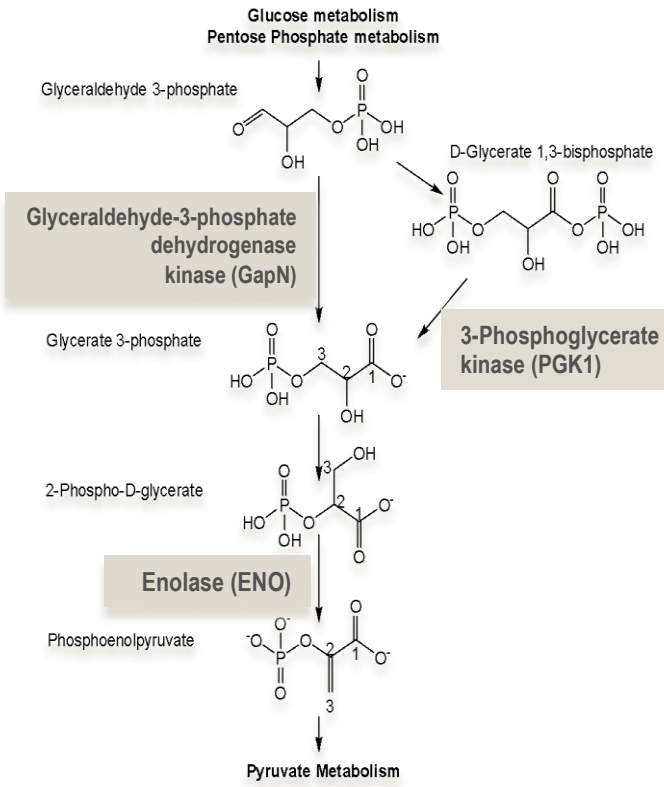
Microbiome-based SCReening of Anal Cancer in PWH (SCRATCH)

Using Multiomics To Guide Biomarker Discovery

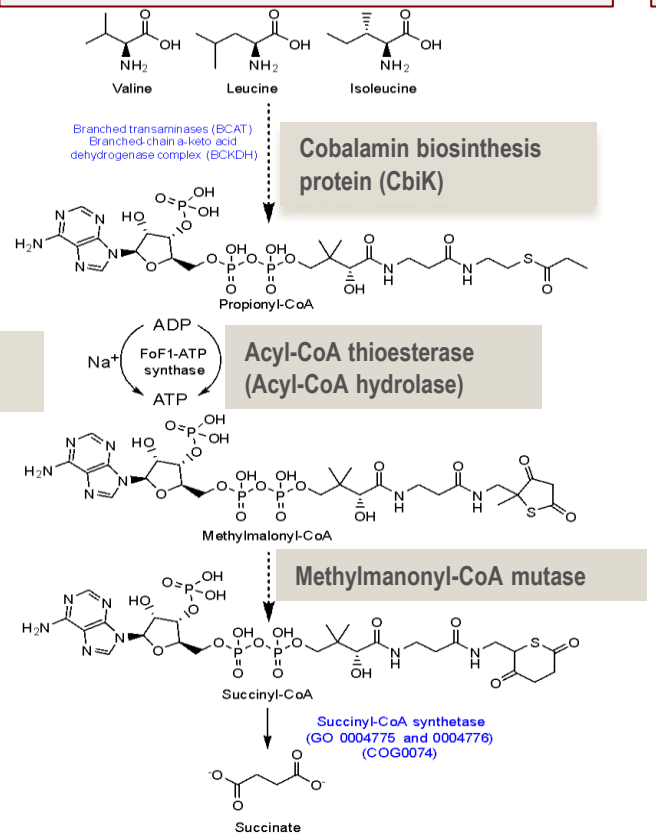
SCRATCH

Proteins overexpressed in HSIL showed biological consistency and plausibility

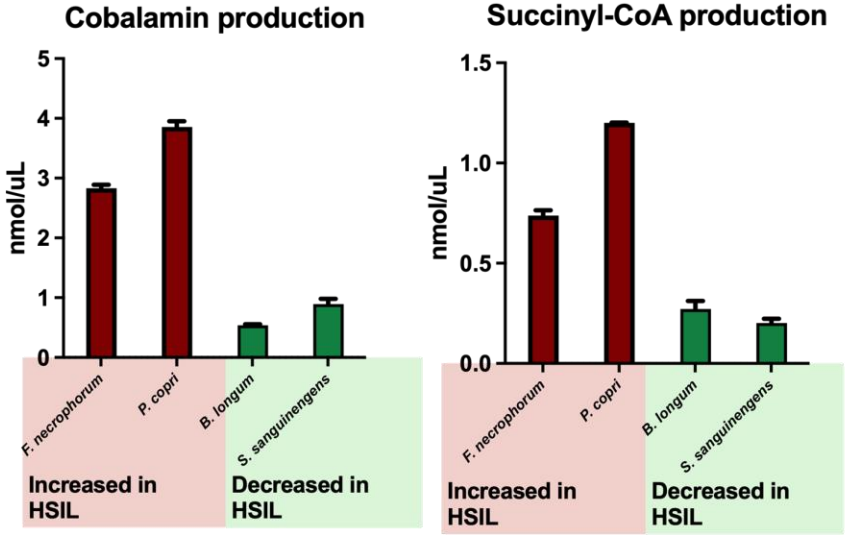
Pathway within the glycolysis and gluconeogenesis overexpressed in HSIL



Pathway within the cobalamin biosynthesis and connections with other proteins overexpressed in HSIL



Bacteria presumably implicated in progression to cancer produced greater concentrations of cobalamin and SucCoA than those presumably protective.



F. necrophorum: associated with cancer pathogenesis *(Shang, World J Gastrointest 2018)*

P. copri: *associated with HSIL in this study.*

B. longum: known anci-carcinogenic effects *(Fahmy, Nutr Cancer 2019)*

S. sanguinengens: decreased in HSIL in this and our previous study *(Ron, JID 2021)*

Serrano-Villar... Ferrer. *Microbiome-Derived Cobalamin and Succinyl-CoA as Biomarkers for Improved Screening of Anal Cancer*. Nature Medicine 2023 Jul;29(7):1738-1749. **Link for free access: https://rdcu.be/dg9g9**

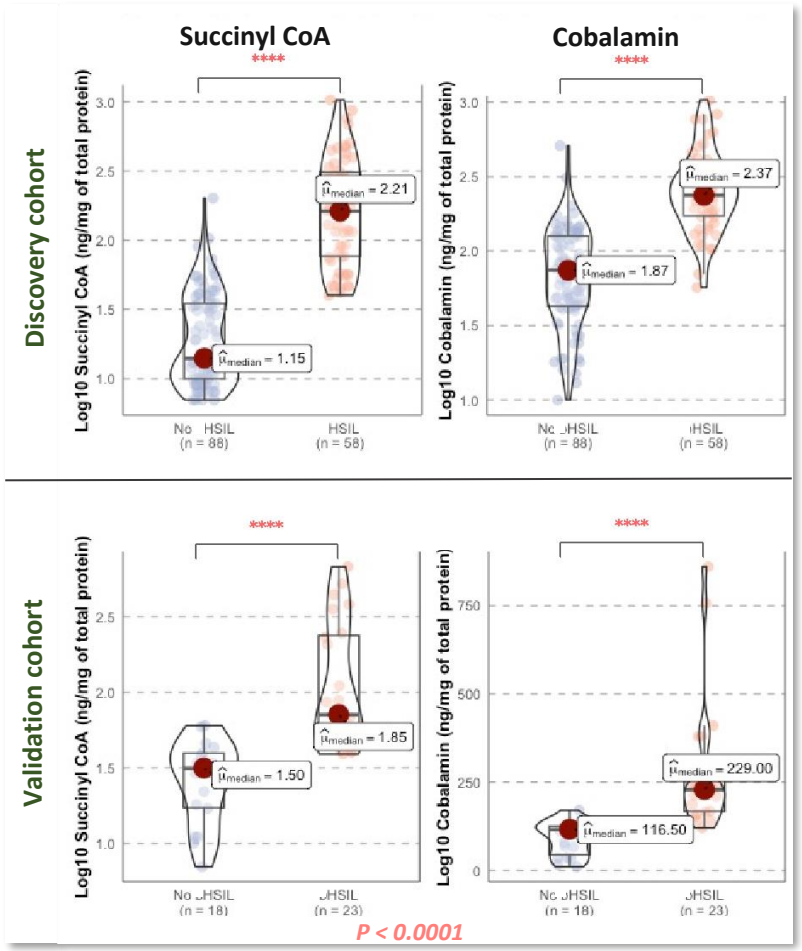
Microbiome-based SCReening of Anal Cancer in PWH (SCRATCH)

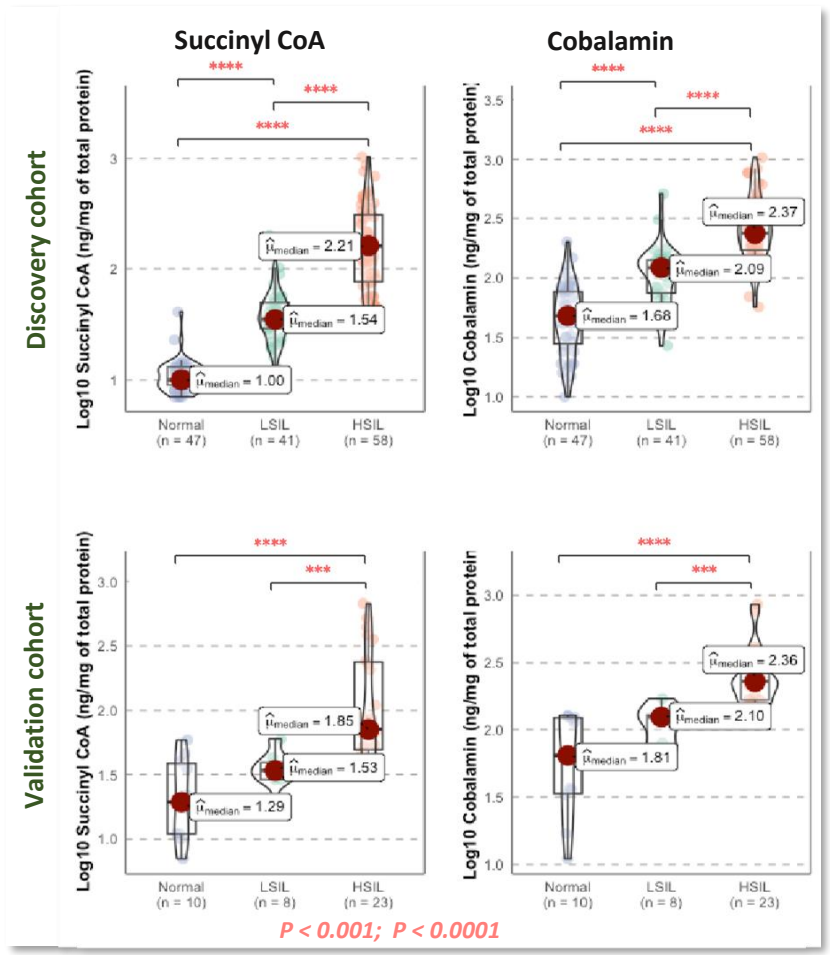
Using Multiomics To Guide Biomarker Discovery

SCRATCH

RESULTS: Targeted metabolite analysis directed by the proteomic findings

Succinyl-CoA and cobalamin are increased in anal cytologic samples from patients with HSIL





Measurements

- Succinyl-CoA Synthetase colorimetric assay kit (ID ab196989; Abcam, Cambridge, UK)
- Cobalamin ELISA kit (ID LS-F13023; LifeSpan BioSciences)

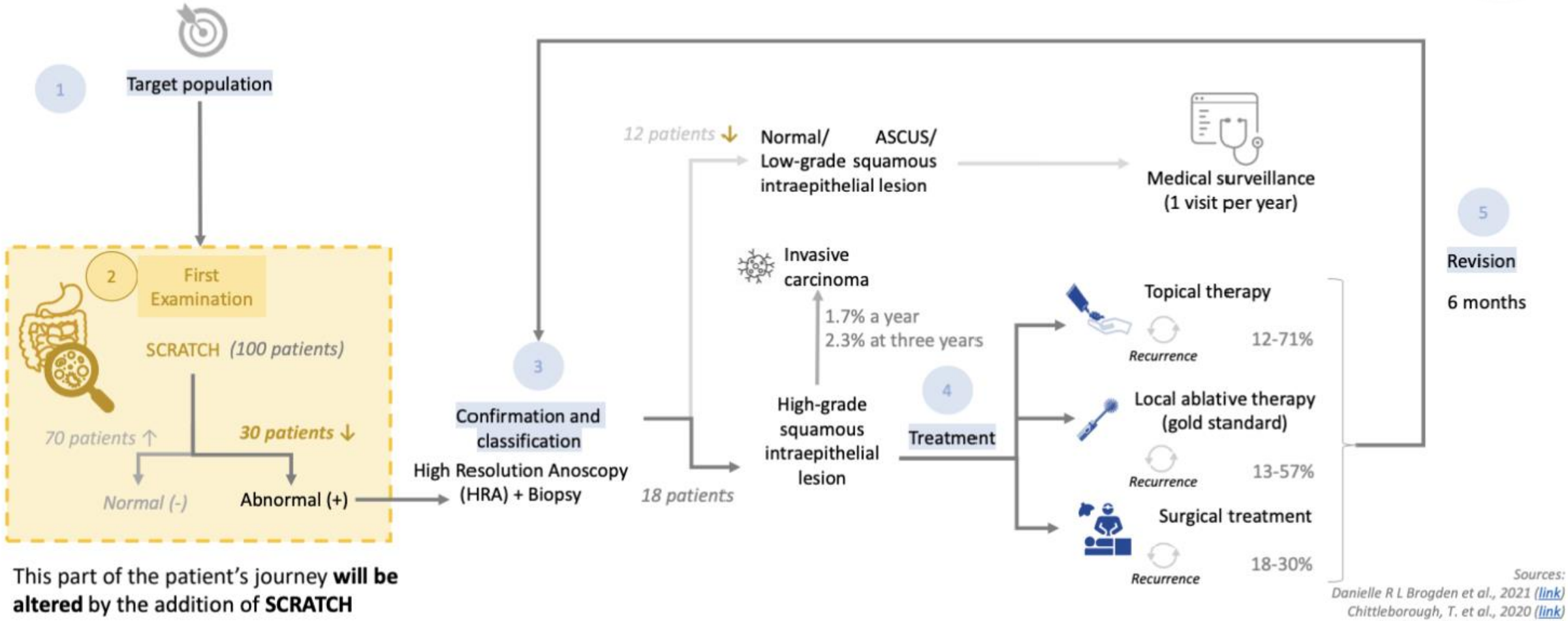
Calibration curves

- Succinyl-CoA (ref. S1129-5MGM, Merck Life Science S.L.U., Madrid, Spain)
- Cobalamin (ref. V6629-100MG, Merck Life Science S.L.U., Madrid, Spain) were prepared before the assay.

Microbiome-based SCReening of Anal Cancer in PWH (SCRATCH)

Using Multiomics To Guide Biomarker Discovery

SCRATCH



Serrano-Villar... Ferrer. *Microbiome-Derived Cobalamin and Succinyl-CoA as Biomarkers for Improved Screening of Anal Cancer*. Nature Medicine 2023 Jul;29(7):1738-1749. **Link for free access: https://rdcu.be/dg9g9**

Translating Science Into Technology

(or at least trying to 😅)

TRANSCAN-2
ERA-NET: Aligning national/regional translational cancer research programmes and activities

Microbiota-based SCReening of Anal Cancer in HIV-infected individuals
SCRATCH

MEDAL KIT — Detección precoz de lesiones anales por metabolitos

Metabolite Early Detection of Anal Lesions

To develop, validate, and start the regulatory pathway of an innovative bacterial metabolite biosensor for detecting precancerous anal lesions, enhancing anal cancer prevention through improved accuracy, patient acceptability, and ease of use.
Assess its utility in other epithelial cancers.

Fundación "la Caixa"

VISIONARIUM
Innovation by Gilead

Environmental factors

MSM vs. non-MSM vs. women, HIV vs. non-HIV, EU-based vs. US-based

Methodological factors

Sampling methods:

- preservation medium, temperature, sampling devices
- Lab performing the assays

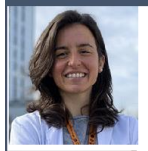
Other cancers

Cervical cancer, colorrectal cancer

Technology

ELONA (Enzyme-Linked Oligonucleotide Assay)
Aptamer-based self-testing device

Clinical Team



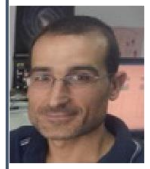
Clara Crespillo
Clinical researcher
Expert in HPV screening
IRICYS

Raquel Ron
Clinical researcher
Expert in HPV screening
IRYCIS

Sergio Serrano-Villar
Project leader
Research Area Director at IRYCIS

Biotech Team

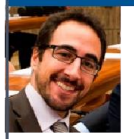
Elena Moreno
PostDoc Fellow
Molecular Biologist
IRYCIS



Manuel Ferrer
Research Profesor
Systems Biotechnology Group
CSIC

Victor González
Head of Aptamer unit
IRYCIS

R & D Team



Diego Velasco
Director
Innovation Unit
IRYCIS

Emma González
Molecular Biologist
Innovation Unit
IRYCIS

aptus biotech
AMADIX
mecwins

Collaborators

Adrián Curran
HPV Specialist
Hospital Vall d'Hebron

Joel Palefsky
UCSF

Outline

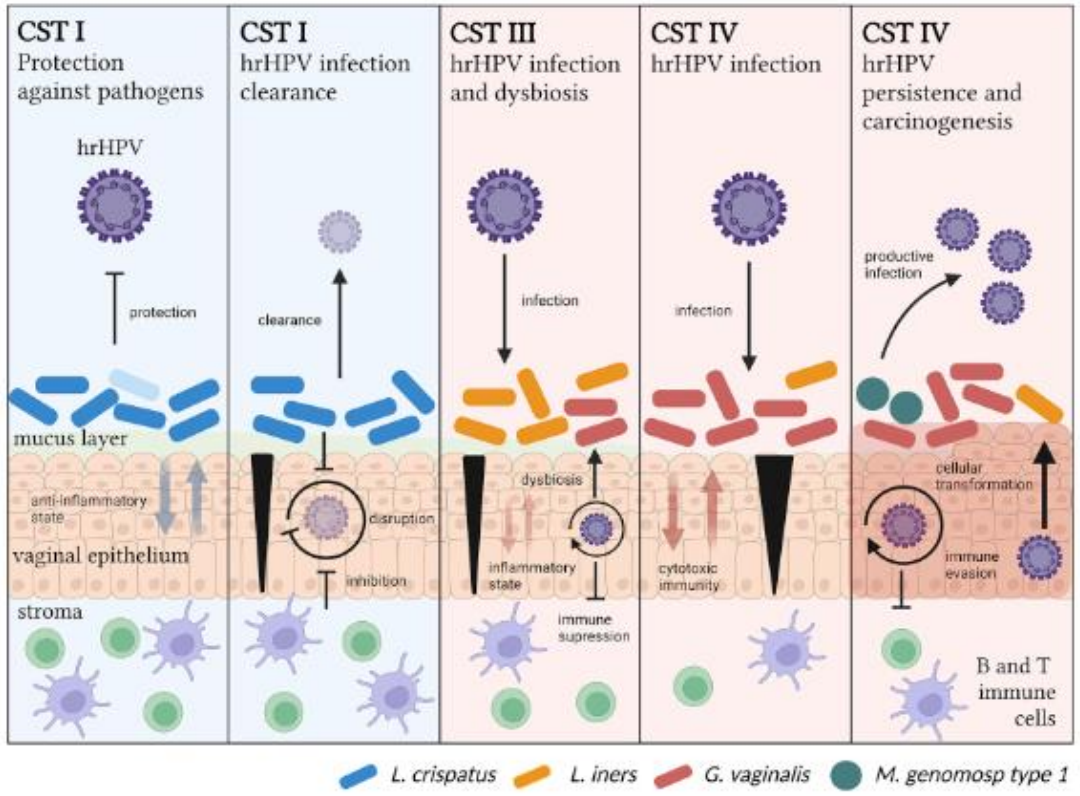
1 Microbiome – HPV Interactions

2 Diagnostic Applications

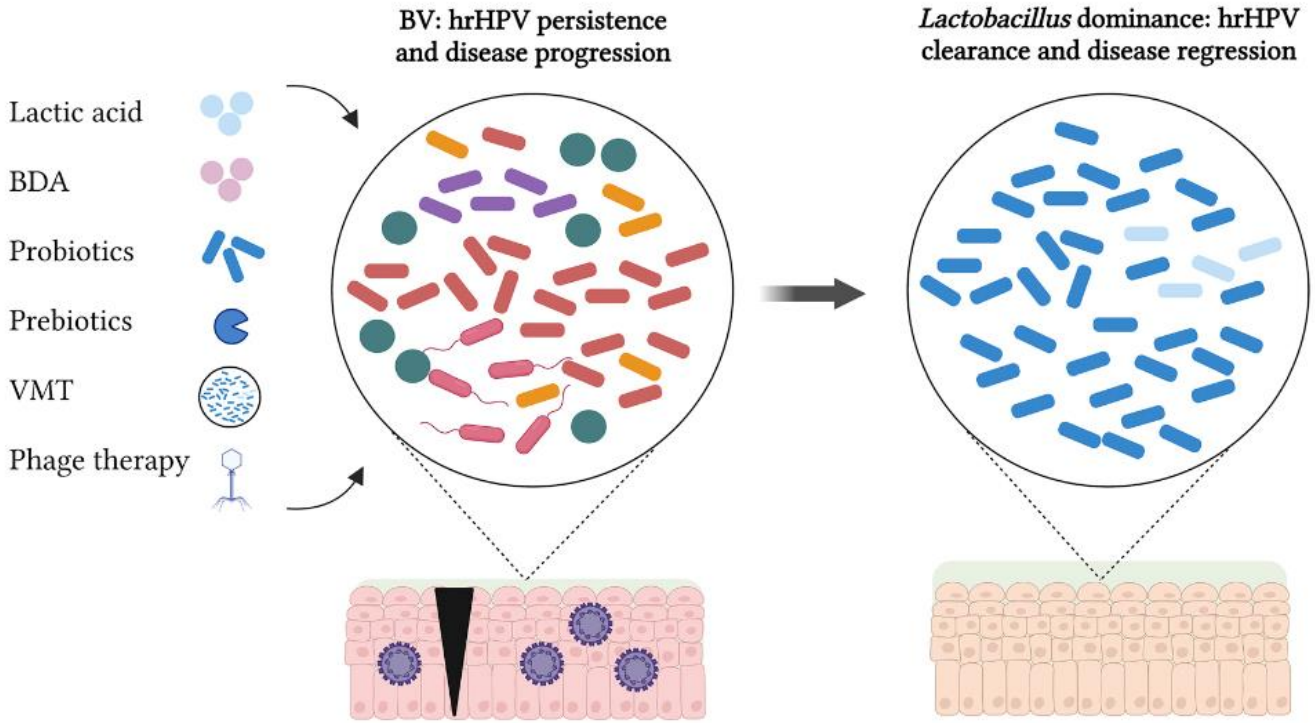
3 Therapeutic Implications

Therapeutic interventions in the microbiome for HPV

Cervico-Vaginal Community States Associated with HPV Progression

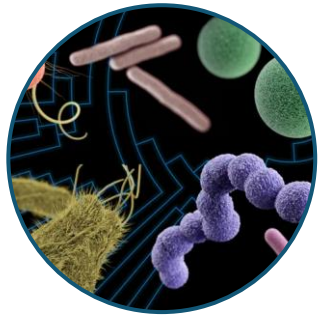


Current Cervicovaginal - Targeted Therapies to Facilitate HPV Clearance



Molina ... Melchers. Assessing the Cervicovaginal Microbiota in the Context of hrHPV Infections: Temporal Dynamics and Therapeutic Strategies. mBIO 2022

Pipeline for Vaginal Microbiome Research



Bacterial vaginosis

Bacterial consortia

Ferring, Rebiotix and MyBiotics

Bacterial vaginosis

Lactobacillus crispatus CTV-05 (Lactin-V)

Osel

Bacterial vaginosis

pH regulator (PHyph)

Gedea therapeutics

Bacterial vaginosis

Phage therapy

Intralytix

Bacterial vaginosis

uBiome transplant

Johns Hopkins University

Ongoing clinical trials targeting the microbiome for HPV

NCT Number	Study Title
NCT05109533	Probiotics Role in HPV Cervico-vaginal Infection Clearance
NCT06245486	Probiotc Lactobacillus Crispatus-M247 (Crispact®) Supplementation in the Sterilization of High-risk Human Papilloma (HPV-HR) Viruses
NCT05316064	Reducing Abundance of Human Papilloma Virus in Women by Taking Probiotic
NCT01599416	Influence of U-relax on Vaginal Health Promotion and HPV DNA Test Change From Positive to Negative
NCT03372395	Probiotic Implementation as Help in Solving Vaginal Infections
NCT04099433	Application of Oral Bacteriotherapy to Promote Anal HPV Clearance in HIV Positive Individuals
NCT01097356	The Effect of Probiotics on the Clearance of the Human Papillomavirus and on Cytological Lesions Caused by the Virus
NCT06001190	The Influence of Oral Probiotic on the Vaginal Flora and Microenvironment Alteration in the Vaginosis Infection Women
NCT06582004	Comparisons of the Effects and Clinical Outcomes of CH2 Vaginal Gel Versus Placebo on CIN1

Google

suplementos frente al VPH

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Patrocinado

Papilocare InmunoCaps 3…
37,99 €
Atida | Mifarma
+3,99 € de gas…
1,27 €/1ct
10 % de...
Suplementos · Cápsula · Zinc,…
De Google

HuPaVir 20 sobres
37,68 €
Amazon.es
Envío gratuito
Suplementos · Polvo · Zinc,…
De Kelkoo

Papilocare inmunocaps 30…
38,69 €
Salunatur.com
+3,99 € de gas…
Suplementos · Cápsula · Zinc,…
De Google

Kijimea PRO I 84 cápsulas
89,95 €
kijimea.es
Envío gratuito
1,07 €/1item
Suplementos · Cápsula · Adultos
De Google

PAPILOXYL 30 capsulas…
27,95 €
Amazon.es
+3,99 € de gas…
Suplementos · Cápsula
De Kelkoo

Theralogix, ProCerv HP, 27…
108,60 €
iHerb
Envío gratuito
Suplementos · Cápsula ·…
De Google

Hupavir, 20 sobres 6 g
36,57 €
Welnia
+1,99 € de gas…
★★★★½ (186)
Suplementos · Polvo · Zinc,…
De Producthero

Papilocare Inmunocaps 30…
29,36 €
.Farmacia 4 Est...
+3,49 € de gas…
5 % de...
Suplementos · Cápsula · Zinc,…
De Google

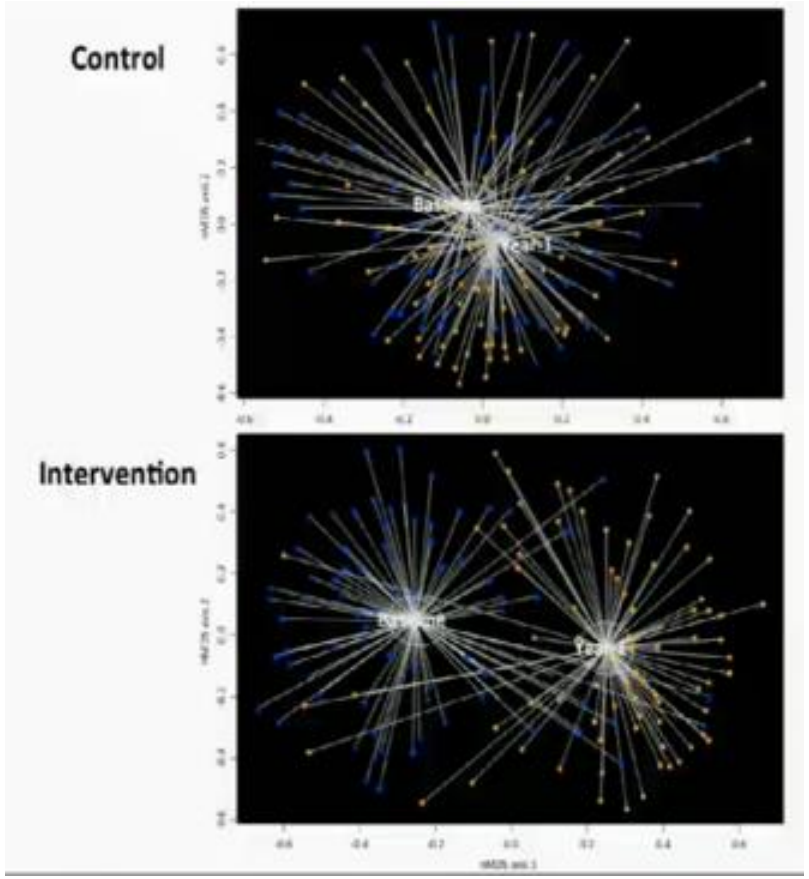
Instituto del Virus del Papiloma Humano
https://imvph.com.mx › que-medicamento-debo-tomar-s...

¿Qué medicamento debo tomar si tengo VPH?

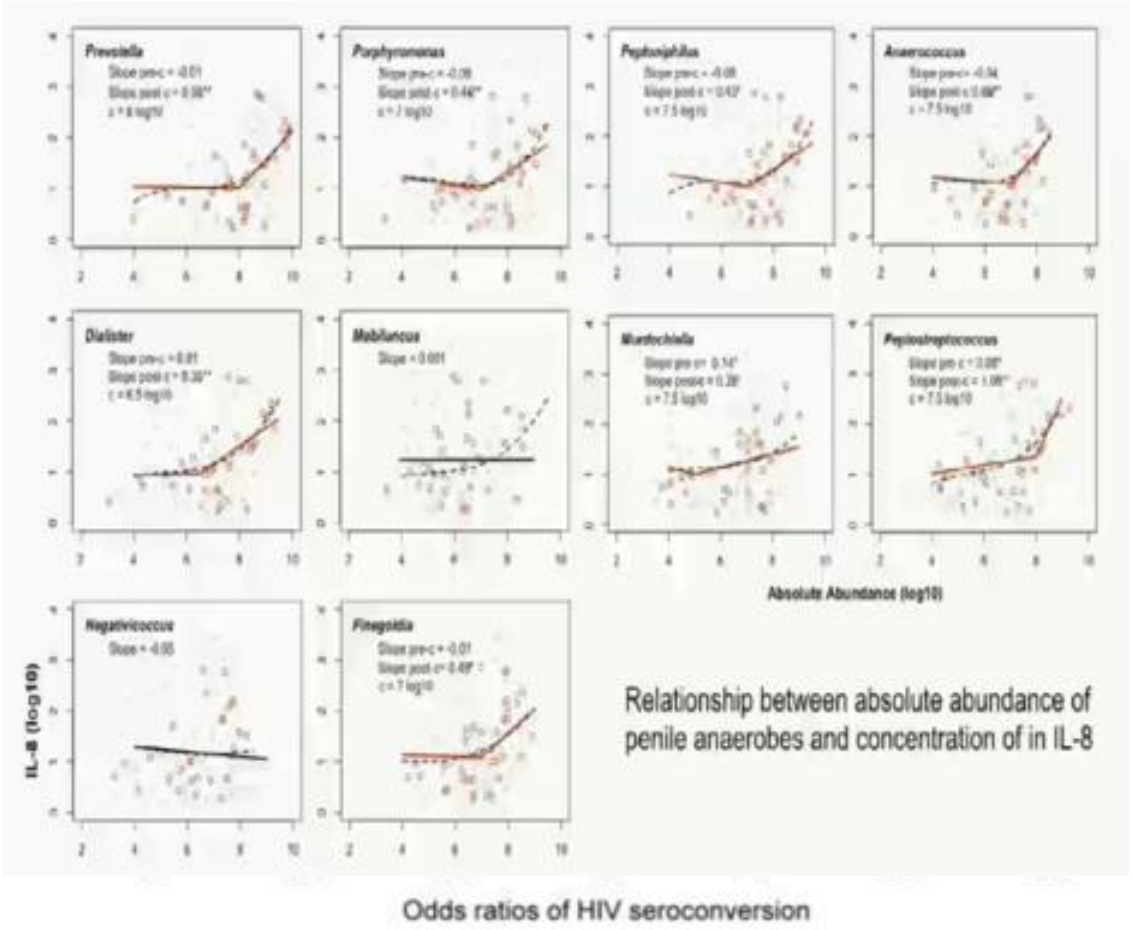
14 dic 2023 — **Hera, un suplemento alimenticio enfocado en el manejo de VPH**
Aporta minerales y vitaminas antioxidantes que refuerzan tu organismo, haciéndolo ...

Interventions On the Penile Microbiome

Male circumcision reduces female-to-male HIV transmission Through Microbiome Changes Reducing Local Inflammation



Liu. mBio 2013



Liu. mBIO2017

Vaginal Microbiome Transplantation in Recurrent BV

MENU nature medicine

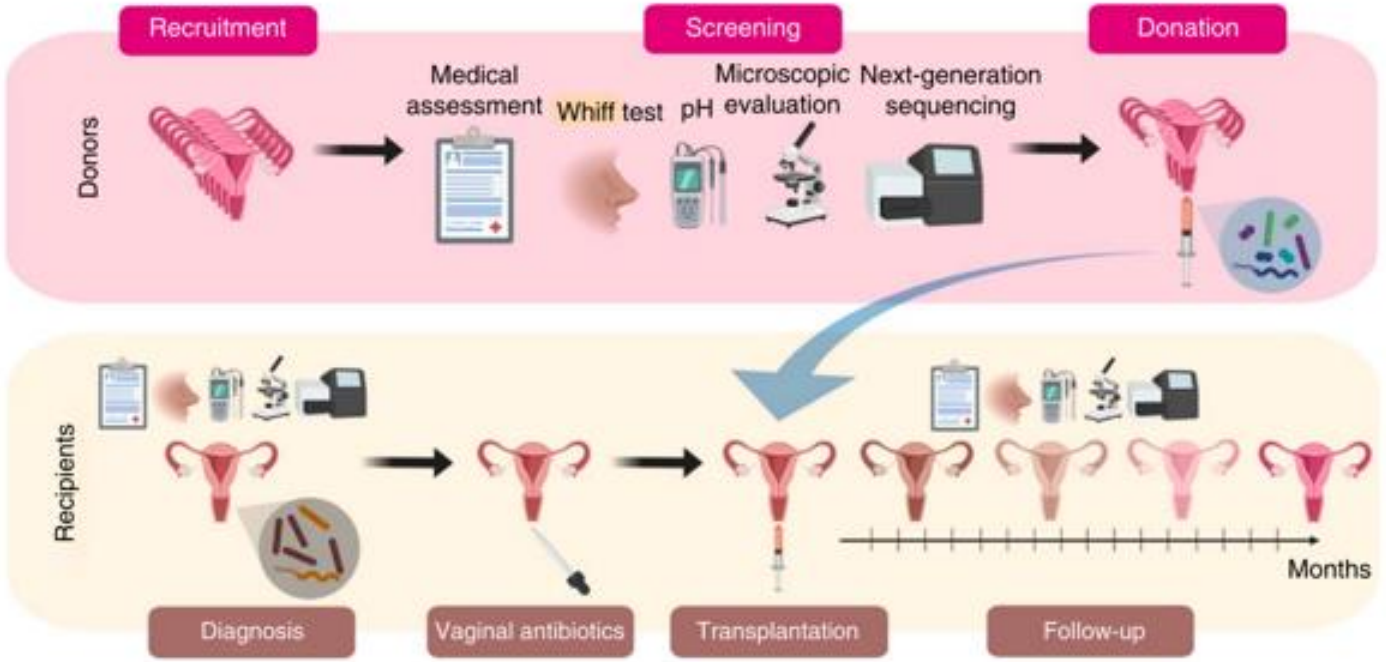
Brief Communication | Published: 07 October 2019

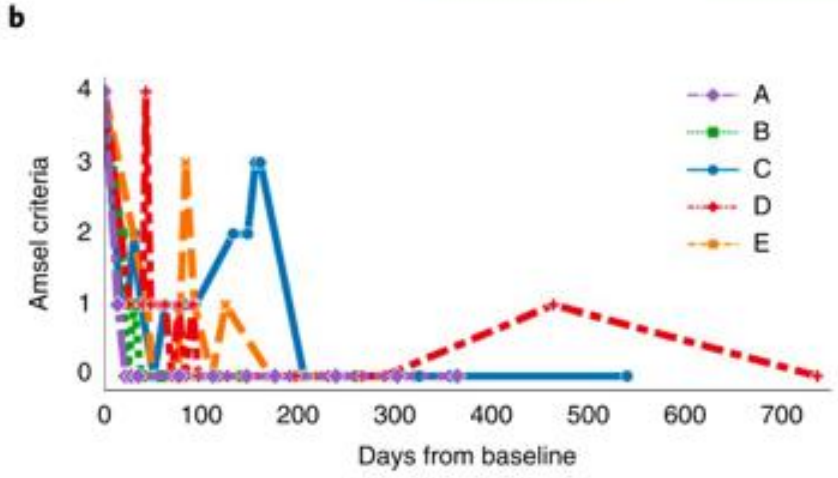
Vaginal microbiome transplantation in women with intractable bacterial vaginosis

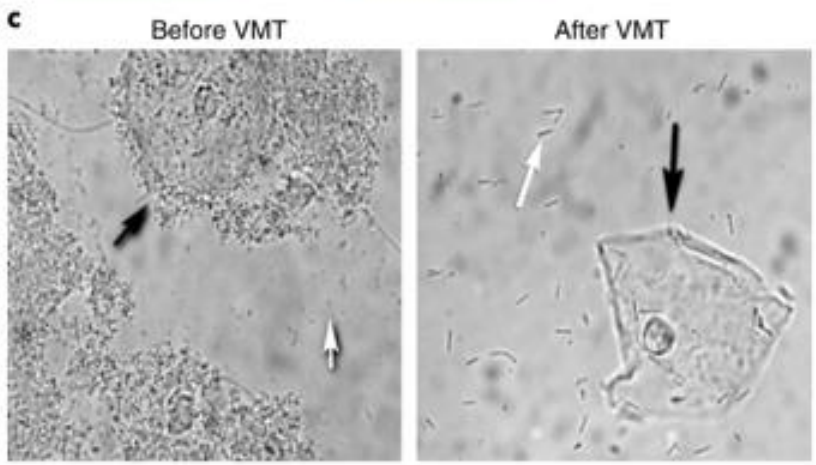
Ahinoam Lev-Sagie, Debra Goldman-Wohl, Yotam Cohen, Mally Dori-Bachash, Avner Leshem, Uria Mor, Jacob Strahilevitz, Allon E. Moses, Hagit Shapiro, Simcha Yagel & Eran Elinav

Nature Medicine **25**, 1500–1504(2019) | Cite this article

6632 Accesses | **2** Citations | **433** Altmetric | Metrics







Google Patents

vaginal microbiota

8 of 1760

← Back to results vaginal; microbiota;

Vaginal microbiota collection device modular preservation unit

Abstract

The present invention discloses a vaginal microbiota collection device and modular preservation unit comprising a means to collect and preserve the vaginal microbiota from an individual, a means to distribute the harvested microbiota, or both. The means to distribute the harvested microbiota comprises a collection apparatus with one or more modular components. The vaginal microbiota is distributed based on need or validation. The collection and preservation of the vaginal microbiota is accomplished by a piston mechanism. The present invention also discloses a method of harvesting vaginal microbiota using the device disclosed herein.

WO2018017658A1
WIPO (PCT)

Download PDF Find Prior Art Similar

Other languages: French

Inventor: Christopher Stevens

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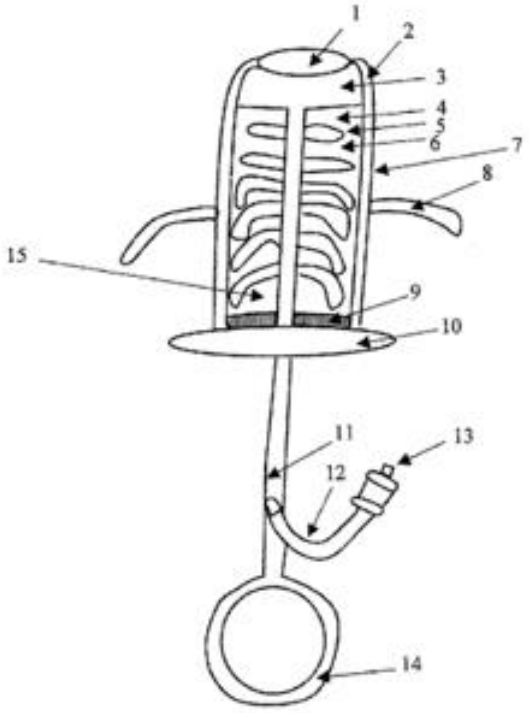
(54) Title: VAGINAL MICROBIOTA COLLECTION DEVICE MODULAR PRESERVATION UNIT

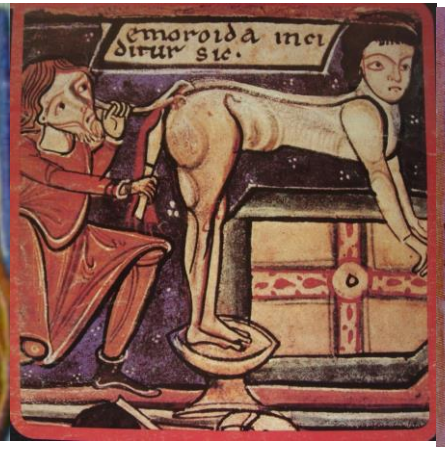
Figure 1

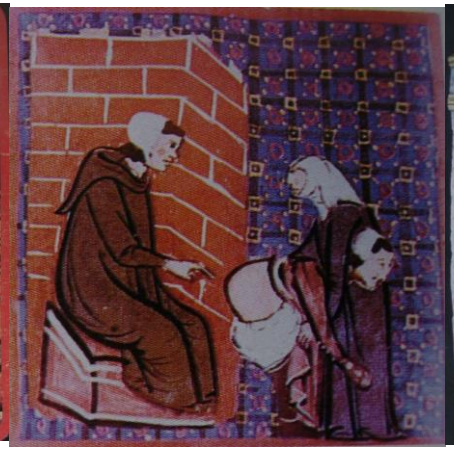


(57) Abstract: The present invention discloses a vaginal microbiota collection device and modular preserv means to collect and preserve the vaginal microbiota from an individual, a means to distribute the harvested microbiota, or both. The means to distribute the harvested microbiota comprises a collection apparatus with one or more modular components. The vaginal microbiota is distributed based on need or validation. The collection and preservation of the vaginal microbiota is accomplished by a piston mechanism. The present invention also discloses a method of harvesting vaginal microbiota using the device disclosed herein.

Interventions on the Anal Microbiome: A Trending Topic but a Neglected Site

Fiat secundum artem





Enema, Galenic texts
129 dC

Hemorrhoidectomy
Salerno school
XII century

DARE
Middle age

Hemorrhoid cauterization
XV century

Delfos oracle
2024

TCA?
IRC?
Imiquimod?
EC?

Conclusions

1 **Emerging Research Area**

- The connections between the microbiome and HPV immunopathogenesis seem evident, but there is still much to learn.

2 **Understanding the cause-effect relationship is a challenge in microbiome studies:**

- If microbiota leads to HPV/dysplasia: therapeutic opportunities
- In any case: diagnostic opportunities

3 **We must strive to transform the knowledge generated in this field into clinical tools that:**

- Stratify the risk of complications,
- Diagnose precancerous lesions and effectively treat them.

sergio.serrano@
salud.madrid.org

@serranovillar
@infecciosasryc
@eiinlab