Il Microbiota vaginale: confronto con il Microbiologo

- MARTEDI' 12 NOVEMBRE 2019
- 11:00-13:00
- **Sala del Castello**
- **Sessione 14 IL MICROBIOTA: NON SOLO INTESTINO**
- a cura del Gruppo di Lavoro analisi del microbiota (GLAM)

Antonio Ragusa

Direttore U.O.C. Ostetricia e Ginecologia Ospedale S.G. Calibita Fatebenefratelli;

Isola Tiberina. Roma.

Vaginal microbiome of reproductive-age women

Jacques Ravel[a,1], Pawel Gajer[a], Zaid Abdo[b], G. Maria Schneider[c], Sara S. K. Koenig[a], Stacey L. McCulle[a], Shara Karlebach[d], Reshma Gorle[e], Jennifer Russell[f], Carol O. Tacket[f], Rebecca M. Brotman[a], Catherine C. Davis[g], Kevin Ault[d], Ligia Peralta[e], and Larry J. Forney[c,1]

PNAS | March 15, 2011 | vol. 108 | suppl. 1

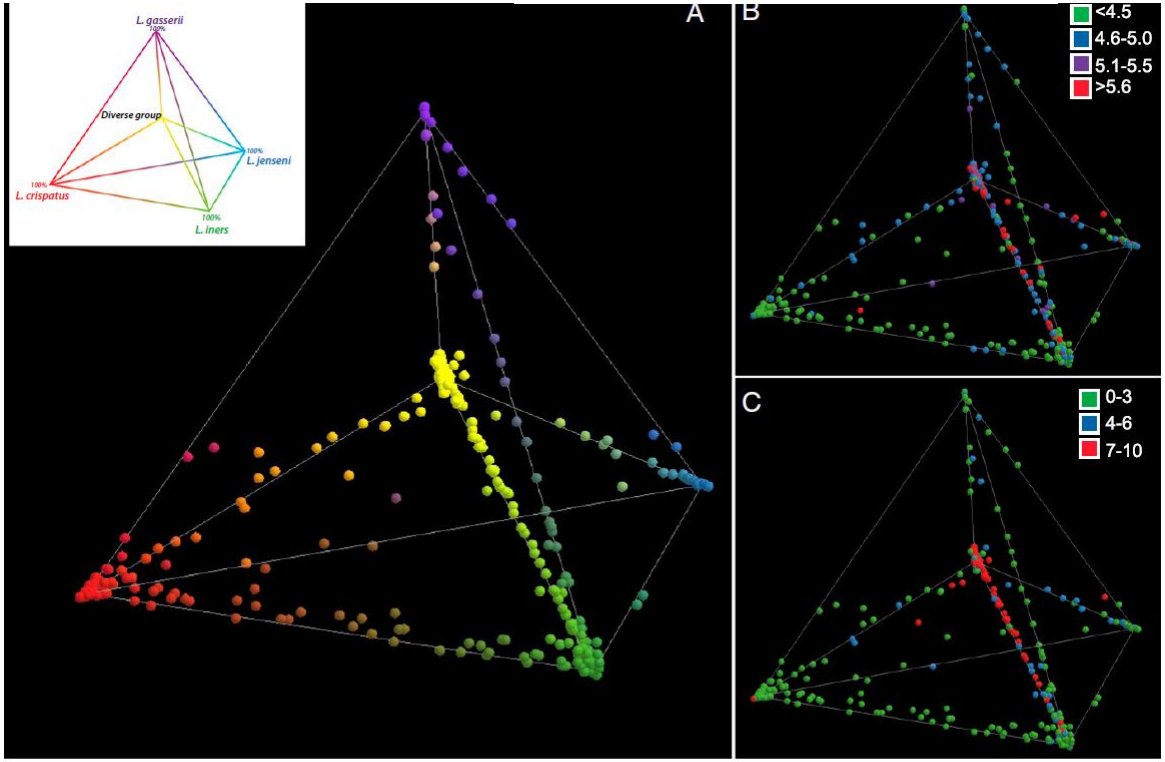


Fig. 4. Relationships among vaginal bacterial communities visualized by principal component analysis in which the relative abundances are expressed as proportions of the total community and displayed in 3D space. Communities dominated by species of *Lactobacillus* and representing community groups I, II, III, and V are shown at each of the four outer vertices of the tetrahedron, with communities of group IV at the inner vertex and shown in the *Inset*. (*A*) Each point corresponds to a single subject and was colored according to the proportions of phylotypes in each community. (*B*) pH of each vaginal community shown in *A*. (*C*) Nugent score category of each vaginal community shown in *A*.

Vaginal microbiome of reproductive-age women

Jacques Ravel[a,1], Pawel Gajer[a], Zaid Abdo[b], G. Maria Schneider[c], Sara S. K. Koenig[a], Stacey L. McCulle[a], Shara Karlebach[d], Reshma Gorle[e], Jennifer Russell[f], Carol O. Tacket[f], Rebecca M. Brotman[a], Catherine C. Davis[g], Kevin Ault[d], Ligia Peralta[e], and Larry J. Forney[c,1]

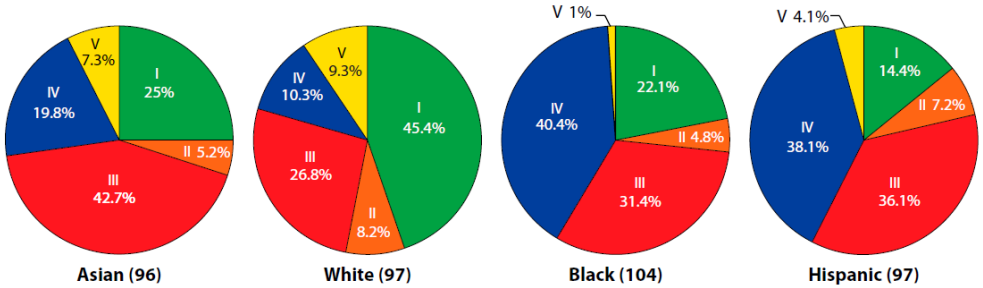


Fig. 3. Representation of vaginal bacterial community groups within each ethnic group of women. The number of women from each ethnic group is in parentheses.

Four were dominated by Lactobacillus iners, L. crispatus, L. gasseri, or L. jensenii, whereas the fifth had lower proportions of lactic acid bacteria and higher proportions of strictly anaerobic organisms,

J Med Primatol doi:10.1111/jmp.12217

ORIGINAL ARTICLE

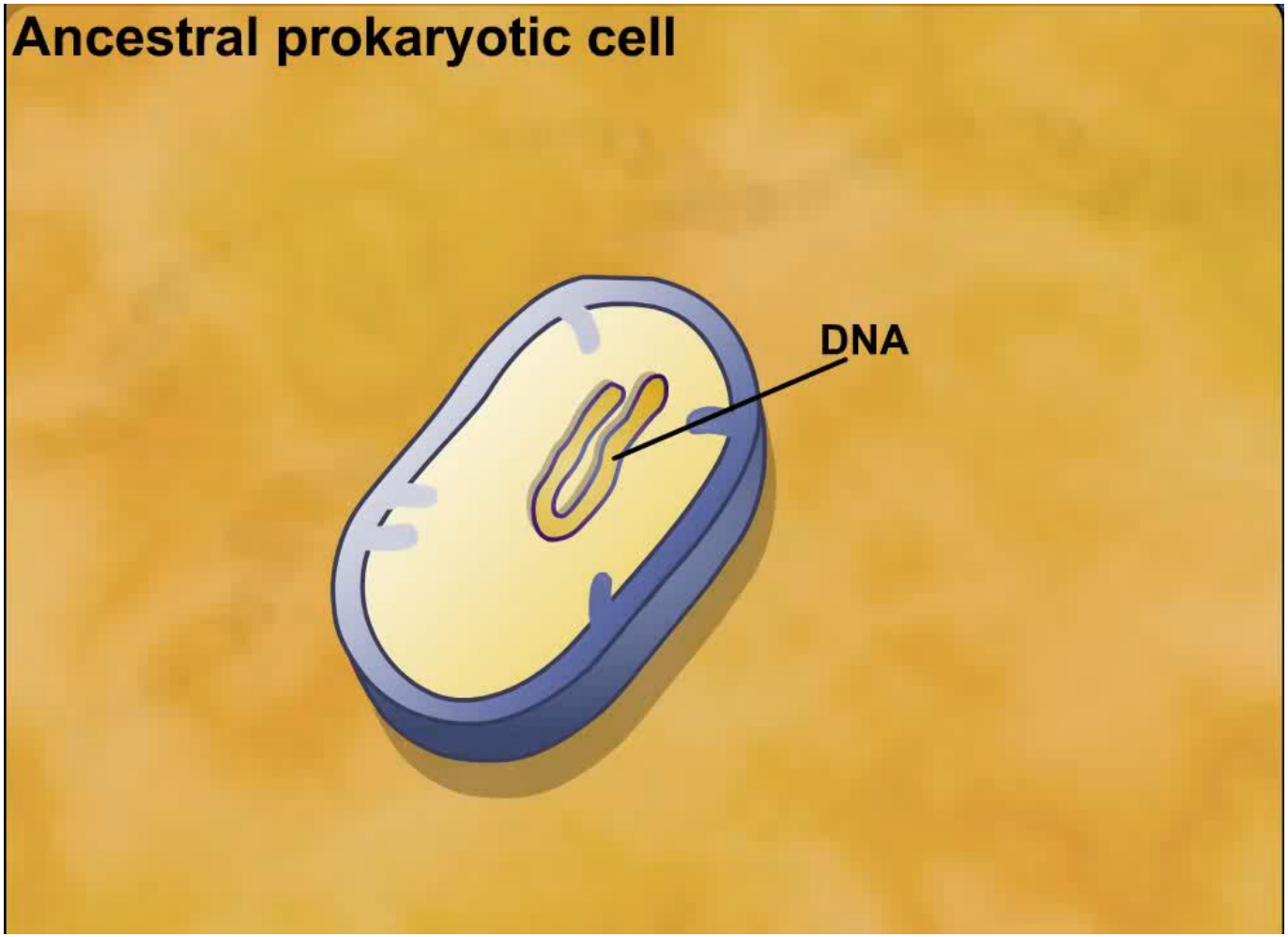
Baboon vaginal microbial flora

Jael A. Obiero[1], Kenneth K. Waititu[1], Isaac Mulei[2], Farah I. Omar[1], Walter Jaoko[3] & Peter G. Mwethera[1]

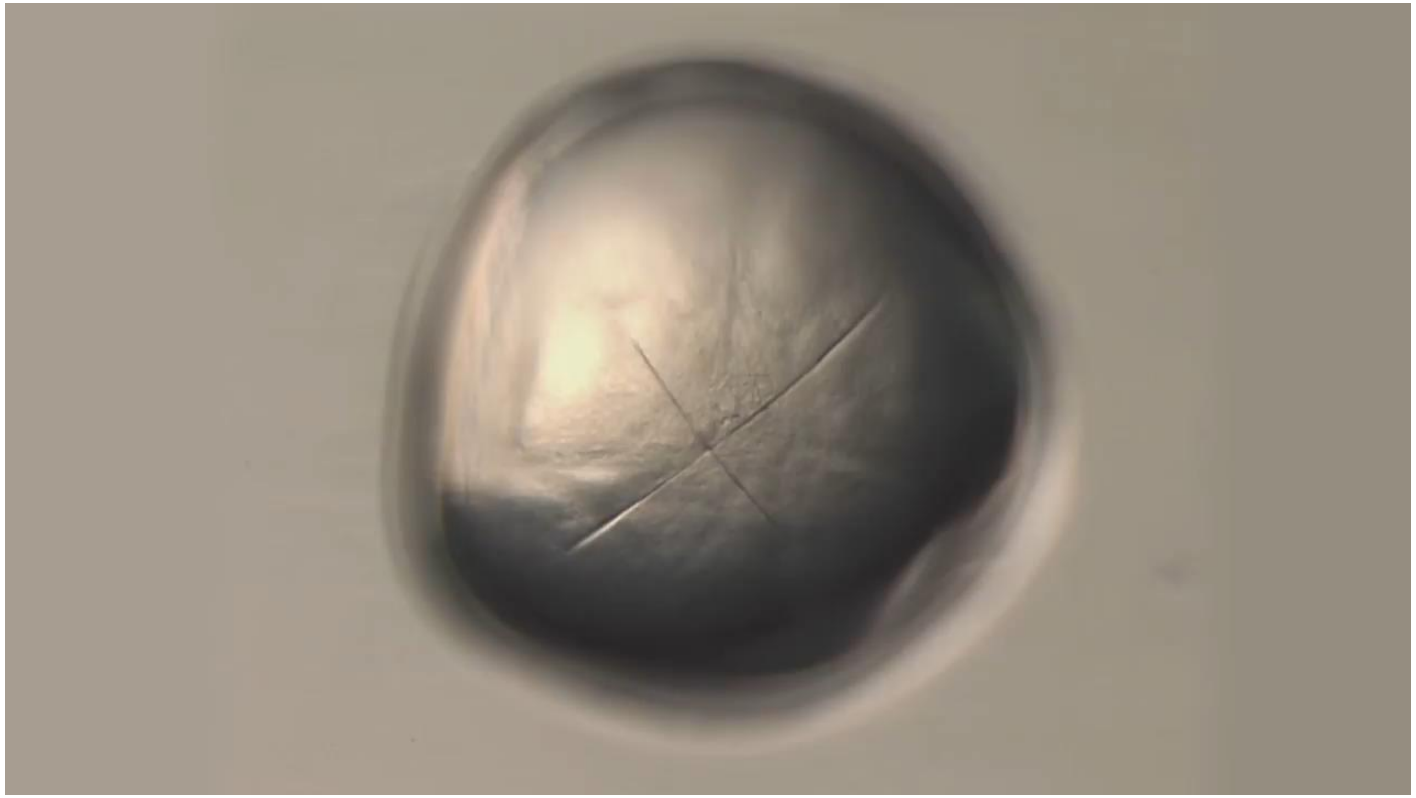
1 Reproductive Health and Biology, Institute of Primate Research, Nairobi, Kenya
2 Veterinary Pathology, University of Nairobi, Nairobi, Kenya
3 Medical Microbiology, University of Nairobi, Nairobi, Kenya

Conclusions The baboon vaginal microbiota is heterogeneous in terms of species composition and is typified by a scarcity of lactobacilli.

Endosimbiosi



The momentous transition to multicellular life may not have been so hard after all



L' evoluzione del nostro microbiota Geneticamente siamo identici agli uomini del paleolitico ma la nostra dieta è profondamente cambiata e la durata della nostra vita enormemente allungata, anche grazie all'uso di antibiotici. I nostri microorganismi ci hanno accompagnato e si sono rapidamente adattati a questi cambiamenti.

OBSTETRICS

Racial disparity in the frequency of recurrence of preterm birth

Zachary A.-F. Kistka; Lisanne Palomar; Kirstin A. Lee, MD; Sarah E. Boslaugh, PhD; Michael F. Wangler, MD; F. Sessions Cole, MD; Michael R. DeBaun, MD, MPH; Louis J. Muglia, MD, PhD

Am J Obstet Gynecol 2007;196;

le gravide di colore hanno una incidenza di parto pretermine e PROM pretermine significativamente maggiore rispetto alle gravide di etnia caucasica, indipendentemente da eventuali fattori materni confondenti, (medici e socio-economici)

Rischio Relativo aumentato di oltre 3 volte

La durata della gestazione è minore negli africani

•La durata media della gravidanza è di 274.8 giorni nelle donne africane (significativamente meno che in donne di origine europea)
•L'individuazione costante di una durata inferiore della gestazione in donne nere, suggerisce il raggiungimento più precoce della maturità a carico dell'unità fetoplacentare.

Omigbodun and Adewuyi. *J Natl Med Assoc* 1997; 89: 617–621

Precoce maturazione dei polmoni nei feti africani

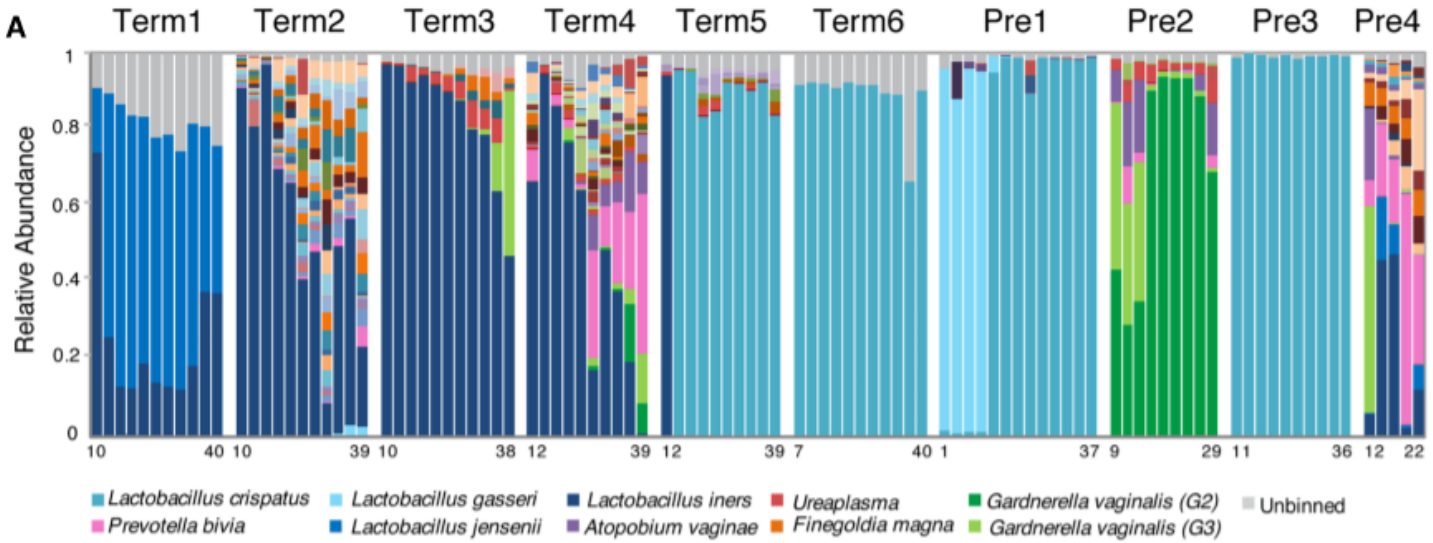
- Farrell PM, Wood RE. Epidemiology of hyaline membrane disease in the United States:analysis of national mortality statistics. *Ped* 1976;**58**:167–76
- Buehler JW, Strauss LT, Hogue CJ, Smith JC. Birth weight-specific causes of infant mortality, United States, 1980. *Public Health Reports* 1987;**102**:162–71
- Coulter JB. The incidence of the respiratory distress syndrome: with particular reference to developing countries. *Tropical & Geographical Medicine* 1980;**32**:277–85
- Richardson DK, Torday JS. Racial differences in predictive value of the lecithin/sphingomyelin ratio. *Am J Obstet Gynecol* 1994;**170**:1273–8
- Robillard PY, Hulsey TC, Alexander GR, Sergent MP, de Caunes F, Papiernik E. Hyaline membrane disease in black newborns: does fetal lung maturation occur earlier? *Europ J Obstet Gynecol Reprod Biol* 1994;**55**:157–61
- Berman S, Richardson DK, Cohen AP, Pursley DM, Lieberman E. Relationship of race and severity of neonatal illness. *Am J Obstet Gynecol* 2001;**184**:668–72

GENOME RESEARCH

Metagenomic analysis with strain-level resolution reveals fine-scale variation in the human pregnancy microbiome

Daniela S. Aliaga Goltsman, Christine L. Sun, Diana M. Proctor, et al.

Genome Res. 2018 28: 1467-1480 originally published online September 19, 2018



la comunità batterica a livello vaginale presenta la minore diversità, al contrario dell'intestino

A differenza della comunità salivare o intestinale, quella vaginale è generalmente dominata da una singola specie batterica, *L. iners* o *L. crispatus* in particolare. Le comunità vaginali dominate da *L. iners* dimostrano di incrementare notevolmente la loro variabilità tassonomica (ricchezza) verso la fine della gravidanza al contrario di quelle caratterizzate dalla presenza di *L. crispatus* che rimangono pressoché stabili nel tempo l'Individualità, intesa come taxon vaginale più espresso, età gestazionale e complicazioni di salute sono le principali fonti di variazione a carico dei pattern di abbondanza genica

Temporal and spatial variation of the human microbiota during pregnancy

Daniel B. DiGiulio[a,b,c,1], Benjamin J. Callahan[a,d,1], Paul J. McMurdie[a,d], Elizabeth K. Costello[a,e], Deirdre J. Lyell[a,f], Anna Robaczewska[a,b,c], Christine L. Sun[a,e], Daniela S. A. Goltsman[a,e], Ronald J. Wong[a,g], Gary Shaw[a,g], David K. Stevenson[a,g], Susan P. Holmes[a,d], and David A. Relman[a,b,c,e,2]

[a]March of Dimes Prematurity Research Center, Stanford University School of Medicine, Stanford, CA 94305; [b]Department of Medicine, Stanford University School of Medicine, Stanford, CA 94305; [c]Veterans Affairs Palo Alto Health Care System, Palo Alto, CA 94304; [d]Department of Statistics, Stanford University, Stanford, CA 94305; [e]Department of Microbiology and Immunology, Stanford University School of Medicine, Stanford, CA 94305; [f]Department of Obstetrics and Gynecology, Stanford University School of Medicine, Stanford, CA 94305; and [g]Department of Pediatrics, Stanford University School of Medicine, Stanford, CA 94305

Prevalence of a *Lactobacillus*-poor vaginal community state type (CST 4) was inversely correlated with gestational age at delivery ($P = 0.0039$). Risk for preterm birth was more pronounced for subjects with CST 4 accompanied by elevated *Gardnerella* or *Ureaplasma* abundances.

There was no association between the composition of the women's saliva, gut, and tooth microbiota and preterm birth,

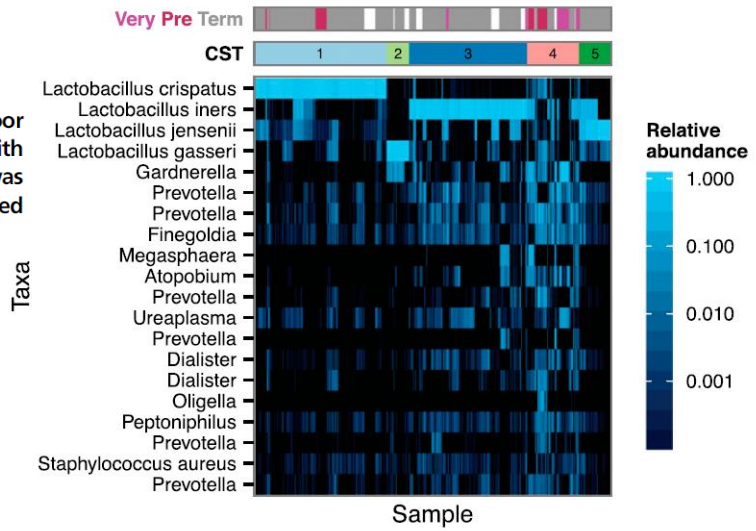


Fig. 2. Heat map of the fractional abundance of the 20 most abundant OTUs in the vaginal communities of 40 women sampled longitudinally during pregnancy. Clustering on the abundance profiles of individual samples (n = 761) using the partitioning around medoids algorithm identified six CSTs. CSTs 1, 2, 3, and 5 were characterized by dominant *Lactobacillus* species that typically account for >90% of the community: *L. crispatus*, *L. jensenii*, *L. iners*, and *L. gasseri*, respectively. CST 4 was significantly more diverse. Pregnancy outcomes are indicated by the bar at the top: term delivery (gray), >37 gestational weeks; preterm (maroon), <36 wk; very preterm (pink), <32 wk; marginal delivery during the 37th gestational week (white).

SCIENTIFIC REPORTS

OPEN

SUBJECT AREAS:
OUTCOMES RESEARCH
MEDICAL RESEARCH

Received
17 February 2014

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15 May 2014

Published
30 May 2014

Characterisation of the vaginal *Lactobacillus* microbiota associated with preterm delivery

Ljubomir Petricevic[1], Konrad J. Domig[2], Franz Josef Nierscher[1], Michael J. Sandhofer[1], Maria Fidesser[2], Iris Krondorfer[2], Peter Husslein[1], Wolfgang Kneifel[2] & Herbert Kiss[1]

[1]Department of Obstetrics and Gynecology, Medical University of Vienna, Waehringer Guertel 18-20, A-1090 Vienna, Austria, [2]Department of Food Science and Technology, BOKU - University of Natural Resources and Life Sciences, Vienna, Muthgasse 18, A-1190 Vienna, Austria.

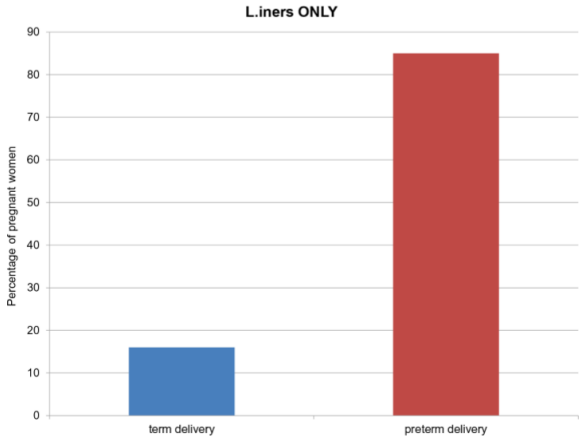


Figure 3 | Percentage of *L. iners* as only single *Lactobacillus* species in women with term (TD) and preterm delivery (PTD) as determined by denaturing gradient gel electrophoresis (DGGE).

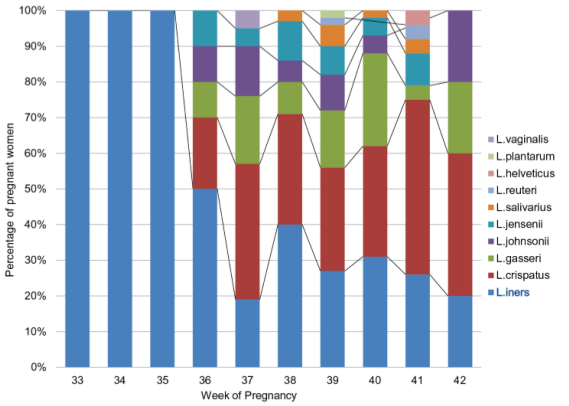


Figure 4 | Lactobacilli status obtained at the beginning of the study (i.e., between 11 + 0 and 14 + 0 weeks of gestation) compared to gestational age at birth.

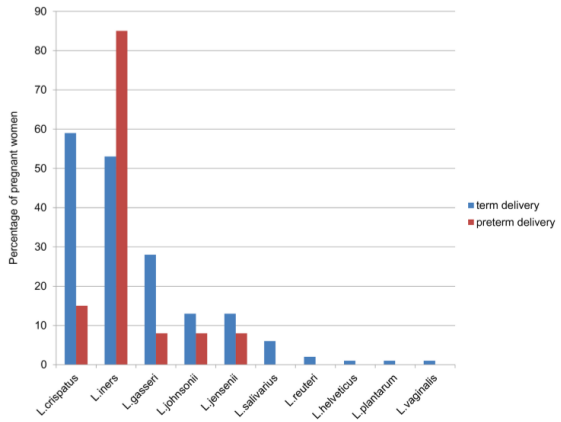


Figure 2 | Percentage of the most frequent vaginal *Lactobacillus* species in women with term (TD) and preterm delivery (PTD) as determined by denaturing gradient gel electrophoresis (DGGE).

ARTICLES
https://doi.org/10.1038/s41591-019-0450-2
nature medicine
OPEN

The vaginal microbiome and preterm birth

Women who delivered preterm exhibited significantly lower vaginal levels of Lactobacillus crispatus and higher levels of BVAB1, Sneathia amnii, TM7-H1, a group of Prevotella species…Preterm-birth-associated taxa were correlated with proinflammatory cytokines in vaginal fluid.

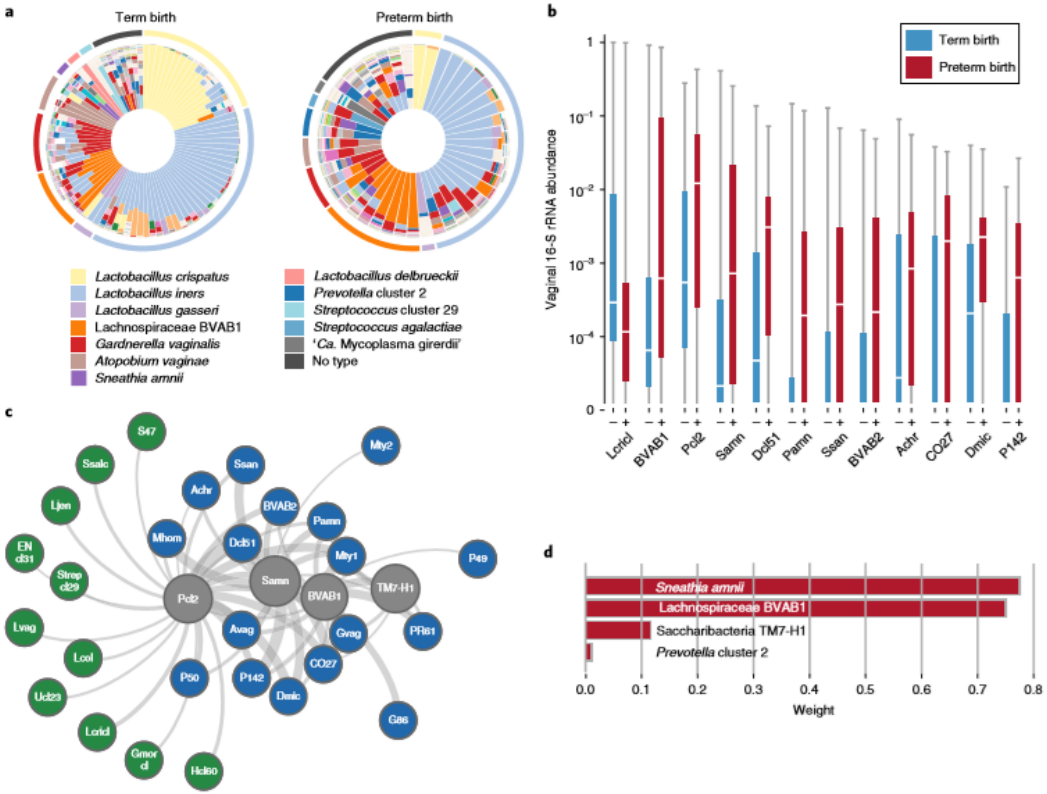


Fig. 2 | Bacterial taxa associated with spontaneous PTB. a, Vagitypes of 90 women who delivered at term (≥39 weeks of gestation), and 45 women who delivered prematurely (<37 weeks of gestation) showing 13 community states, or vagitypes. **b**, Abundance of taxa significantly different in PTB ($n=45$) and TB ($n=90$) cohorts. These taxa have $P<0.05$ for the Mann–Whitney U-test (two-sided) for difference in proportional abundance between the cohorts, corrected using the Benjamini–Hochberg procedure with an FDR of 5%. TB is indicated in blue as (−) and PTB in red as (+). Boxes show the median and interquartile range; whiskers extend from minimum to maximum values within each cohort. **c**, Network analysis of four taxa highly associated with PTBs. Negative correlations are shown in green, positive correlations in blue and predictive taxa in gray. Edge weights represent the strength of correlation. See Supplementary Table 3 for abbreviations. **d**, Predictive linear model for PTBs that produces a score based on weighted log(abundances) of four taxa in vaginal 16S rRNA profiles in the 6- to 24-week gestational age range. Taxa abbreviations: Lcricl, *L. crispatus* cluster; BVAB1, Lachnospiraceae BVAB1; Pcl2, *Prevotella* cluster 2; Samn, *S. amnii*; Dcl51, *Dialister* cluster 51; Pamn, *P. amnii*; BVAB2, Clostridiales BVAB2; CO27, Coriobacteriaceae OTU27; Dmic, *Dialister micraerophilus*; P142, *Parvimonas* OTU142.

nature COMMUNICATIONS

ARTICLE

https://doi.org/10.1038/s41467-019-09285-9 OPEN

Cervicovaginal microbiota and local immune response modulate the risk of spontaneous preterm delivery

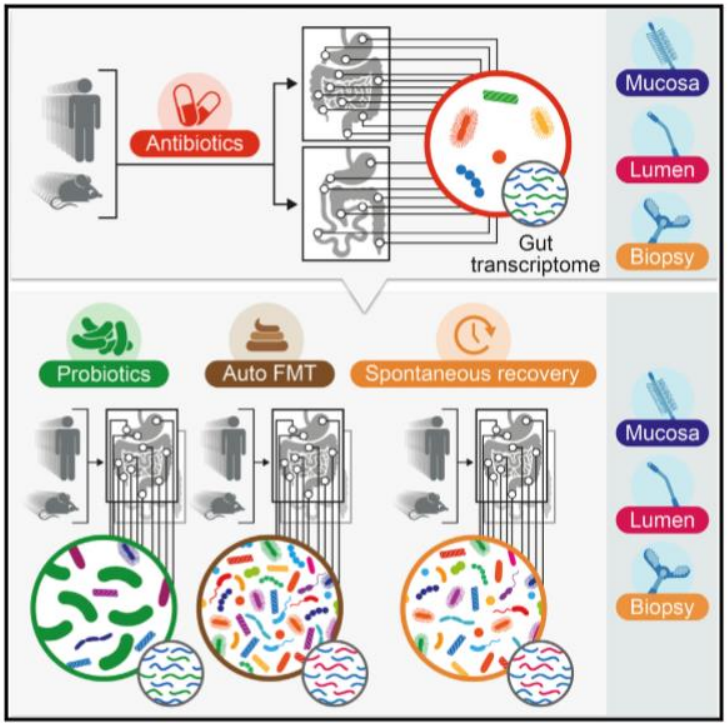
Michal A. Elovitz[1], Pawel Gajer[2], Valerie Riis[1], Amy G. Brown[1], Michael S. Humphrys[2], Johanna B. Holm[2] & Jacques Ravel[2]

…However, higher vaginal levels of β-defensin-2 lowered the risk of sPTB associated with cervicovaginal microbiota in an ethnicity-dependent manner. Surprisingly, even in Lactobacillus spp. dominated cervicovaginal microbiota, low β-defensin-2 was associated with increased risk of sPTB. These findings hold promise for diagnostics to accurately identify women at risk for sPTB early in pregnancy. Therapeutic strategies could include immune modulators and microbiome-based therapeutics to reduce this significant health burden.

Cell

Post-Antibiotic Gut Mucosal Microbiome Reconstitution Is Impaired by Probiotics and Improved by Autologous FMT

Graphical Abstract



Authors

Jotham Suez, Niv Zmora, Gili Zilberman-Schapira, ..., Zamir Halpern, Eran Segal, Eran Elinav

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In Brief

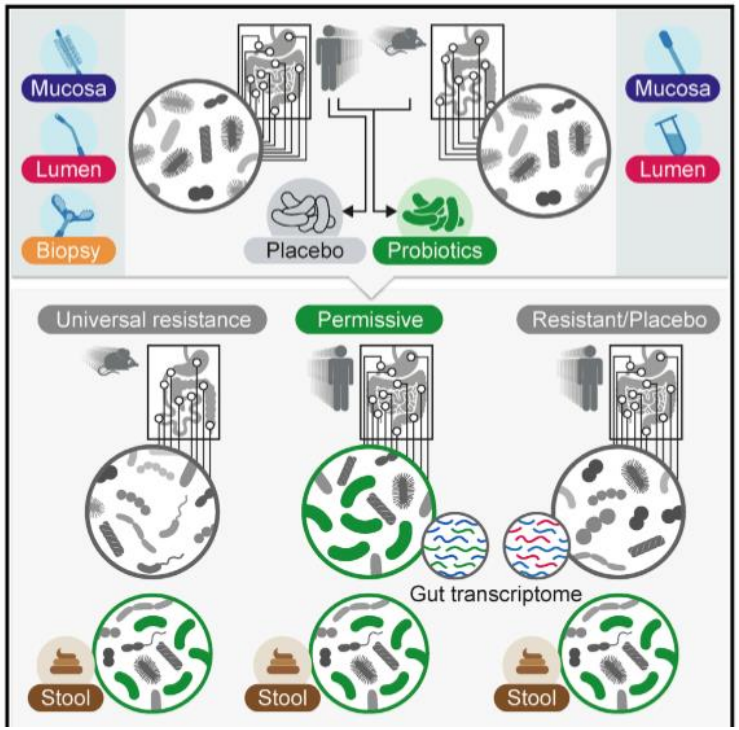
Probiotics perturb rather than aid in microbiota recovery back to baseline after antibiotic treatment in humans.

Article

Cell

Personalized Gut Mucosal Colonization Resistance to Empiric Probiotics Is Associated with Unique Host and Microbiome Features

Graphical Abstract



Authors

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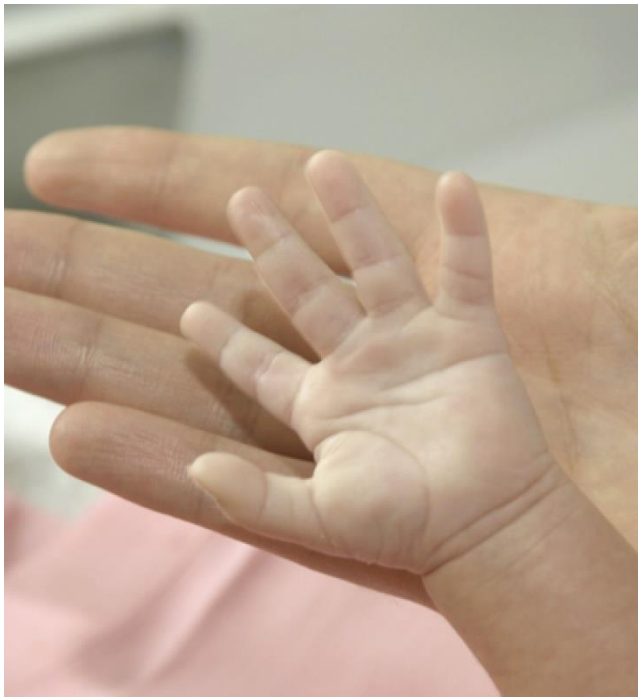
zamir@tlvmc.gov.il (Z.H.), eran.segal@weizmann.ac.il (E.S.), eran.elinav@weizmann.ac.il (E.E.)

In Brief

Probiotics transiently colonize the human gut mucosa in highly individualized patterns, thereby differentially impacting the indigenous microbiome and host gene-expression profile, a trait which is predictable by baseline host and microbiome features, but not by stool shedding.

Esiste un microbiota fetale?



"Ciascuno di noi entra nel mondo privo di colonizzazione microbica a causa dell'ambiente sterile del grembo materno"

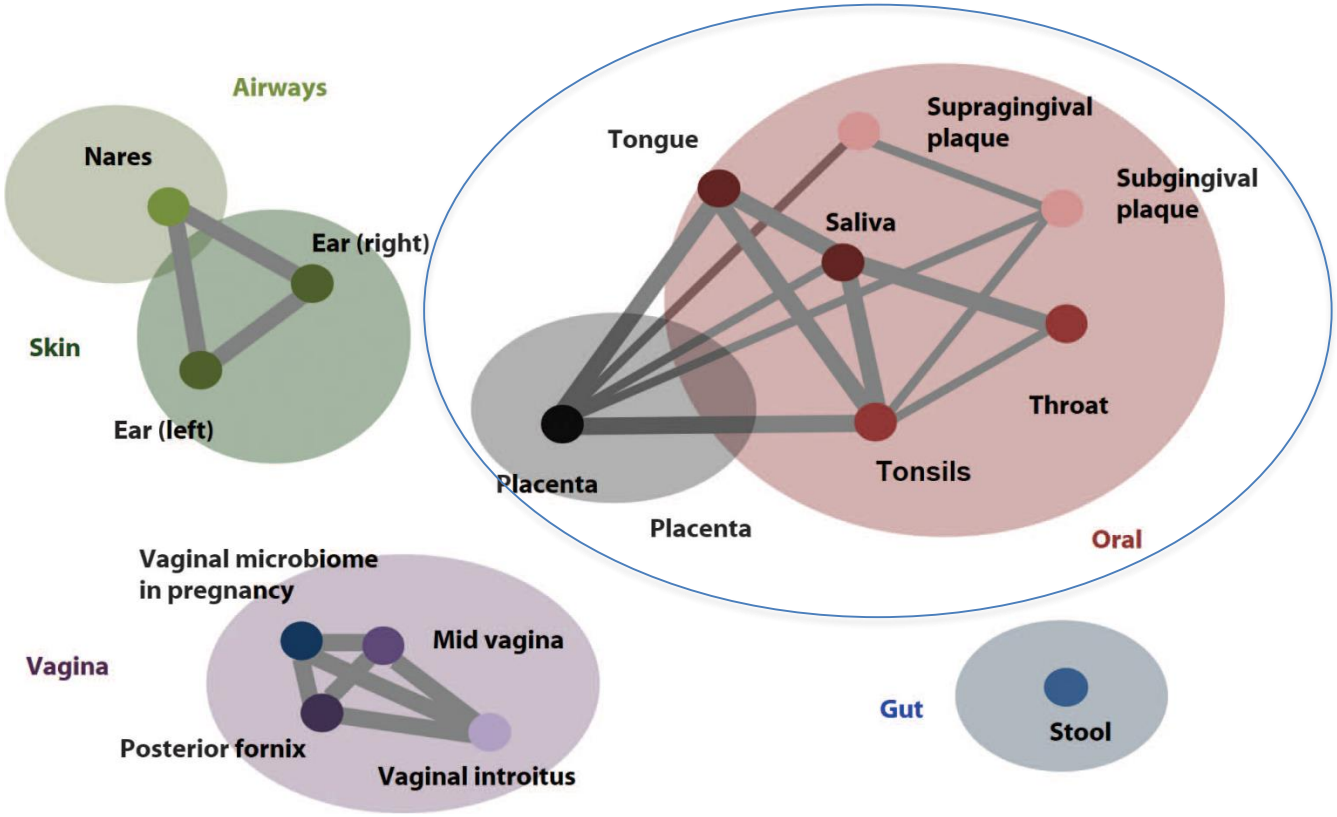
Maynard et al. Nature, 12, Sept 2012, Vol. 489

Science Translational Medicine
AAAS

The Placenta Harbors a Unique Microbiome

Kjersti Aagaard *et al.*

Sci Transl Med **6**, 237ra65 (2014);
DOI: 10.1126/scitranslmed.3008599



Original Research ajog.org

OBSTETRICS

Is amniotic fluid of women with uncomplicated term pregnancies free of bacteria?

Eva Maria Rehbinder, MD; Karin C. Lødrup Carlsen, MD, PhD[1]; Anne Cathrine Staff, MD, PhD[1]; Inga Leena Angell, MSc; Linn Landrø, MD, PhD; Katarina Hilde, MD; Peter Gaustad, MD, PhD; Knut Rudi, PhD

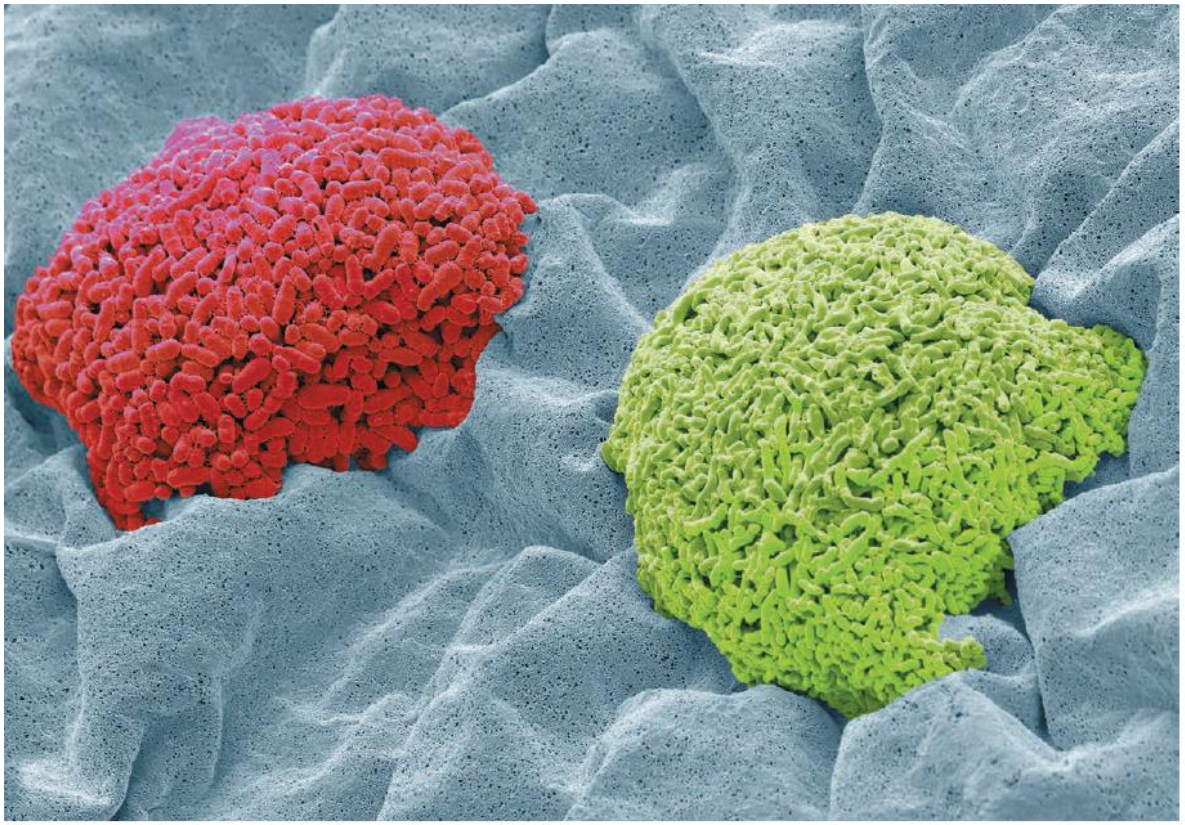
CONCLUSION: We conclude that fetal development in uncomplicated pregnancies occurs in the absence of an amniotic fluid microbiota and that the offspring microbial colonization starts after uterine contractions and rupture of amniotic membrane.

nature 17 January 2018

Baby's first bacteria

THE WOMB WAS THOUGHT TO BE STERILE. SOME SCIENTISTS ARGUE IT'S WHERE THE MICROBIOME BEGINS.

"IF WE DO NOT HAVE MICROBES IN UTERO, I THINK WE WOULD BE THE ONLY SPECIES THAT HAS BEEN INTERROGATED THAT DOESN'T."



Bacterial culture from a belly button: there is some debate as to how different parts of the body are first seeded with microbes.

SHARE

0

REPORT

Transmission modes of the mammalian gut microbiota

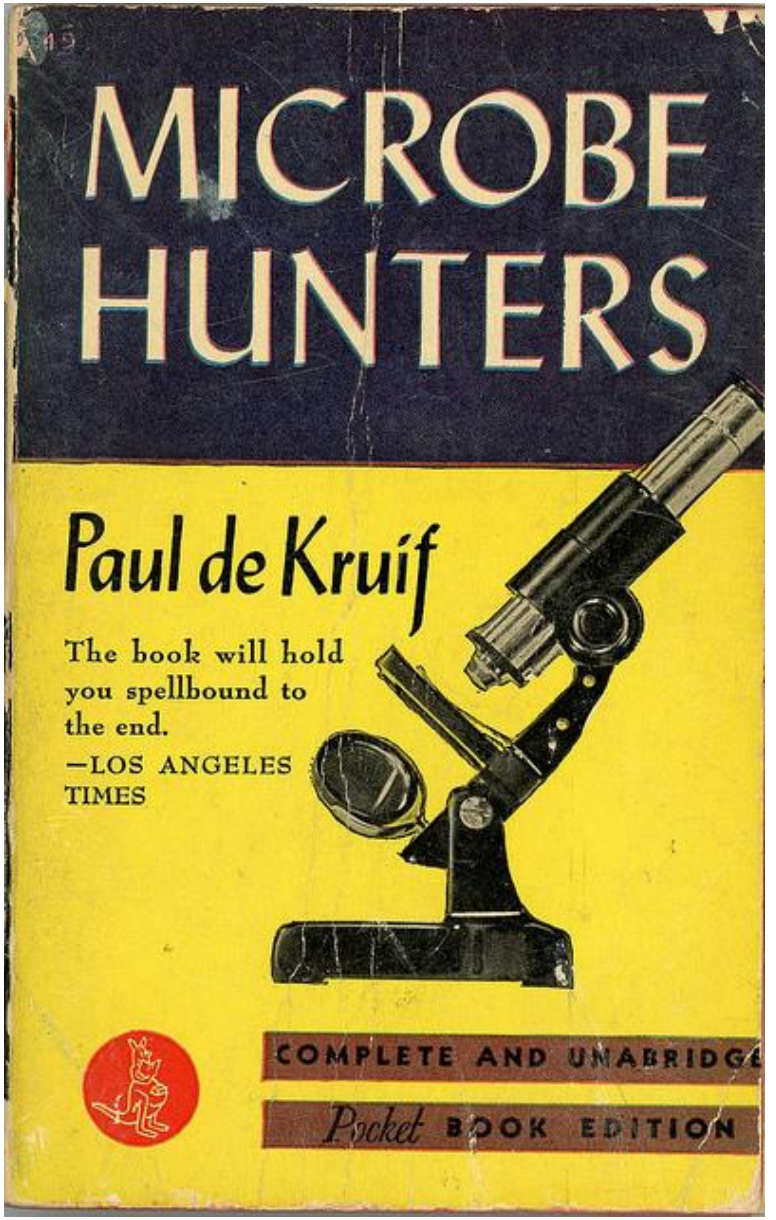
Andrew H. Moeller[1,2,3,*,†], Taichi A. Suzuki[2,3], Megan Phifer-Rixey[4,2,3], Michael W. Nachman[2,3,*]

+ See all authors and affiliations

Science 26 Oct 2018:
Vol. 362, Issue 6413, pp. 453-457
DOI: 10.1126/science.aat7164

Science

Il microbiota intestinale si eredita soprattutto dalla madre



Are bacteria our enemies to be killed or friends to be conquered?

“Biology has entered a new era with the capacity to understand that an organism’s genetics and fitness are inclusive of its microbiome.”

Chi siamo noi?

Brucker, R. M. & Bordenstein, S. R. Response to Comment on “The hologenomic basis of speciation: gut bacteria cause hybrid lethality in the genus *Nasonia*”. *Science.* **345**, 1011 (2014).

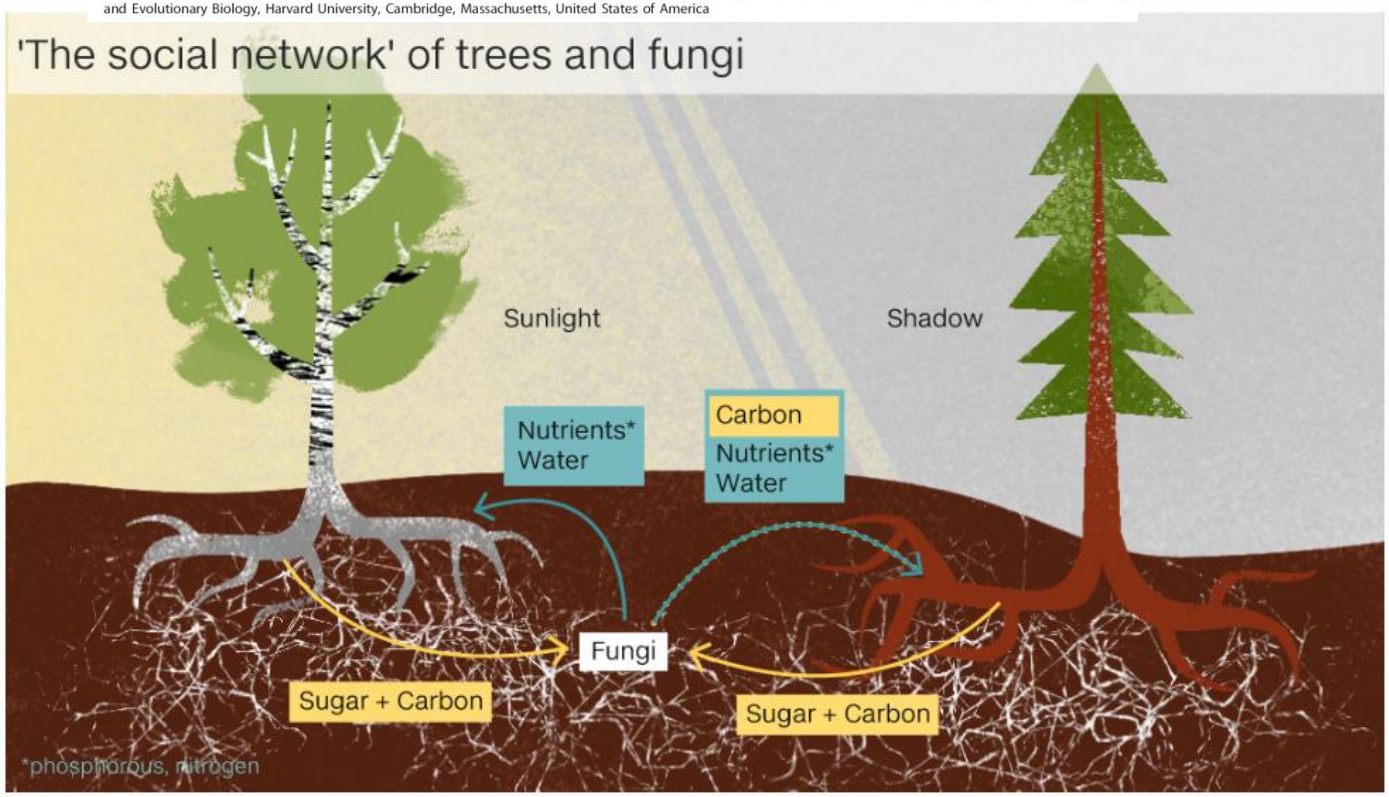
OPEN ACCESS Freely available online

PLoS one

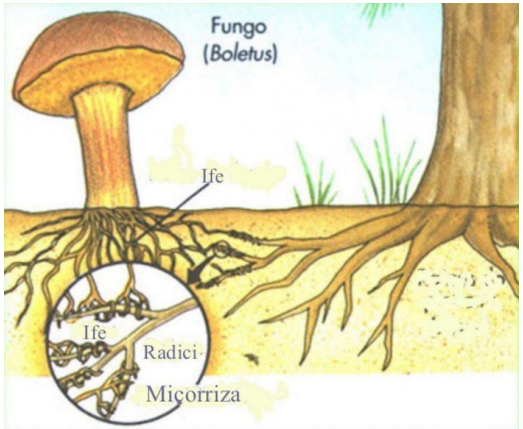
The Irreversible Loss of a Decomposition Pathway Marks the Single Origin of an Ectomycorrhizal Symbiosis

Benjamin E. Wolfe[1]*, Rodham E. Tulloss[2,3], Anne Pringle[4]

1 FAS Center for Systems Biology, Harvard University, Cambridge, Massachusetts, United States of America, **2** Herbarium Rooseveltensis Amanitarum, Roosevelt, New Jersey, United States of America, **3** Honorary Research Associate, the New York Botanical Garden, Bronx, New York, United States of America, **4** Department of Organismic and Evolutionary Biology, Harvard University, Cambridge, Massachusetts, United States of America



Le piante si parlano con un internet sotterraneo di funghi. Ma ci sono anche hacker e ladri
Il "wood wide web« (definizione di Nature, che connette gli esseri viventi della Terra



Virulence

201
6

ISSN: 2150-5594 (Print) 2150-5608 (Online) Journal homepage: http://www.tandfonline.com/loi/kvir20

The vaginal mycobiome: A contemporary perspective on fungi in women's health and diseases

L. Latéy Bradford & Jacques Ravel

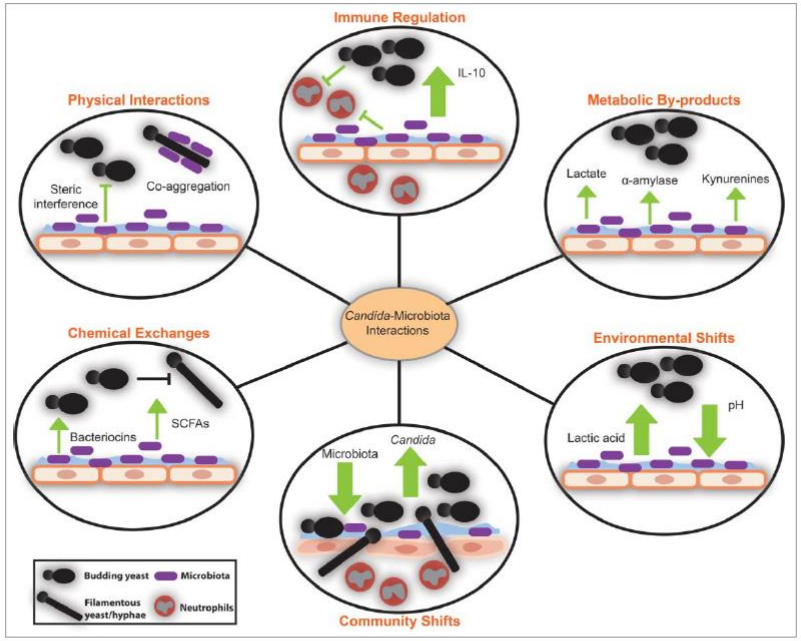


Figure 1. Interactions between *Candida* and microbiota at the mucosal interface have profound effects on the vaginal ecosystem.[109,120-125] Metabolites and small molecules made by the microbiota affect the metabolism and morphology of *Candida* species. Changes in microbiota relative abundance also impact the abundance of *Candida* and its ability to access the mucosal surface, where invasion occurs. In healthy states, when microbiota-derived lactic acid is produced, *Candida* can alter host cytokine production and promote anti-inflammatory signaling. The contribution of bacterial-fungal interactions to the ecology of the vaginal microbiota remains to be described.

Ravel and Brotman *Genome Medicine* (2016) 8:35
DOI 10.1186/s13073-016-0291-2

Genome Medicine

COMMENT Open Access

Translating the vaginal microbiome: gaps and challenges

Jacques Ravel[1,2*] and Rebecca M. Brotman[1,3]

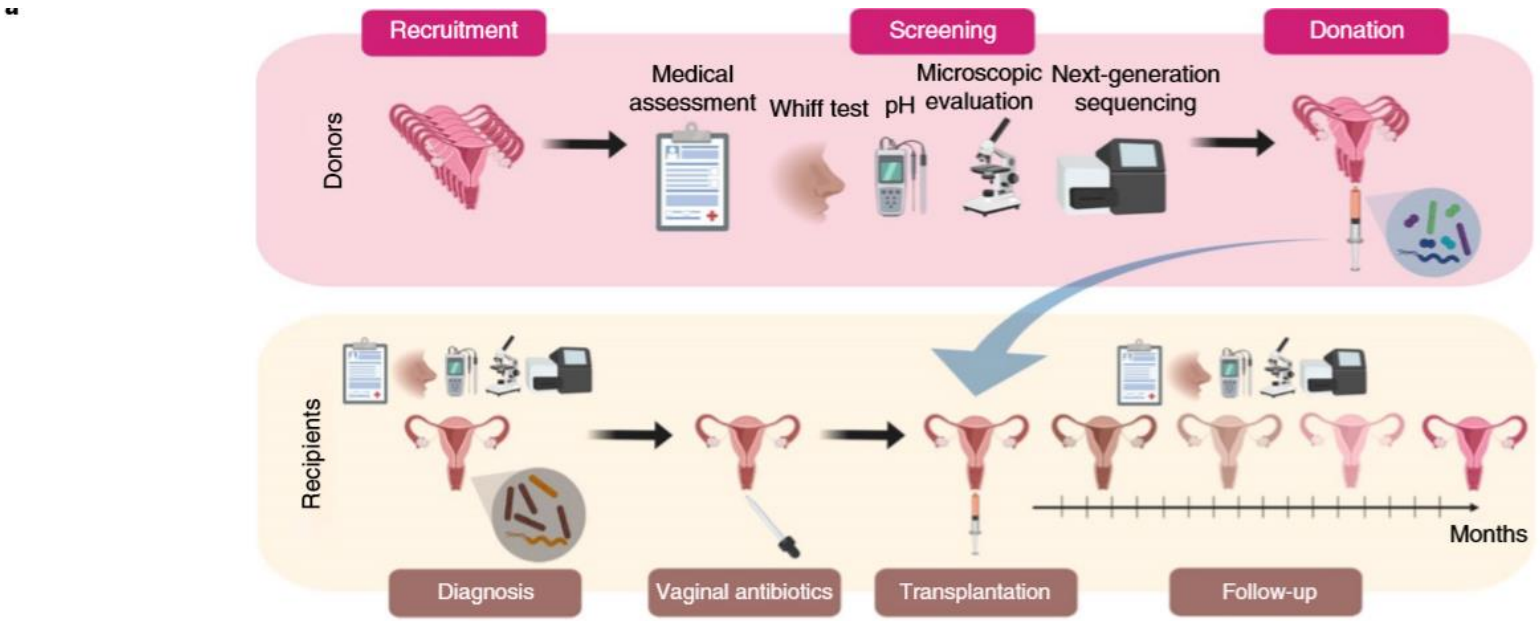
Conclusions

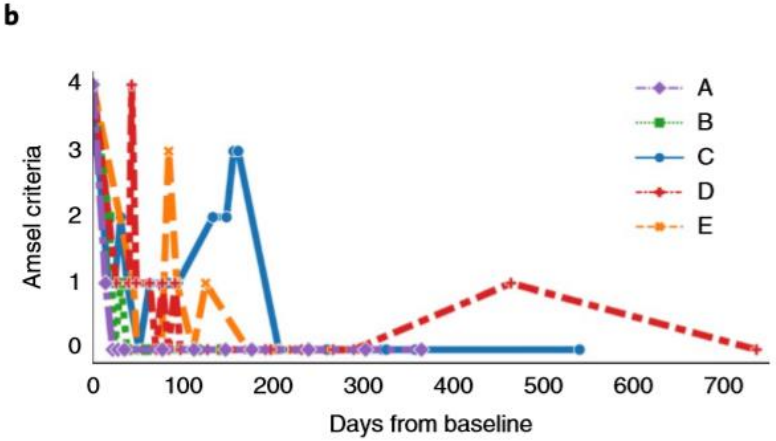
In the near future, manipulation of the vaginal microbiota has the potential to change the way clinicians approach women's health and preventive care. Although we understand the protective role of the vaginal microbiota as a whole, much detail remains to be clarified. Humans are highly unique among mammals in that women can carry *Lactobacillus* spp. as the dominant or minor member of the vaginal microbiota, which leads us to ask what roles other vaginal bacteria might have and how their manipulation might affect their ancillary functions. The interaction between microbiota at other body sites with the vaginal microbiota should also be considered and, just like the newly appreciated gut–brain axis, a gut–vagina axis might have an important role in women's health. The next decade of systems biology and epidemiologic research on the vaginal microbiota is expected to lead to antibiotic-sparing strategies designed to manage, modulate, and restore a robust vaginal microenvironment and ultimately improve the health of women and their children.

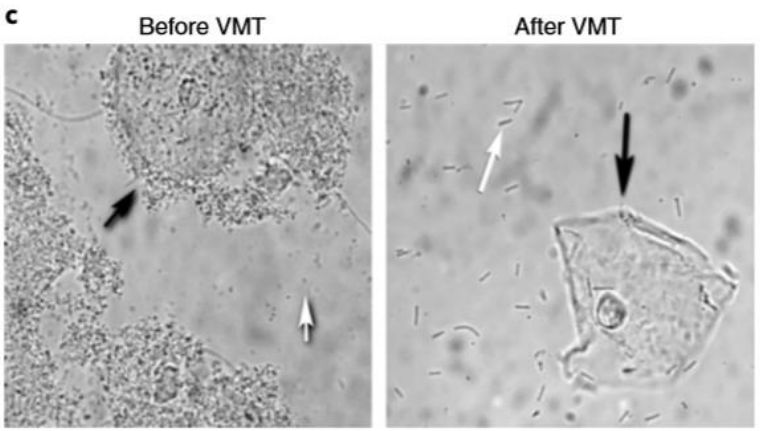
BRIEF COMMUNICATION
https://doi.org/10.1038/s41591-019-0600-6
nature medicine

Vaginal microbiome transplantation in women with intractable bacterial vaginosis

Ahinoam Lev-Sagie[1,6*], Debra Goldman-Wohl[1,6], Yotam Cohen[2,6], Mally Dori-Bachash[2], Avner Leshem[2,3], Uria Mor[2], Jacob Strahilevitz[4], Allon E. Moses[4], Hagit Shapiro[2], Simcha Yagel[1] and Eran Elinav[2,5*]







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SCIENTIFIC REPORTS

OPEN

Cervical intraepithelial neoplasia disease progression is associated with increased vaginal microbiome diversity

Received: 18 September 2015
Accepted: 21 October 2015
Published: 17 November 2015

A. Mitra[1,2], D. A. MacIntyre[1], Y. S. Lee[1], A. Smith[3], J. R. Marchesi[3,4], B. Lehne[5], R. Bhatia[6], D. Lyons[7], E. Paraskevaidis[8], J. V. Li[6], E. Holmes[4], J. K. Nicholson[4], P. R. Bennett[1,2] & M. Kyrgiou[1,2]

The vaginal microbiome in HSIL was characterised by higher levels of Sneathia sanguinegens (P < 0.01), Anaerococcus tetradius (P < 0.05) and Peptostreptococcus anaerobius (P < 0.05) and lower levels of Lactobacillus jensenii (P < 0.01) compared to LSIL.

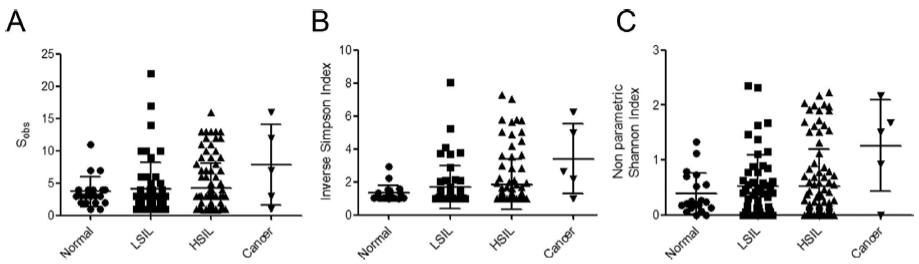


Figure 4. Vaginal microbiome richness and diversity indices associated with disease status (normal, LSIL, HSIL and cervical cancer patients). The number of species observed increased with disease severity with lowest richness observed in healthy controls and highest in HSIL and ICC (**A**). Diversity, as assessed by Inverse Simpson (**B**) and non-parametric Shannon (**C**) indices followed the same pattern. KEY - HSIL: High-grade squamous intra-epithelial lesion; ICC: invasive cervical cancer; LSIL: Low-grade squamous intra-epithelial lesion; S_{obs}: Species observed; ** = $P < 0.01$; *** = $P < 0.001$.

Science
AAAS
Editor's Summary

Vaginal microbiome affects HIV risk
Jon Cohen (July 21, 2016)
Science 353 (6297), 331. [doi: 10.

INFECTIOUS DISEASE

Vaginal microbiome affects HIV risk

Unusual bacteria in vagina help explain high infection rates in South African women

By **Jon Cohen**, *in Durban, South Africa*

The makeup of a woman's vaginal microbiome strongly influences her susceptibility to HIV infection, suggest studies presented at the 21st International AIDS Conference here this week. The microbiome may also explain why pre-exposure prophylaxis (PrEP)—giving anti-HIV drugs to prevent infection—works better in men than in women. These findings have particular relevance here in South Africa's KwaZulu-Natal province, which has perplexingly high levels of HIV infection in teenage girls and young women.

"It's a really important insight into why young women in Africa are getting infected at such high rates," says Douglas Kwon, an immunologist at Massachusetts General Hospital in Boston, who has studied the vaginal microbiome and HIV.

The new findings come from follow-up studies of women in a PrEP trial of a vaginal gel containing the anti-HIV drug tenofovir. Conducted by the Centre for the AIDS Programme of Research in South Africa (CAPRISA) based here, the trial took place in a region where 66% of 30-year-old women are infected. The CAPRISA team made headlines in 2010 by showing that the gel reduced a woman's risk of infection by 44%. But many wondered why the gel wasn't more effective—and indeed it failed in a later trial.

The more provocative of the two new studies compared the vaginal microflora in 49 women who became infected during the trial with that of 70 who remained HIV negative. A previous study of women in this trial had shown that those with increased genital tract inflammation were more likely to become infected. Vaginal biopsies suggest a reason: Inflammation brings more of HIV's favorite target, CD4 white blood cells, to the mucosal surface. And in a separate study of women in KwaZulu-Natal, Kwon and colleagues reported last year that inflammation in the vagina is linked to a decrease in *Lactobacillus*, which creates an acidic environment inhospitable to many pathogens. As the researchers noted but could not explain, *Lactobacillus* dominated in the vaginas of only 37% of the women, compared with 90% of U.S. white women.

Until now, however, no one had clearly linked specific vaginal microbiomes to an increased risk of HIV infection. "Now we have actual data," says CAPRISA's director, epidemiologist Salim Abdool Karim.

The data come from a massive effort to identify bacterial species on vaginal swabs from the women in the CAPRISA tenofovir gel study. By extracting thousands of bacterial ribosomal RNAs from each swab, Ian Lipkin's lab at Columbia University identified a total of 1368 species.

One relatively rare species, *Prevotella bivia*, stood out. Women whose vaginal microbiome included more than 1% of *P. bivia* had the highest levels of genital inflammation and the highest likelihood of becoming infected. These women had markedly reduced levels of *Lactobacilli*, and the researchers showed that *P. bivia* itself releases an inflammation-promoting compound called lipopolysaccharide. Women with more than 1% *P. bivia* were nearly 13 times more likely to become infected by HIV than those with less.

In the second study, of vaginal washings from 688 women in the CAPRISA trial, Adam Burgener from the Public Health Agency of Canada in Winnipeg and Nichole Klatt of the University of Washington, Seattle, showed that the vaginal microbiome can directly interfere with PrEP. The tenofovir gel protected only 18% of the women whose microbiome contained less than 50% *Lactobacilli*. The efficacy jumped to 61% when the *Lactobacillus* proportion was above 50%. In the lab, the researchers found that drug levels drop by half in the presence of *Gardnerella*, a genus that flourishes when *Lactobacilli* are scarce.

Anthony Fauci, head of the U.S. National Institute of Allergy and Infectious Diseases in Bethesda, Maryland, says these findings open the possibility of manipulating the vaginal microbiome with antibiotics or beneficial microbes. "If this pans out, it seems like a relatively low-tech way to make an impact on whether you get infected or not," Fauci says.

Kwon cautions that efforts to manipulate the microbiome to treat inflammatory diseases of the gut have had limited success. But Fauci is more optimistic. The vaginal vault has far less susceptible tissue than the gut, he points out. "You're talking inches rather than feet," he says. "This is an interesting issue that needs to be pursued." ■

SCIENTIFIC AMERICAN

English Cart 0

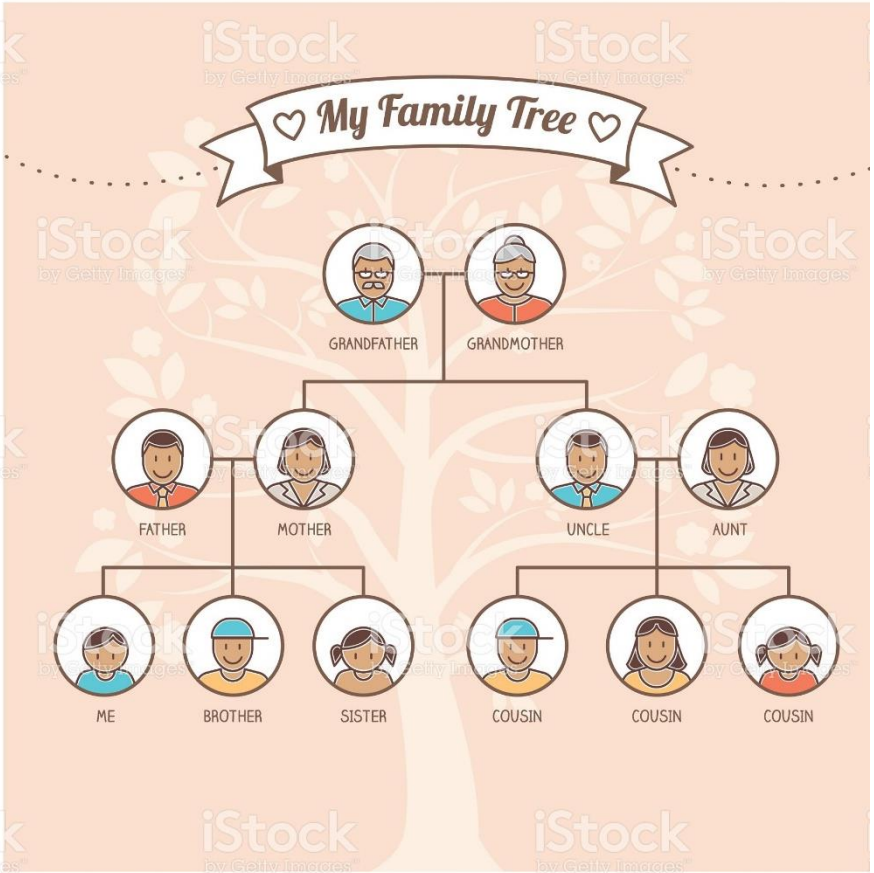
SCIENCES MIND HEALTH TECH SUSTAINABILITY EDUCATION VIDEO PODCASTS BLOGS ST

Guest Blog

Shortchanging a Baby's Microbiome

C-sections and formula feeding could be interfering with a critical biological process

By Toni Harman on February 14, 2017



HMO Human Milk Oligosaccaride

Journal of
Gynecology and Women's Health
ISSN 2474-7602

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Mini Review
Volume 8 Issue 1 - January 2018
DOI: 10.19080/JGWH.2018.08.555732

J Gynecol Women's Health

Childbirth and New Omics Sciences: an Ecological Perspective

Antonio Ragusa[1*] and Alessandro Svelato[2]

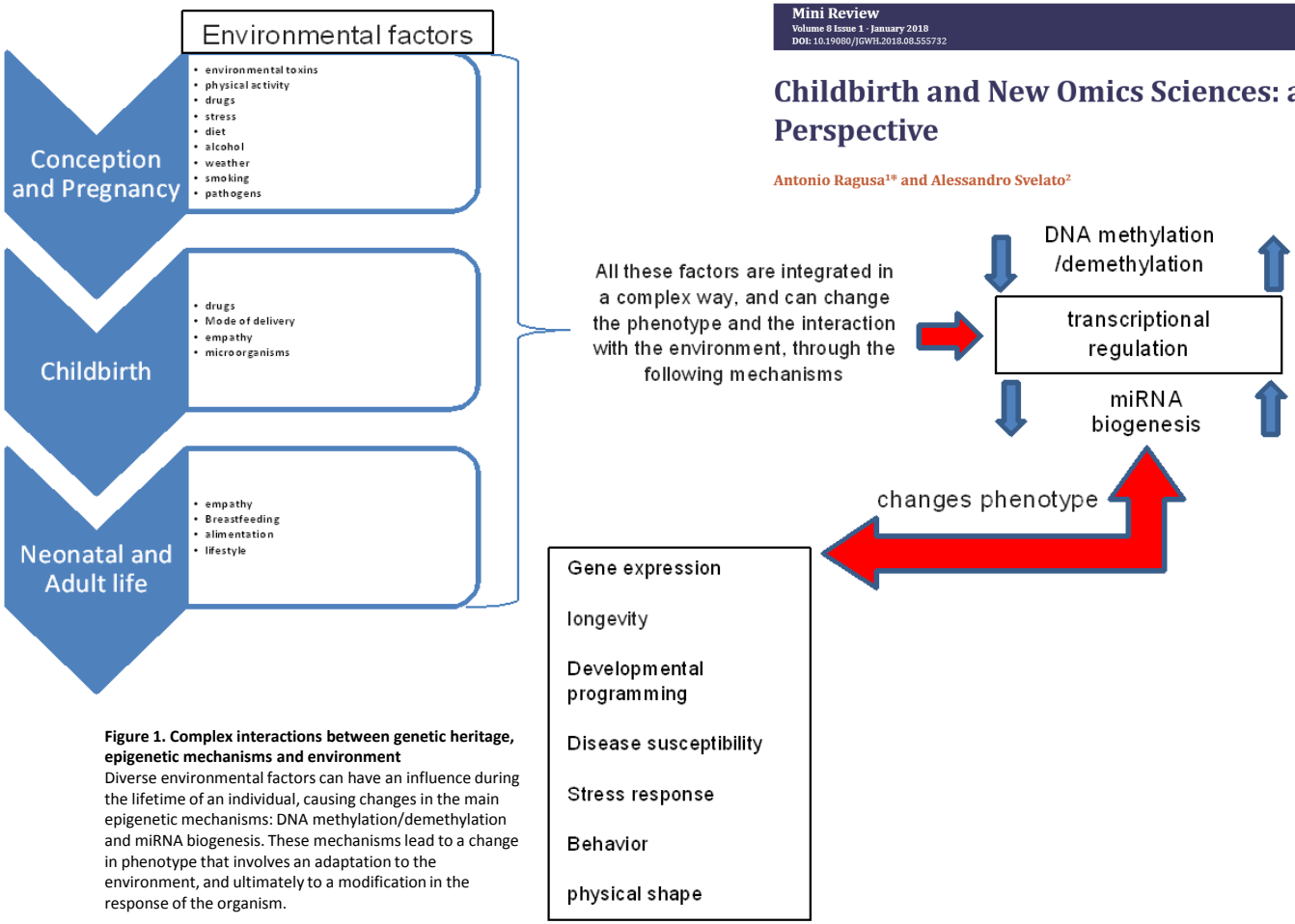

Figure 1. Complex interactions between genetic heritage, epigenetic mechanisms and environment
Diverse environmental factors can have an influence during the lifetime of an individual, causing changes in the main epigenetic mechanisms: DNA methylation/demethylation and miRNA biogenesis. These mechanisms lead to a change in phenotype that involves an adaptation to the environment, and ultimately to a modification in the response of the organism.

Cancer Epidemiology, Biomarkers & Prevention

Research Article

Mode of Delivery and Risk of Childhood Leukemia

Stephen Starko Francis[1], Steve Selvin[2], Catherine Metayer[1], Amelia D. Wallace[1], Vonda Crouse[4], Theodore B. Moore[5], Joseph L. Wiemels[3], and Patricia A. Buffler[1,†]

Journal of
Gynecology and Women's Health
ISSN 2474-7602

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Mini Review
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J Gynecol Women's Health

Childbirth and New Omics Sciences: an Ecological Perspective

Antonio Ragusa and Alessandro Svelato.

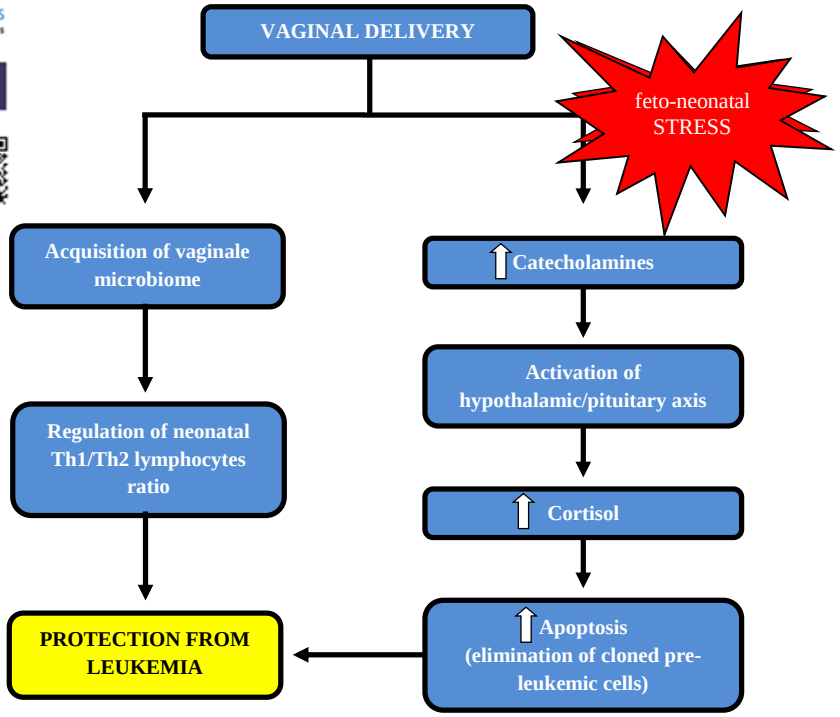


Figure 2. Hypothetical mechanism through which vaginal birth can protect newborns from leukemia

Vaginal birth causes higher stress in the foetus/newborn, which, by means of the activation of the foetal hypothalamic/pituitary axis, increases the neonatal ability of apoptosis, which, in turn, eliminates cloned pre-leukemic cells. Moreover, the acquisition of the vaginal microbiome enables acquisition of micro-organisms that positively regulates the newborn's Th1/Th2 ratio.

Disease Markers

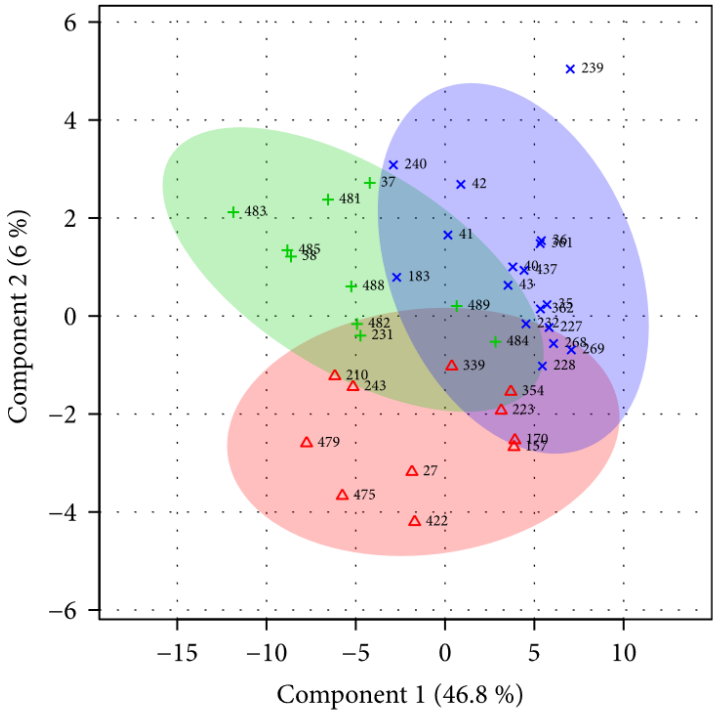
Impact Factor 2.348

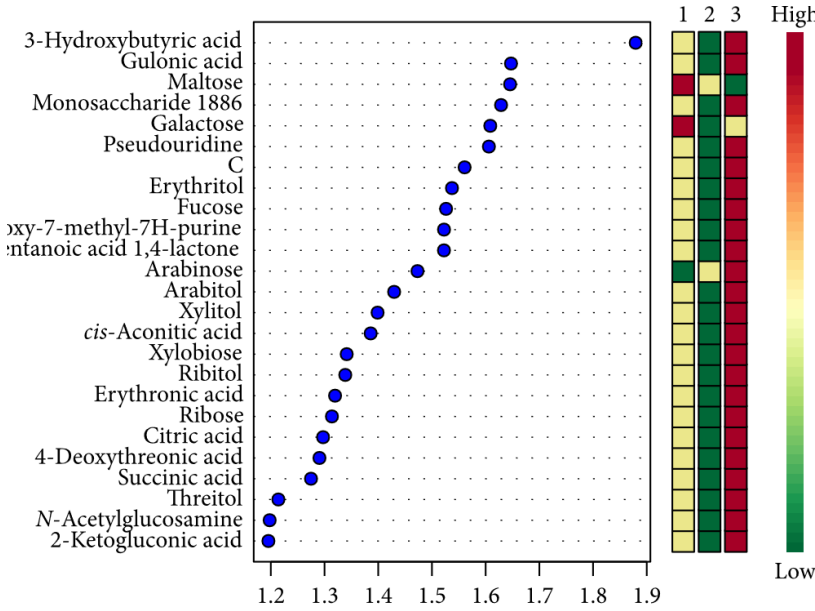
201
8

PROM and Labour Effects On Urinary Metabolome: A Pilot Study

Alessandra Meloni[1]*, Francesco Palmas[2]*, Luigi Barberini[3], Rossella Mereu[1], Sara Francesca Deiana[1], Maria Francesca Fais[1], Antonio Noto[4], Claudia Fattuoni[2], Michele Mussap[5], Antonio Ragusa[6], Angelica Dessì[4], Roberta Pintus[4], Vassilios Fanos[4], Gian Benedetto Melis[1].

Fig.1: A) 2D scores plot showing PLS-DA discrimination between Ph1 (red, out of labour, intact membranes), Ph2 (green, out of labour, PROM) and Ph3 (blue, in labour, PROM) and B) the corresponding VIP score plot.





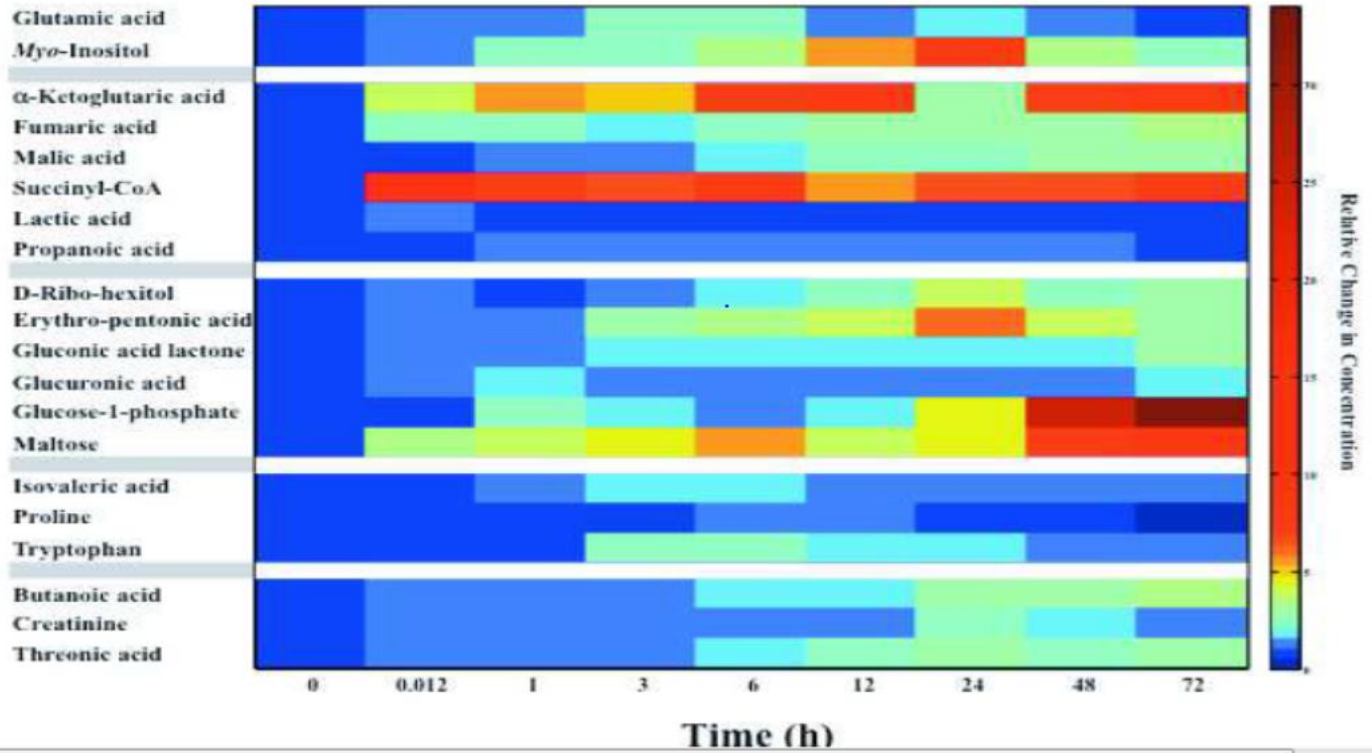
FEMS Microbiology Letters

Volume 159, Issue 2, 15 February 1998, Pages 293-297

Poly-β-hydroxybutyrate production by lactic acid bacteria

Belma Aslıma, Fikret Çalışkana, Yavuz Beyatlıa, Ufuk Gündüzb

The fetal to neonatal transition



we identified 100 metabolites that changed during this transition. Of these 100 metabolites, 23 demonstrated significant change during the first 72 hours. Of note, four intermediates of the tricarboxylic acid (TCA) cycle were identified (□-ketoglutaric acid, fumaric acid, malic acid, and succinyl-CoA), demonstrating a consistent rate of rise during the study.

The Perinatal Transition of the Circulating M 1 etabolome in a Nonhuman Primate Andrew C. Beckstroma, Pattaraporn Tanyaa, Elizabeth M. Humstonb, Laura R. Snyderc3 , Robert E. Synovecb and Sandra E. Juula,*

Volume 5, Issue 2, April 2017, Pages 163-169

The importance of faulty perinatal imprinting

Hormonal imprinting occurs perinatally, when the developing hormone receptors connect to their target hormones. This is required for the normal development of the receptor-hormone connection. At this time, the selectivity of receptors is weak and can be misdirected to related endogenous or exogenous molecules, such as other members of the same hormone family, synthetic hormones, drugs, hormone-like environmental pollutants, and endocrine disruptors. In this situation, faulty hormonal imprinting develops with lifelong consequences, which are manifested by altered receptor binding capacity, hormone production, changed bone formation, and brain neurotransmitter content. The effect of faulty imprinting is epigenetically inherited and manifested in progeny

Antonio Ragusa

La diade Madre Bambino è in realtà una triade! (UN OLOBIONTE!)

- solo 1 cellula su 10 della madre è umana
- 1/3 dei metaboliti ematici dei mammiferi è di derivazione batterica

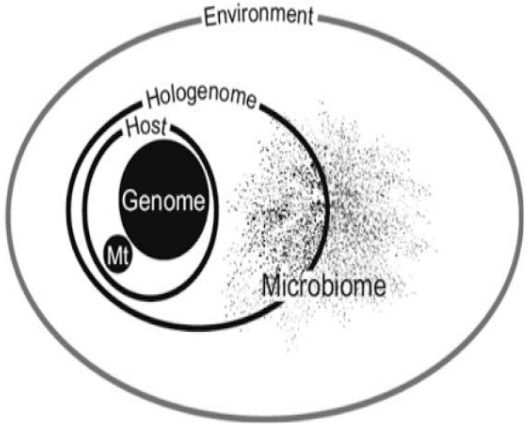


Fig. 6.5 A simplified diagram of the hologenome. The hologenomic concept of a species is that the beneficial microbiome (*black*) is an extension of the animal species' genome and mitochondria (Mt). That beneficial microbiome is deterministically acquired. Although there is some plasticity in the host-associated microbiome derived from the environment (such as diet and abiotic factors, *gray*), the host limits the potential members of the total microbiome (Taken from Brucker and Bordenstein (2013a, b), Zoology)

frontiers in GENETICS

HYPOTHESIS AND THEORY ARTICLE
published: 19 August 2014
doi: 10.3389/fgene.2014.00282

A holobiont birth narrative: the epigenetic transmission of the human microbiome

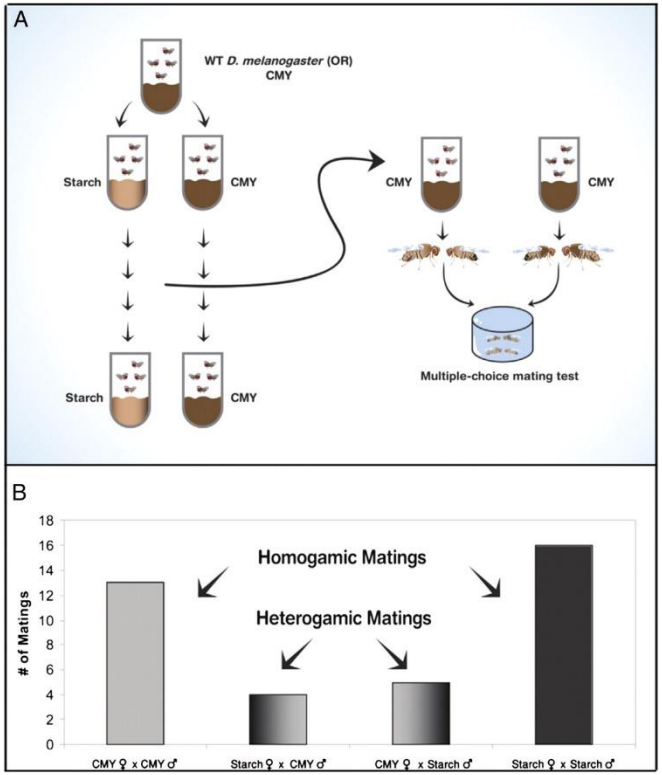
Scott F. Gilbert[1,2]*

[1] Department of Biology, Swarthmore College, Swarthmore, PA, USA
[2] Biotechnology Institute, University of Helsinki, Helsinki, Finland

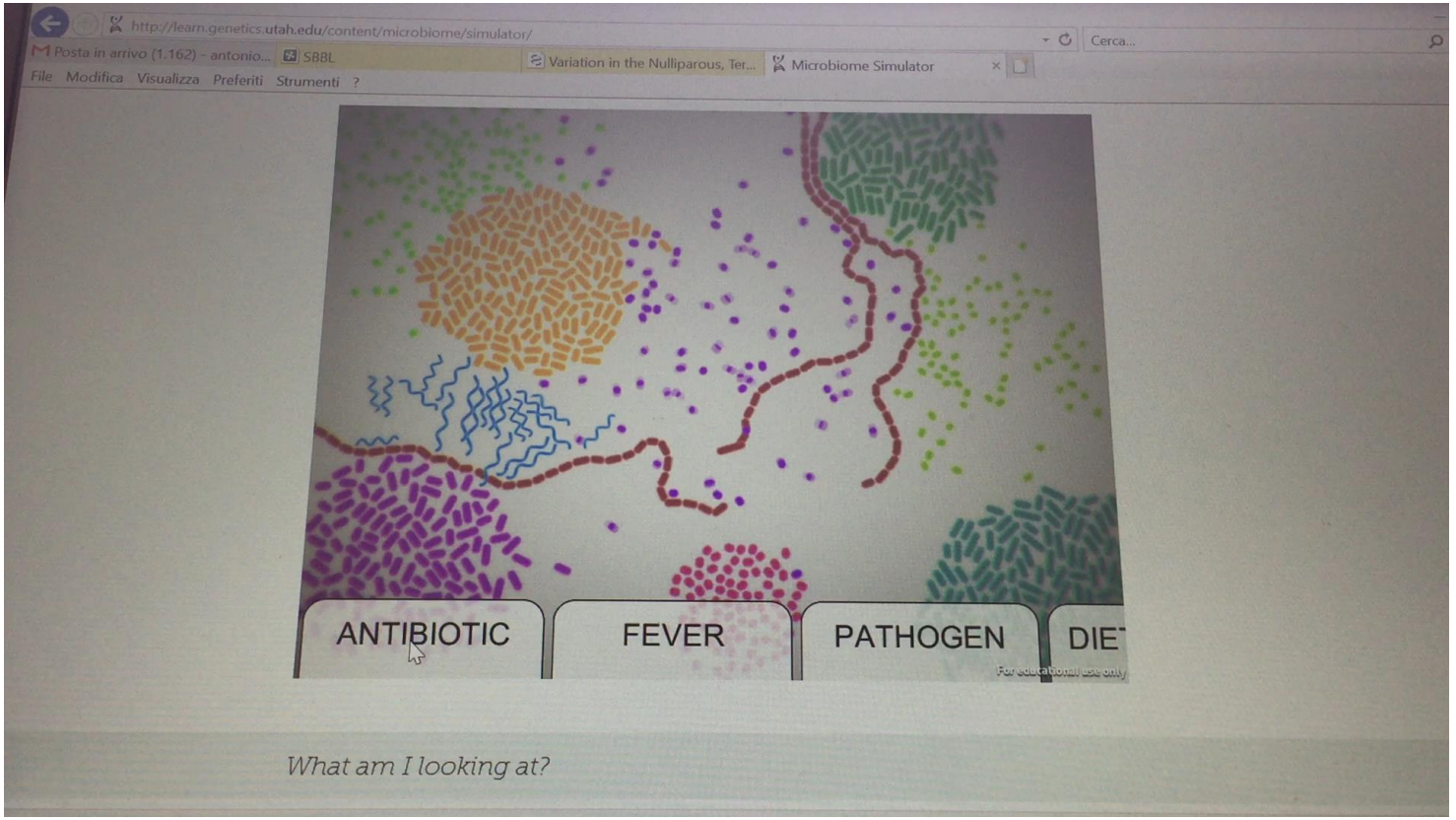
Cortesia Prof. Fanos

(A) Schematic representation of the experimental procedure.

Commensal bacteria play a role in mating preference of *Drosophila melanogaster*



Gil Sharon et al. PNAS 2010;107:20051-20056

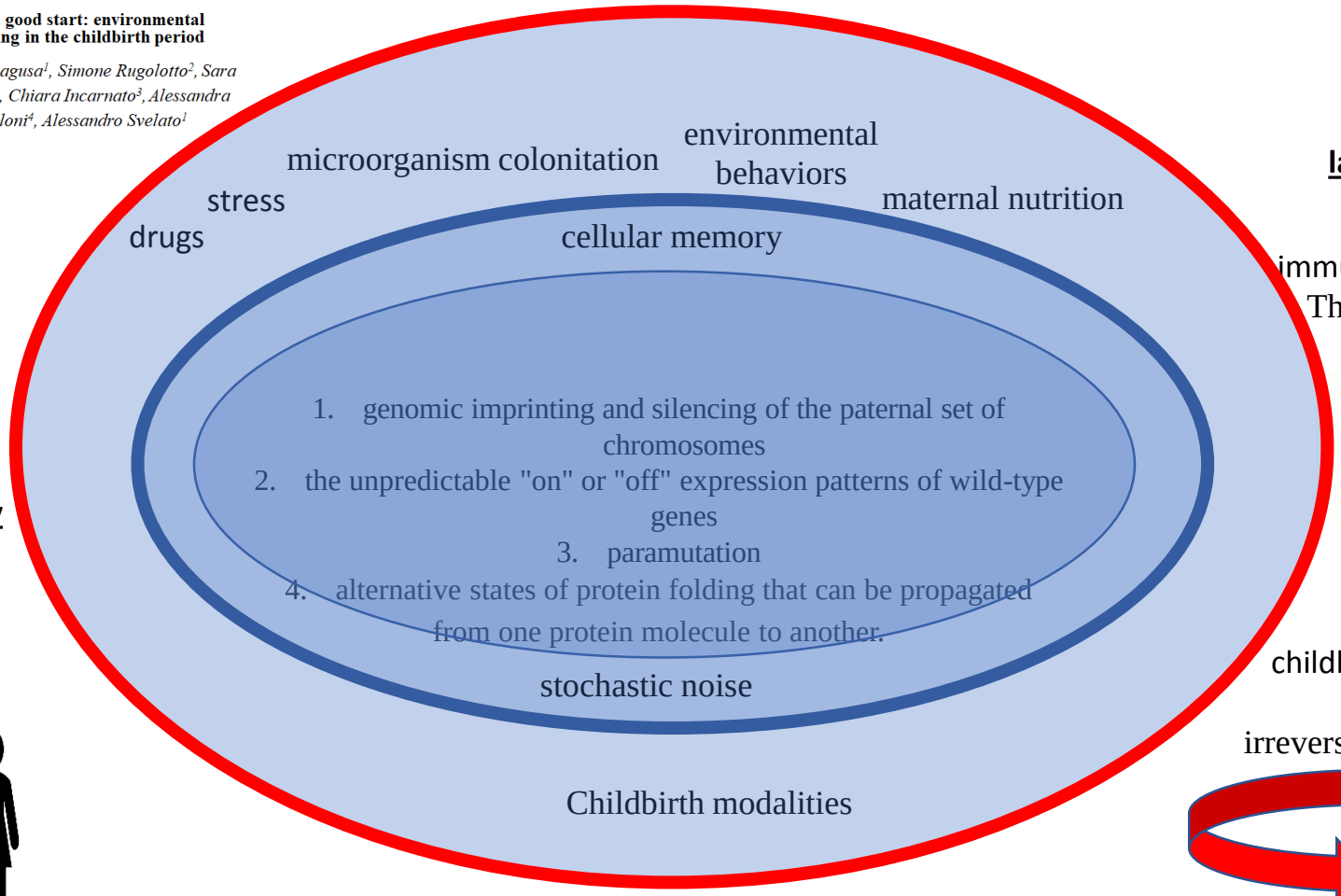


http://learn.genetics.utah.edu/content/microbiome/simulator/

Off to a good start: environmental imprinting in the childbirth period

Antonio Ragusa[1], Simone Rugolotto[2], Sara D'Avino[1], Chiara Incarnato[3], Alessandra Meloni[4], Alessandro Svelato[1]

In press, 2018



pregnancy

genetic heritage

labour and birth

immunological system
Th1/Th2 cell ratio

childbirth imprinting
as
irreversible phenomenon

health or future illness

Fig 1 Pregnancy, labor and birth as complex systems. They are characterized by a huge amount of interdependencies

Prevalence of and risk factors for abnormal vaginal flora and its association with adverse pregnancy outcomes in a rural district in north-east Bangladesh

Key Message

One-sixth of the pregnant women in our study had abnormal vaginal flora; a third did not resolve after treatment. Persistent abnormal vaginal flora was significantly associated with increased risk of adverse pregnancy outcomes. Further research on timely diagnosis, treatment, better characterization of the microbiome may improve outcomes.

Acta Obstet Gynecol Scand. 2018 Oct 22.

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

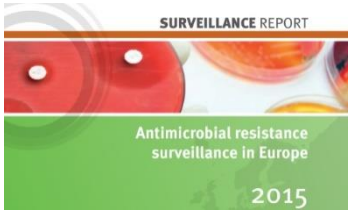
Adjunctive Azithromycin Prophylaxis for Cesarean Delivery

Antonio Ragusa, M.D. and Alessandro Svelato
Massa Carrara General Hospital, Massa Carrara, Italy

Disturbances in the establishment of the indigenous intestinal microbiome because of cesarean delivery or antibiotic exposure in early life, either directly or through modifications of the breast microbiome, have been linked to the risk of immune-mediated and inflammatory conditions such as atopic disorders, inflammatory bowel disease, and obesity later in life. In our opinion, the addition of another antibiotic to prophylaxis before nonelective cesarean section may have medium-term and long-term effects on neonatal health, and these effects should evaluated before clinical practice is changed. Studies to evaluate these effects are lacking.

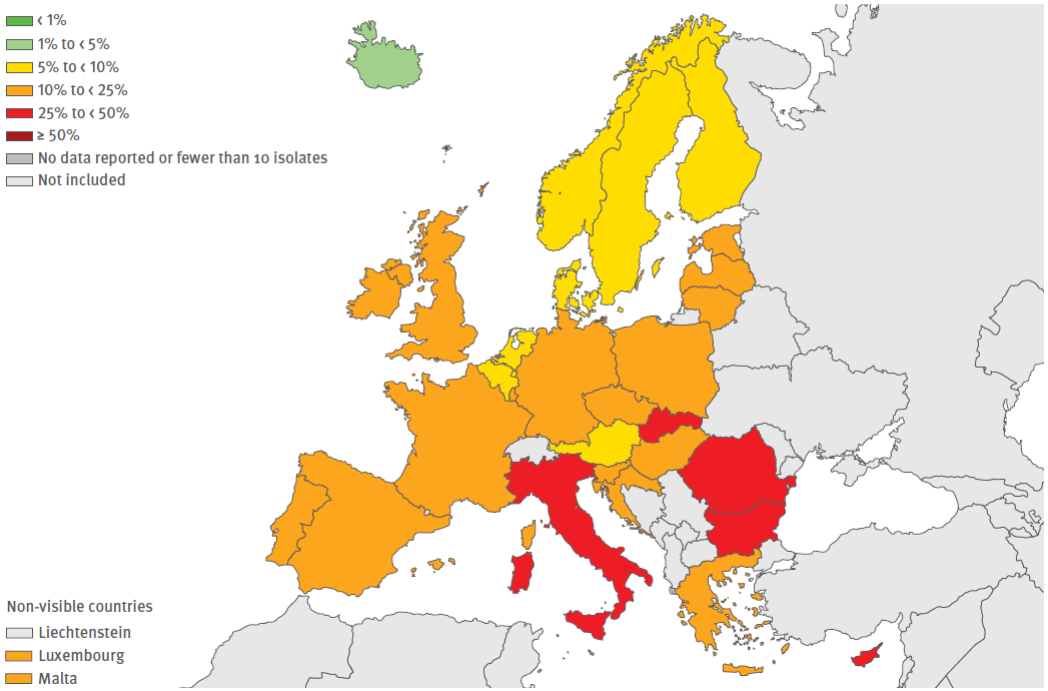
Bias del presente

- detto anche hyperbolic discounting, le decisioni vengono prese per ottenere una gratificazione immediata, ignorando le possibilità di guadagno differite nel tempo. Questo atteggiamento influenza i nostri comportamenti in 3 importanti aree della nostra vita: l'alimentazione, la vita professionale e i risparmi.
- In uno studio condotto da Read & van Leeuwen (1998), il 74% dei partecipanti sceglieva la frutta quando doveva decidere cosa mangiare la settimana successiva. Ma dovendo decidere cosa mangiare subito il 70% sceglieva il cioccolato! Lo stesso vale per denaro: siamo molto ben disposti ad approfittare di sconti nel momento presente, rimandando al futuro la preoccupazione per le spese più impegnative. Chi si occupa di marketing crea infatti proposte ad hoc che ci inducano ad accettare di comprare un prodotto grazie a uno sconto o a un "regalo" iniziale, vantaggio che viene perso sul lungo periodo ma che, proprio per effetti del **bias del presente**, non valutiamo.



ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

Figure 3.2. ***Escherichia coli*****. Percentage (%) of invasive isolates with resistance to third-generation cephalosporins, by country, EU/EEA countries, 2015**



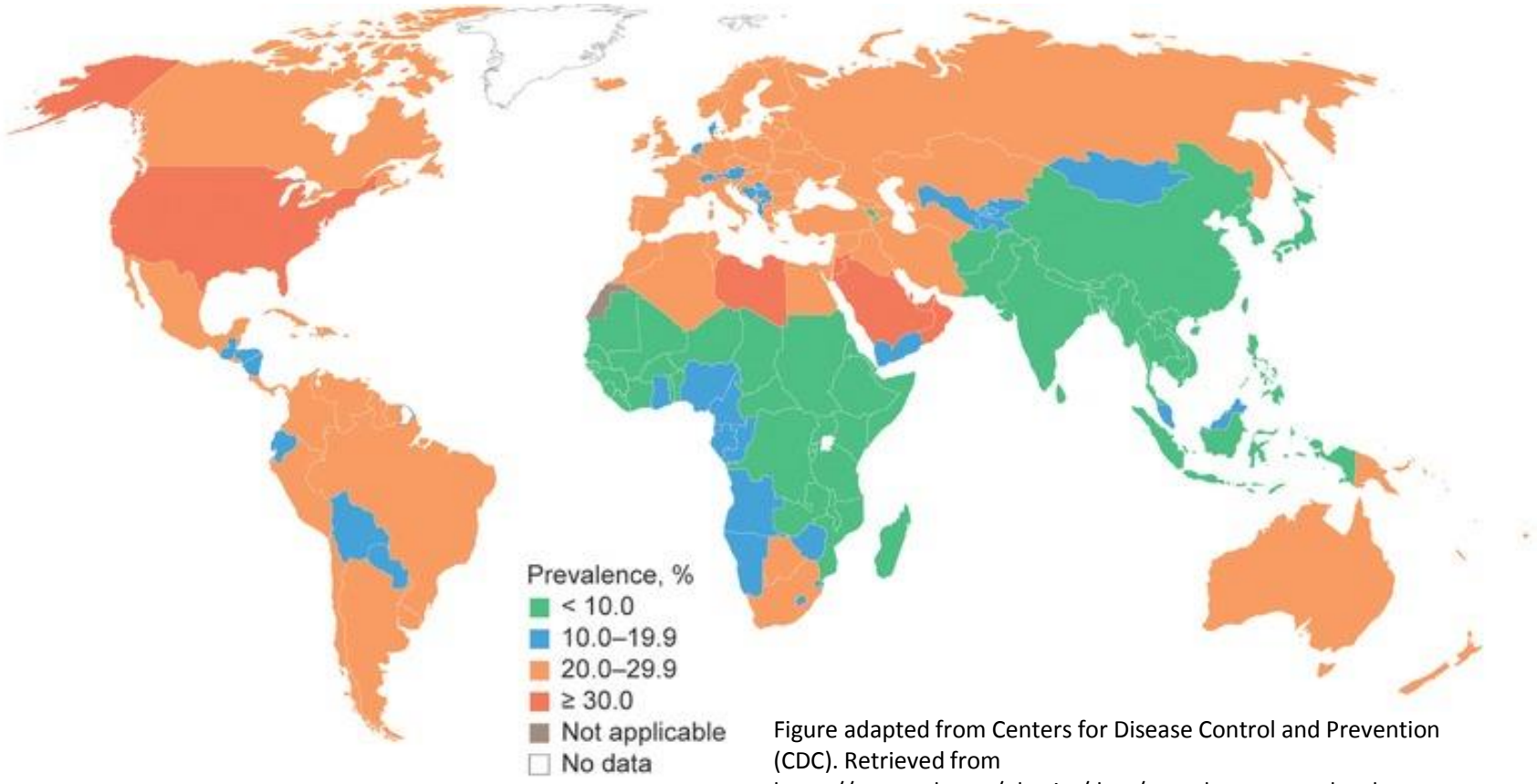
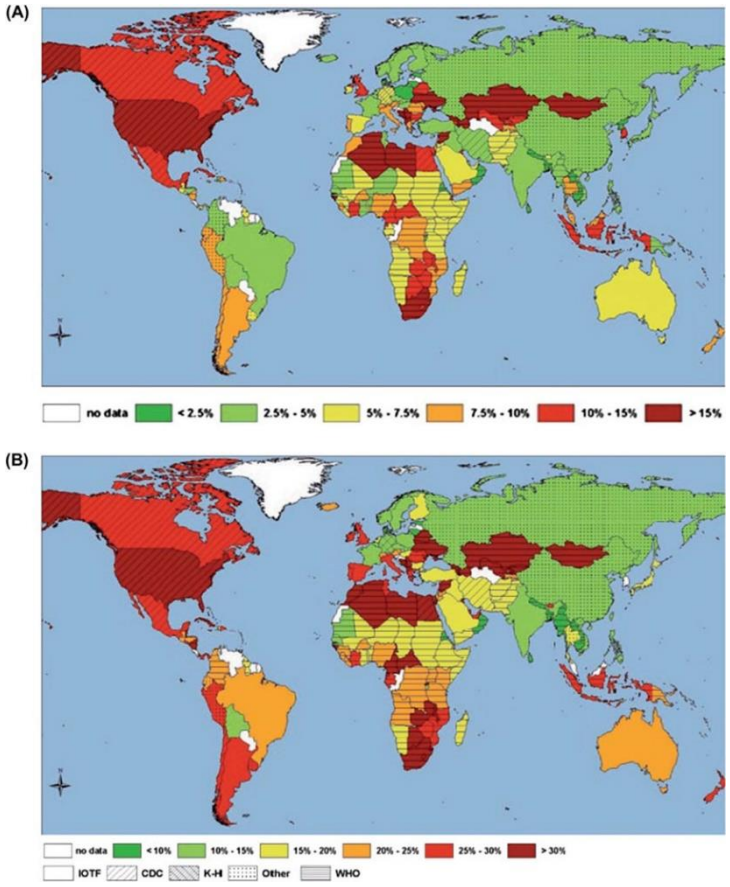


Figure adapted from Centers for Disease Control and Prevention (CDC). Retrieved from https://www.cdc.gov/obesity/data/prevalence-maps.html.

(A) Worldwide prevalence of obesity in children and adolescents. (B) Worldwide combined prevalence of overweight and obesity in children and adolescents. The prevalence estimates were calculated as the arithmetic mean of the age-specific estimates. Adapted from *Epidemiology of Obesity in Children and Adolescents* (Pigeot et al., 2011, p. 228, Figure 13.2) with kind permission of Springer Science & Business Media.



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Pharmacological Research xxx (xxxx) xxxx

Contents lists available at ScienceDirect

Pharmacological Research

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Review

Gut microbiota and probiotic intervention as a promising therapeutic for pregnant women with cardiometabolic disorders: Present and future directions

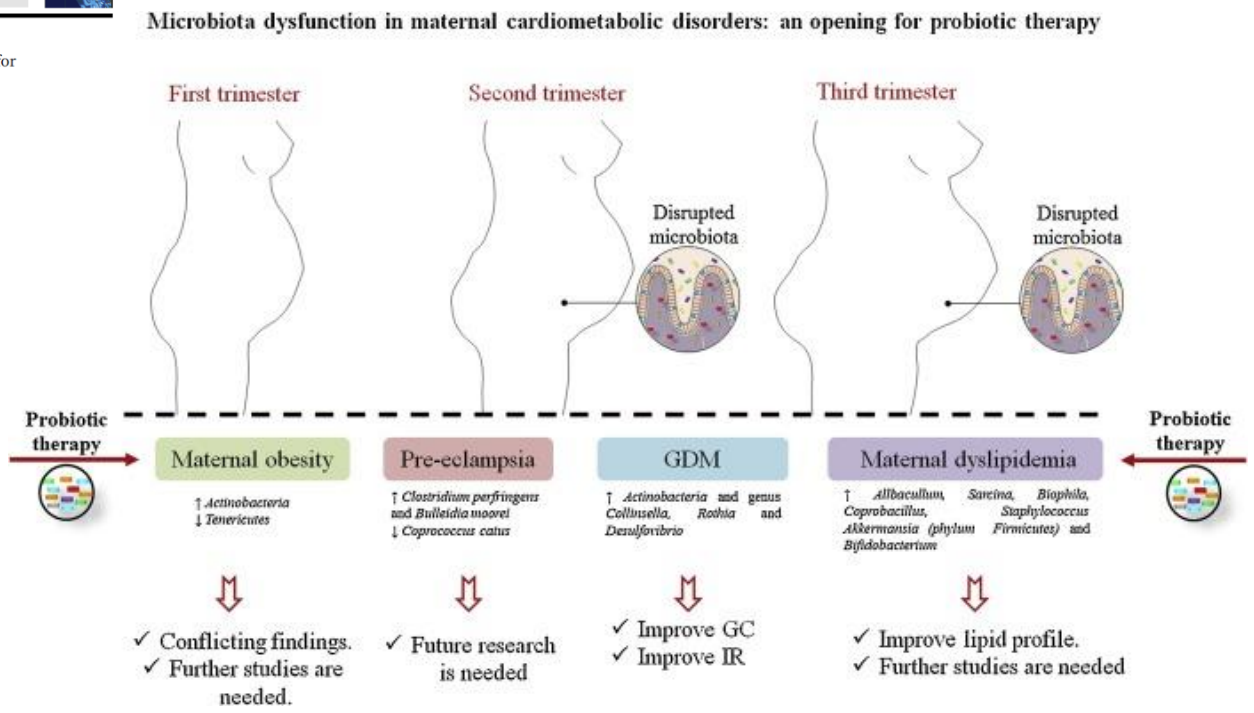


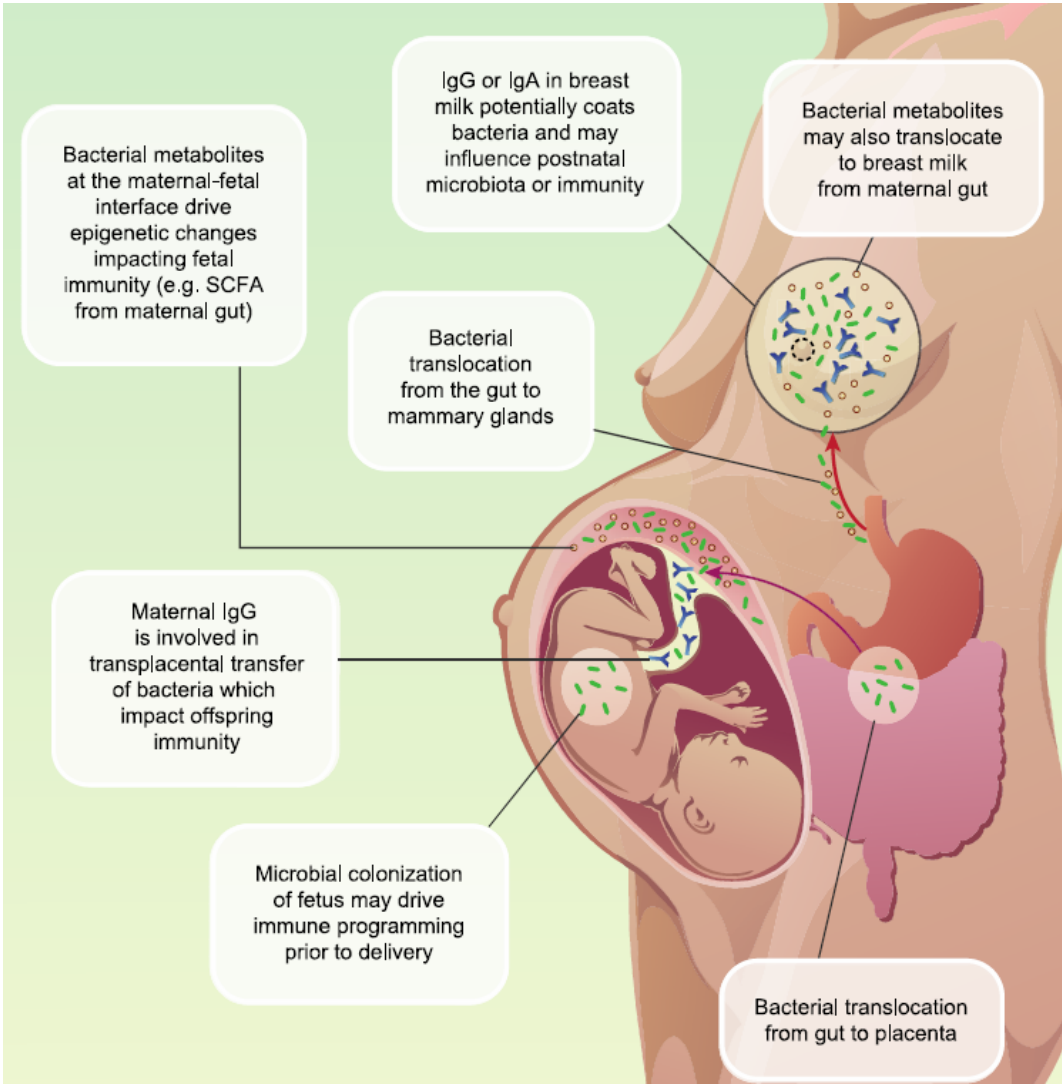
Fig. 1. Schematic drawing showing that maternal cardiometabolic disorders, such as gestational diabetes mellitus (GDM), pre-eclampsia, obesity and dyslipidemias, are associated with disrupted microbiota and that probiotic intervention could improve glycemic control (GC), insulin resistance (IR) and lipid profiles in pregnant women

Influence of maternal microbiota during pregnancy on infant immunity

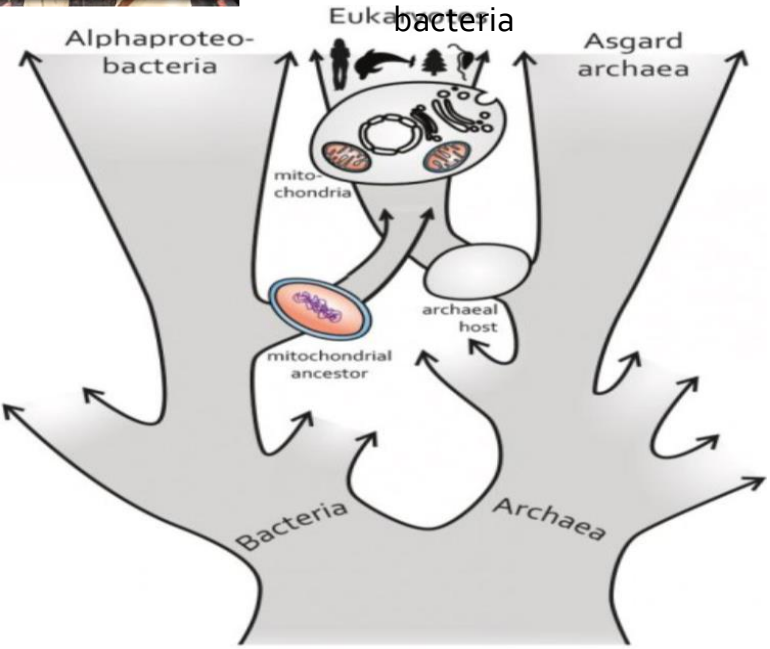
Donald D Nyangahu[1] and Heather B Jaspan[1,2,3]

Clin Exp Immunol. 2019 May 23.

Figure 2: Potential mechanisms of crosstalk between maternal microbiota and offspring immunity. Maternal gut microbiota during pregnancy translocate to the maternalfetal interface. Commensals microbes translocate from the maternal gut to the placenta or fetal gut during pregnancy (maternal gut placenta axis) or to mammary glands. These microbes impact developing fetal immunity via various mechanisms including epigenetic changes, release of short chain fatty acids and alteration of the cytokine environment. Bacteria or bacterial metabolites transfer to the mammary glands (gut-breastmilk axis) impacting infant gut colonization and continued immune development after delivery.



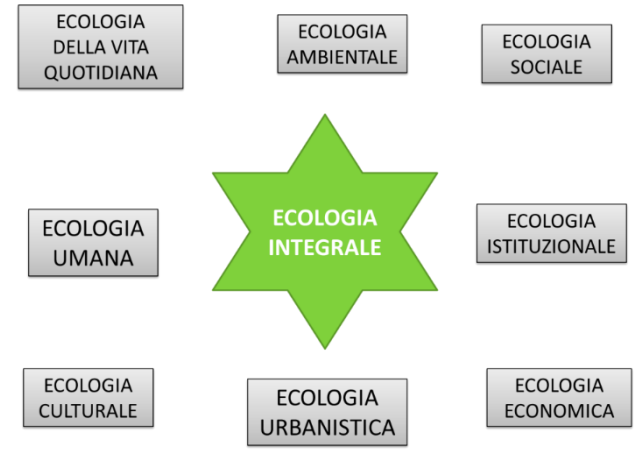
1967, Lynn Margulis (then Lynn Sagan) as first, proposed that mitochondria originate from endosymbiotic bacteria



Le parole da tre lettere del codice genetico sono le stesse in ogni creatura: CGA significa arginina e GCG significa alanina, tanto nei pipistrelli quanto negli scarafaggi o nei batteri. Hanno lo stesso significato anche negli archeobatteri…… che vivono a temperature di ebollizione nelle sorgenti sulfuree centinaia di metri sotto la superfice dell'Oceano Atlantico o in quelle microscopiche capsule di devianza chiamate virus. Ovunque si vada nel mondo, qualsiasi animale, pianta, insetto o essere informe si stia guardando, se è vivo userà lo stesso dizionario e conoscerà lo stesso codice.

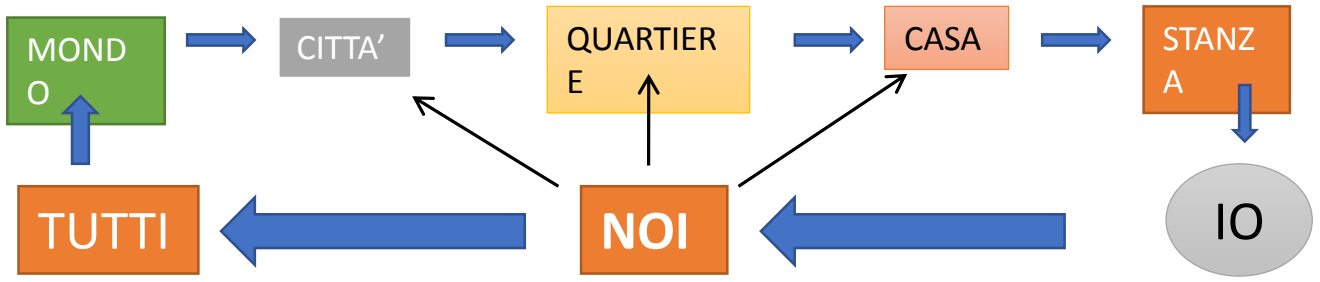
La vita è una. Il codice genetico, con l'eccezione di poche e minime aberrazioni locali, per lo più presenti per ragioni inspiegabili nei protozoi ciliati, è lo stesso in tutte le creature. Usiamo tutti lo stesso linguaggio. Ciò significa- e le persone religiose potrebbero trovarla un argomentazione utile- che vi è stata un'unica creazione, un unico evento in cui è nata la vita.

Matt Ridley, 1999



Ecologia della vita quotidiana

IL MONDO COMINCIA DALLA MIA STANZA




visit Micropia
and discover the invisible life

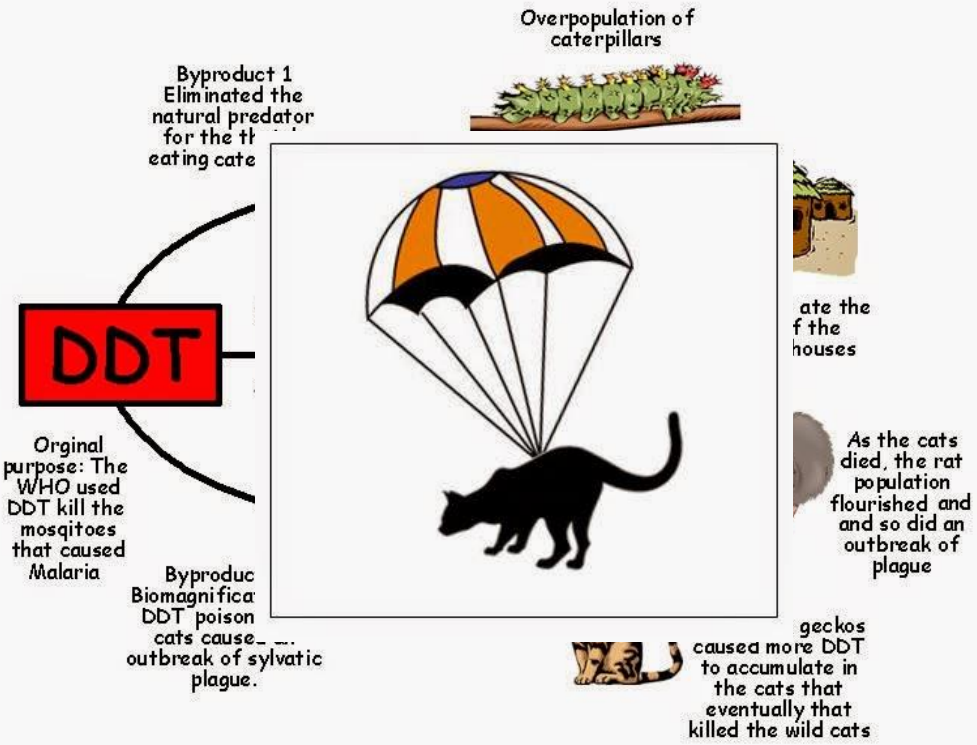
> *Spengiti, spengiti breve candela! La vita non è che un'ombra che cammina, un povero commediante che si pavoneggia e si agita, sulla scena del mondo, per la sua ora, e poi non se ne parla più; una favola raccontata da un idiota, piena di rumore e di furore, che non significa nulla.*
>
> CIT.
>
> Macbeth: atto V, scena V

Non è vero!

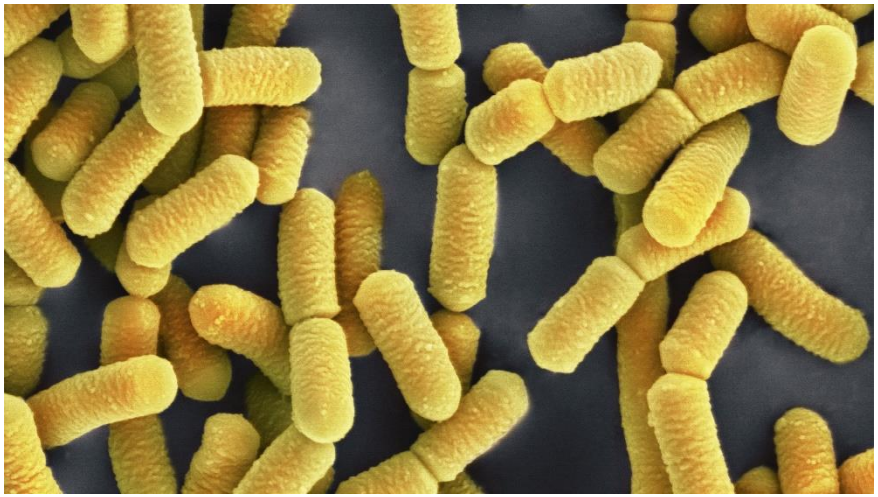
World Health Organization

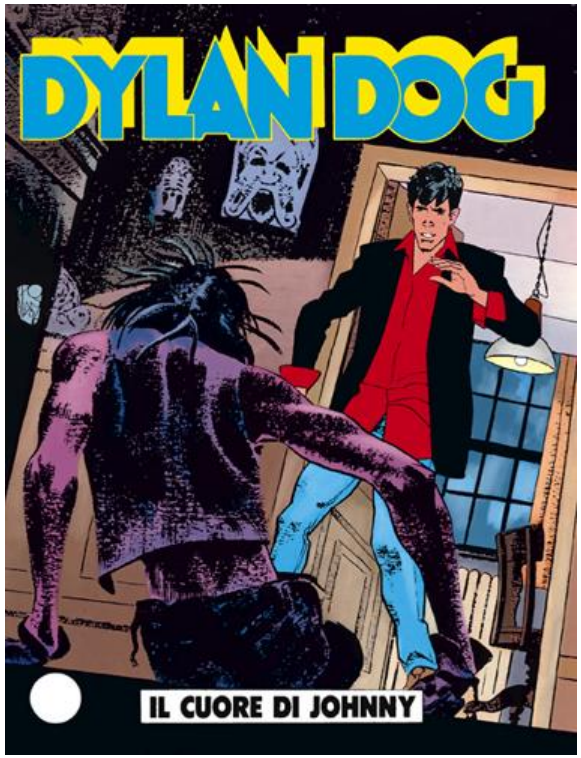
Effect of DDT Use in Borneo

In the early 1950's the people in Borneo, suffered from Malaria the World Health Organization had a solution, kill the mosquitoes with DDT. This is what happened.



Lactic acid bacteria (such as *Lactobacillus*), are used to make the bioplastic PLA (Polylactic Acid). Lactic acid bacteria transform the plant-based material into a sustainable and innovative alternative to traditional plastic
The various types of PLA have numerous applications, from drinking cups to surgical sutures and screws for repairing fractures. The production of PLA is virtually CO2-neutral as it is made from organic materials. Other properties which contribute to a circular economy include the fact that plant-based plastic can be recycled, composted and reused, as long as it is collected and processed correctly.





Grazie di avermi ascoltato