Functionality of the Maternal Microbiome

Sixth Arab-American Frontiers symposium

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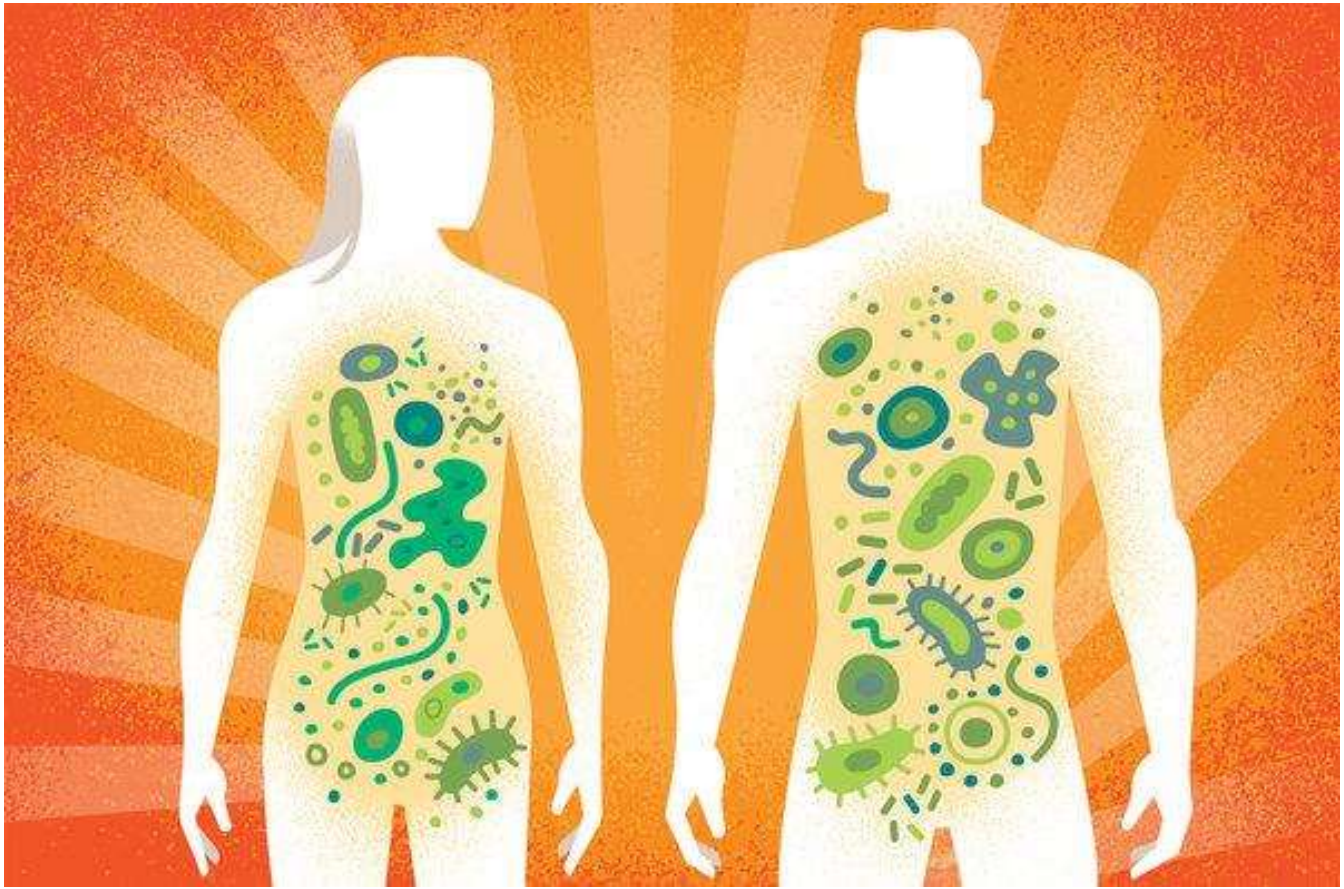
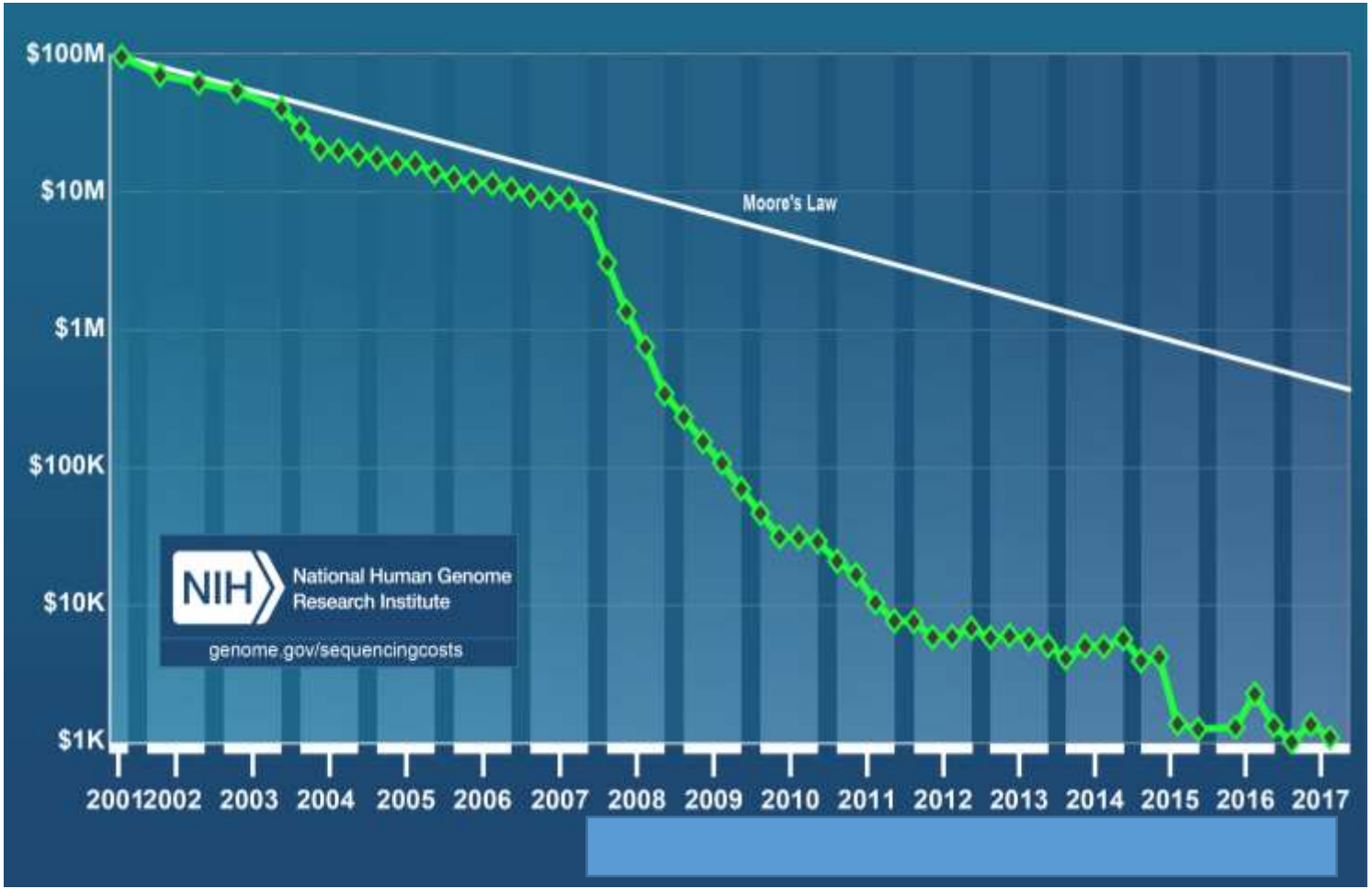


https://www.nytimes.com/2017/11/06/well/live/unlocking-the-secrets-of-the-microbiome.html


$100M
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Moore's Law
NIH
National Human Genome Research Institute
genome.gov/sequencingcosts
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Sequence an informative gene to get a census of what microbes are present

Extract and sequence all DNA from a sample (couple hundred base pairs at a time)

Human genome: ~3 billion base pairs
Bacterial genome: ~0.5 – 10 million base pairs

Image source: http://commonfund.nih.gov/hmp

https://hmpdacc.org/ihmp

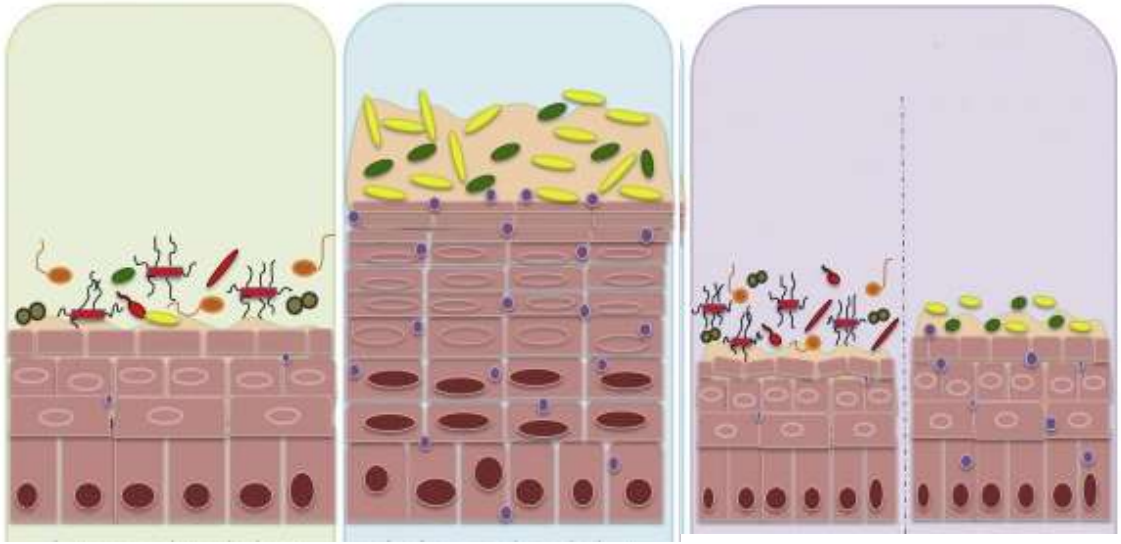
vmc.vcu.edu

Paradigms for health

Female reproductive tract
Lactobacillus dominance
Low bacterial diversity

Gut

The environment of the female reproductive and microbiome change with hormonal shifts across a woman's life



Pre-puberty

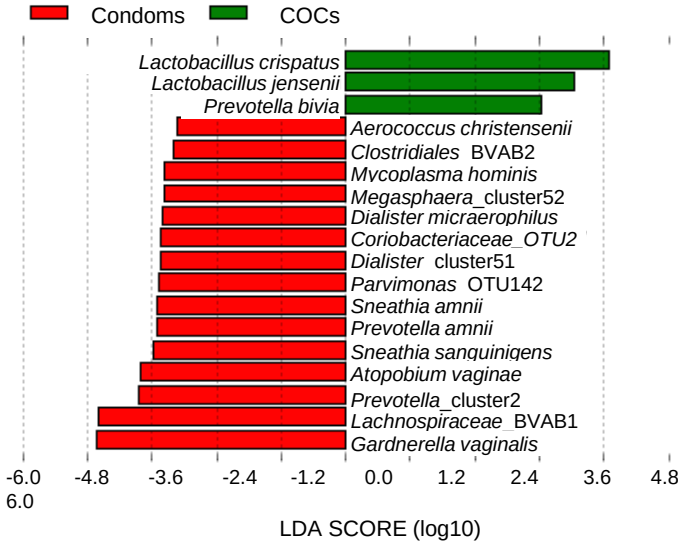
Reproductive years

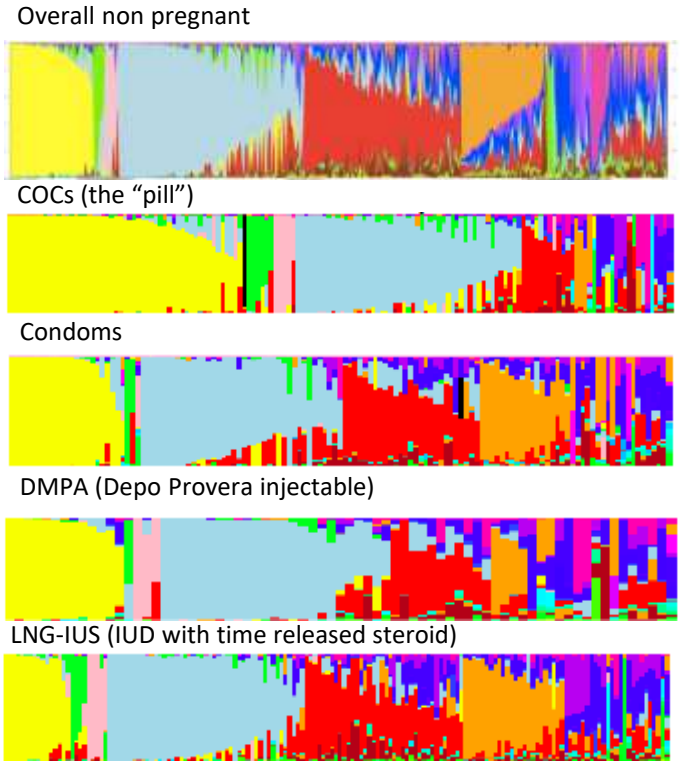
Post-menopause

Image adapted from: Muhleisen et al./*Maturitas* 2016.

Oral contraceptives associated with decreased diversity

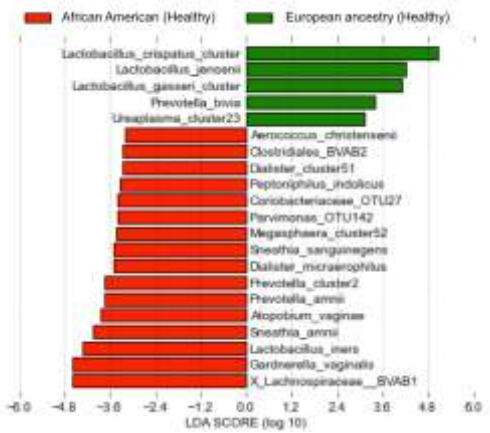
Combined oral contraceptives seem to favor *lower diversity and some taxa:*





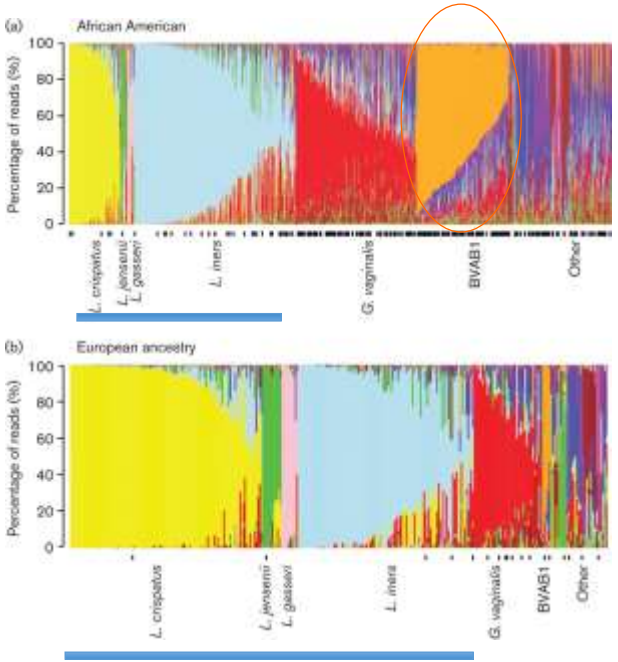
Brooks et al. 2016

Microbiome composition of the female reproductive tract correlates significantly with ethnicity



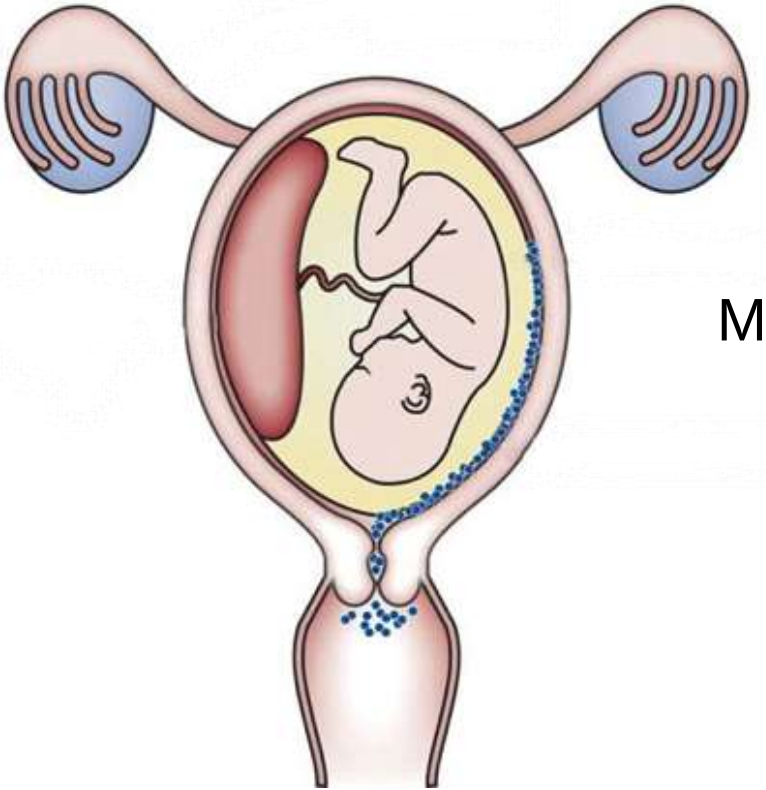
African American

European ancestry



Lactobacillus dominance

Fettweis JM, Brooks JP *et al. Microbiology* 2014;160:2272-2282



Microbial etiology suspected in up to

40-50%

of preterm deliveries*

Image adapted from: Goldenberg, R. L., Culhane, J. F., Iams, J. D. & Romero, R. Epidemiology and causes of preterm birth. *Lancet* **371,** 75–84 (2008).

*Lockwood, C. J. Predicting premature delivery--no easy task. *N. Engl. J. Med.* **346,** 282–284 (2002).

*Lamont, R. F. Infection in the prediction and antibiotics in the prevention of spontaneous preterm labour and preterm birth. *BJOG* **110 Suppl 20,** 71–75 (2003).

C-sections, antibiotics and impaired infant microbiome development

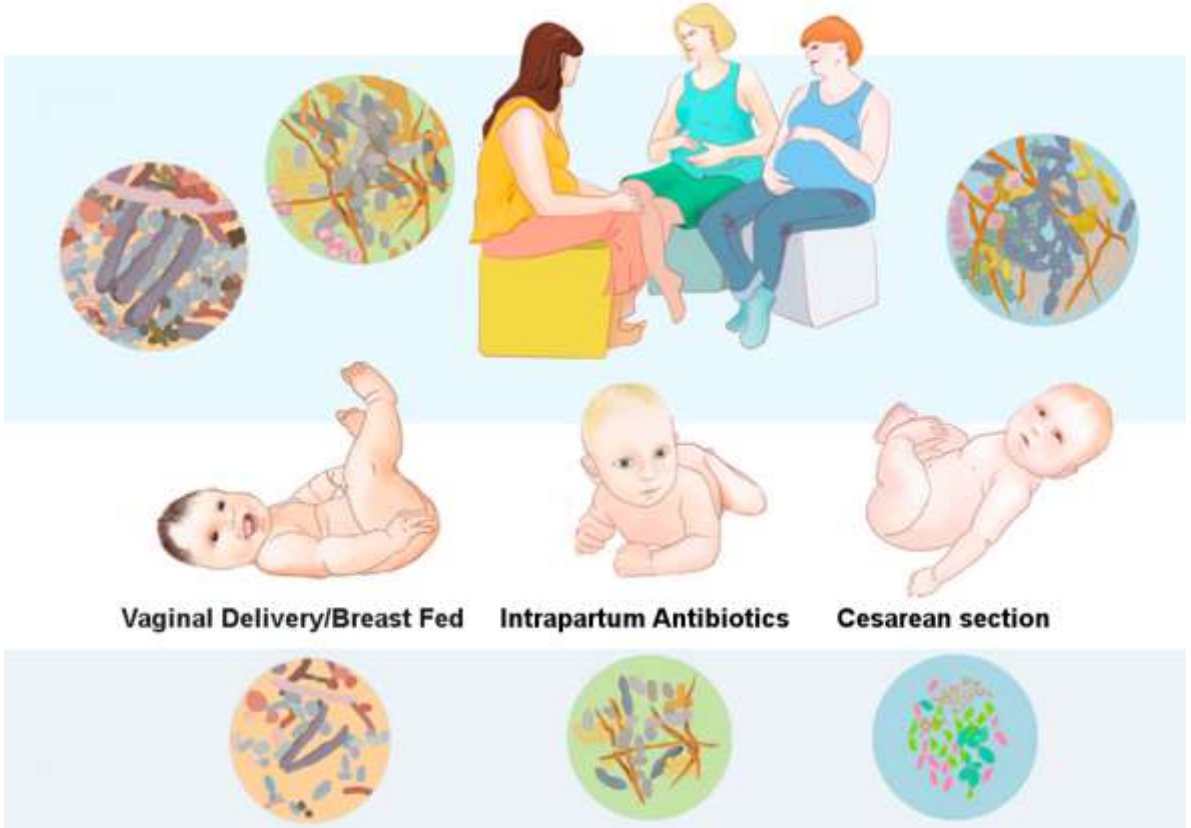


Image adapted from: Bäckhed, F. *et al.* Dynamics and Stabilization of the Human Gut Microbiome during the First Year of Life. *Cell Host Microbe* **17,** 852 (2015).

Host genetics also plays a role in shaping microbiome

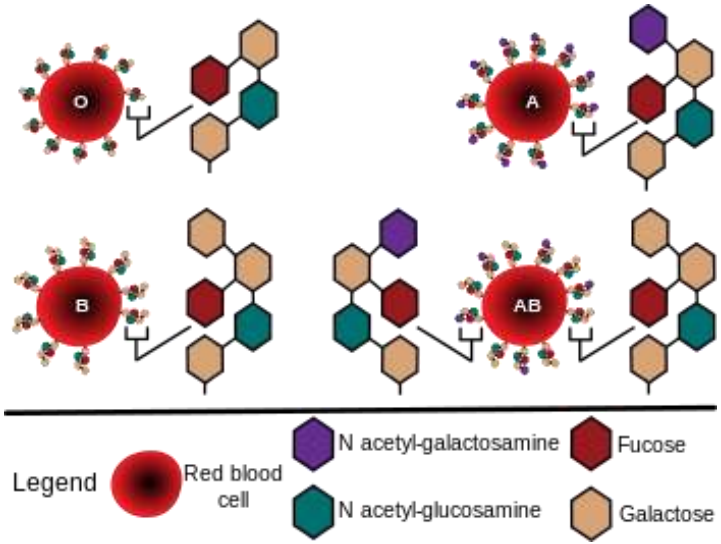


Image adapted from: Bäckhed, F. *et al.* Dynamics and Stabilization of the Human Gut Microbiome during the First Year of Life. *Cell Host Microbe* **17,** 852 (2015).
Image: https://en.wikipedia.org/wiki/Blood_type

Maternal secretor status (FUT2 gene) impacts gut microbiome of breast fed infants

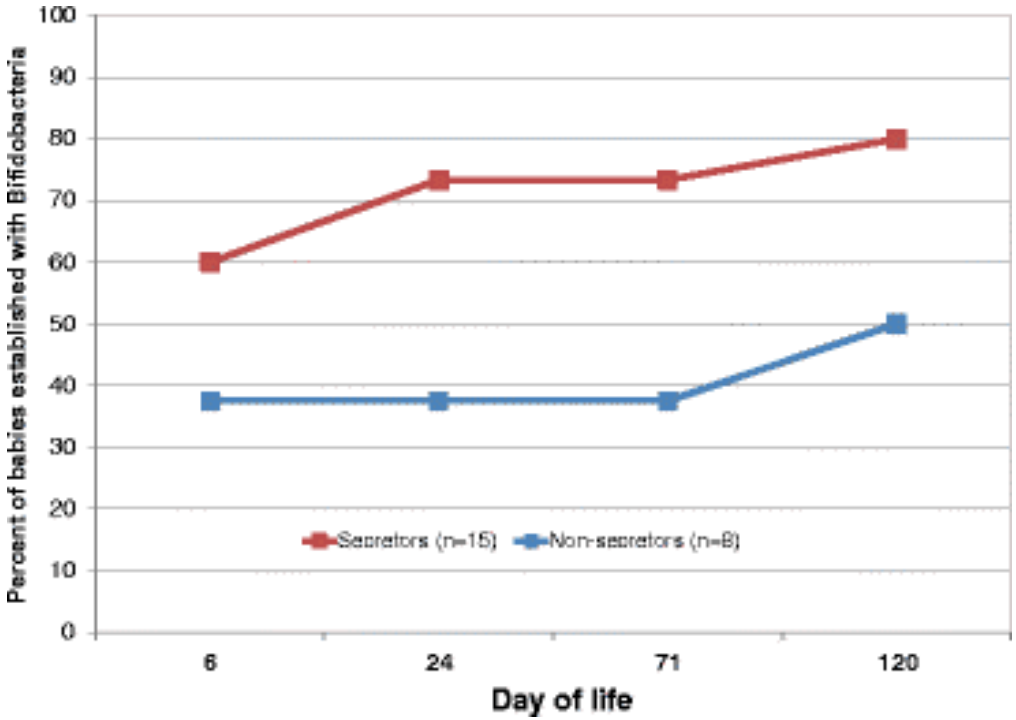
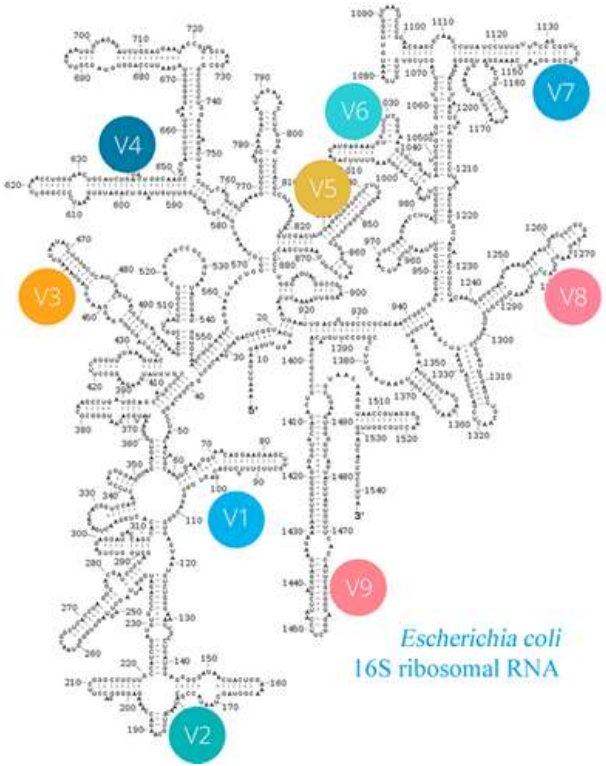


Image adapted from: Bäckhed, F. *et al.* Dynamics and Stabilization of the Human Gut Microbiome during the First Year of Life. *Cell Host Microbe* **17,** 852 (2015).
Image: https://en.wikipedia.org/wiki/Blood_type

Impact on Lifelong Health?

Images: http://www.thebluediamondgallery.com/wooden-tile/a/asthma.html, http://www.picserver.org/o/obesity.html , http://thebluediamondgallery.com/a/autism.html

Technical Challenge 1: Developing standards for 16S rRNA marker gene surveys



Fettweis et al. BMC Genomics 2012, 13(Suppl 8):S17
http://www.biomedcentral.com/1471-2164/13/S8/S17

BMC Genomics

RESEARCH Open Access

Species-level classification of the vaginal microbiome

Jennifer M Fettweis[1,2], Myrna G Serrano[1,2], Nihar U Sheth[2], Carly M Mayer[1], Abigail L Glascock[1], J Paul Brooks[2,3], Kimberly K Jefferson[1], Vaginal Microbiome Consortium (additional members), Gregory A Buck[1,2*]

From The International Conference on Intelligent Biology and Medicine (ICIBM)
Nashville, TN, USA. 22-24 April 2012

Brooks et al. BMC Microbiology (2015) 15:66
DOI 10.1186/s12866-015-0351-6

BMC Microbiology

METHODOLOGY ARTICLE Open Access

The truth about metagenomics: quantifying and counteracting bias in 16S rRNA studies

J Paul Brooks[1,2*], David J Edwards[1], Michael D Harwich Jr[1], Maria C Rivera[4], Jennifer M Fettweis[5], Myrna G Serrano[2,3], Robert A Reris[1], Nihar U Sheth[2], Bernice Huang[5], Philippe Girerd[5], Vaginal Microbiome Consortium (additional members), Jerome F Strauss III[5], Kimberly K Jefferson[2,3] and Gregory A Buck[2,3]

MICROBIAL ECOLOGY IN HEALTH AND DISEASE, 2017
VOL. 28, 1353255
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Taylor & Francis

RESEARCH ARTICLE OPEN ACCESS

Changes in vaginal community state types reflect major shifts in the microbiome

J. Paul Brooks[a,c], Gregory A. Buck[b,c], Guanhua Chen[d], Liyang Diao[a], David J. Edwards[a], Jennifer M. Fettweis[b], Snehalata Huzurbazar[e], Alexander Rakitin[b], Glen A. Satten[b], Ekaterina Smirnova[b], Zeev Waks[f], Michelle L. Wright[a], Chen Yanover[g] and Yi-Hui Zhou[a]

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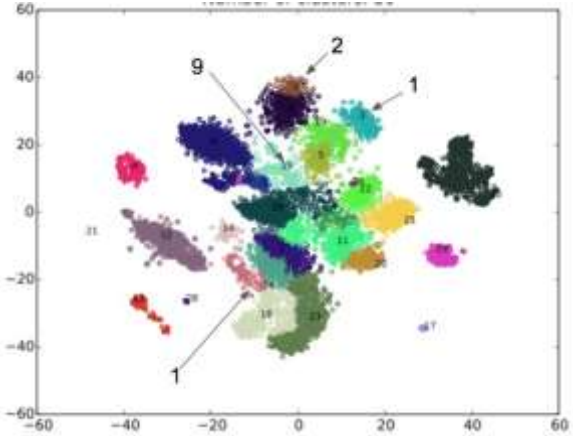
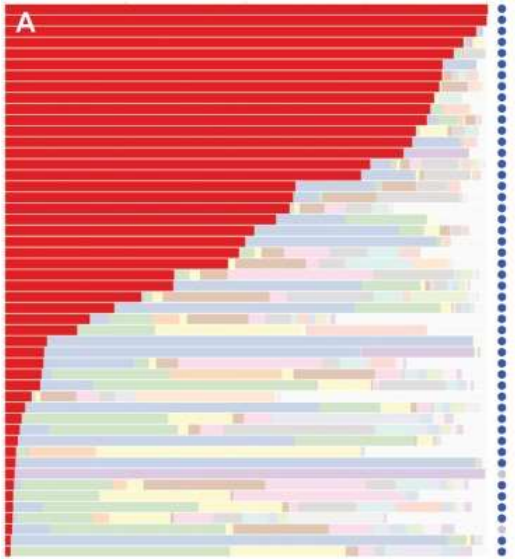
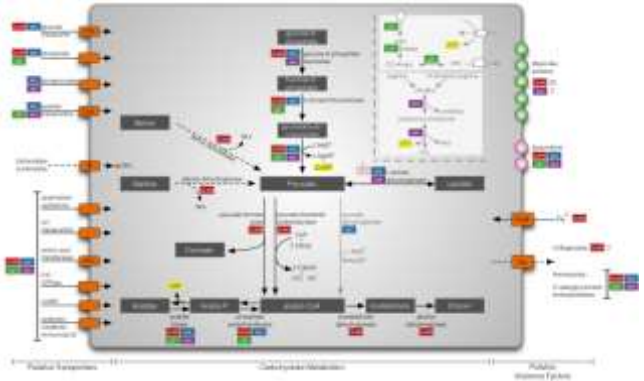
Technical Challenge 2: Uncovering Dark Matter—References Genomes for Microbes in the Female Reproductive Tract



“*Ca*. Mycoplasma girerdii” as a novel pathogen-associated organism



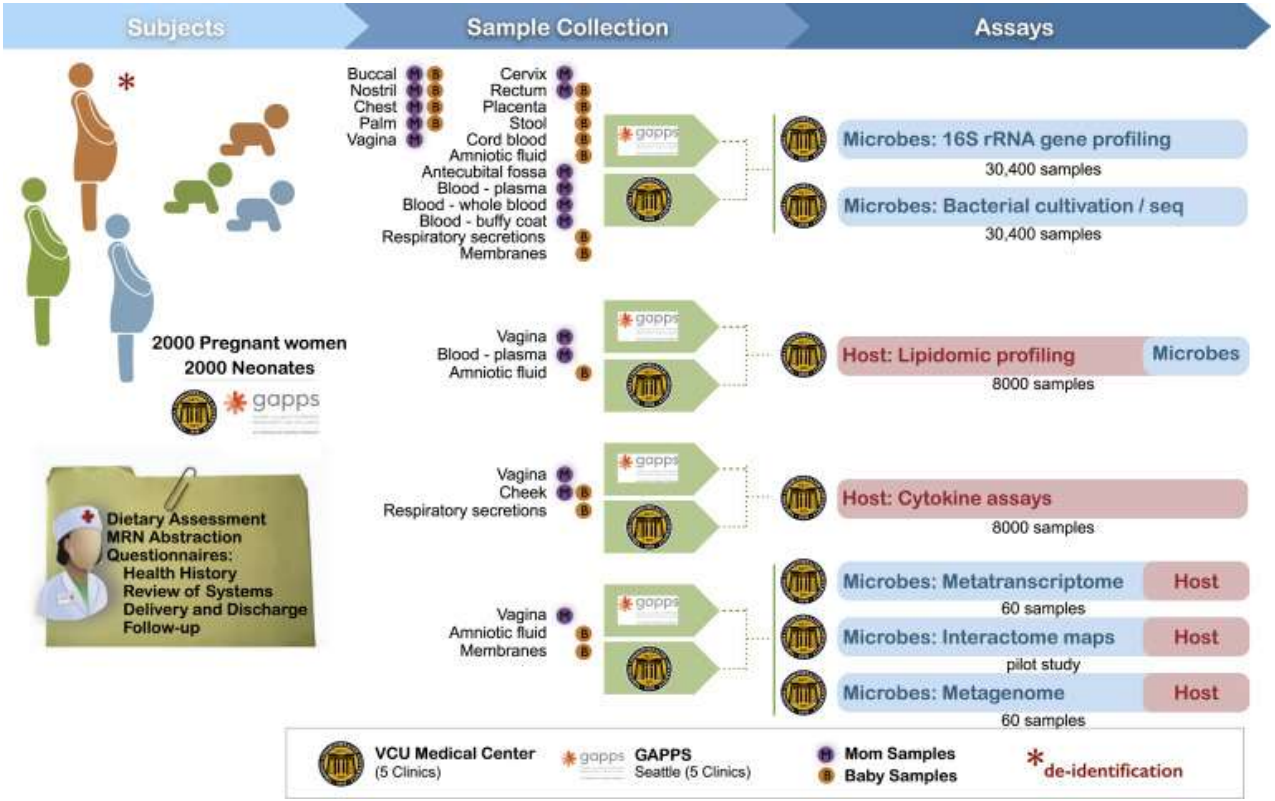


” is glycolytic with unique strategies in pyruvate metabolism

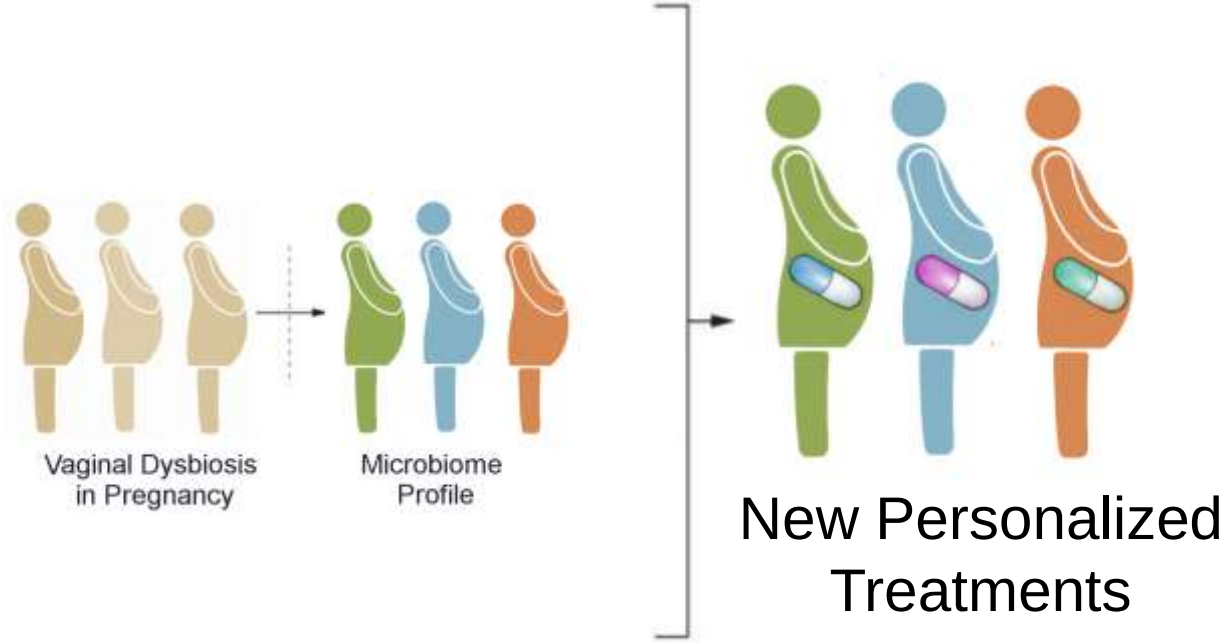
An Emerging Mycoplasma Associated with Trichomoniasis, Vaginal Infection and Disease

***Candidatus* Mycoplasma girerdii replicates, diversifies, and co-occurs with *Trichomonas vaginalis* in the oral cavity of a premature infant**

Technical Challenge 3: Data Storage, Distribution, and Integrated Omics Analysis



Precision Medicine Approaches



- Reduce incidence of preterm birth
- Improve pregnancy outcomes

- Reduce risk for transmission and acquisition of sexually-transmitted infections (Community as unit of pathogenicity)

- Maintain healthy human microbiome across generations
- Prevent increase in antimicrobial resistance genes in human microbial gene pool

Thank you!

<u>Fettweis Lab</u>
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Others…..

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