

The Gut Microbiome (and HIV)

5th of October 2018

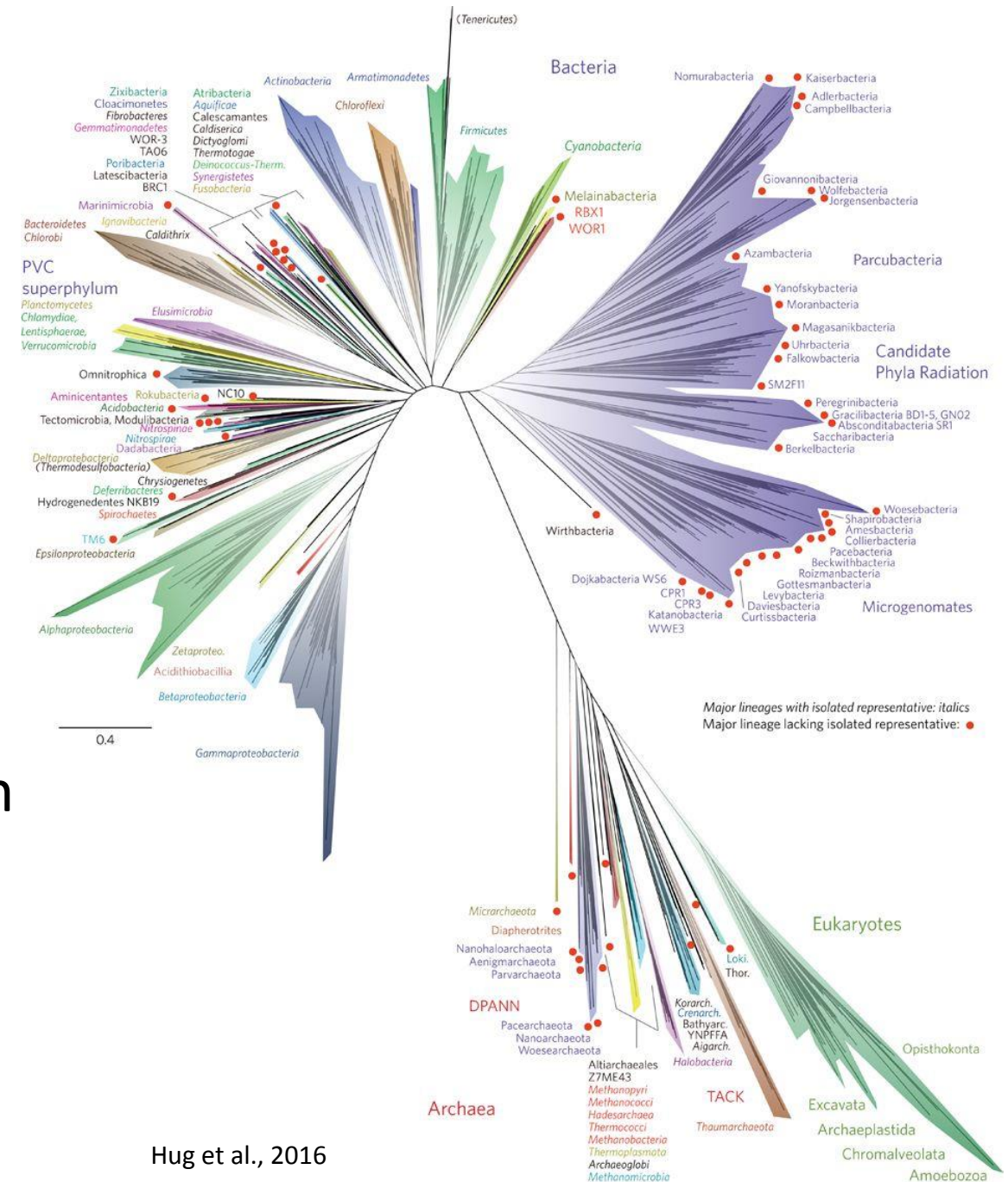
BHIVA Autumn Conference 2018

- I have no relationships to declare with pharmaceutical, diagnostic, or such similar companies involved in HIV/STI related products for the preceding twelve months.

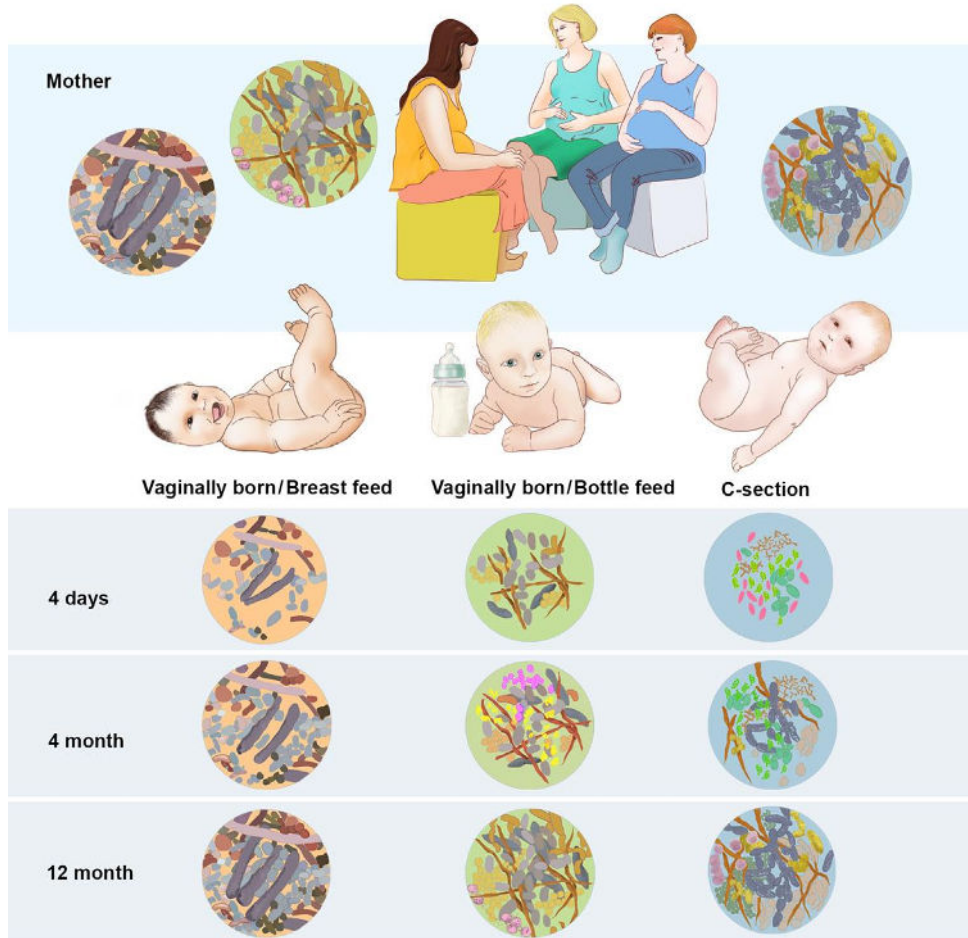
The gut microbiome

In numbers

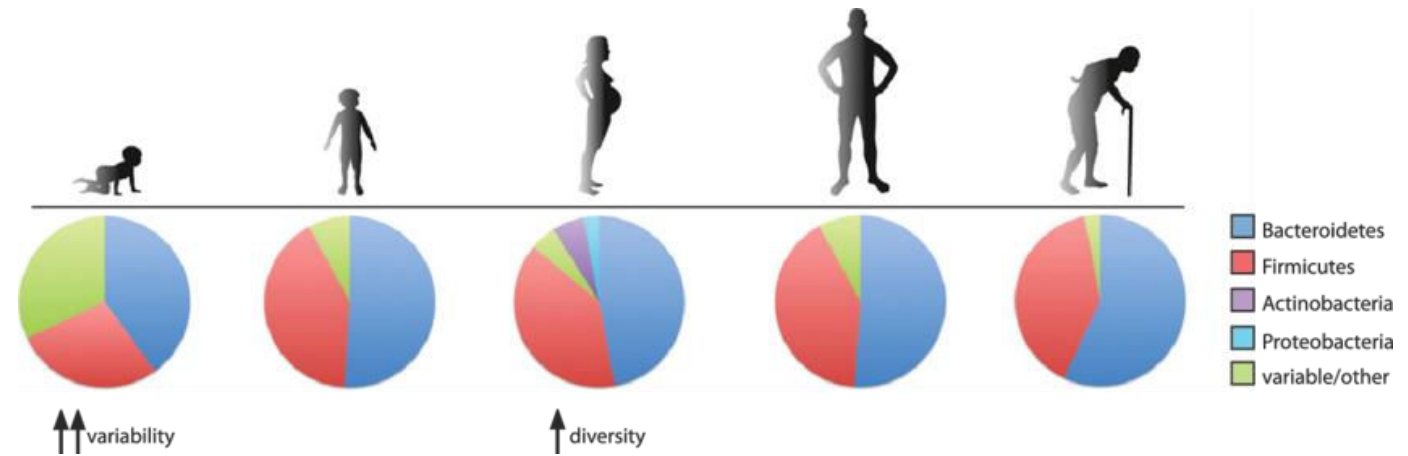
- 100 trillions of microbes
 - 95% in the gut
- 5:1 viruses:bacteria
- 150 microbial genes for 1 human
- Unique fingerprint



Acquisition of the gut microbiome

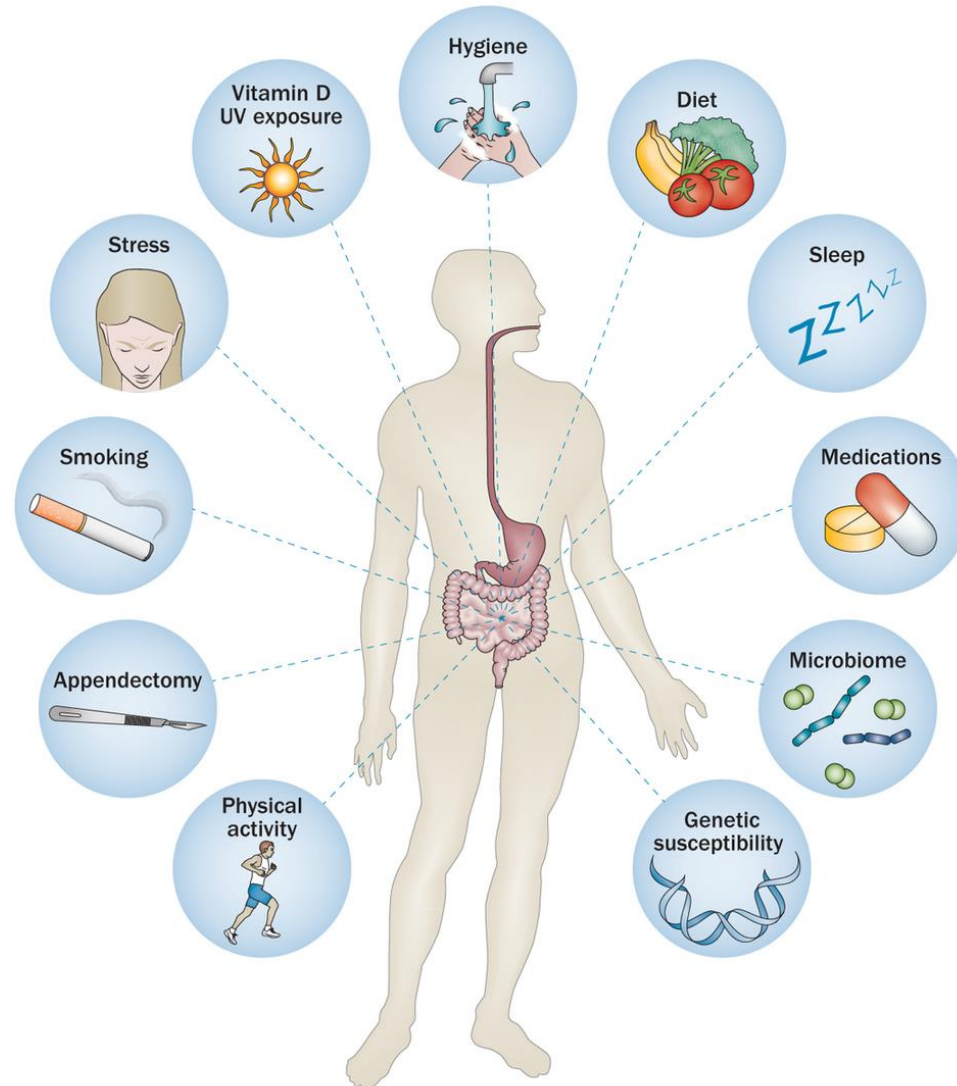


Bäckhed et al. 2015

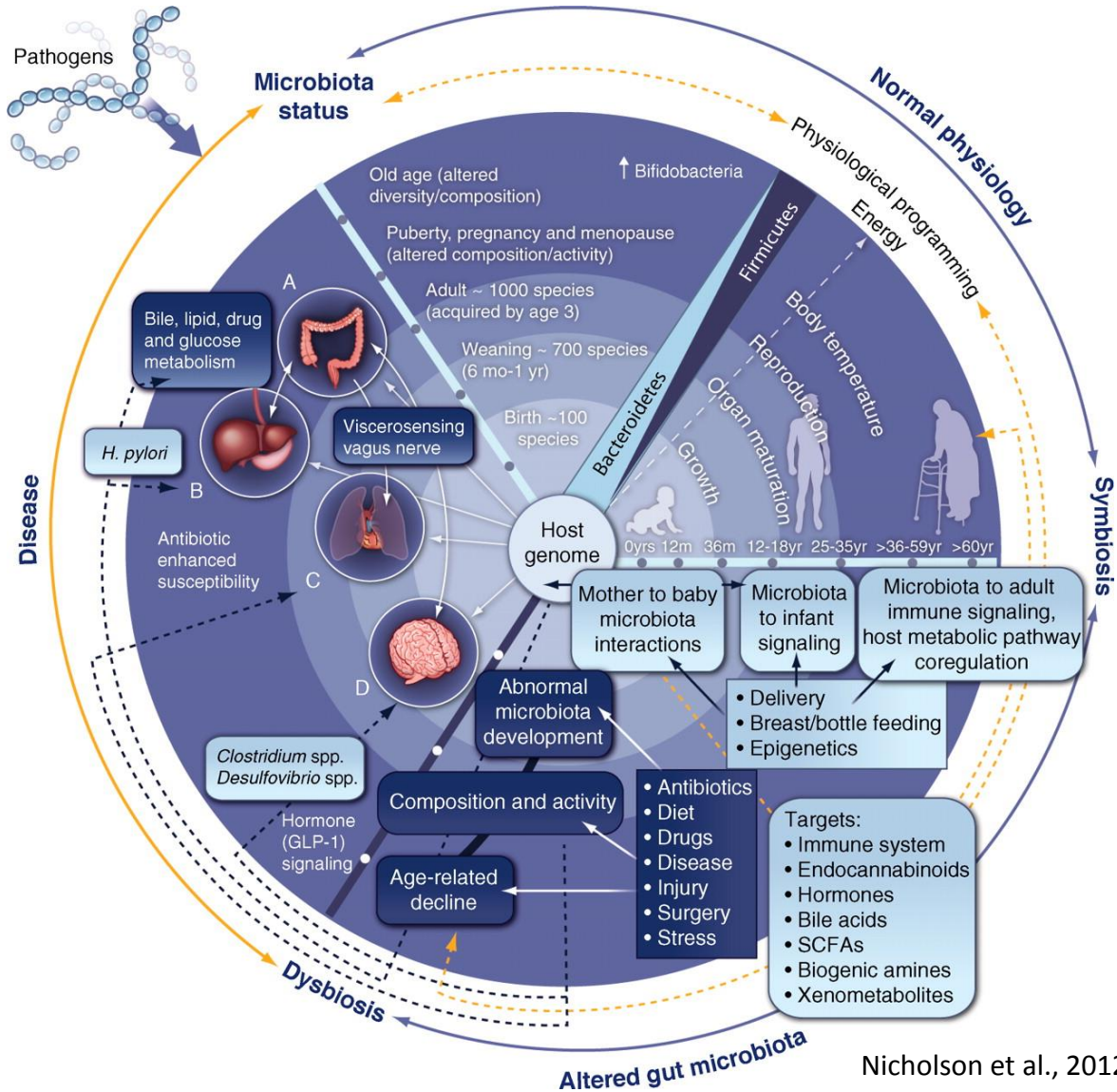


Kostic et al. 2013

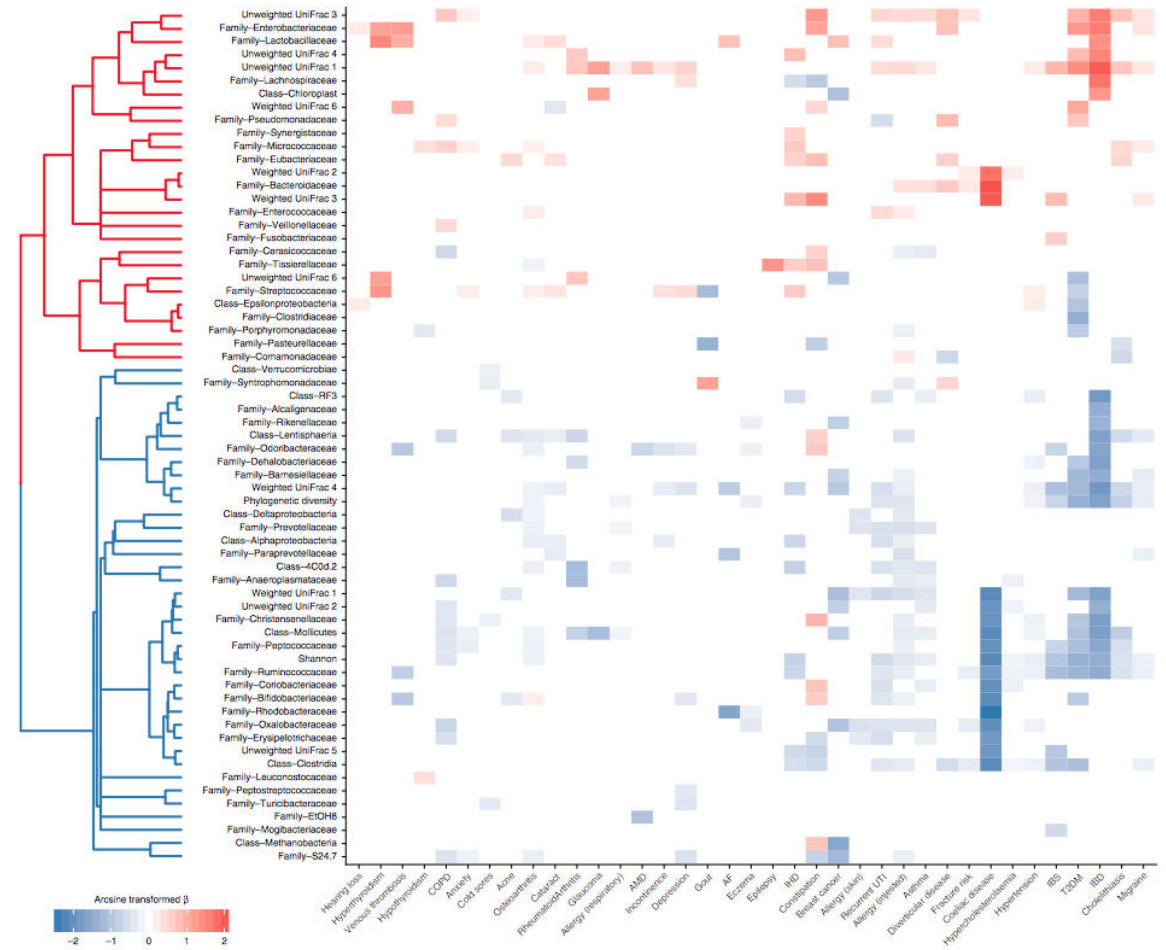
Shaping the gut microbiome



The gut microbiome and health



Nicholson et al., 2012



Jackson et al., 2018

Characterising the microbiome



Sampling the microbiome

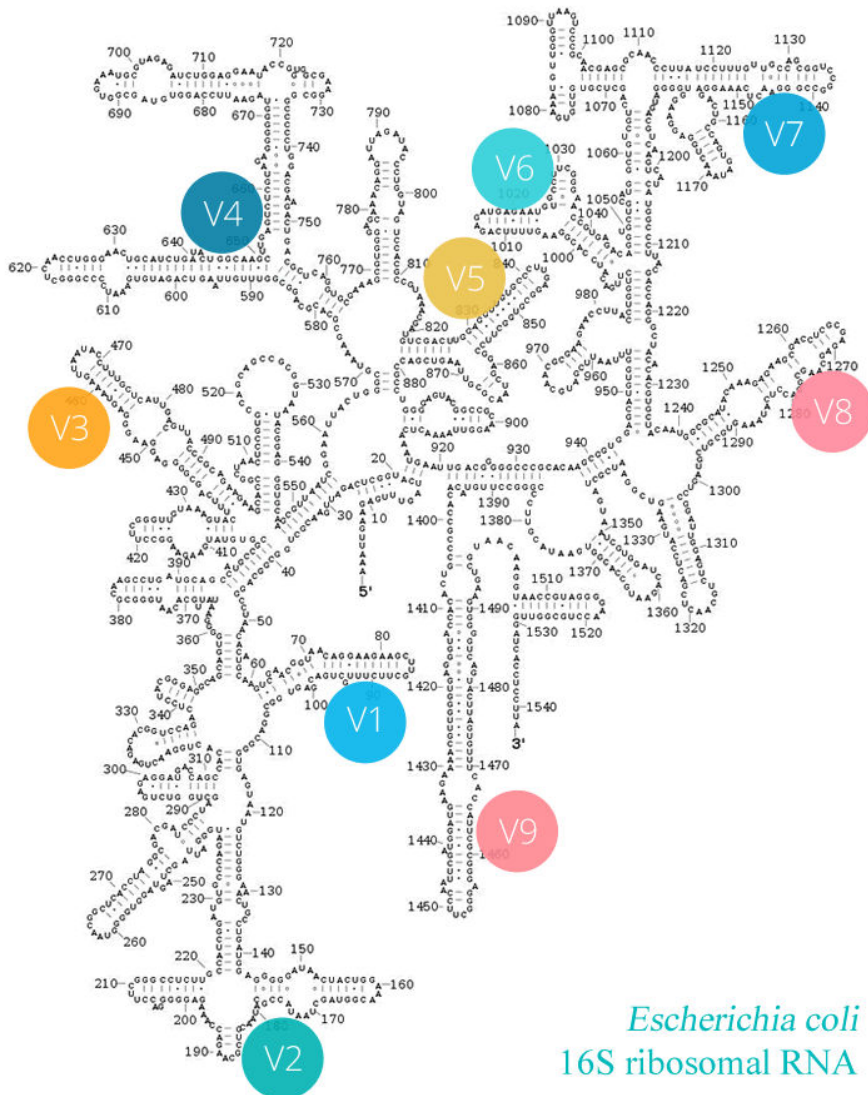
- Faecal sample
- Swab
- Colonoscopy
- The gut is mostly anaerobic!
- Think carefully about:
 - Collection
 - Storage
 - ...

Characterizing the microbiome – Culture -

- Most microbes in the gut are:
 - Anaerobes
 - Fastidious growth
 - May have very specific requirements
 - Depend on one another



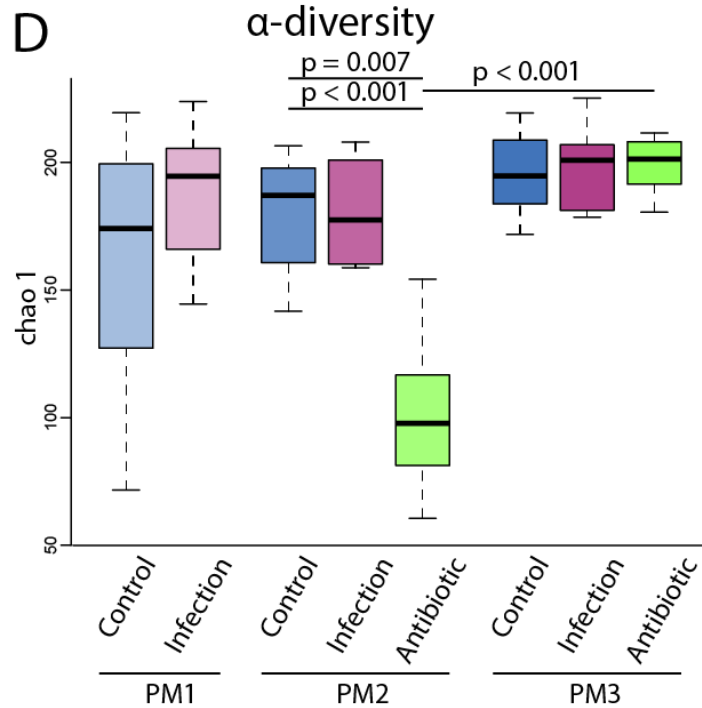
Characterizing the microbiome – Sequencing-



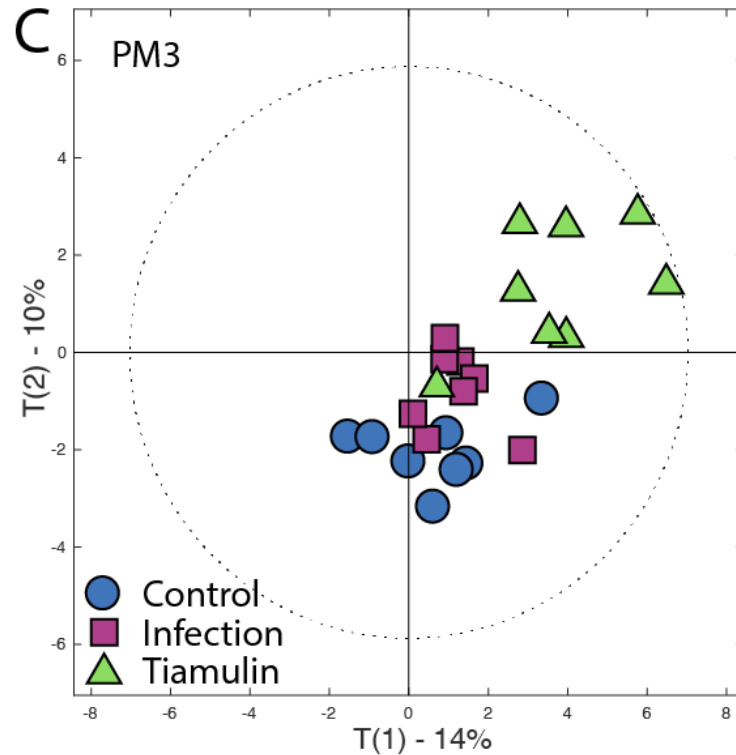
- 16S rRNA -> who
 - Amplification step
 - ~ £30/sample
- Shotgun metagenomics -> who & what
 - Untargeted
 - ~ £200/sample

Data analysis

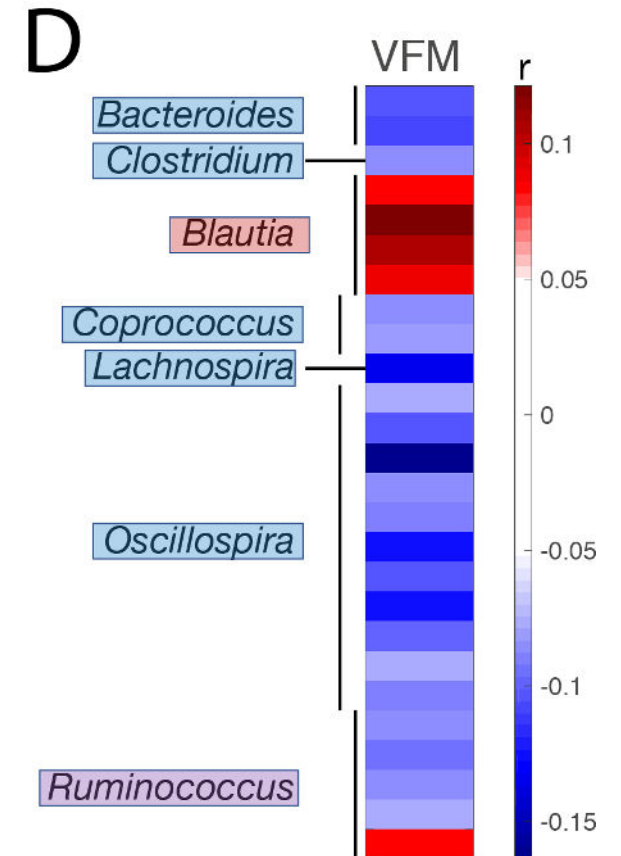
- Alpha diversity



- Beta diversity



- Associations



HIV and the gut microbiome

Unique gut microbiota signature

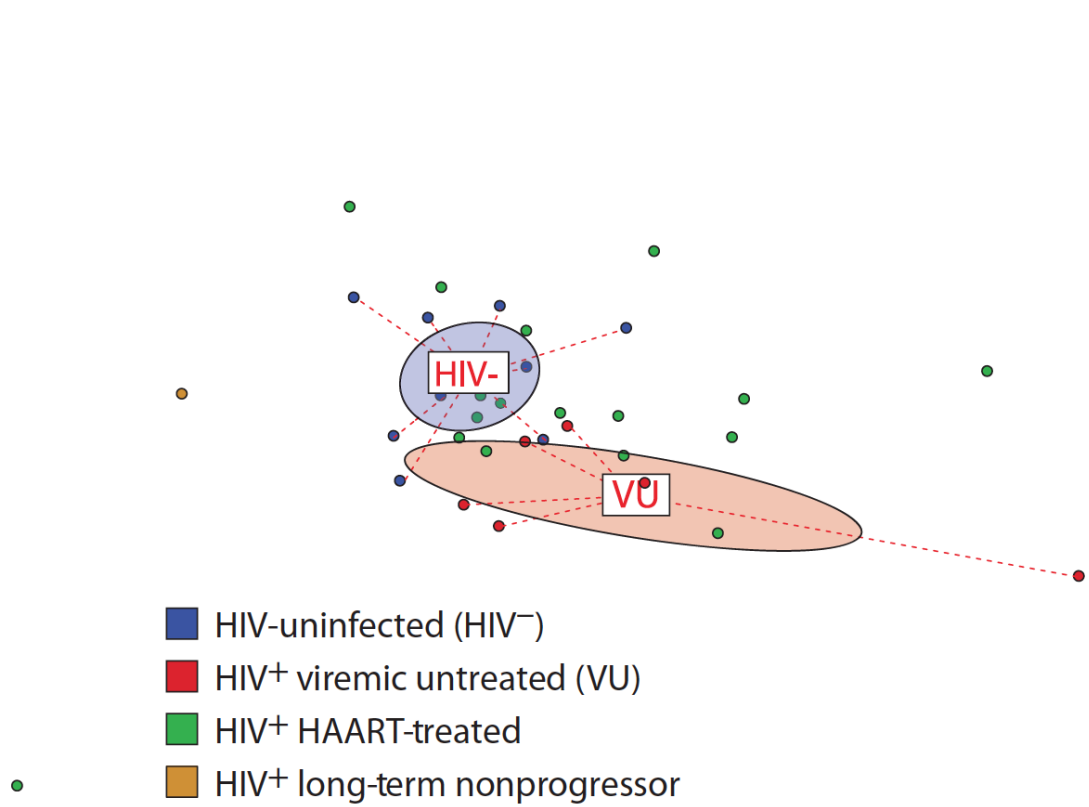
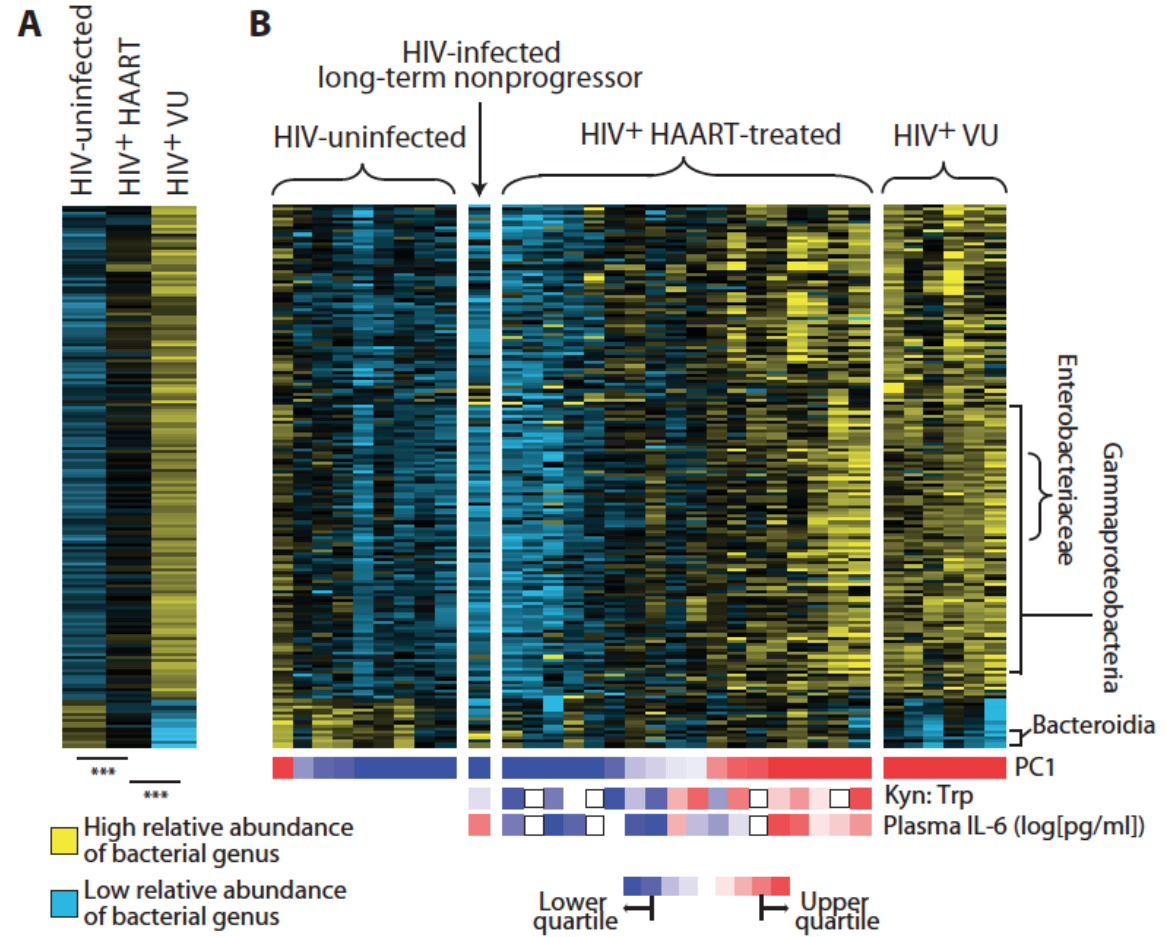


Fig. 1. Gut bacterial microbiota composition in HIV-infected VU subjects differs from that of HIV-uninfected risk-matched controls.

P = 0.002



Unique gut microbiota signature

Alterations in the Gut Microbiota Associated with HIV-1 Infection

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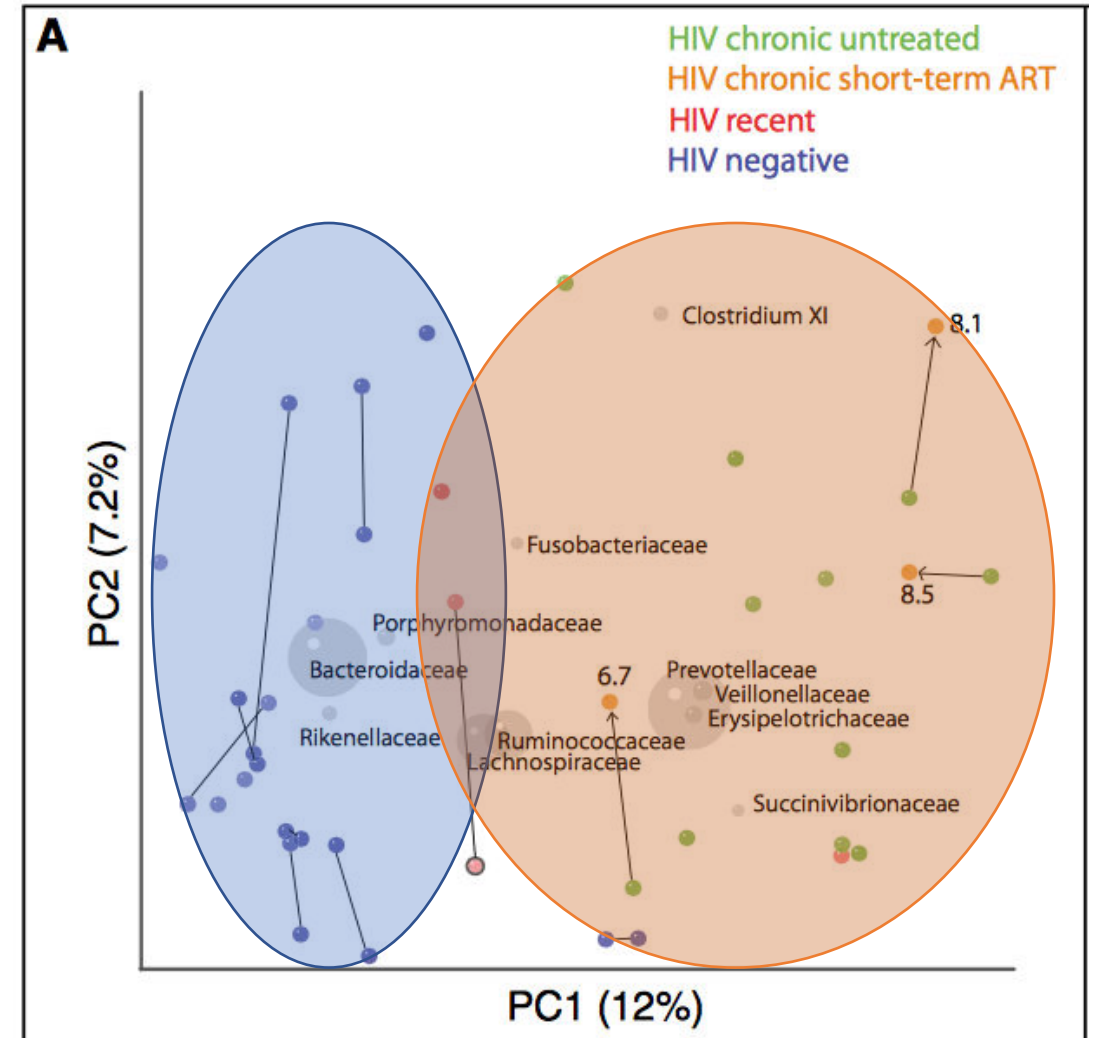
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<http://dx.doi.org/10.1016/j.chom.2013.08.006>

Table 2. Comparison of Alpha Diversity in HIV-Positive and -Negative Individuals with and without ART Treatment

	Observed Species	Shannon	PD
HIV negative	508 ± 21.6	5.6 ± 0.19	27.9 ± 1.46
Chronic HIV, ART untreated	563 ± 30.5	6.3 ± 0.15	36.4 ± 1.31
Chronic HIV on long-term ART	469 ± 39.6	5.68 ± 0.16	28.69 ± 1.19
Recent HIV	517 ± 64.4	5.76 ± 0.49	31.7 ± 3.06
p value (ART untreated versus negative) t test	0.144	0.013	0.0003
p value (ART untreated versus ART treated) t test	0.070	0.016	0.0006

Values are given as mean ± SD.





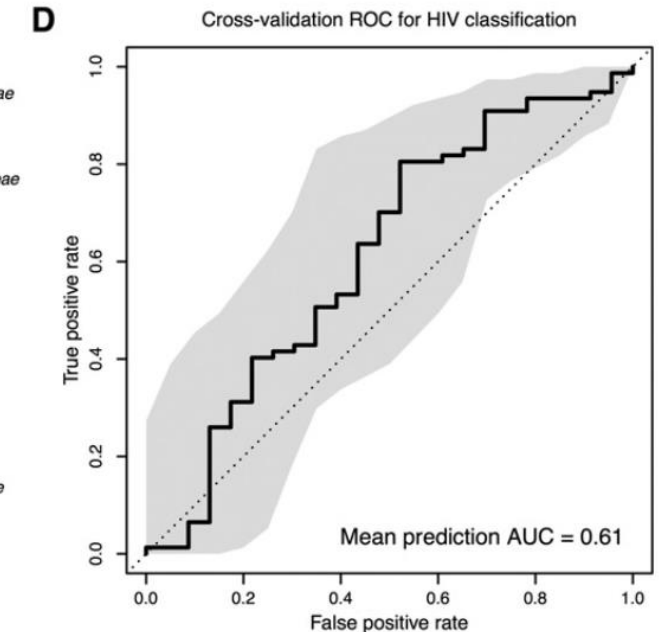
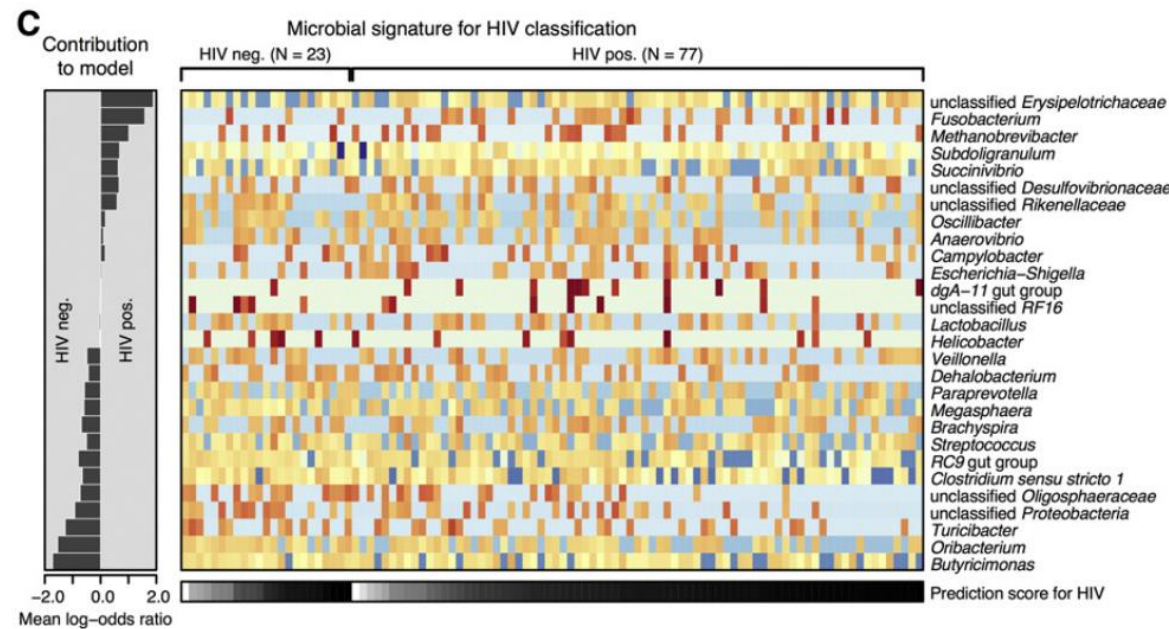
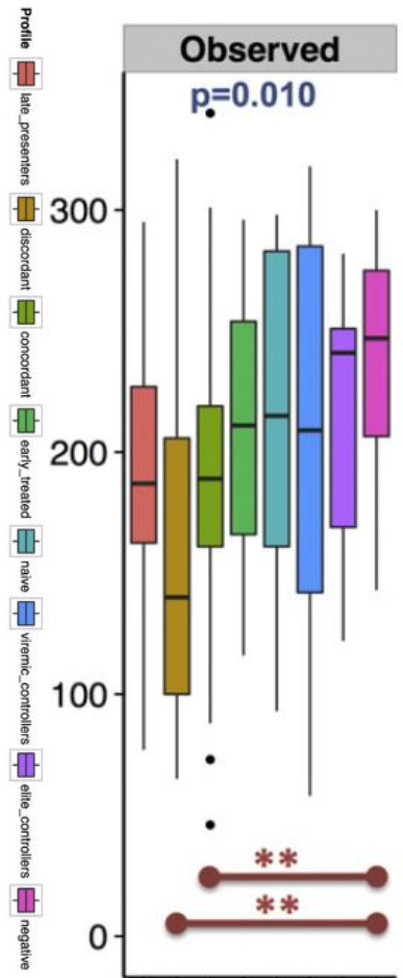
Prediction

Research Paper

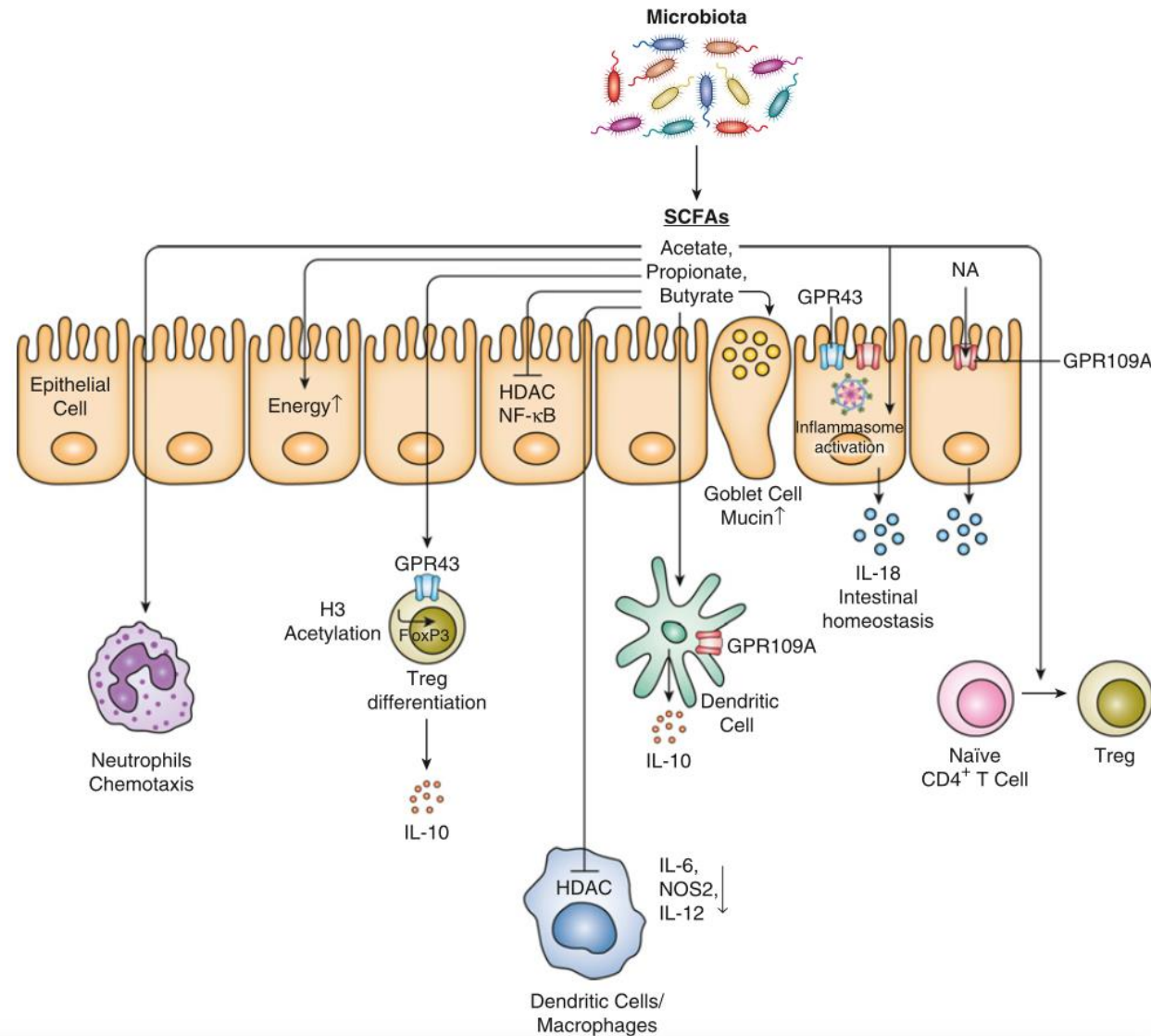
Gut Microbiota Linked to Sexual Preference and HIV Infection



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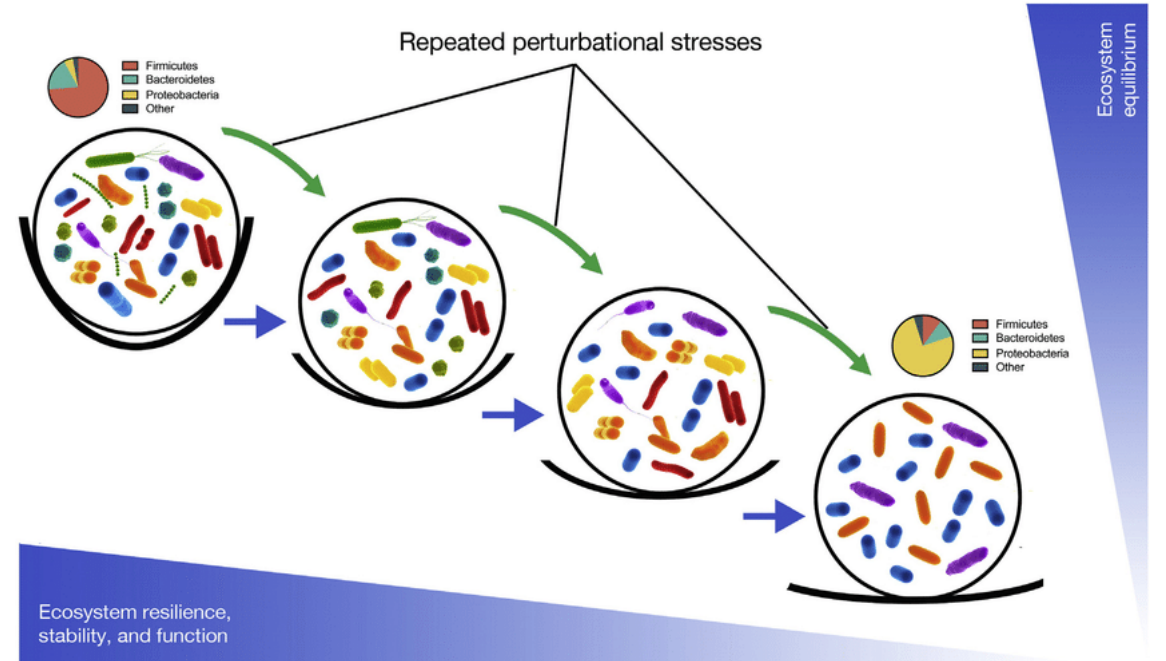
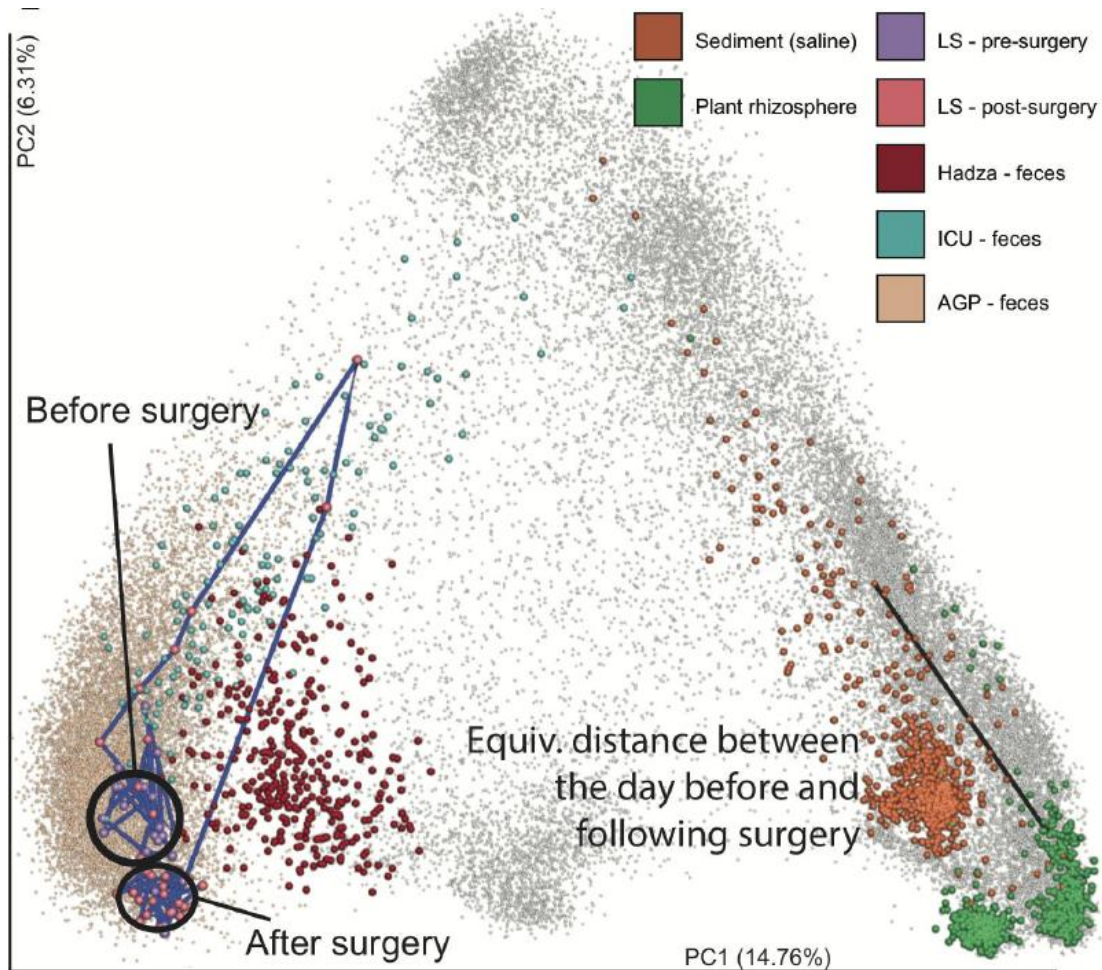


Probably because:



Possible consequences

Resilience of the gut microbiome



The gut microbiome and HIV treatment

Vaccination?



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HUTCH NEWS

Gut microbiome may have interfered with experimental HIV vaccines

Inoculating infants instead of adults could bypass problem, researchers say

July 30, 2015 | By Dr. Rachel Tompa / Fred Hutch News Service



Vaccination?

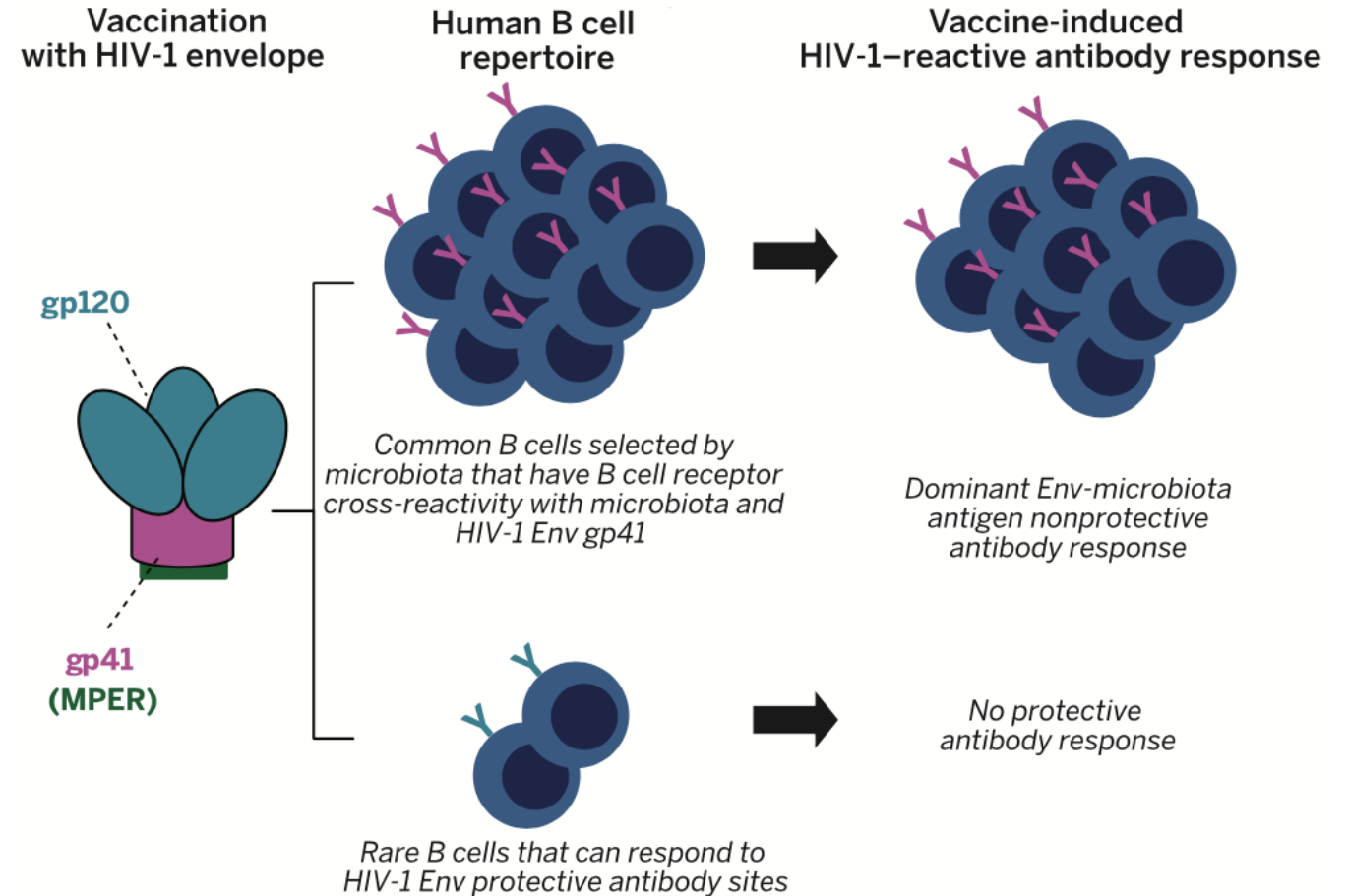
RESEARCH

RESEARCH ARTICLE

HIV-1 VACCINES

Diversion of HIV-1 vaccine-induced immunity by gp41-microbiota cross-reactive antibodies

Wilton B. Williams,^{1*} Hua-Xin Liao,¹ M. Anthony Moody,¹ Thomas B. Kepler,² S. Munir Alam,¹ Feng Gao,¹ Kevin Wiehe,¹ Ashley M. Trama,¹ Kathryn Jones,¹ Ruijun Zhang,¹ Hongshuo Song,¹ Dawn J. Marshall,¹ John F. Whitesides,¹ Kaitlin Sawatzki,² Axin Hua,² Pinghuang Liu,¹ Matthew Z. Tay,¹ Kelly E. Seaton,¹ Xiaoying Shen,¹ Andrew Foulger,¹ Krissey E. Lloyd,¹ Robert Parks,¹ Justin Pollara,¹ Guido Ferrari,¹ Jae-Sung Yu,¹ Nathan Vandergrift,¹ David C. Montefiori,¹ Magdalena E. Sobieszcyk,³ Scott Hammer,³ Shelly Karuna,⁴ Peter Gilbert,⁵ Doug Grove,⁵ Nicole Grunenberg,⁴ M. Juliana McElrath,⁴ John R. Mascola,⁶ Richard A. Koup,⁶ Lawrence Corey,⁴ Gary J. Nabel,^{6†} Cecilia Morgan,⁵ Gavin Churchyard,⁷ Janine Maenza,⁴ Michael Keefer,⁸ Barney S. Graham,⁶ Lindsey R. Baden,⁹ Georgia D. Tomaras,¹ Barton F. Haynes^{1*}



Diversion of HIV-1 vaccine-induced immunity by Env gp41-microbiota cross-reactive antibodies. Immunization of humans with a vaccine containing HIV-1 Env gp120 and gp41 compo-

The microbiome & side effects

Side effects

Short-term:

- Feeling tired
- Nausea (upset stomach)
- Vomiting
- Diarrhea
- Headache
- Fever
- Muscle pain
- Occasional dizziness
- Insomnia

Long-term:

- Kidney problems, including kidney failure
- Liver damage
- Heart disease
- Diabetes
- An increase in fat levels in the blood
- Changes in how the body uses and stores fat
- Osteoporosis
- Nerve damage
- Insomnia & depression

Take home messages

- HIV patients have a distinct gut microbiome
- The gut microbiome could affect response to HIV treatment
 - Personalized medicine
- Could probiotic/prebiotic help minimizing long-term side effects?

Thank you!