



**1st ASEICA
EDUCATIONAL
SYMPOSIUM**

Madrid, 14th and 15th November 2017

Microbiome and the modulation of the immune system

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CIBEResp

A humbling note... or: How i learned to stop
worrying about eukaryotes...
and love small things

2015

by the numbers

Humans



7.4×10^9

Trees



3.04×10^{12}

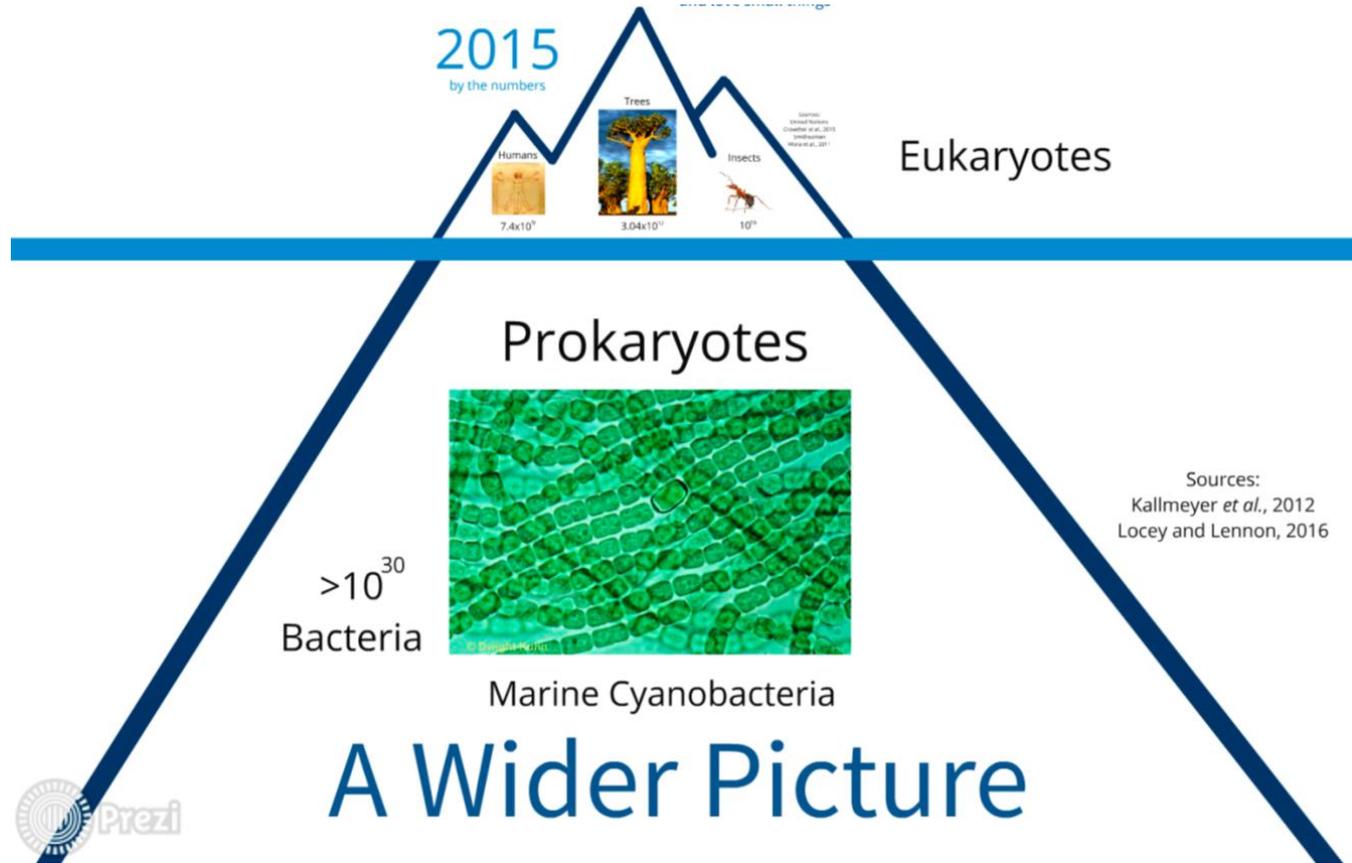
Insects

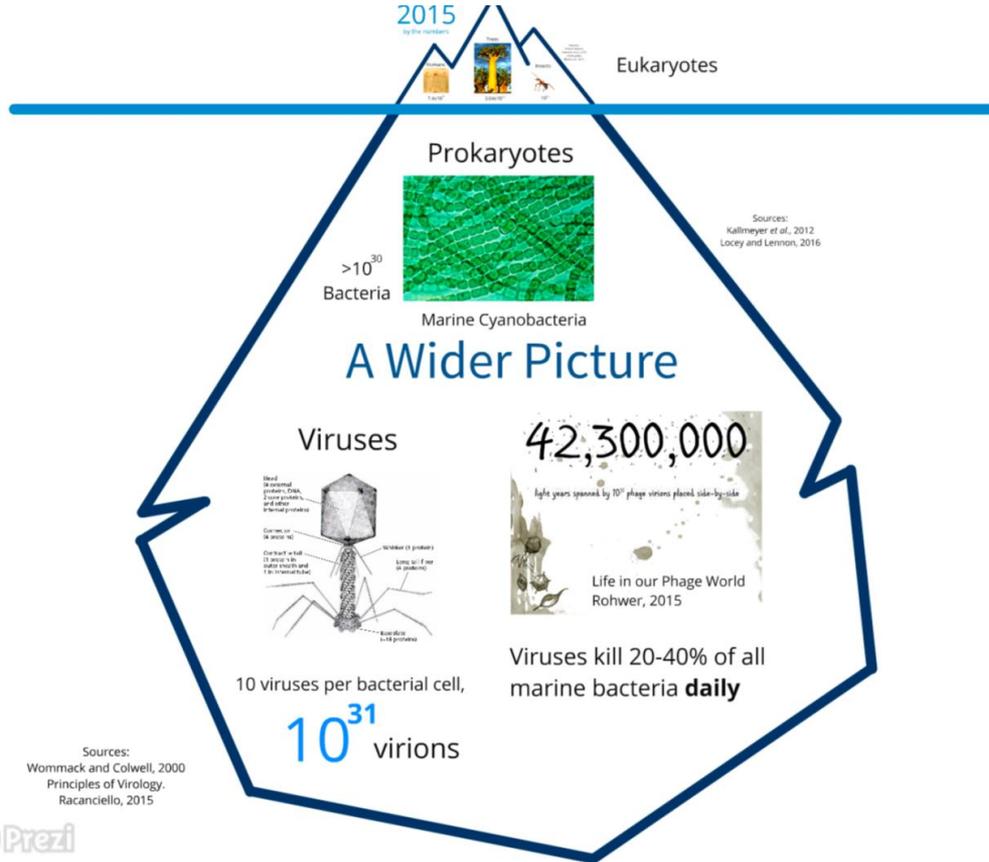


10^{19}

Sources:
United Nations
Crowther *et al.*, 2015
Smithsonian
Mora *et al.*, 2011



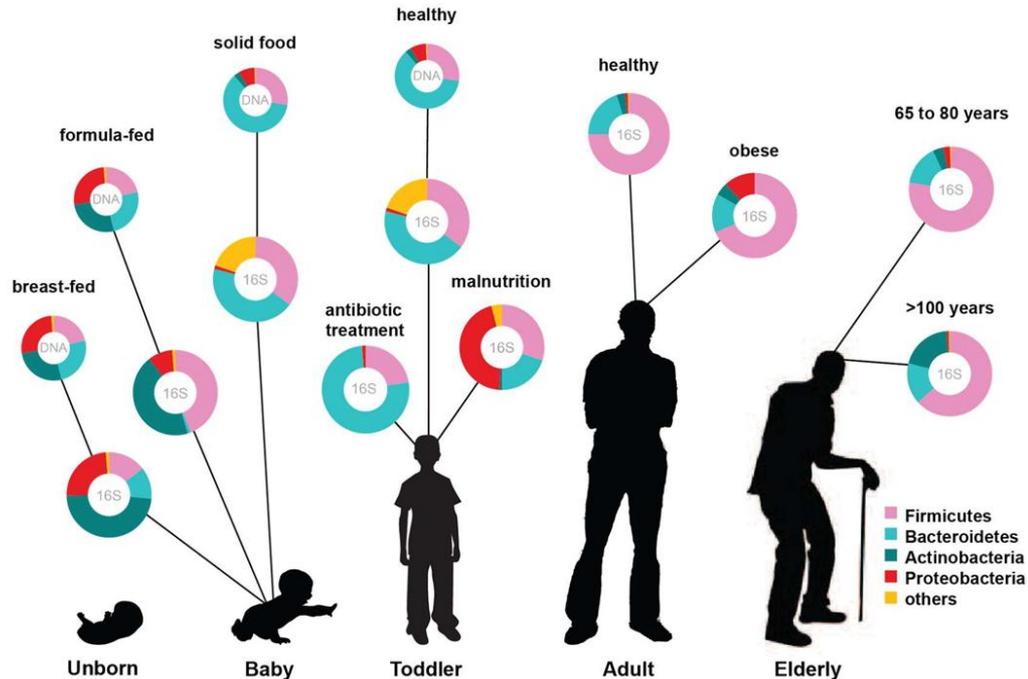




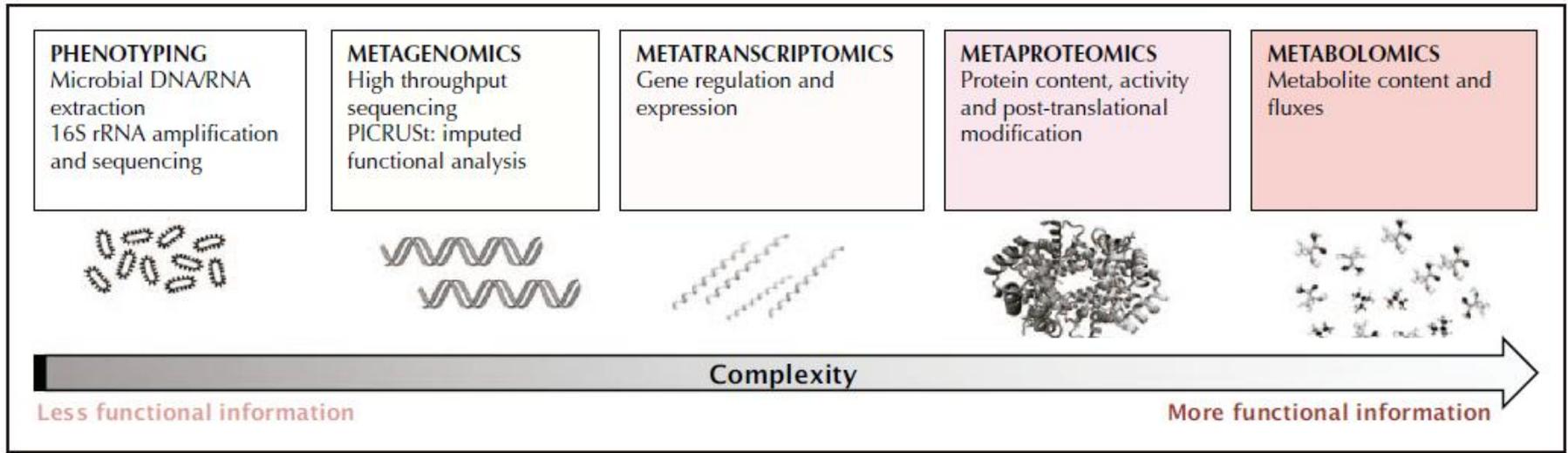
Bacterial diversity in an adult body

Body site	Rough surface area ¹	Rough number of genera ¹
Gastrointestinal tract	300–400 m ²	1183–3180
Oral cavity	215 cm ²	600
Respiratory tract	160 m ²	314
Skin	1.8 m ²	113
Urinary tract	350 cm ²	20–500
Vagina cavity	90 cm ²	282

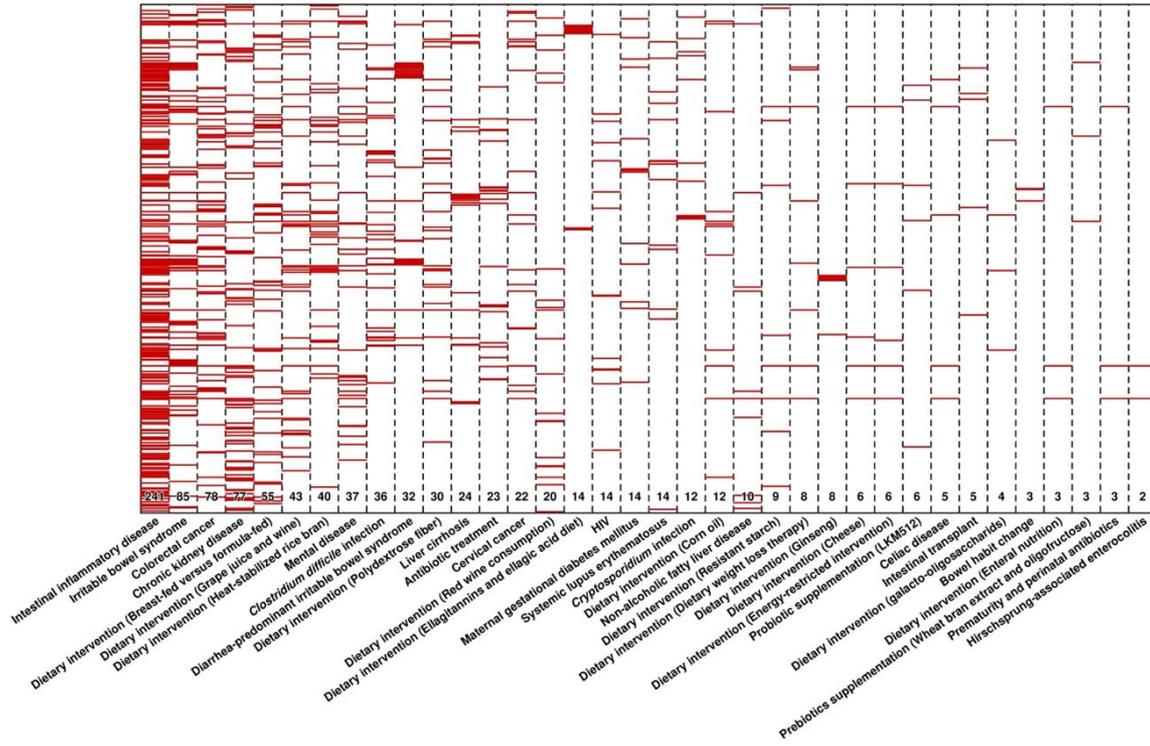
Microbiota through life stages and perturbations



High-throughput approaches used to study variations in the function of the human microbiota



Microbial metabolite biomarkers found to discriminate healthy controls and patients: 621 metabolites



40% of the human metabolites are of microbial origin

Altered metabolism of gut microbiota contributes to chronic immune activation in HIV-infected individuals

JF Vázquez-Castellanos, S Serrano-Villar, A Latorre, A Artacho, ML Ferrús, N Madrid, A Vallejo, T Sainz, J Martínez-Botas, S Ferrando-Martínez, M Vera, F Dronda, M Leal, J Del Romero, S Moreno, V Estrada, MJ Gosalbes and A Moya

Mucosal Immunology | VOLUME 8 NUMBER 4 | JULY 2015

Different clinical measurements of disease progression

Markers of innate immune activation

Systemic inflammation

- Interleukin-6 (IL6)
- High-sensitivity C-reactive protein (hs-CRP)
- Viral load

Thrombosis

Fibrin degradation product D-dimers (DIM)

Bacterial translocation markers

- Bactericidal permeability increasing protein (BPI)
- soluble CD14 (sCD14)

Markers of adaptive immune activation

- CD4+, and CD8+ T-cells count
- The percentage of cells expressing markers of activation: CD25+, CD38+, HLADR+ or CD38+/HLA-DR+
- The percentage of cells expressing markers of senescence: CD57+

Thymic function

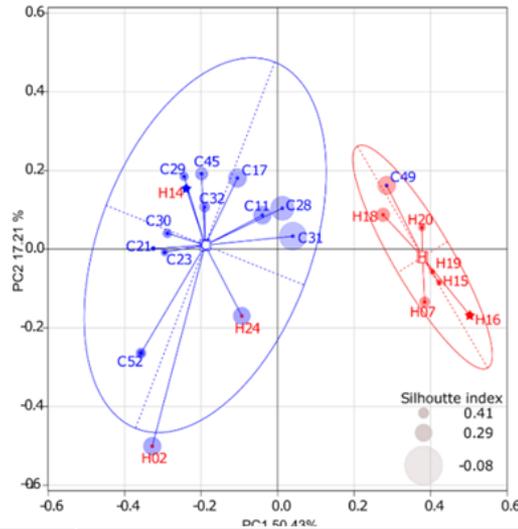
sj/ β -TREC ratio

Endothelial function

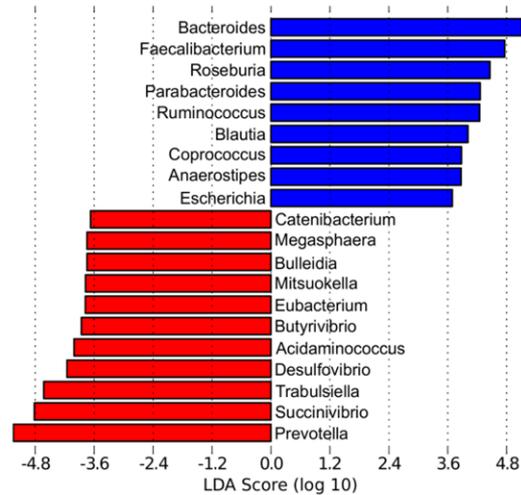
ADMA (μ M/L)

Differences in gut microbiota composition between HIV-infected individuals under ART and healthy subjects

Genus level
PCoA

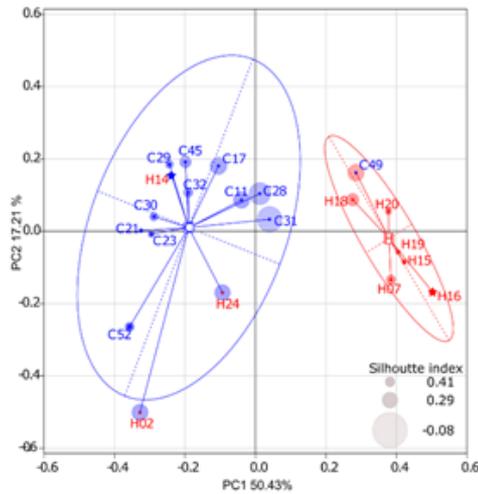


Taxonomic
biomarkers

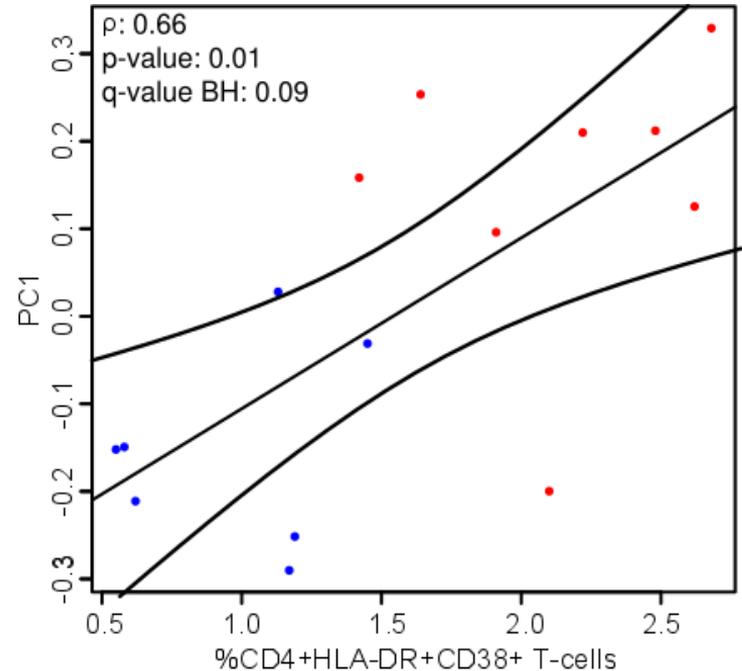


	IR	Controls	p-value	q-value
Shannon index	5.96 ± 1.03	7.00 ± 0.51	0.01	0.04
Chao1 estimator	567.69 ± 175.21	776.27 ± 166.63	0.02	0.05
Ace estimator	563.69 ± 176.44	794.90 ± 172.46	0.01	0.04

Dysbiosis correlates with immune activation and inflammation



50% variance

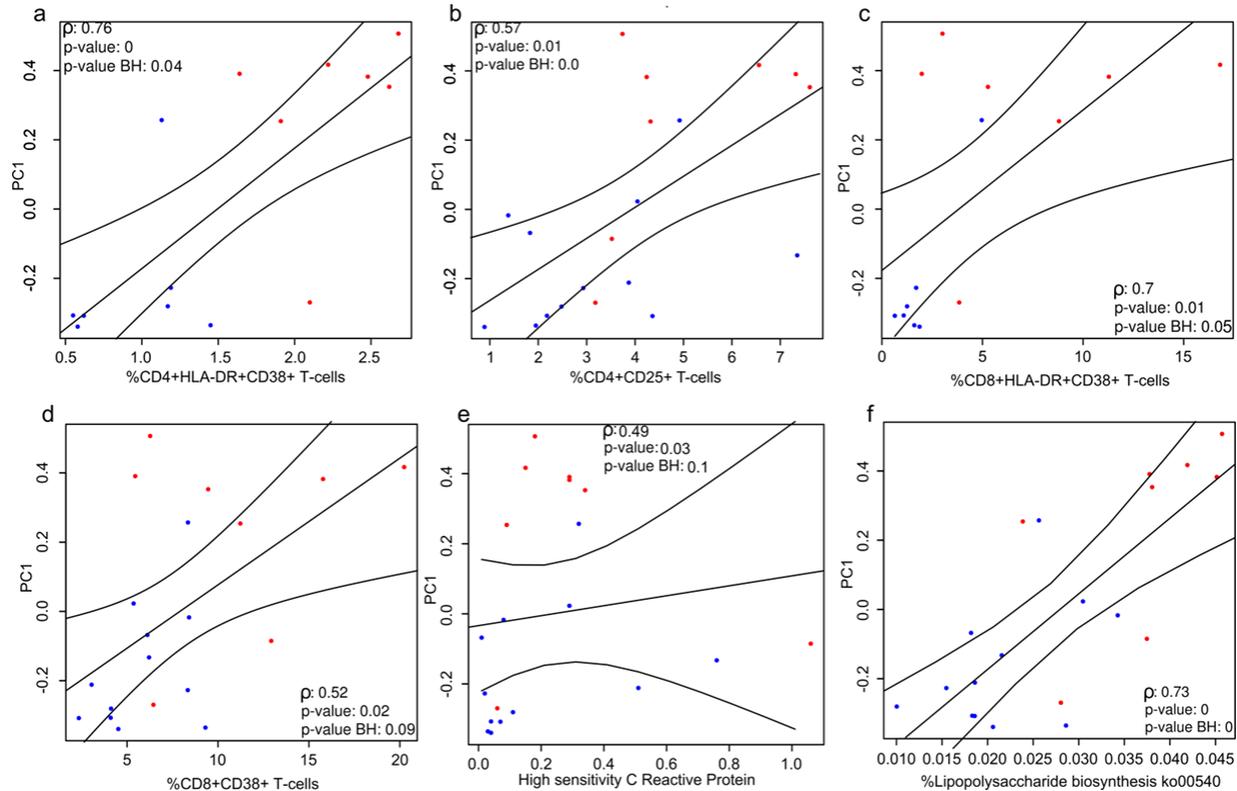
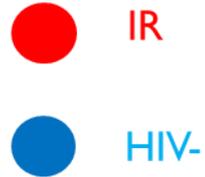


IR

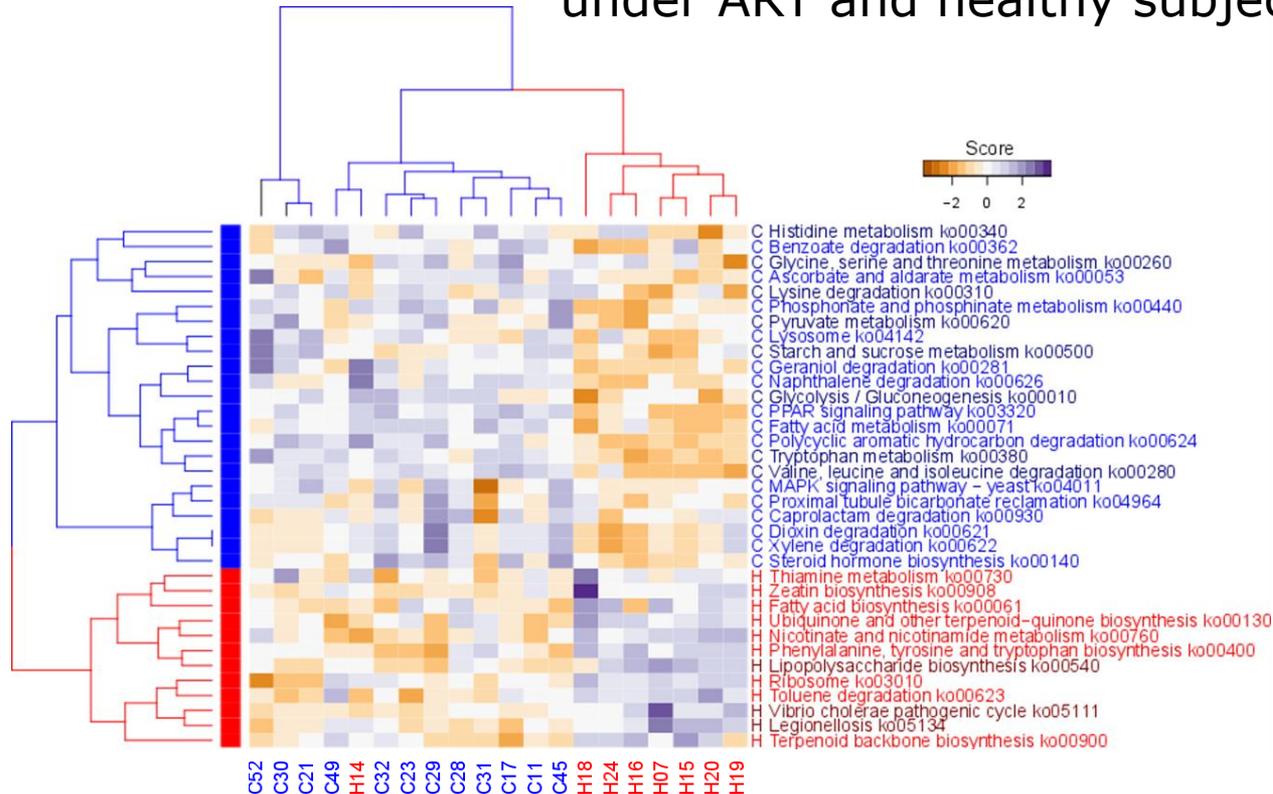


HIV-

The impact of total microbiota on immunological predictors of disease progression



Differences in gut metabolic composition between HIV-infected individuals under ART and healthy subjects



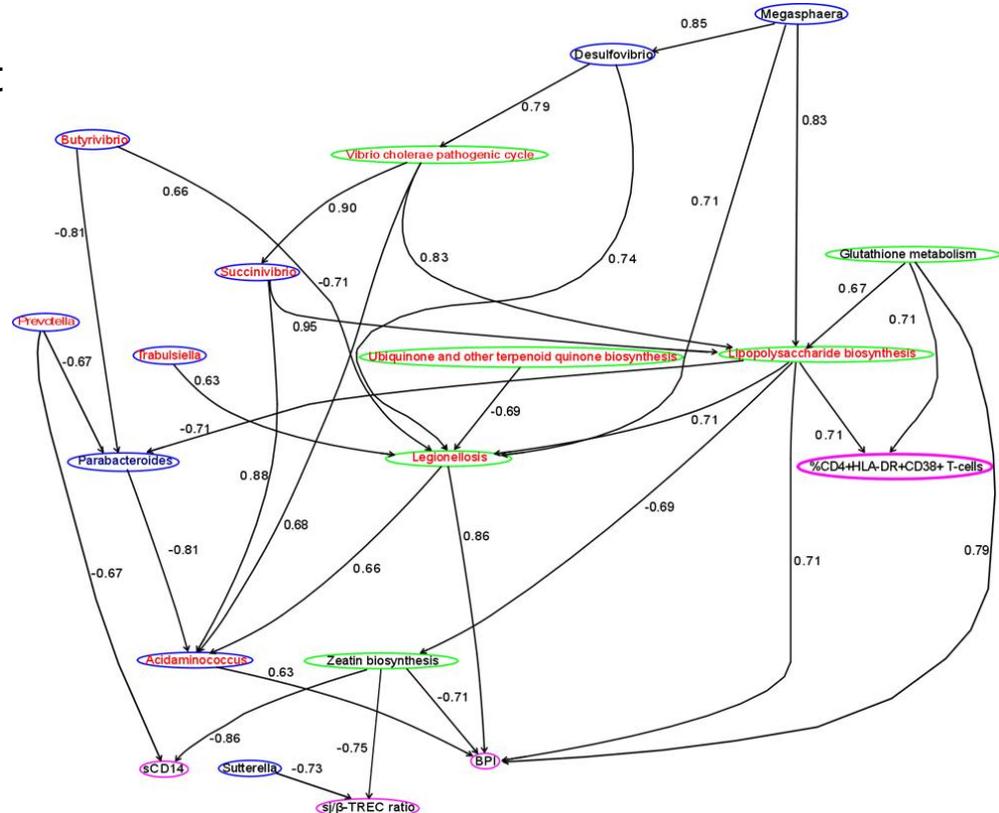
Heat map of the functional biomarkers for patients and controls



Bayesian networks and Markov blankets estimation

LPS Markov blanket

- Ellipse legend**
- KEGG pathway
 - Genus
 - Immune activation variables
- Text legend**
- HIV+ LefSe biomarkers
 - HIV- LefSe biomarkers



Summary

- ✓ To date, 105 diseases and disorders are associated with changes in gut, respiratory, oral, skin and urinary/vaginal microbiotas.
- ✓ 40% of metabolites in the human body are produced by our microbiota.
- ✓ The HIV-gut associated dysbiosis is enriched in Gram-negative bacteria species and presents a decay in their bacterial diversity.
- ✓ The long-term effective ART response does not recover a healthy microbiome composition.
- ✓ The HIV-gut associated microbiota present proinflammatory metabolic pathways.
- ✓ The bacterial dysbiosis is associated with the systemic immune activation.

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Asociación Española
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sobre el Cáncer



Fundación para el Fomento de la
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de la Comunitat Valenciana

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