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XXXIV Congreso Sociedad Andaluza de Medicina Interna (SADEMI)

V Encuentro de Enfermería de Medicina Interna de Andalucía

14, 15 y 16 de Junio 2018
CAMPUS DE LA SALUD
- GRANADA -

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Microbiota Intestinal y Salud

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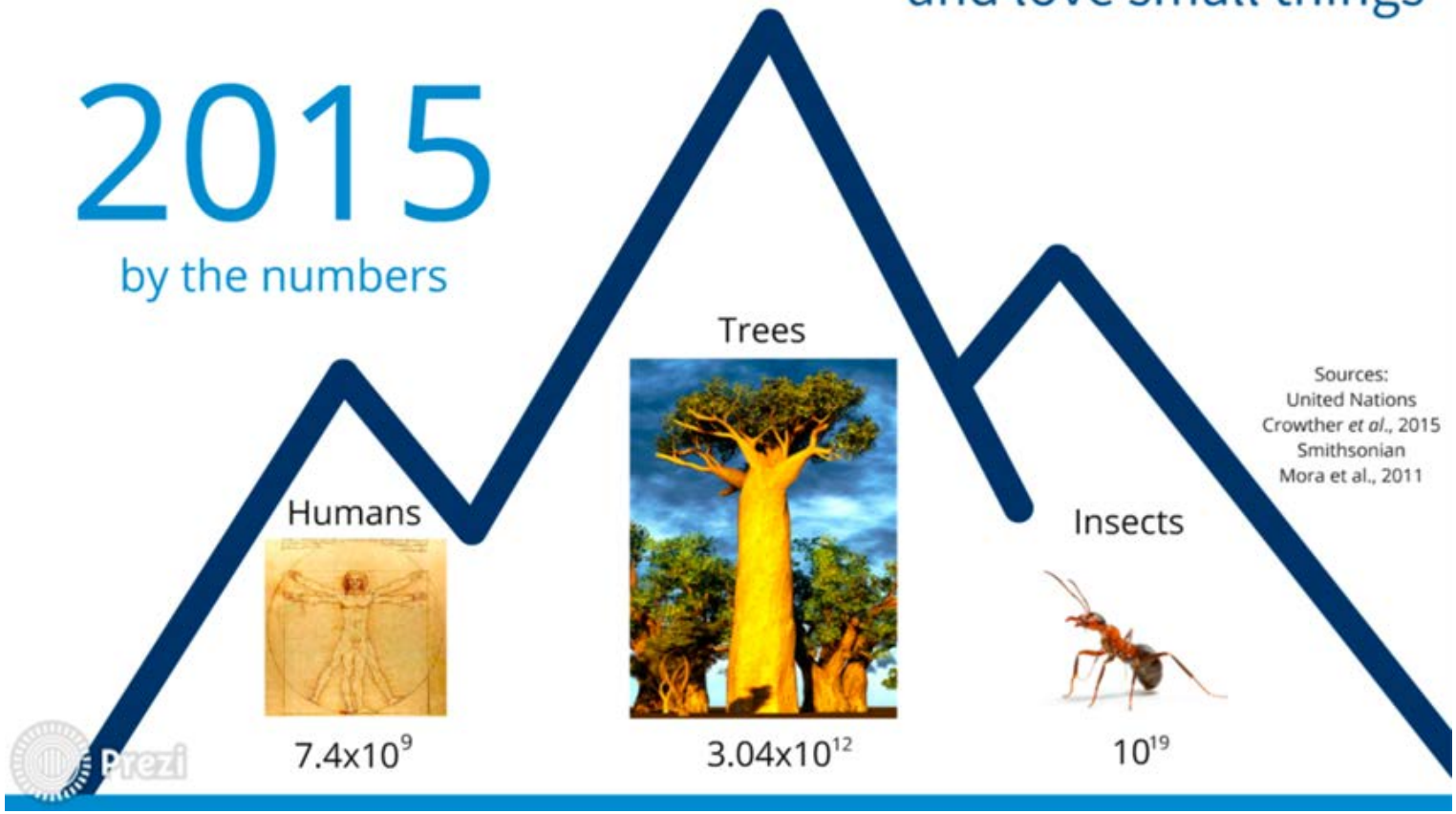
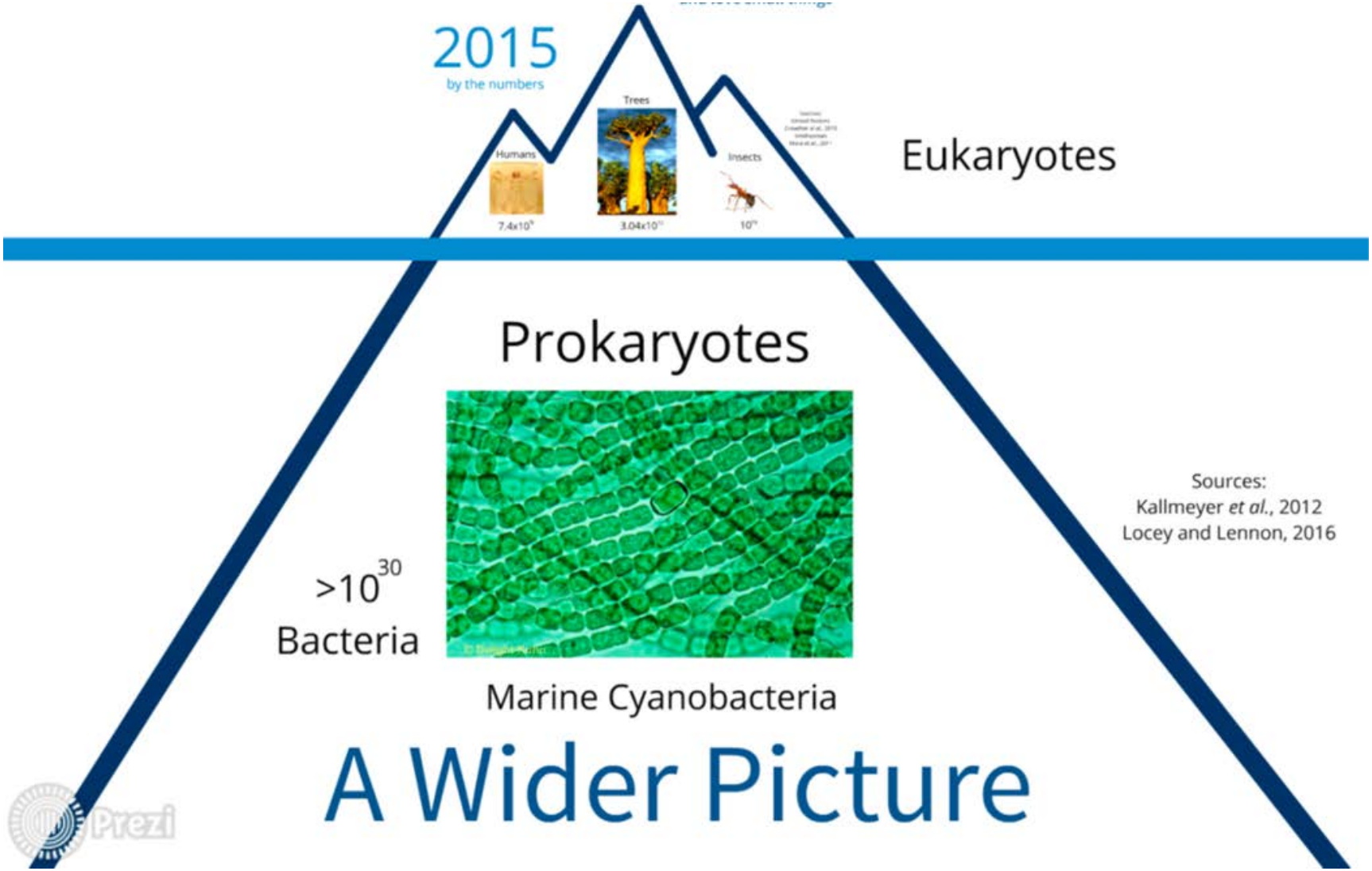
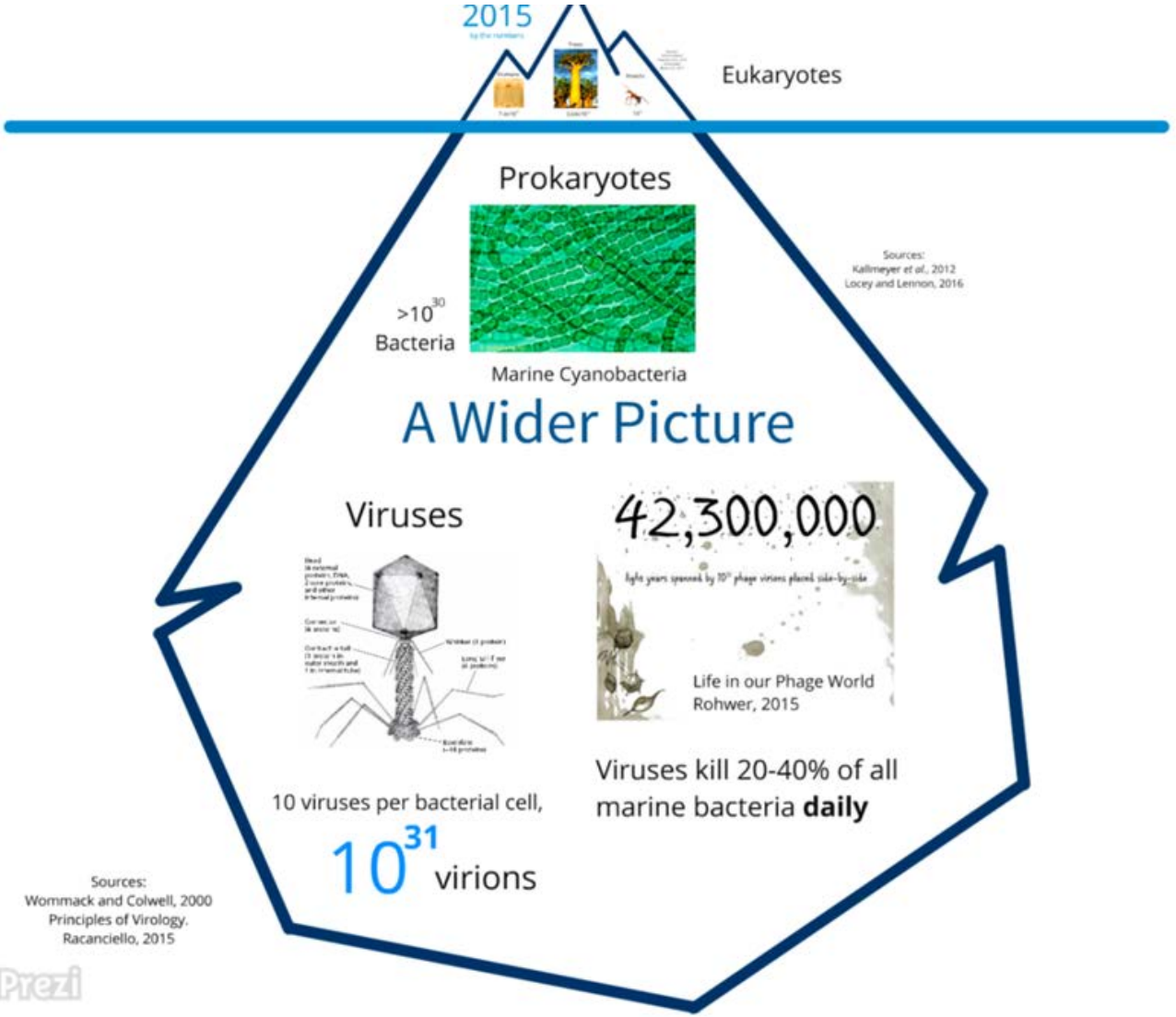
CIBER en Epidemiología y Salud Pública

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

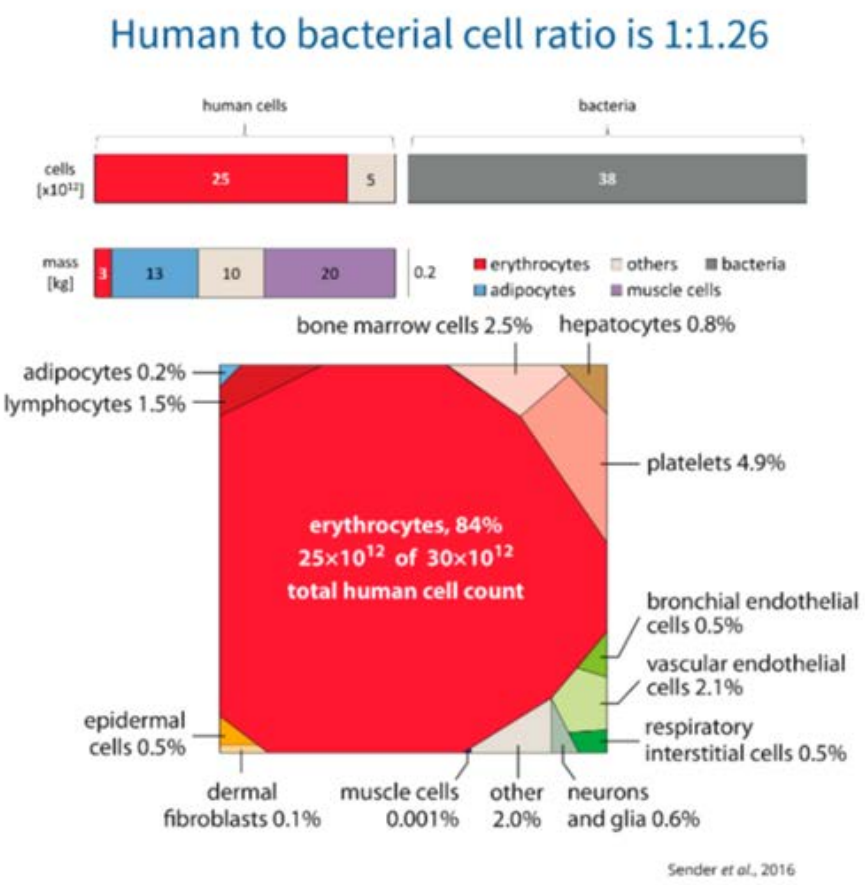
2015
by the numbers

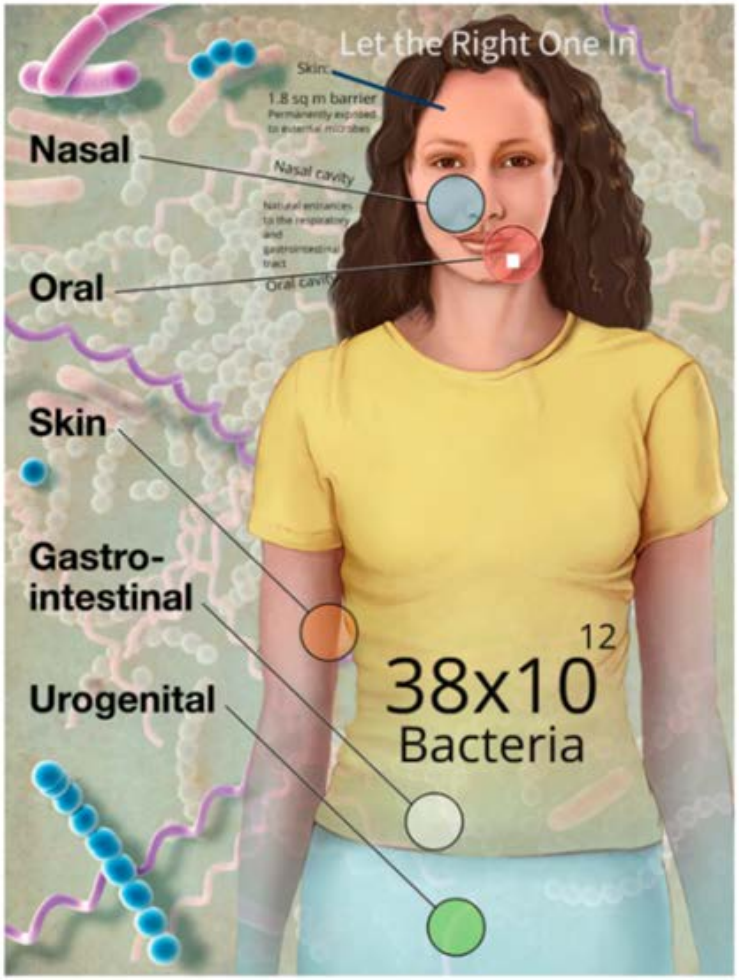



2015
by the numbers
Humans
Trees
Insects
Eukaryotes
Prokaryotes
>10^30
Bacteria
Marine Cyanobacteria
Sources:
Kallmeyer et al., 2012
Locey and Lennon, 2016
A Wider Picture


2015
Eukaryotes
Prokaryotes
>10^30
Bacteria
Marine Cyanobacteria
Sources:
Kallmeyer et al., 2012
Locey and Lennon, 2016
A Wider Picture
Viruses
42,300,000
Life in our Phage World
Rohwer, 2015
10 viruses per bacterial cell,
10^31 virions
Viruses kill 20-40% of all marine bacteria **daily**
Sources:
Wommack and Colwell, 2000
Principles of Virology.
Racanciello, 2015

Human to bacterial cell ratio

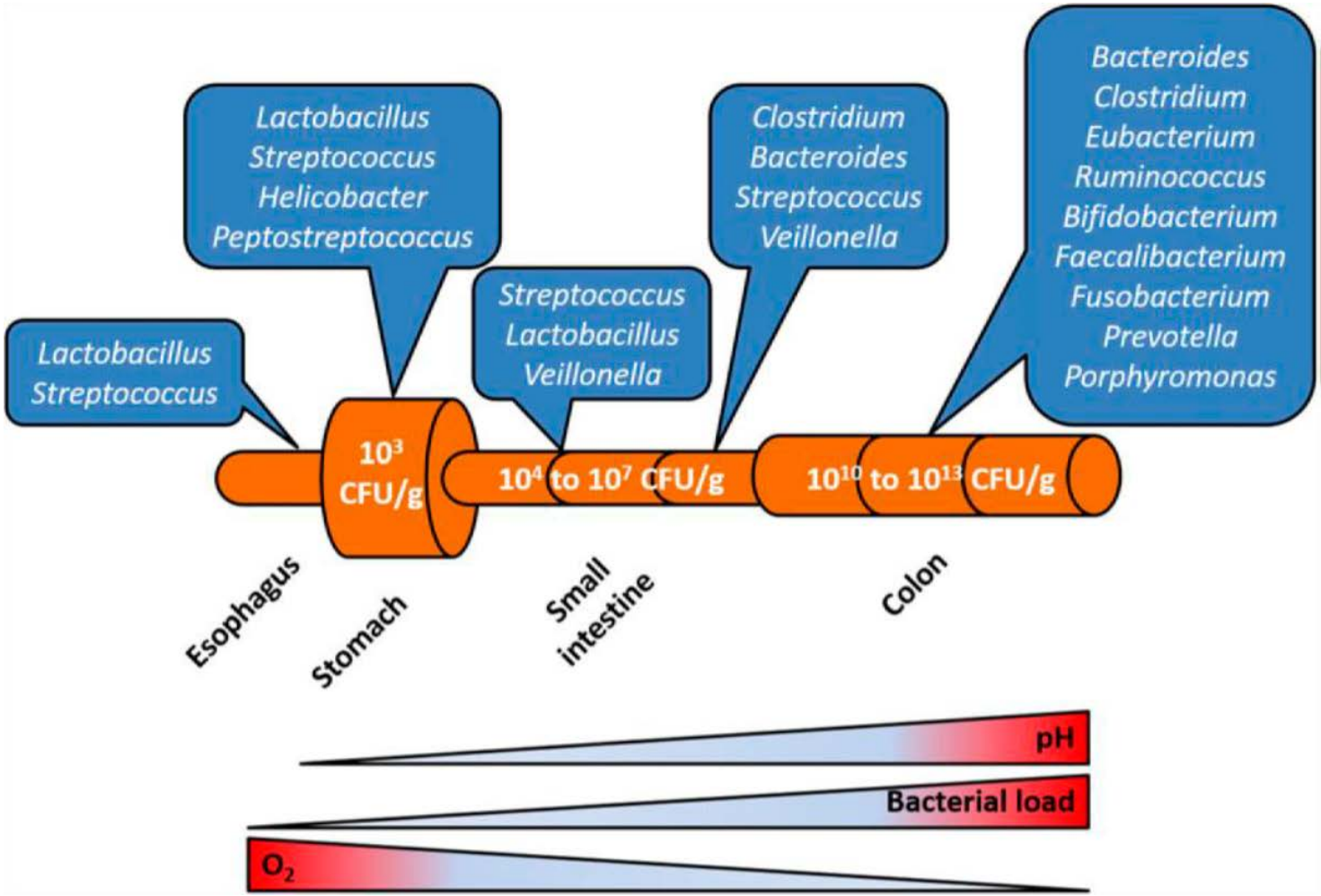




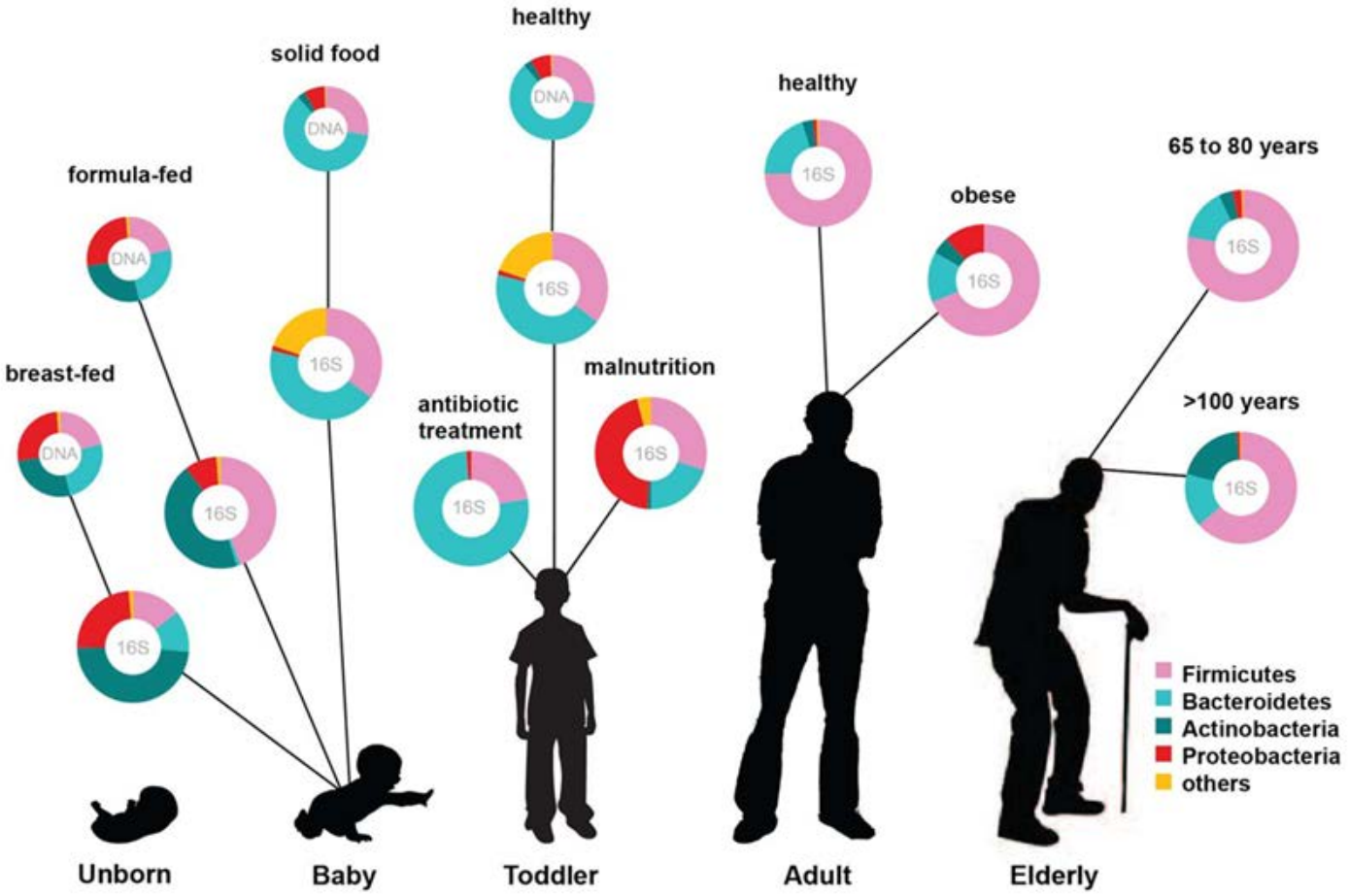
Bacterial diversity in an adult body

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

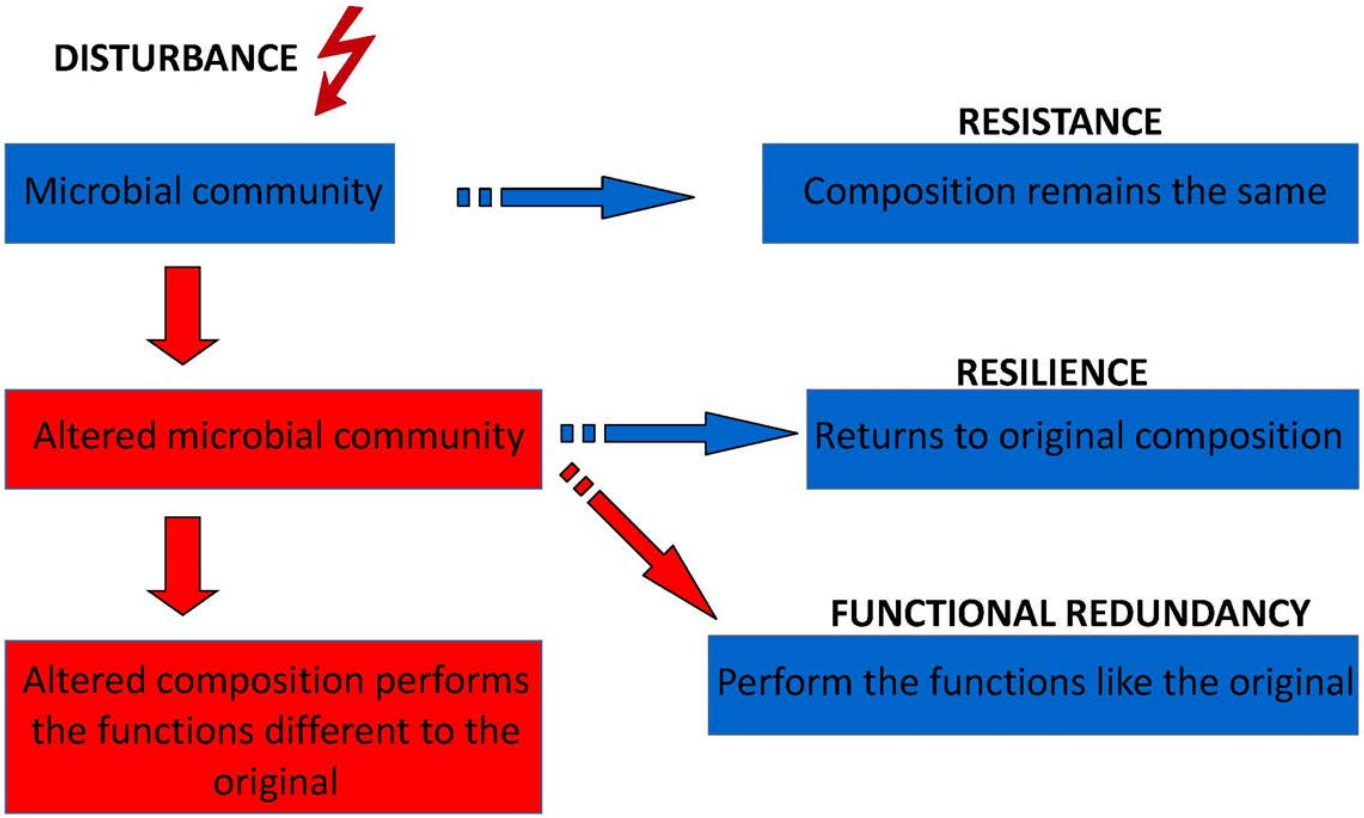
Microbiota composition and pysiological conditions along the digestive tract



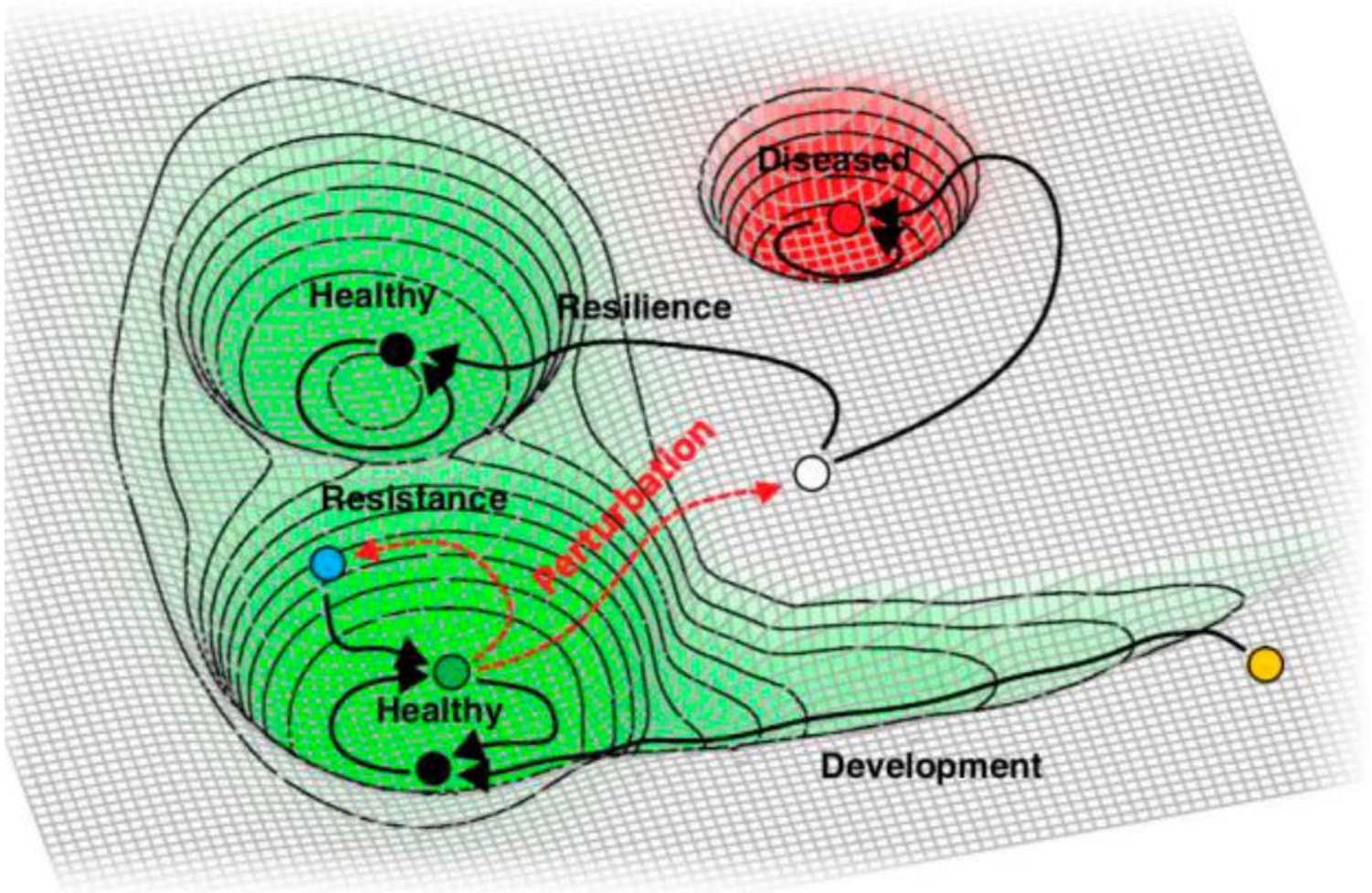
Microbiota through life stages and perturbations



Functional stability against disturbance



The microbiome landscape



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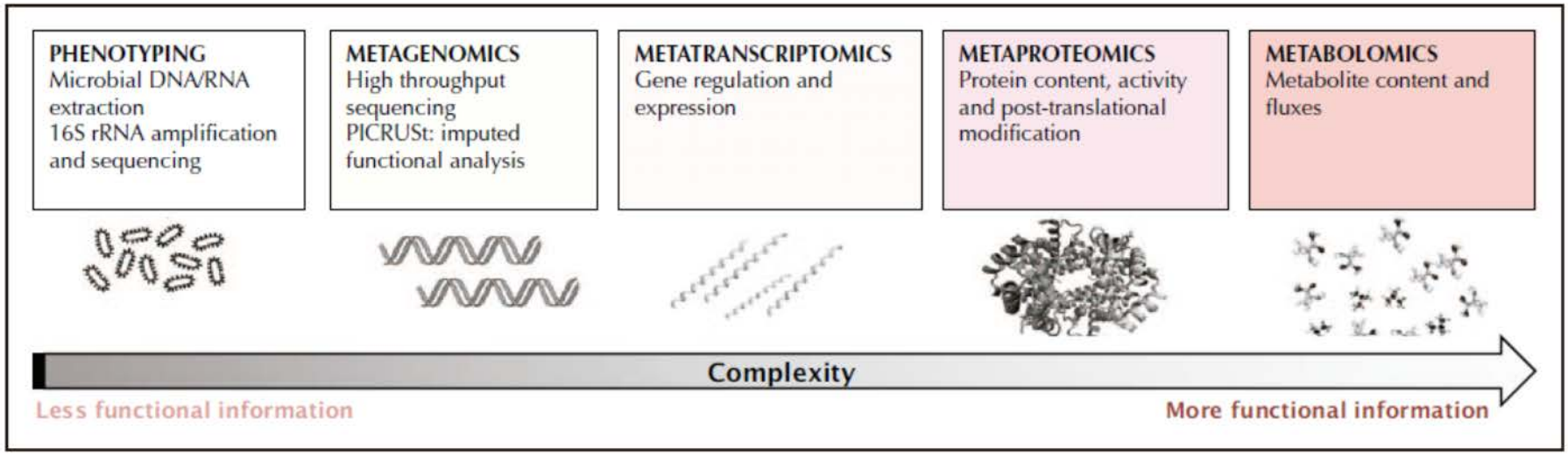
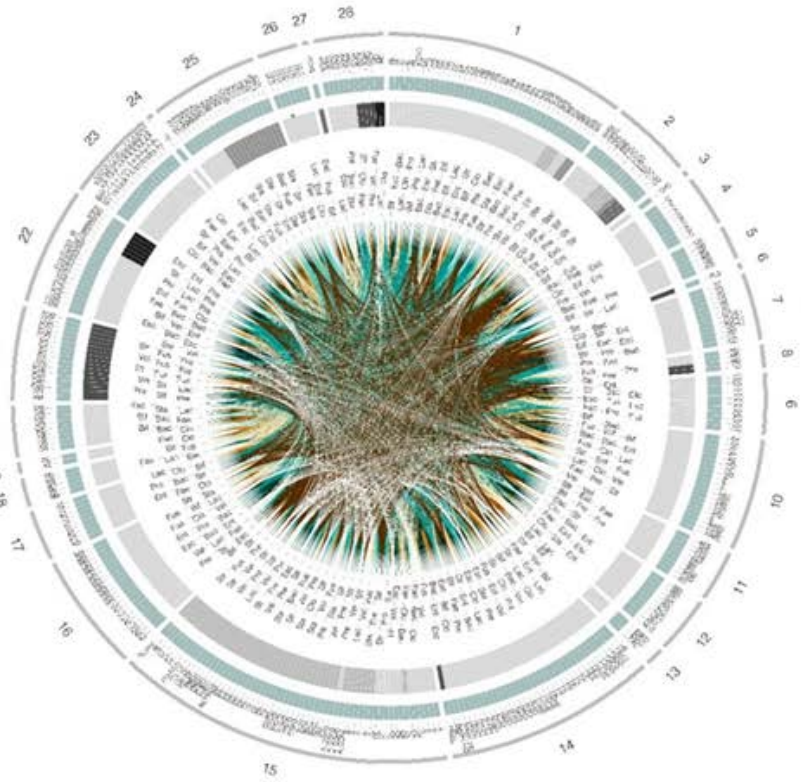
Exploring the human microbiome from multiple perspectives: factors altering its composition and function

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



Diseases associated with alterations to the total microbiota



Type of microbiota
- Gut
- Oral
- Respiratory tract
- Skin
- Urinary tract
- Vaginal

Genera
- *Bacteroides* [Bac]
- *Bifidobacterium* [Bif]
- *Clostridium* [Clo]
- *Enterococcus* [Ent]
- *Escherichia* [Esc]
- *Faecalibacterium* [Fae]
- *Fusobacterium* [Fus]
- *Lactobacillus* [Lac]
- *Prevotella* [Pre]
- *Staphylococcus* [Sta]
- *Streptococcus* [Str]
- *Veillonella* [Vei]

1 AUTOIMMUNE/IMMUNE

AL	Allergy
AICAD	Anti-islet cell autoimmunity
CD	Celiac disease
EA	Enthesitis-related arthritis
HR	Hepatitis R
RA	Rheumatoid arthritis
SJS	Sjögren's syndrome
SLE	Systemic lupus erythematosus
RS	Rhinosinusitis
WA	Hyper-IgE, Wiskott-Aldrich & cytokinesis 8 syndromes

2 CANCER (other than gastrointestinal)

AMBL	Acute myeloblastic leukaemia
AML	Acute myeloid leukaemia
LAC	Laryngeal cancer
LC	Lung cancer
BC	Breast cancer
UC	Urothelial carcinoma

3 CARDIOVASCULAR DISEASE

CHD	Congenital heart disease

4 CROHN'S DISEASE

C	Crohn's disease

5 DEMYELINATING DISEASE

MS	Multiple sclerosis

6 DENTAL AND SKIN DISEASE

PLS	Papillon–Lefèvre syndrome

7 DIARRHEA

TD	Traveller's diarrhea
DCHLI	Diarrhea in children from low income countries
OD	Osmotic diarrhea

8 GANGRENOUS DISEASE

ND	Noma disease

9 GASTROINTESTINAL CANCER

CC	Colorectal cancer

10 INFLAMMATORY DISEASE

AA	Acute apendicitis
AP	Acute pancreatitis
AS	Ankylosing spondylitis
HD	Hirschsprung's disease
P	Pouchitis
PSC	Primary sclerosing cholangitis
S	Spondyloarthritis
AIABL	Arthritis with induced alveolar bone loss

11 INFLAMMATORY DISEASE (blood vessel)

AFS	Atherosclerosis
BD	Behcet's disease
CAD	Coronary artery disease
KD	Kawasaki disease

12 INFLAMMATORY BOWEL DISEASE

IBD	Inflammatory bowel disease
NEC	Necrotizing enterocolitis

13 KIDNEY DISEASE

ESRD	End-stage renal disease
CKD	Chronic kidney disease

14 LIVER DISEASE

HE	Hepatic encephalopathy
HRICI	Hepatitis R-induced chronic liver disease
HLS	Histological liver steatosis
LC	Liver cirrhosis (alcoholic)
LCI IL	liver cirrhosis (alcoholic) with hepatic encephalopathy
NAFL	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
NASH_HC	Non-alcoholic steatohepatitis and hepatocellular carcinoma
PBC	Primary biliary cirrhosis

15 LUNG AND RESPIRATORY DISEASE

A	Asthma
CF	Cystic fibrosis
A_COPD	Asthma and chronic obstructive pulmonary disease
BVL	Benign vocal fold lesion
BCH	Bronchiectasis
COPD	Chronic obstructive pulmonary disease
IPF	Idiopathic pulmonary fibrosis
NCFBCH	Non-cystic fibrosis bronchiectasis
PNEU	Pneumonia
PD_CF	Pulmonary disease and cystic fibrosis
PDAIDS	Pulmonary disease with lung transplant and human immunodeficiency virus (HIV) infection
PT	Pulmonary tuberculosis
RI	Respiratory infection
RI_viral	Respiratory infection (viral)

16 MALNUTRITION DISORDER

KU	Kwashiorkor undernutrition
MN	Malnutrition

17 MENTAL DISEASE

AD	Anxiety and depression
AI	Autism disorder

18 METABOLIC SYNDROME

MS	Metabolic syndrome

19 NEURODEGENERATIVE DISEASE

AZ	Alzheimer's disease
PK	Parkinson's disease

20 OBESITY AND OVERWEIGHT

OB	Obesity
OW	Overweight

21 ODONTOGENIC INFECTION

AEI	Acute endodontic infection
CAR	Caries
CO	Chronic osteomyelitis
GV	Gingivitis
POD	Periodontitis

22 PATHOGENIC INFECTION

AENI	Acute enteric infection
CHL	Cholera
CDIFI	*Clostridium difficile* infection
SHI	Shigellosis
BCYS	Blastocystis
BV	Bacterial vaginosis
PID	Pelvic inflammatory disease

23 DIABETES

GLUI	Glucose intolerance
Type_1_D	Type 1 diabetes
Type_2_D	Type 2 diabetes

24 RADIATION ENTEROPATHY

RE	Radiation enteropathy

25 SKIN DISEASE

ATOD	Atopic dermatitis
ATOF	Atopic eczema
GUD	Genital ulcer disease
AVR	Acne vulgaris and rosacea
ASA	Acute skin abscesses
CFU	Chronic foot ulcer
PSO	Psoriasis
PSOA	Psoriatic arthritis
SSTI	Skin and soft tissue infection

26 ULCERATIVE COLITIS

UC	Ulcerative colitis

27 URINARY TRACT INFECTION

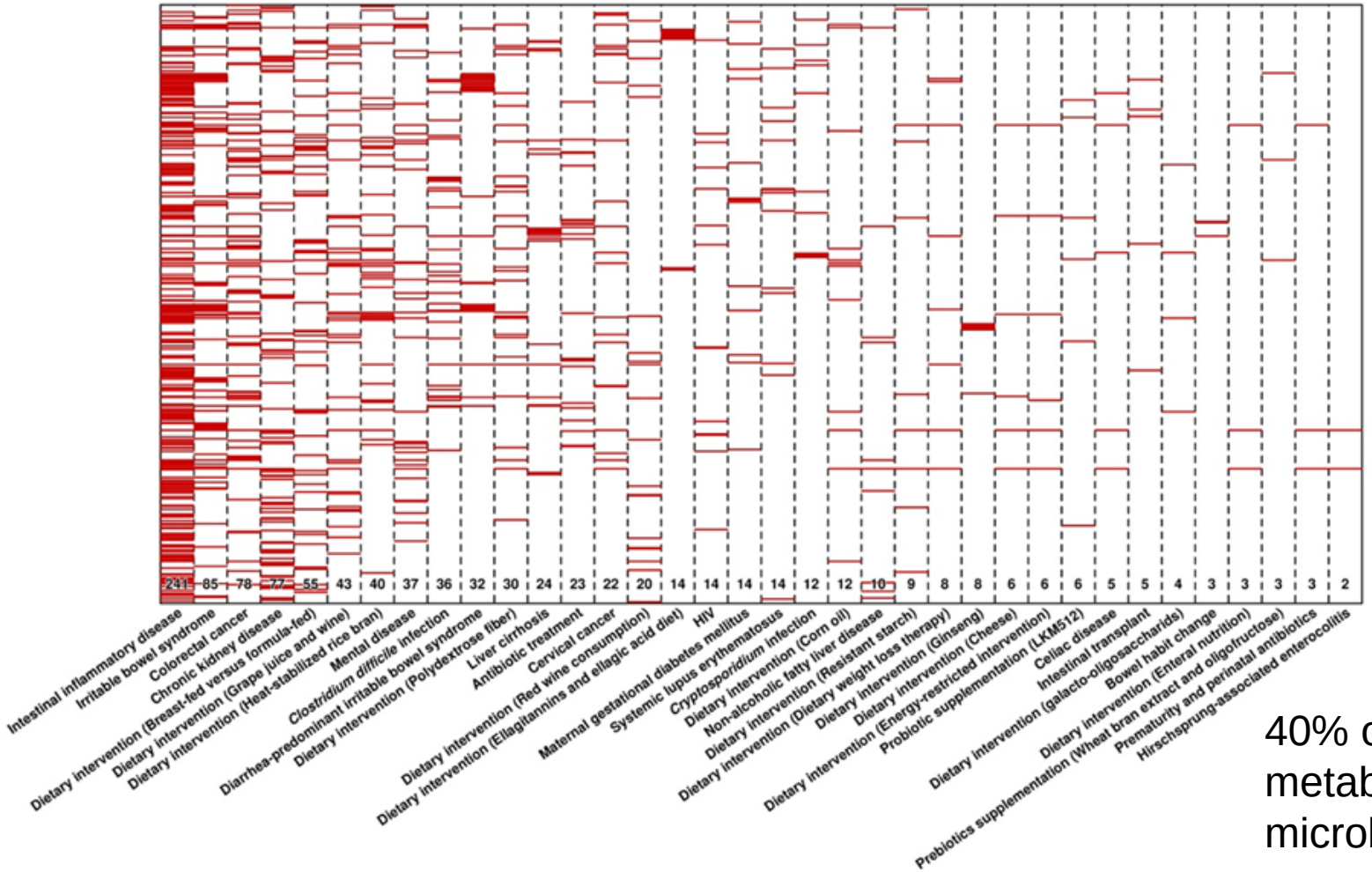
ITCYS	Interstitial cystitis

28 VIRAL INFECTION

AIDS	Human immunodeficiency virus (HIV) infection
GH	Genital herpes

- ✓ 28 types of disease
- ✓ 105 diseases
- ✓ 231 non-redundant genera
- ✓ 15 different phyla
- ✓ 12 genera associated with at least 50% of diseases

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



40% of the human metabolites are of microbial origin

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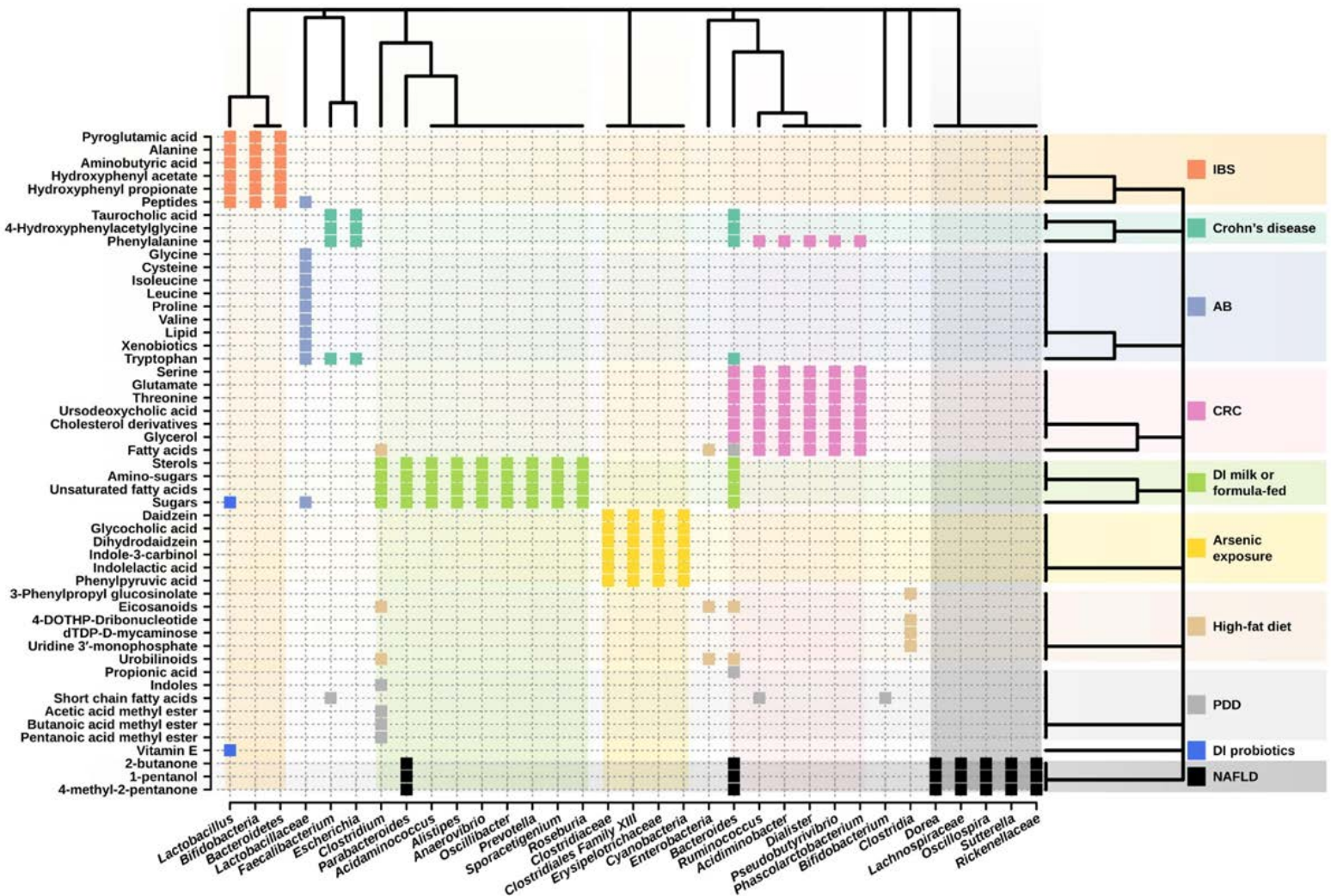
Clustering of the metabolic biomarkers and the gut microbiota members in the context of multiple diseases and interventions



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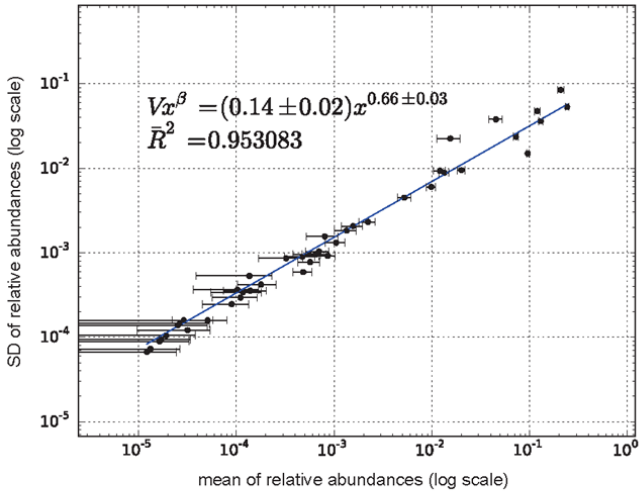
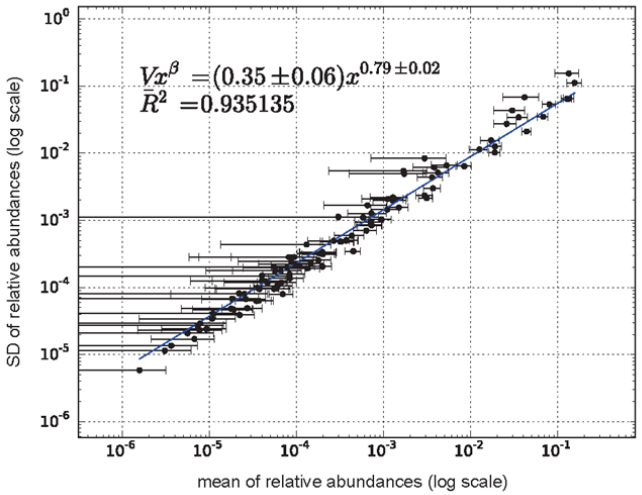
Health and disease imprinted in the time variability of the human microbiome

Power law fits of the standard deviation (SD) vs. mean of the relative abundance of bacterial genus monitored over time

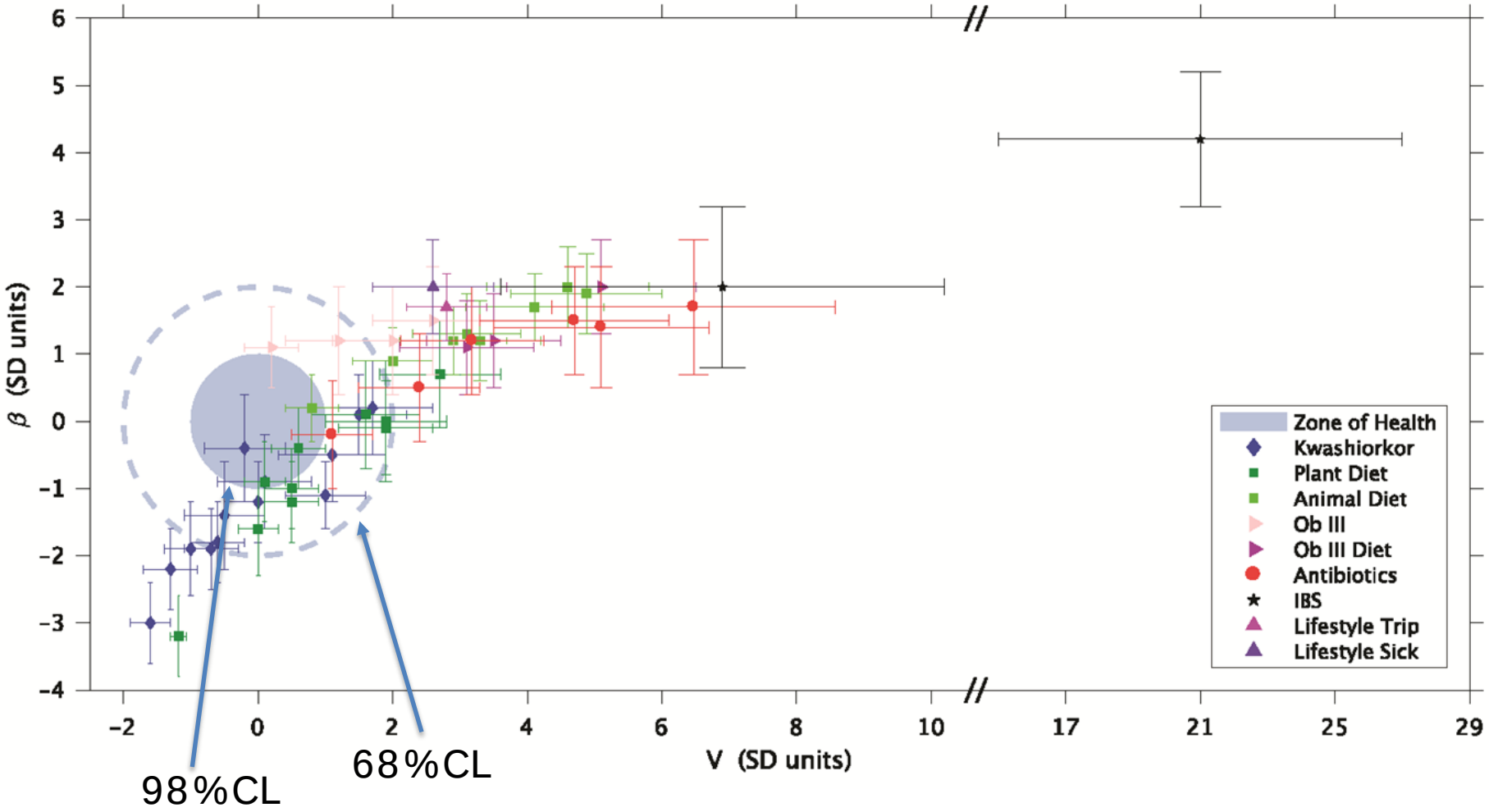


Healthy subject

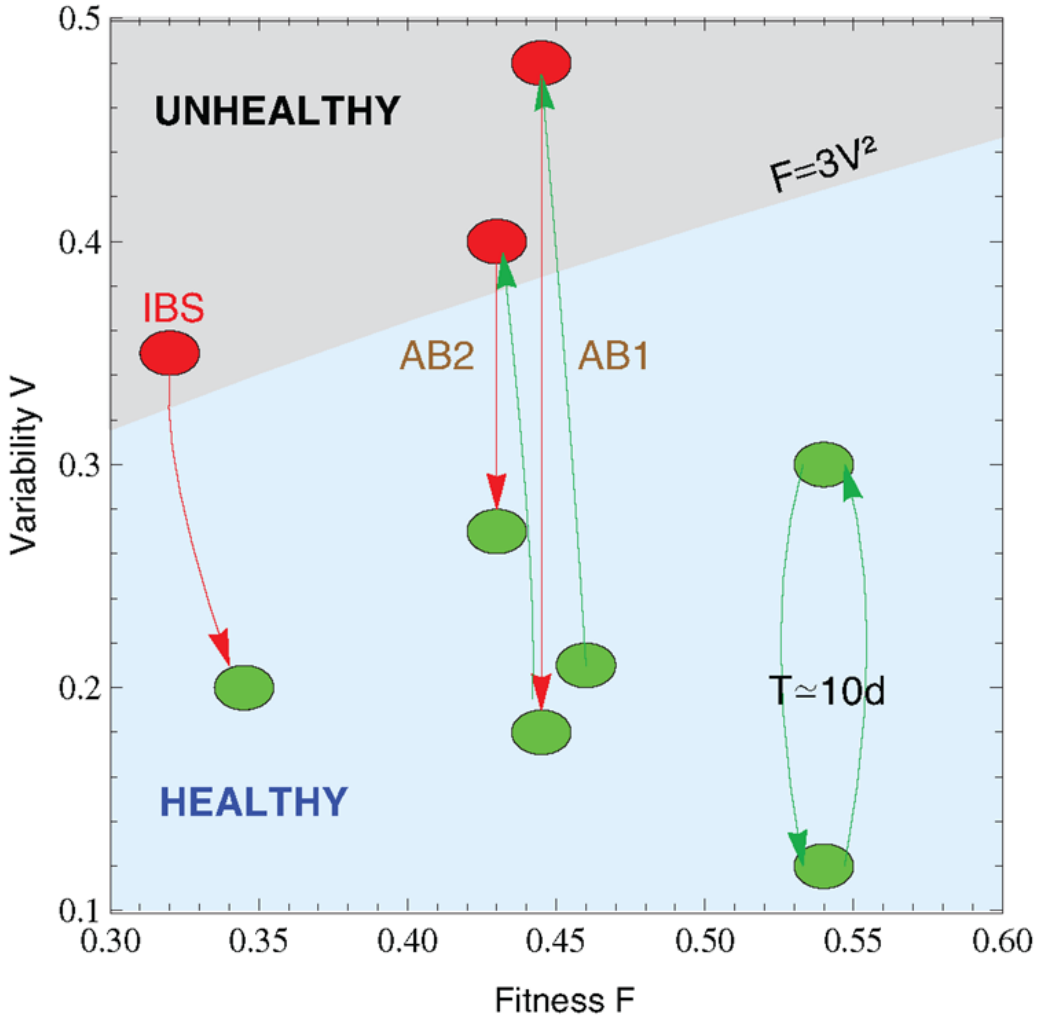


IBS subject

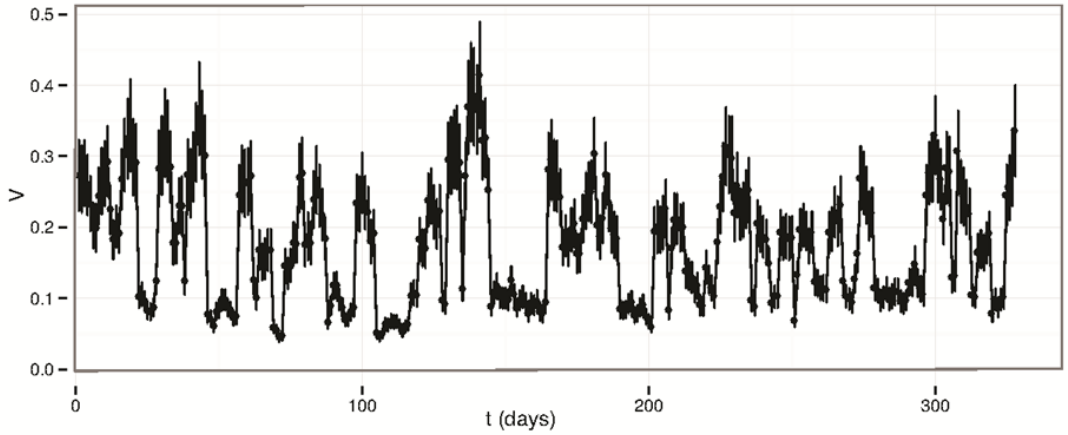
Taylor's law parameter space for diferente studies

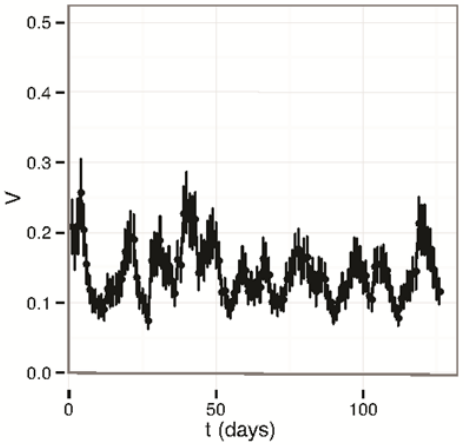


Microbiota states can be placed in the phase space

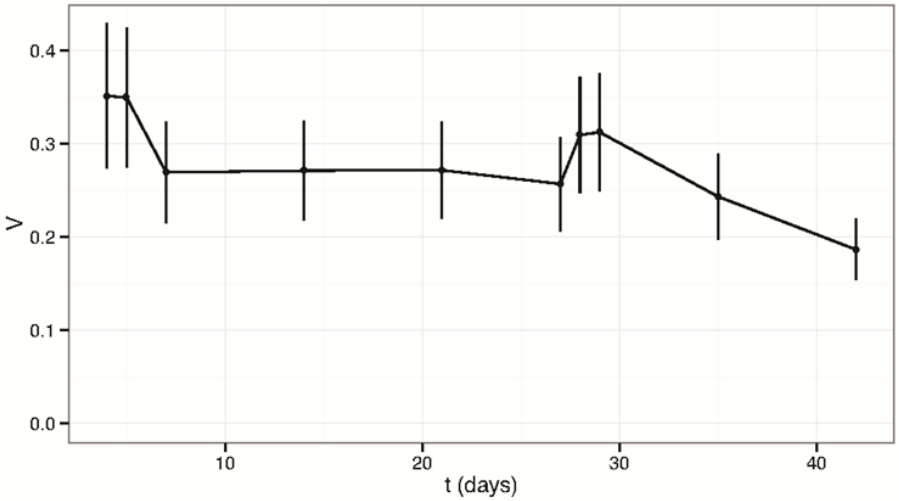


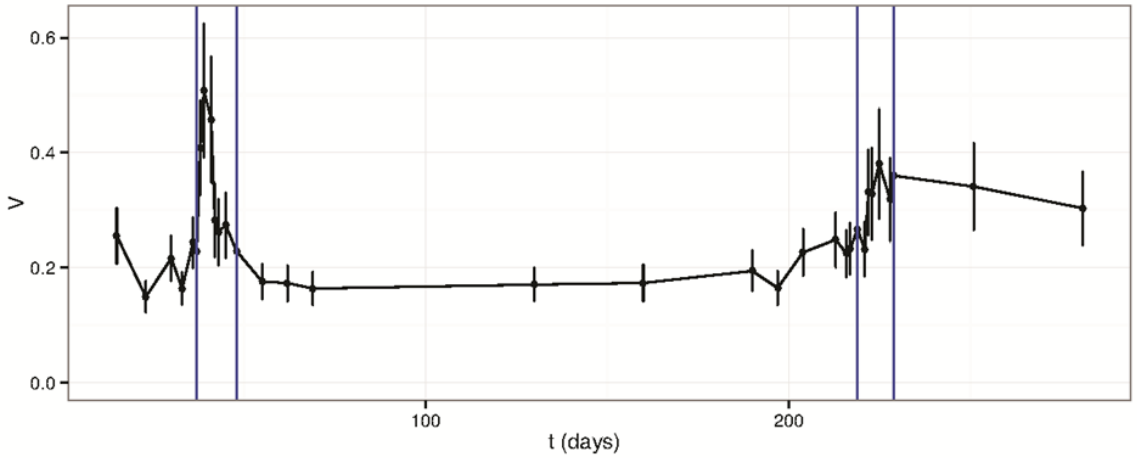
V of the two subjects (male, top) and female (bottom) as a function of time





V as a function of time for a IBS patient (top) and another one that has taken antibiotics in two periods





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Time series analysis of the microbiota of children suffering from acute infectious diarrhea and their recovery after treatment

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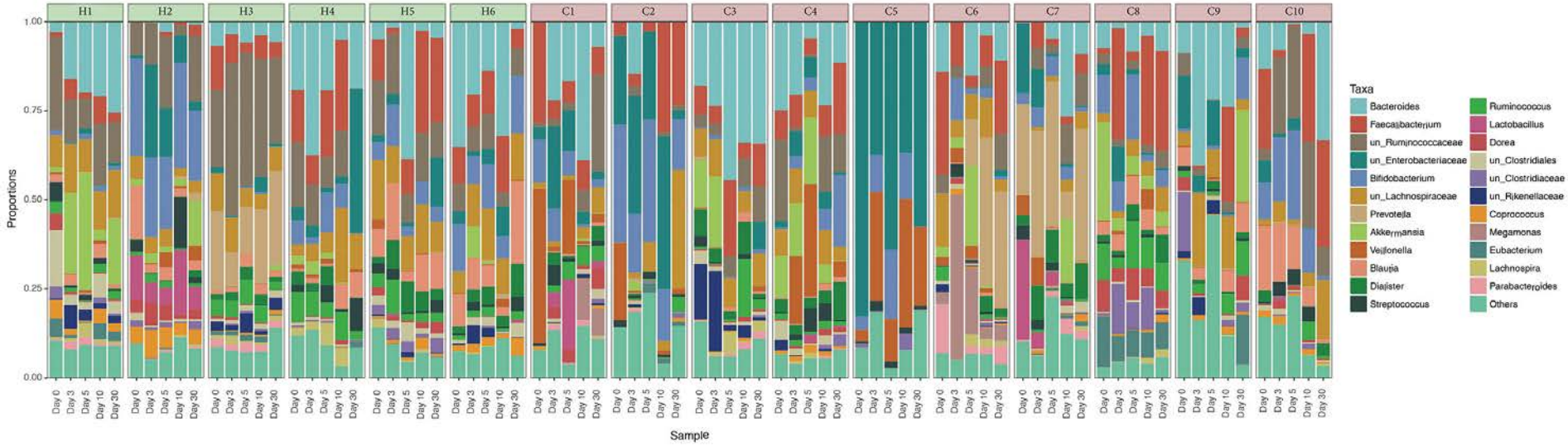
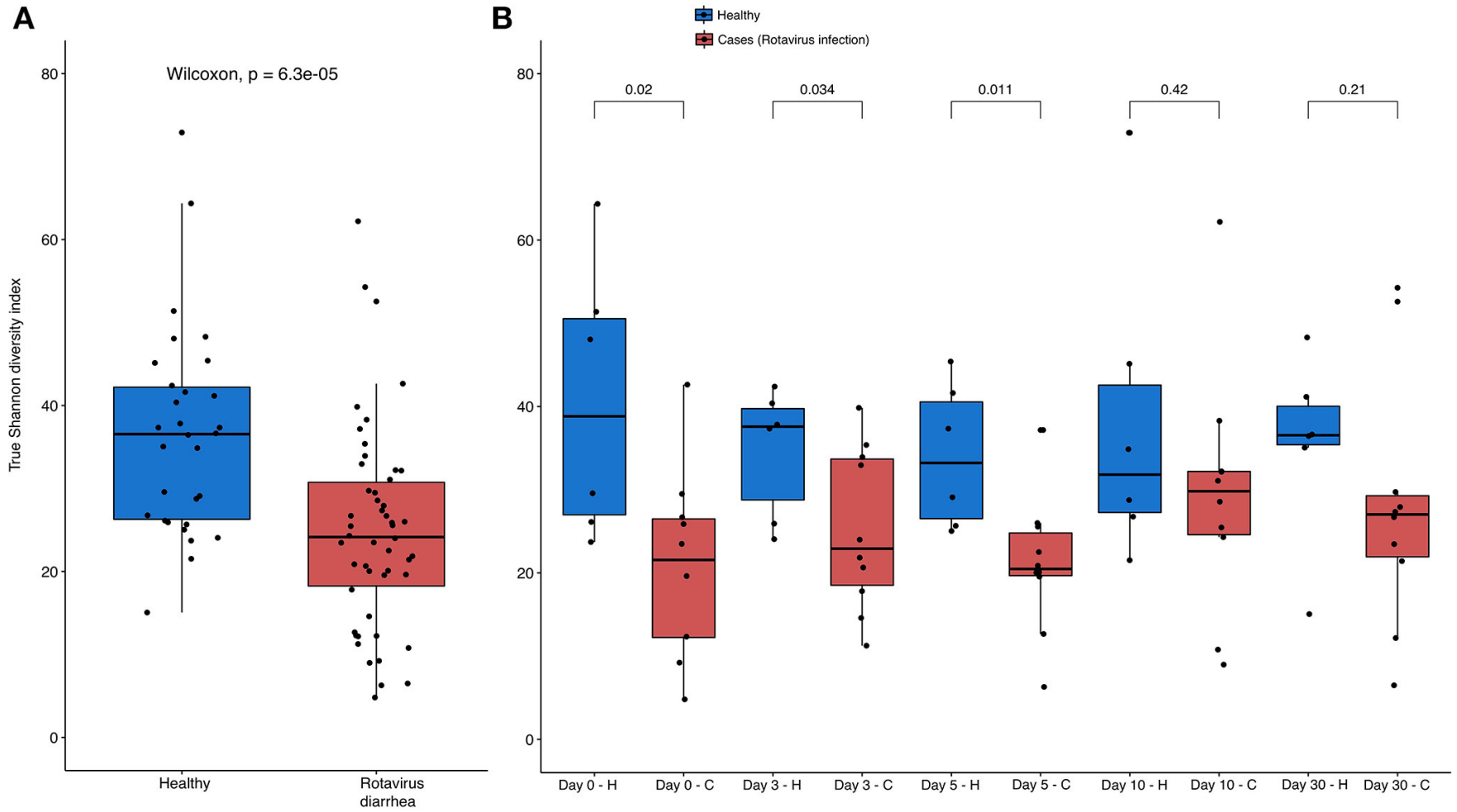
Changes in the gut microbiota of healthy children and cases

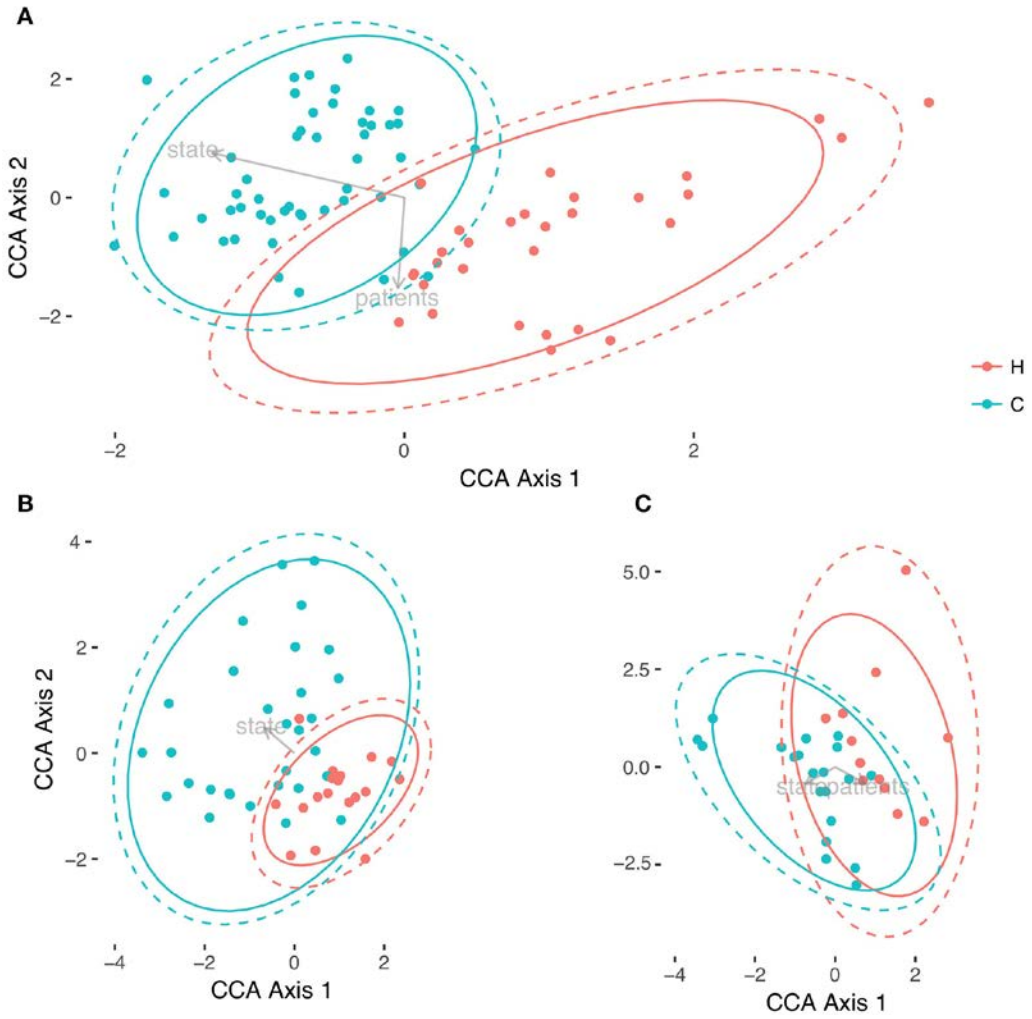


Healthy children: H1-H6
Cases: C1-C10

Shannon diversity index per health status (A) and per day (B)



Comparison of microbiotas between healthy children and children with acute diarrhea

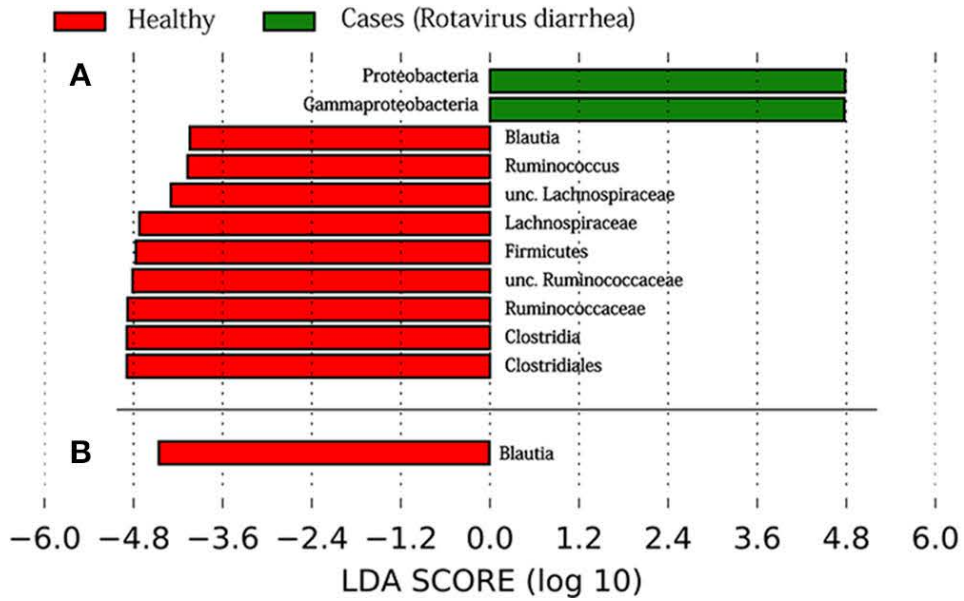


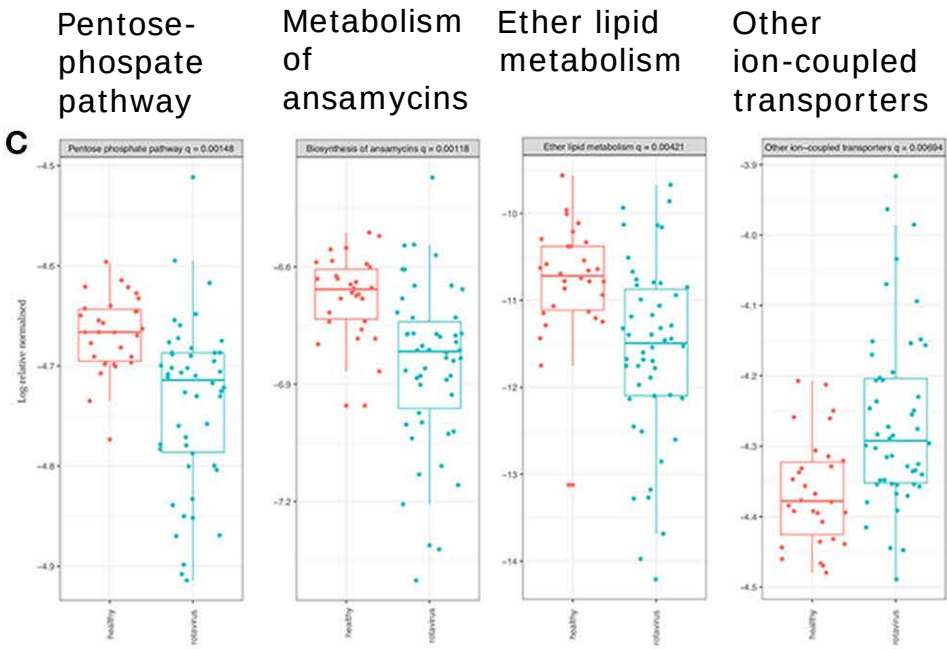
(A) Global differences between both health status, Healthy (H, in red), and Cases (C, in green) for all times.

(B) CCA for the individuals from time 0 to 5

(C) CCA of samples belonging to days 10 and 30

Taxonomic biomarkers and functions enriched

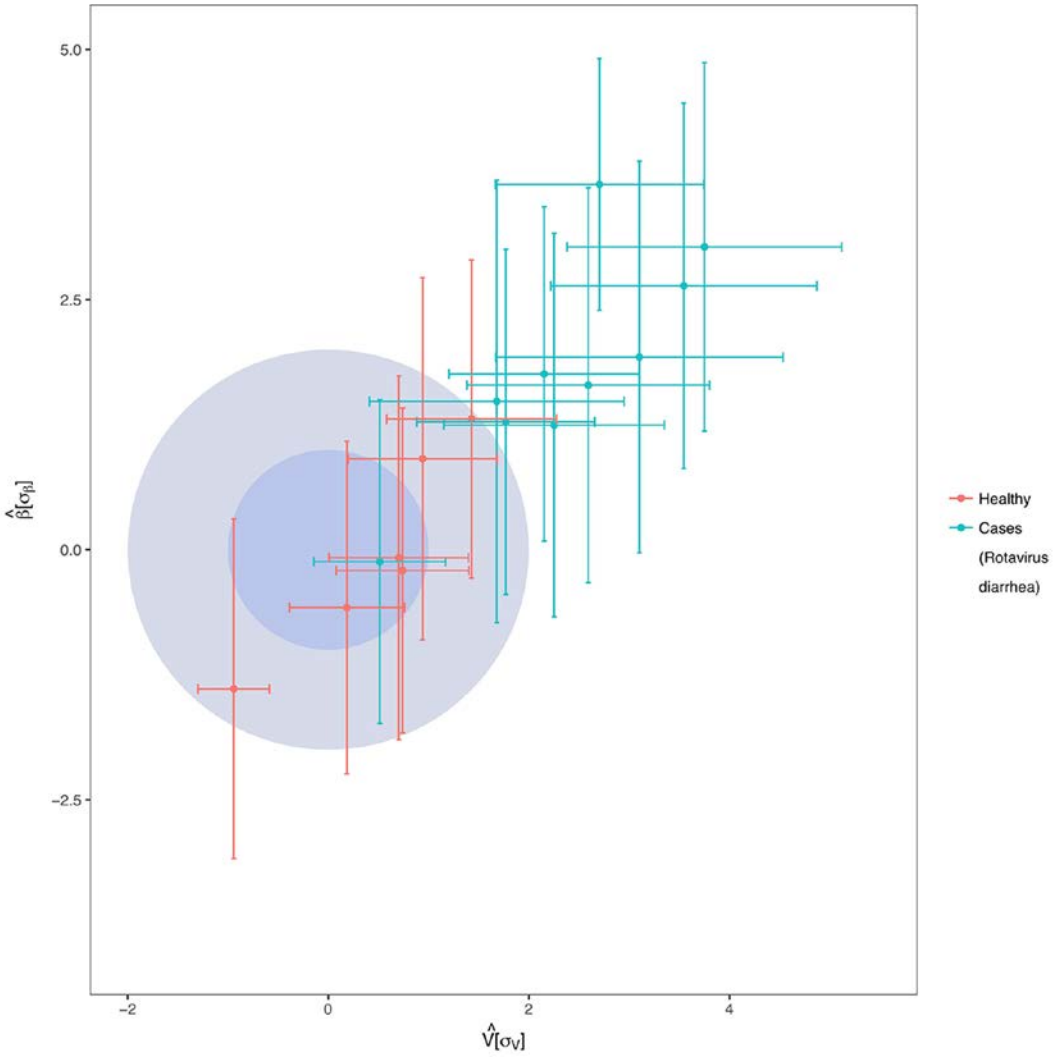




LEfSe analysis between the healthy children (in red) and case children (in green).
(A) from days 0 to 5
(B) from days 10 to 30

(C) KEGG (Kyoto Encyclopedia of Genes and Genomes) pathways at level 3 of hierarchy validated by Kruskal-Wallis test

Taylor's law parameter space



The inner darker-blue circle corresponds to the 68% CL region of healthy children in the Taylor's parameter space, while the bigger light-blue circle delimits the 98% CL region

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.
- ✓ A fluctuation scaling law describe the temporal changes in the gut microbiota.
- ✓ Stable microbiotas can be distinguished from unstable microbiotas.
- ✓ We identified the microbiota transition from a diseased state to a healthy one with time, whose characterization may lead to relevant clinical data.
- ✓ Our work highlights the importance of using time series for the study of dysbiosis related to diarrhea, and many other diseases

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