Gemelli

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Il Microbiota come strumento diagnostico

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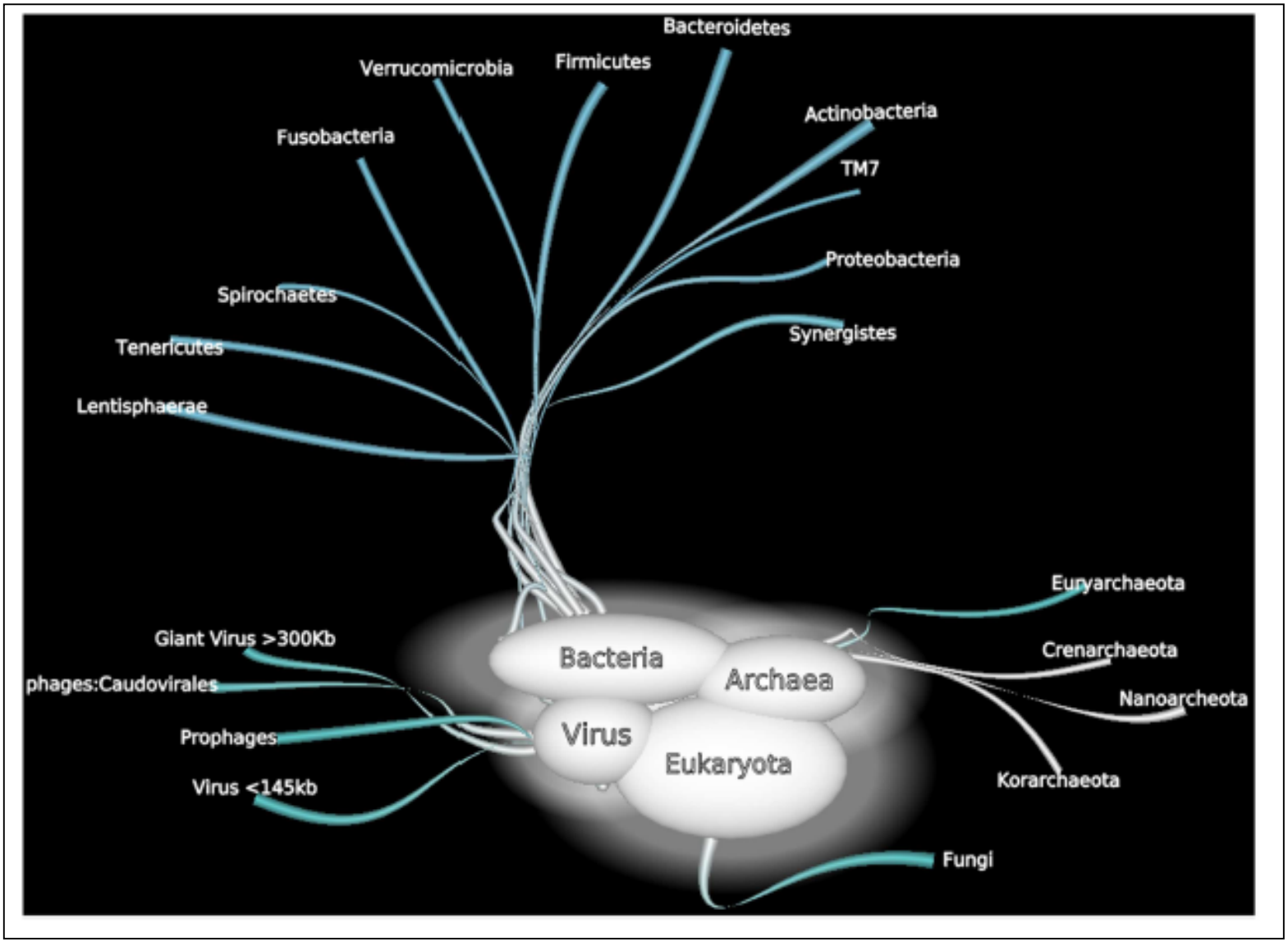
Glossary of terms (2)

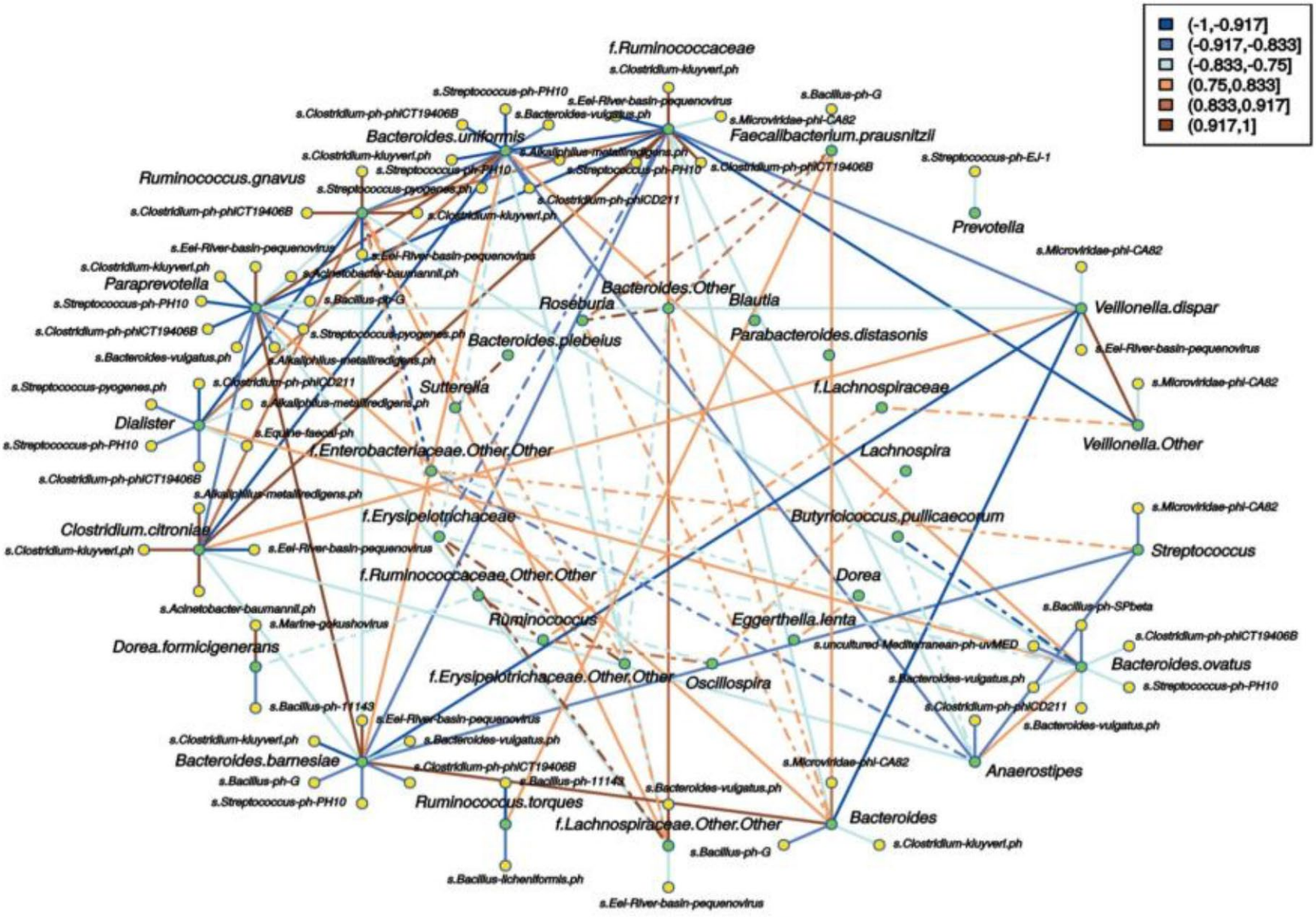
Definition	Explanation
Microbiota	All the microbes that are found in a particular region or habitat; the term “microflora” is no longer used
Microbiome	The totality of the microbes with their genes that are harbored by the microbiota and the milieu in which they interact
Operational taxonomic unit (OTU)	Specific sequences based on sequence similarity (typically threshold is 97%) to reference genes. This is taken as a proxy for species-level
Taxon	A group of phylogenetically related microbes that belong to the same taxonomic group, such as order, family, or genus
Richness	Number of different taxa within a single population
α Diversity	How many types of sequences in a sample
β Diversity	How many different types of sequences are shared among samples

- Humans are viewed as composites of human and microbial cells.
- Human microbiota are complex and dynamic microbial communities composed mainly of bacteria, but also includes protozoa, archaea, viruses, and fungi that resides in and on different body niches (oral cavity, throat, esophagus, stomach, colon, urogenital tract, respiratory tract, and skin).
- The colonic microbiota constitutes the most abundant microbial domain within the human body, with the vast majority belonging to the bacterial phyla of *Firmicutes* and *Bacteroidetes*.

A non-exhaustive overview of human gut microorganisms among bacterial, Archaea, viral, and *Eukaryota* domains



Correlation network between relative abundance of *bacterial, yeast and bacteriophage*-matching reads



Microbiota influencers

- **Sanitation**
- **Mode of delivery, breast-feeding..**
- **Diet**
  - ***Composition (calories, fat, fibres, vegetable, meat..)***
  - ***Cooking***
  - ***Natural food additives (safrol..)***
  - ***Artificial chemical food additives:***
    - ***Preservatives (benzoic acid, sodium benzoate, nitrite/nitrate, sulfur dioxide/sulfite..)***
    - ***Sweeteners, emulsifiers and stabilizers, flavors, thickeners, antifoaming, anticaking, bulking, antioxidants..)***
    - ***Others (titanium dioxide..)***
- **Exercise**
- **Sleep**
- **Stress**
- **Violence**
- **Drugs**

How to define an EUBIOTIC enterotype?

EU= good ***BIOS= life***

- **Composition:** ***Diversity***
  Richness
  Relative Abundance

Our gut is a sophisticated ecosystem that is regulated by the logic of RELATIONAL HARMONY

Microbiota and Host live in a COOPERATIVE SYSTEMIC AGGREGATION MODEL

EUBIOSIS

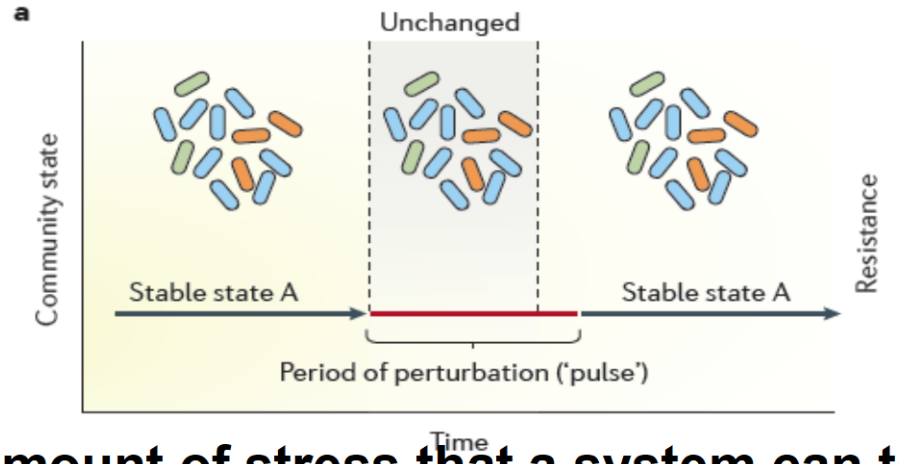
Failure of HOST-MICROBIOTA equilibrium

Quali-quantitative alterations of oral, esophageal, gastric, small bowel and/or colonic microbiota

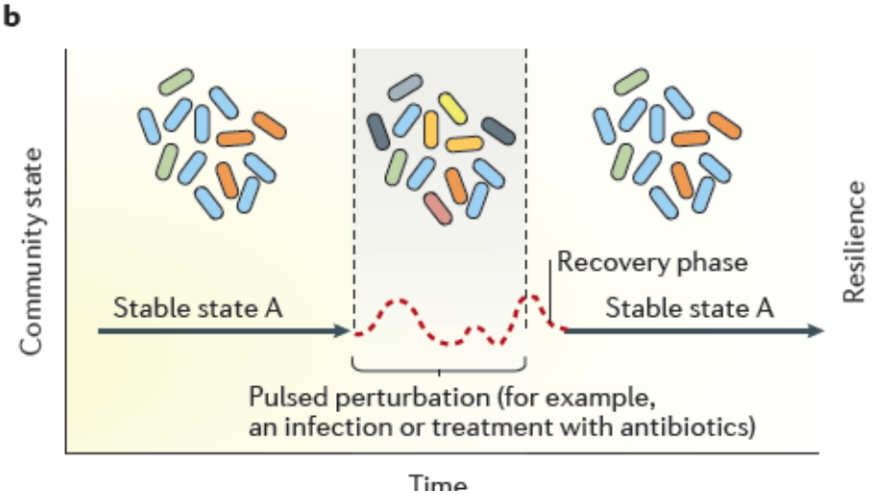
DYSBIOSIS

From EUBIOSIS to DYSBIOSIS

RESISTANCE: **a given ecosystem to stand unchanged in the face of a disturbance**



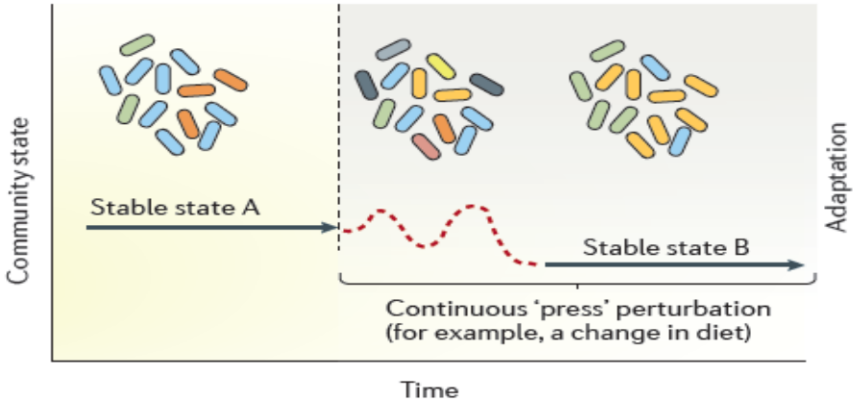
RESILIENCE: **amount of stress that a system can tolerate before its homeostatic state shifts towards a new equilibrium with different functions and services**



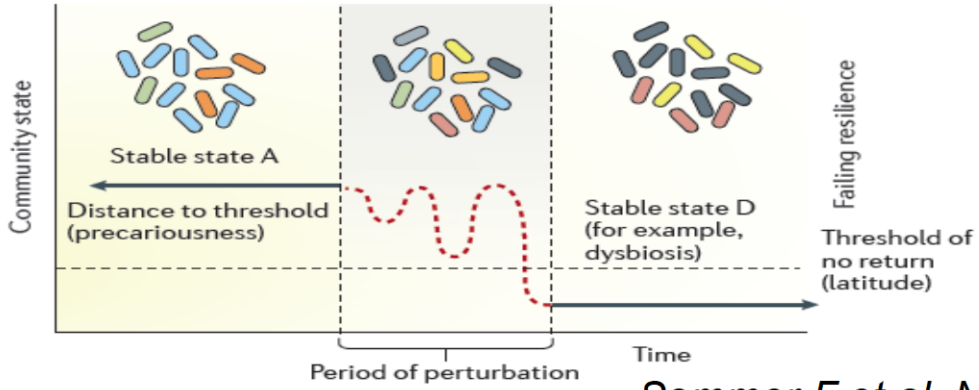
Sommer F et al.
Nat Rev Microbiol 2017

From EUBIOSIS to DYSBIOSIS

Facing a continuous perturbation, the composition of the microbiota may adopt a new beneficial or detrimental state: ADAPTATION



Acquisition of an unhealthy and dysbiotic microbiota with high resilience potential may contribute to chronicity of human microbiota-associated diseases



Sommer F et al. Nat Rev Microbiol 2017

nature microbiology

PERSPECTIVE

PUBLISHED: 24 AUGUST 2017 | VOLUME: 2 | ARTICLE NUMBER: 17121

Stress and stability: applying the Anna Karenina principle to animal microbiomes

Jesse R. Zaneveld[1]*, Ryan McMinds[2] and Rebecca Vega Thurber[2]*

- **“all happy families look alike; each unhappy family is unhappy in its own way”**
- **“Tutte le famiglie felici sono simili le une alle altre; ogni famiglia infelice è infelice a modo suo”**


АННА КАРЕНИНА

РОМАНЪ

ГРАФА

Л. Н. ТОЛСТАГО

ВЪ ВОСЬМИ ЧАСТЯХЪ

ТОМЪ ПЕРВЫЙ

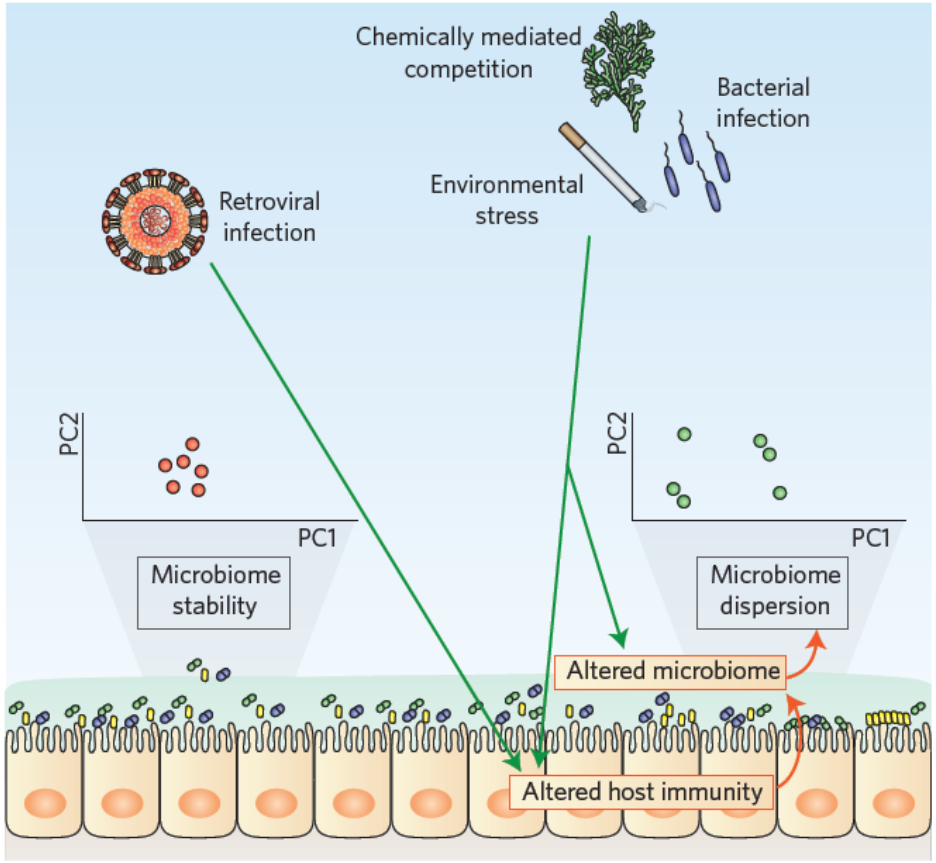
МОСКВА.

1878.

“all healthy microbiomes are similar; each dysbiotic microbiome is dysbiotic in its own way”

- Typically, healthy hosts possess relatively stable microbiomes that form tight clusters in ordination space.
- In contrast to movement of these clusters to a new place in ordination space a variety of external stressors have been shown to disrupt this stability, resulting in more dispersed microbiomes.
- More dispersed microbiomes have been associated with a variety of negative outcomes for the host, including increased invasibility and altered clinical parameters (for example, endotoxaemia in alcoholics).
- In principle, these disruptions may act indirectly by affecting host immunity (as in HIV and SIVcpz), indirectly by altering the microbiome (for example, by displacing protective mutualists like antibiotic producers), or through a combination of both mechanisms.

Anna Karenina principle of perturbations inducing microbiome destabilization



From: Zaneveld *et al*, Nat. Microbiol., 2017

MICROBIOTA ASSOCIATED DISEASES

- *Gatrointestinal, lung, genito-urinary tract infections*
- *Irritable Bowel Syndrome*
- *Inflammatory Bowel Disorders*
- *Diverticulosis*
- *Celiac disease and Malabsorption*
- *Food Intolerance/Allergy*
- *Gastrointestinal Cancers*
- *Liver diseases*
- *Pancreatic diseases*
- *Obesity, Diabetes and Metabolic Syndrome*
- *Nephrological, Gynecological, Urological, Oncological, Rheumatological/autoimmune, Cardiovascular, Neurological (Parkinson, Alzheimer, MS..), Psichiatric disorders (schizofrenia, anxiety/depression, autism..)*

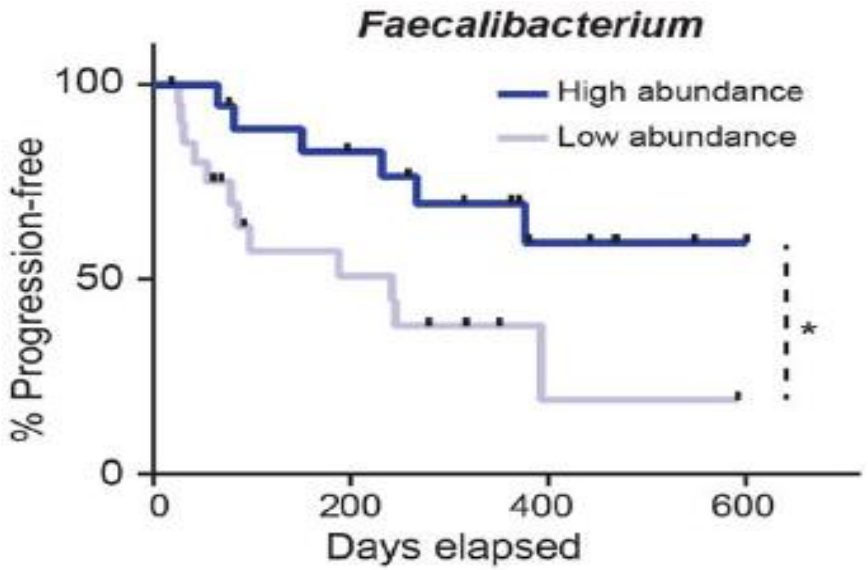
GI Cancers associated to DYSBIOSIS

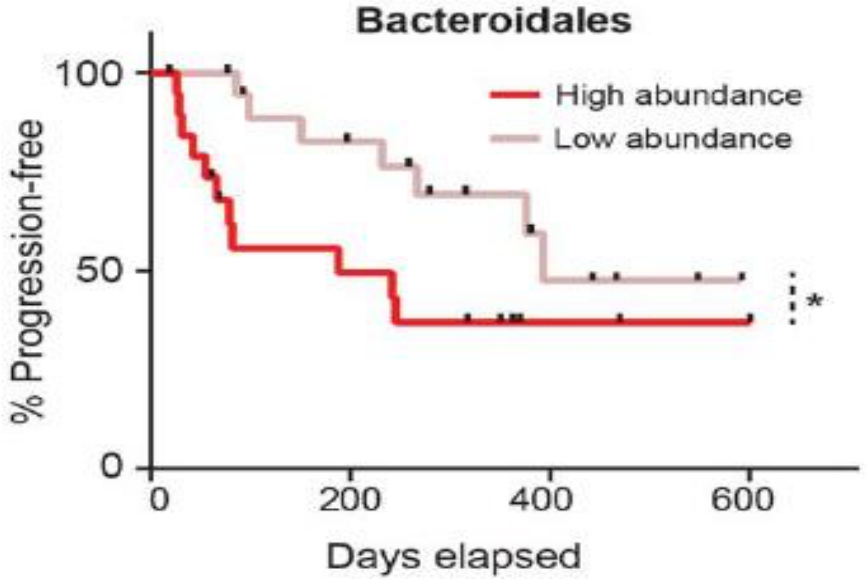
- ***Oral cavity***
- ***Esophagus***
- ***Stomach***
- ***Small Bowel***
- ***Colon***
- ***Liver***
- ***Bile trat***
- ***Pancreas***

METAGENOMIC ANALYSES PREDICTS PD-1 IMMUNOTHERAPY RESPONSE: 1

- ***Faecalibacterium*** **abundance correlate with longer Progression Free Survival**

- ***Bacteroidales*** **abundance correlate with shorter Progression Free Survival**





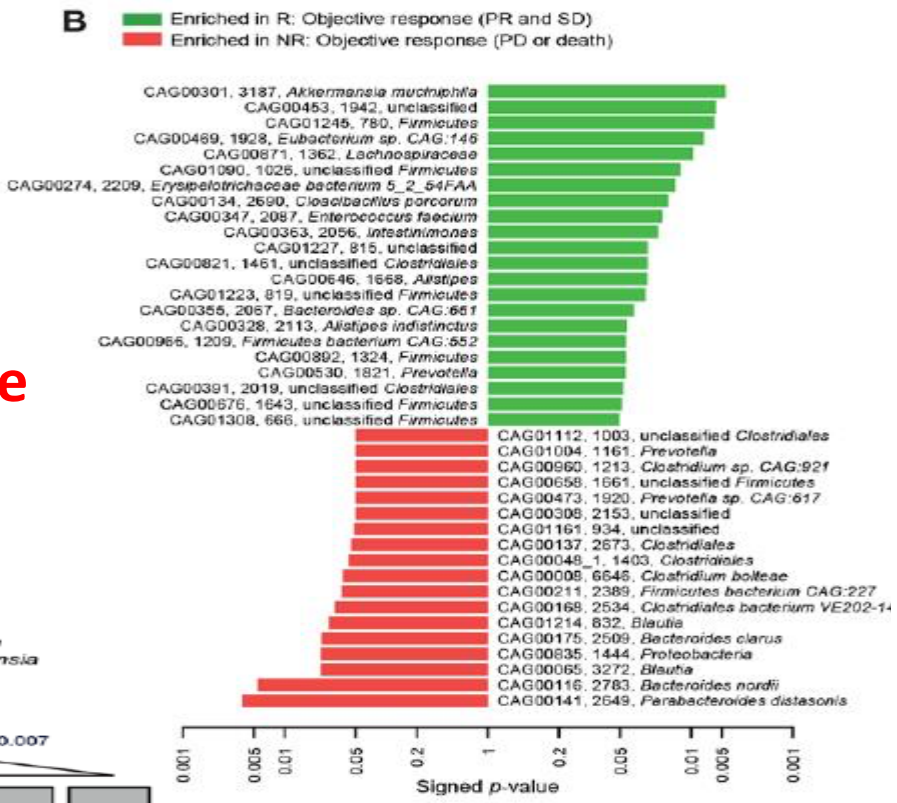
Gopalakrishnan, Science 2017

METAGENOMIC ANALYSES PREDICTS PD-1 IMMUNOTHERAPY RESPONSE: 2

Shot gun sequencing of fecal samples at diagnosis in PD-1 therapy:

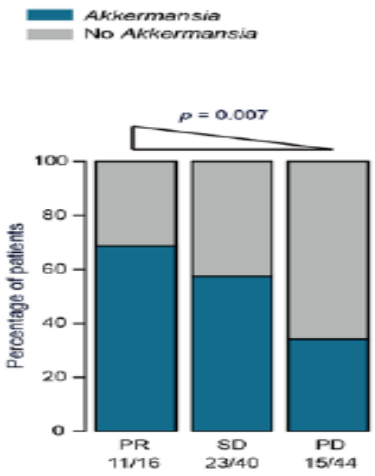
- **RESPONDER**
- **NON RESPONDER**

Akkermansia muciniphila abundance correlate with longer Progression Free Survival



Frequency of patients with detectable ***A. muciniphila*** in their feces according to:

- **PR**: partial response
- **SD**: stable disease
- **PD**: progressed or died



Routy, Science 2017

HOW WE CAN STUDY THE MICROBIOTA AND HOW WE CAN ANALYSE THE OBTAINED RESULTS?

Flores et al. Microbiome (2015) 3:33
DOI 10.1186/s40168-015-0092-7

Microbiome

METHODOLOGY Open Access

Collection media and delayed freezing effects on microbial composition of human stool

- The effect of collection media and delayed freezing up to 7 days on microbial composition were evaluated.
- Ten participants collected triplicate stool samples each into no media as well as RNAlater® with and without kanamycin or ciprofloxacin. For each set of conditions, triplicate samples were frozen on dry ice immediately (time = 0) or frozen at −80 ° C after 3-days and 7-days incubation at 25 ° C.
- Microbiota metrics were estimated from Illumina MiSeq sequences of 16S rRNA gene fragments (V3–V4 region). Intraclass correlation coefficients (ICC) across triplicates, collection media, and incubation time were estimated for taxonomy and alpha and beta diversity metrics.

Flores et al. Microbiome (2015) 3:33
DOI 10.1186/s40168-015-0092-7

Microbiome

METHODOLOGY Open Access

Collection media and delayed freezing effects on microbial composition of human stool

- Results showed that the bacterial community composition was stable for 7 days at room temperature in RNAlater® alone.
- RNAlater® provides some stability for beta diversity analyses, but analyses of rare taxa will be inaccurate if specimens are not frozen immediately.
- RNAlater® could be used as collection media with minimal change in the microbiota composition.

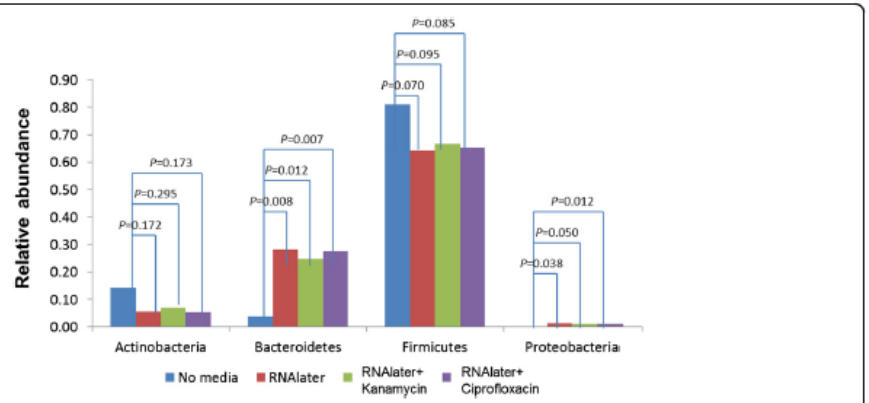


Fig. 1 Comparison of major phyla in fecal samples stored in different media at baseline

PLOS ONE

Storage up to 24 hours (at +4° C or room temperature) or freezing at -20° C did not significantly alter the fecal microbial community structure compared to direct freezing of samples from healthy subjects and patients with gastrointestinal disorders.

RESEARCH ARTICLE

The Effect of Sampling and Storage on the Fecal Microbiota Composition in Healthy and Diseased Subjects

Table 2. Effect of sampling and storage methods on alpha diversity metrics.

Diversity indices	Sampling & storage methods				
	-80°C (n = 28)	1w -20°C (n = 27)	24h RT (n = 28)	24h +4°C (n = 28)	48–72h FecalSwab (n = 18)
Observed species	540.1 (112.5–811.2)	545.5 (93.8–995.9)	549.2 (95.3–830.6)	529.1 (90.6–791.4)	593.9* (280.8–746.9)
Chao1	955.8 (206.0–1457.3)	935.2 (143.6–1780.6)	963.8 (180.1–1525.6)	936.36 (130.1–1440.3)	1042,62* (544.4–1308.4)
Shannon	7.0 (4.4–8.4)	6.9 (4.1–8.7)	7.0 (4.1–8.4)	6.9 (4.4–8.5)	7.4* (5.5–8.1)
PD whole tree	27.5 (8.6–37.3)	27.5 (6.8–46.0)	28.4 (7.8–37.7)	27.6 (7.0–37.2)	30.0* (14.5–37.3)

Median and range are shown in the table. (*p<0.05 compared to -80°C).

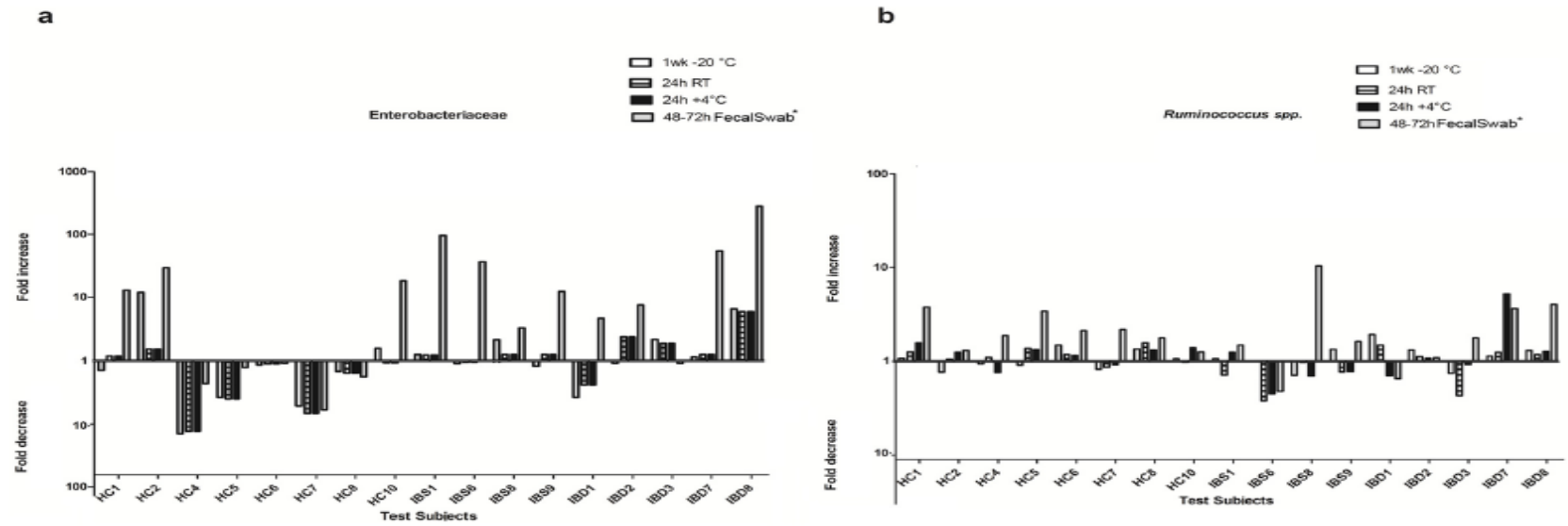


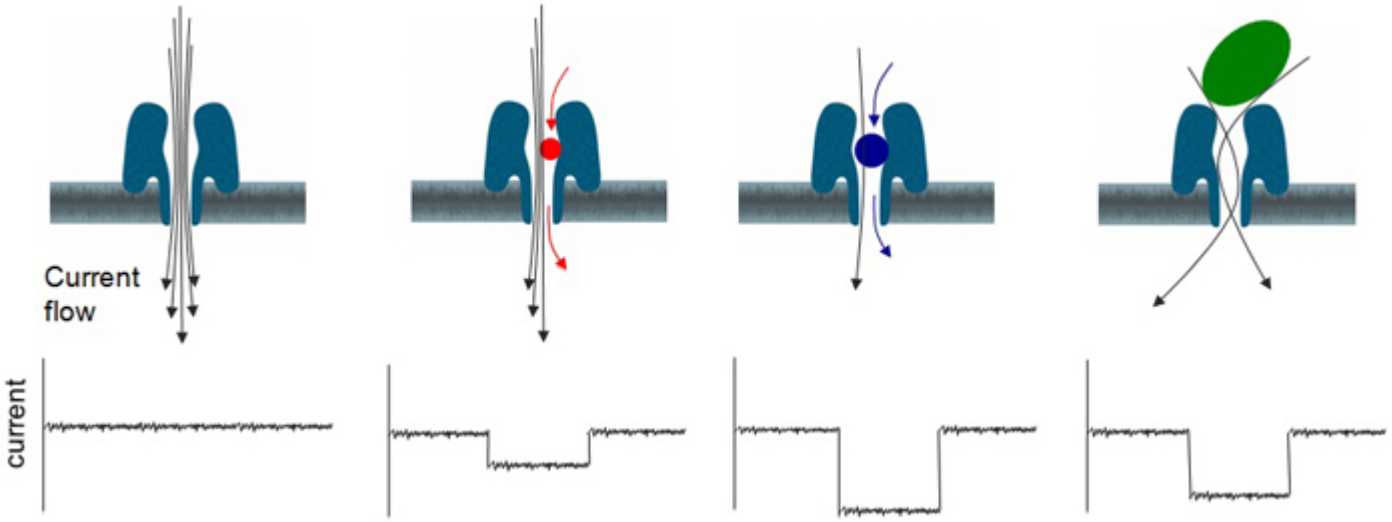
Fig 5. Fold change of relative abundance of Enterobacteriaceae (a) and *Ruminococcus spp.* (b) compared to -80°C. Only test subjects (17/28) with a complete set of samples (5 different sampling and storage methods) available are shown. Fold changes are shown at the y axis (logarithmic scale). * Relative abundance in FecalSwabs was significantly higher as compared to reference storage method (p<0.05 as determined by Wilcoxon signed rank test).

METAGENOMICS AND PYROSEQUNECING

- Molecular methods detected bacteria present at concentrations greater than approximately 10^6 and neglected minority populations.
- Among these neglected populations are potentially pathogenic bacteria such as *S. typhi*, *Yersinia enterocolitica*, and *Tropheryma whipplei*, which may be present in human stools at concentrations below 10^5 cfu per ml, the current threshold of the latest next-generation sequencing (NGS) method.
- The depth is directly correlated with the number of generated sequences, and no plateau was obtained in the number of phylotypes observed, although close to 1,000,000 16S rRNA gene amplicons have been sequenced by Turnbaugh *et al.* (2010).

High-throughput bacterial genome sequencing: an embarrassment of choice, a world of opportunity

Machine (manufacturer)	Chemistry	Modal read length* (bases)	Run time	Gb per run	Current, approximate cost (US$)‡	Advantages	Disadvantages
Bench-top instruments							
454 GS Junior (Roche)	Pyrosequencing	500	8 hours	0.035	100,000	• Long read lengths	• Appreciable hands-on time • High reagent costs • High error rate in homopolymers
Ion Personal Genome Machine (Life Technologies)	Proton detection	100 or 200	3 hours	0.01–0.1 (314 chip), 0.1–0.5 (316 chip) or up to 1 (318 chip)	80,000 (including OneTouch and server)	• Short run times • Appropriate throughput for microbial applications	• Appreciable hands-on time • High error rate in homopolymers
Ion Proton (Life Technologies)	Proton detection	Up to 200	2 hours	Up to 10 (Proton I chip) or up to 100 (Proton II chip)	145,000 +75,000 for compulsory server	• Short run times • Flexible chip reagents	• Instrument not available at time of writing
MiSeq (Illumina)	Reversible terminator	2×150	27 hours	1.5	125,000	• Cost-effectiveness • Short run times • Appropriate throughput for microbial applications • Minimal hands-on time	• Read lengths too short for efficient assembly



- This diagram shows a protein nanopore set in an electrically resistant membrane bilayer. An ionic current is passed through the nanopore by setting a voltage across this membrane.
- If an analyte passes through the pore or near its aperture, this event creates a characteristic disruption in current. Measurement of that current makes it possible to identify the molecule in question.
- For example, this system can be used to distinguish between the four standard DNA bases G, A, T and C.
- It can be used to identify target proteins and small molecules, or to gain rich molecular information, for example to distinguish between the enantiomers of ibuprofen or study molecular binding dynamics.

The MinION system: the future for deep sequencing?

- The MinION™ system is a disposable device that contains the sensor chip, Application-Specific Integrated Circuit (ASIC) and nanopores that are needed to perform a complete single-molecule sensing experiment.
- Plugging directly into a laptop or desktop computer through a USB port, it is a self-contained device to deliver real-time experimental data.
- The MinION device is adaptable for DNA sequencing, protein sensing and other nanopore sensing techniques.

Gut microbiome precision medicine

Moving to a Microbiota signature for any disease or pathological status?

Gut Online First, published on February 7, 2017 as 10.1136/gutjnl-2016-313235

OPEN ACCESS

ORIGINAL ARTICLE

A microbial signature for Crohn's disease

How might it impact on clinical practice in the foreseeable future?

- Considering CD and UC as two distinct subtypes of IBD at the microbiome level could help designing specific therapeutic targets.
- The microbial signature specific to CD combined with either imaging techniques or calprotectin data could help decision-making when the diagnosis is initially uncertain among CD, UC and IBS.

What are the new findings?

- Dysbiosis is greater in CD than in UC, with a lower microbial diversity, a more altered microbiome composition and a more unstable microbial community.
- Different microbial groups are associated with smoking habit and localisation of the disease in CD and UC.
- Eight groups of microorganisms including *Faecalibacterium*, an unknown Peptostreptococcaceae, *Anaerostipes*, *Methanobrevibacter*, an unknown Christensenellaceae, *Collinsella* and *Fusobacterium*, *Escherichia* could be used to discriminate CD from non-CD; the six first groups being in lower relative abundance and the last two groups in higher relative abundance in CD.

Gut Online First, published on February 7, 2017 as 10.1136/gutjnl-2016-313235

OPEN ACCESS

ORIGINAL ARTICLE

A microbial signature for Crohn's disease

Victoria Pascal,[1] Marta Pozuelo,[1] Natalia Borruel,[1,2] Francesc Casellas,[1,2] David Campos,[1] Alba Santiago,[1] Xavier Martinez,[1] Encarna Varela,[1] Guillaume Sarrabayrouse,[1] Kathleen Machiels,[3] Severine Vermeire,[3] Harry Sokol,[4] Francisco Guarner,[1,2] Chaysavanh Manichanh[1,2]

- We analysed a cohort of 2045 non-IBD and IBD faecal samples from four countries (Spain, Belgium, the UK and Germany), applied a 16S rRNA sequencing approach and analysed a total dataset of 115 million sequences.
- In the Spanish cohort, dysbiosis was found significantly greater in patients with CD than with UC, as shown by a more reduced diversity, a less stable microbial community and eight microbial groups were proposed as a specific microbial signature for CD.
- Tested against the whole cohort, the signature achieved an overall sensitivity of 80% and a specificity of 94%, 94%, 89% and 91% for the detection of CD versus healthy controls, patients with anorexia, IBS and UC, respectively.
- Although UC and CD share many epidemiologic, immunologic, therapeutic and clinical features, these results showed that they are two distinct subtypes of IBD at the microbiome level.
- For the first time, microbiomarkers were proposed to discriminate between CD and non-CD independently of geographical regions.

Gut Online First, published on February 7, 2017 as 10.1136/gutjnl-2016-313235

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ORIGINAL ARTICLE

A microbial signature for Crohn's disease

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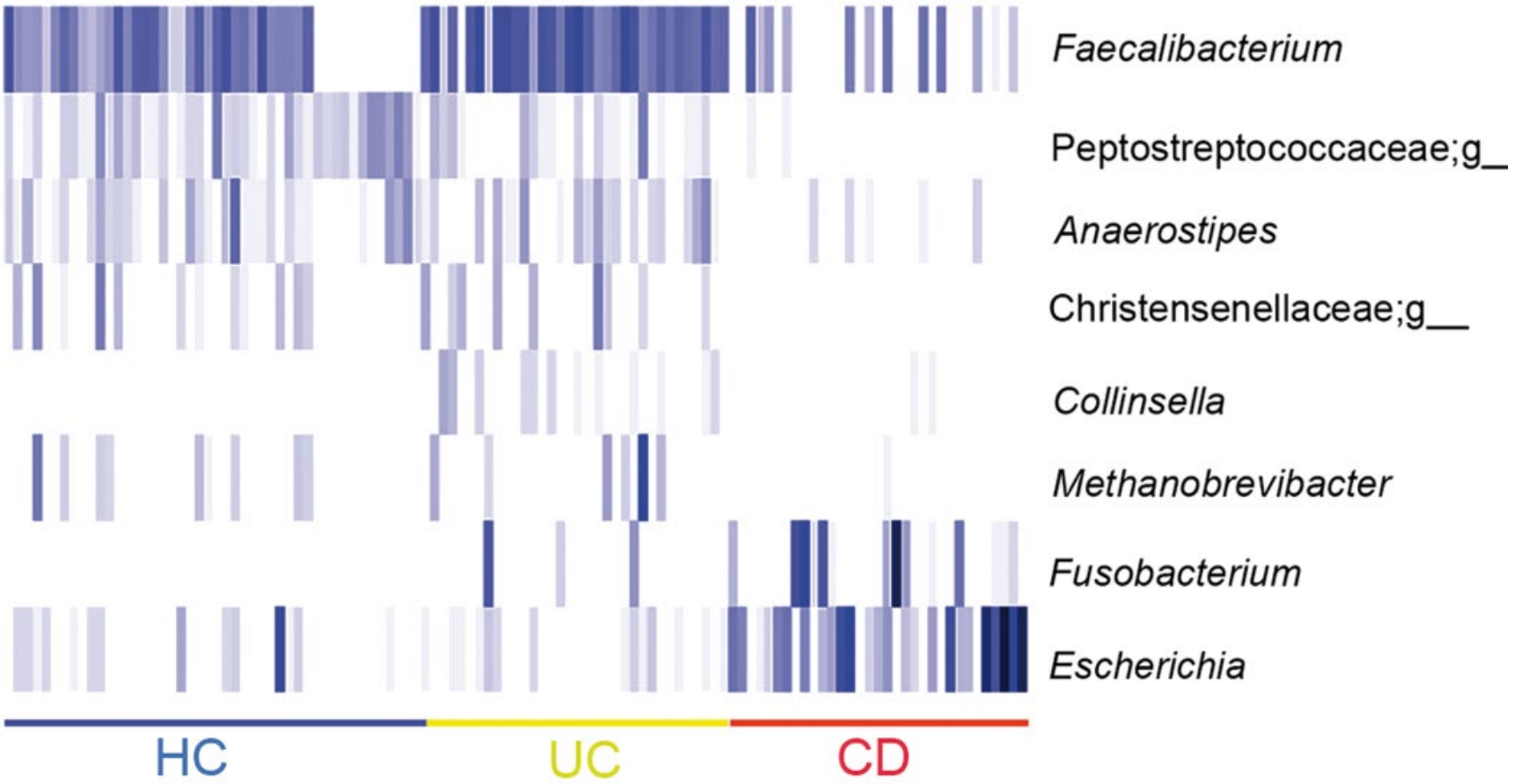
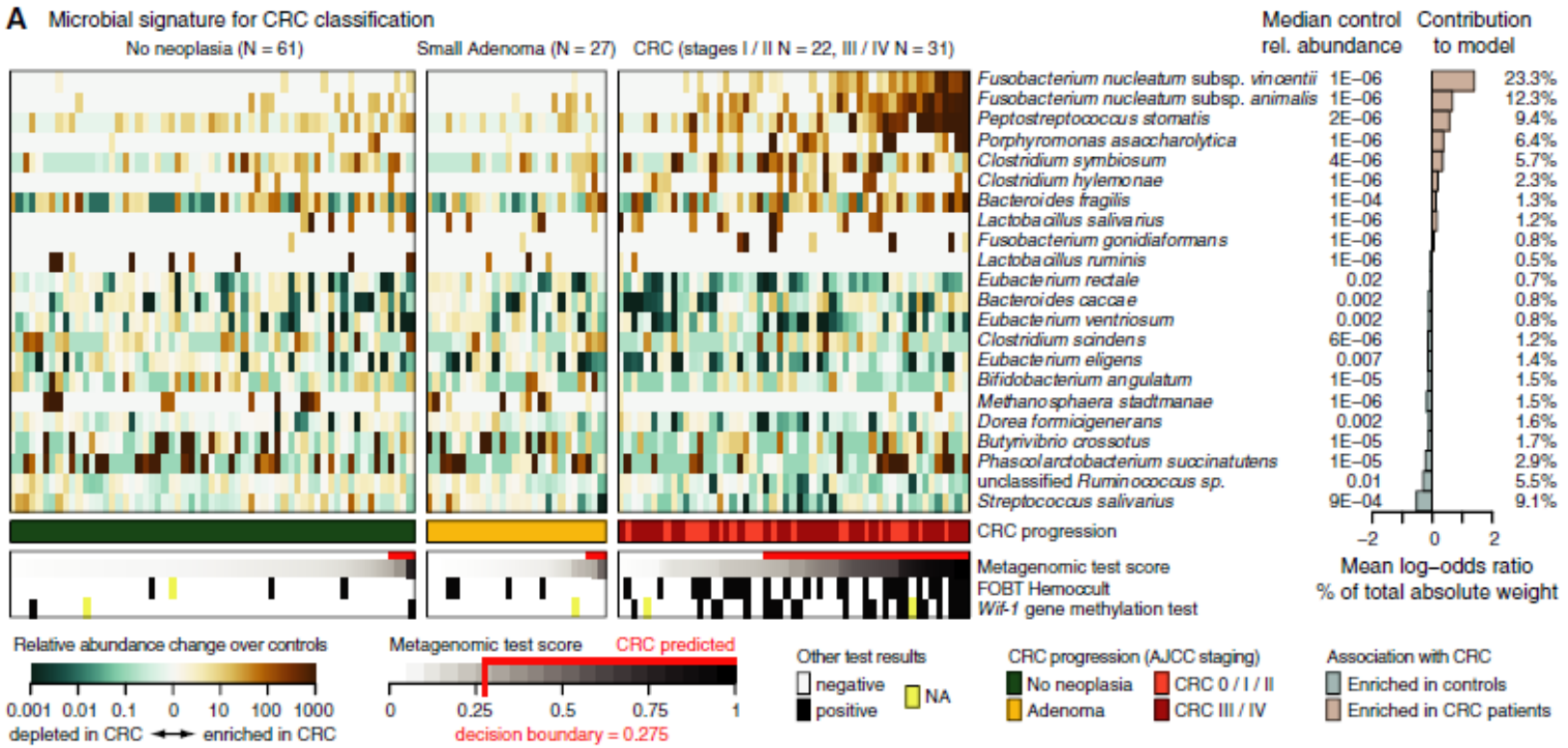


Published online: November 28, 2014

Article

molecular systems biology

Potential of fecal microbiota for early-stage



Signature of CRC-associated gut microbial species. Relative abundances of 22 gut microbial species, collectively associated with CRC, are displayed as heatmap in the left panel as fold change over the median relative abundance observed in controls (indicated to the right); the control group included neoplasia-free and small adenoma patients. Below, the classification score of the microbial signature (from cross-validation) is shown as gray scale (see key) with the decision boundary and resulting false positives and true positives indicated in red (using colonoscopy results as a ground truth). Displayed alongside are the results of the standard Hemoccult FOBT routinely applied for CRC screening and an experimental CRC screening test based on methylation of the wif-1 gene, a Wnt pathway member.

Gut Online First, published on October 24, 2016 as 10.1136/gutjnl-2016-312766

OPEN ACCESS

ORIGINAL ARTICLE

Quantitation of faecal *Fusobacterium* improves faecal immunochemical test in detecting advanced colorectal neoplasia

Table 2 Diagnostic performance of faecal immunochemical test (FIT), marker *Fusobacterium nucleatum (Fn)* and the combined test for colorectal cancer (CRC) and advanced adenoma

Marker/AUC	Discovery cohort	Validation cohort	All samples
CRC model			
FIT	0.86 (0.81–0.90)	0.85 (0.76–0.94)	0.85 (0.81–0.89)
Fn	0.83 (0.78–0.89)	0.89 (0.80–0.98)	0.85 (0.80–0.90)
FIT+*Fn*	0.95 (0.92–0.98)	0.96 (0.92–0.99)	0.95 (0.92–0.98)
(FIT+*Fn*) vs FIT	p<0.001	p=0.0014	p<0.001
Advanced adenoma model			
FIT	0.57 (0.53–0.61)	0.56 (0.51–0.61)	0.56 (0.53–0.59)
Fn	0.59 (0.51–0.67)	0.58 (0.49–0.67)	0.59 (0.53–0.65)
FIT+*Fn*	0.65 (0.58–0.73)	0.63 (0.55–0.72)	0.65 (0.59–0.70)
(FIT+*Fn*) vs FIT	p=0.007	p=0.031	p<0.001

The AUC values of the discovery cohort, the validation cohort and the combined cohort were shown, fitting the logistic regression model from the discovery cohort. The one-sided Delong's test was used to test for incremental gain in AUC for the combined test over FIT.
AUC, area under the receiver-operating characteristic curve.

How might it impact on clinical practice in the foreseeable future?

- Our study identifies faecal quantification of *Fusobacterium* to improve the diagnostic performance of FIT, and might have an impact on the diagnosis of colorectal neoplasia. This simple approach will enhance clinical applicability and utility of this finding. Our study takes one step further towards a non-invasive, potentially more accurate and affordable diagnosis of advanced colorectal neoplasia.

What are the new findings?

- *Fusobacterium* is significantly increased in patients with CRC and advanced adenoma. Faecal quantification of *Fusobacterium* can serve as a biomarker to differentiate patients with CRC and advanced adenoma from controls.
- Combining FIT with this marker significantly increases its detection rates for CRC with a sensitivity of 92.3% and a specificity of 93.0%, and for advanced adenoma with a sensitivity of 38.6% and a specificity of 89.0%. The combined test salvages more than 75% of the CRC samples missed by stand-alone FIT.
- Further addition of two microbial markers does not improve the diagnostic performance. *Fusobacterium* quantification is key in supplementing FIT in diagnosing advanced colorectal neoplasia.

JAMA Oncol. 2017 Jan 26. doi: 10.1001/jamaoncol.2016.6374.

Association of Dietary Patterns With Risk of Colorectal Cancer Subtypes Classified by *Fusobacterium Nucleatum* in Tumor Tissue

Question Does the association between prudent diets (rich in whole grains and dietary fiber) and risk of colorectal cancer vary by presence of the bacterial species *Fusobacterium nucleatum* in tumor tissue?

Findings In this cohort study of 137 217 adults, the association of a prudent diet with colorectal cancer was more evident for a cancer subgroup enriched with tumor *F nucleatum* than a subgroup without detectable tumor *F nucleatum*.

Meaning There may be a potential role for intestinal microbiota, such as *F nucleatum*, in mediating the complex association between diet and the development of colorectal cancer.

Importance *Fusobacterium nucleatum* appears to play a role in colorectal carcinogenesis through suppression of the hosts' immune response to tumor. Evidence also suggests that diet influences intestinal *F nucleatum.* However, the role of *F nucleatum* in mediating the relationship between diet and the risk of colorectal cancer is unknown.

Objective To test the hypothesis that the associations of prudent diets (rich in whole grains and dietary fiber) and Western diets (rich in red and processed meat, refined grains, and desserts) with colorectal cancer risk may differ according to the presence of *F nucleatum* in tumor tissue.

JAMA Oncol. 2017 Jan 26. doi: 10.1001/jamaoncol.2016.6374.

Association of Dietary Patterns With Risk of Colorectal Cancer Subtypes Classified by Fusobacterium Nucleatum in Tumor Tissue

Results Of the 173 229 individuals considered for the study, 137 217 were included in the analysis, 47 449 were male (34.6%), and mean (SD) baseline age for men was 54.0 (9.8) years and for women, 46.3 (7.2) years. A total of 1019 incident colon and rectal cancer cases with available *F nucleatum* data were documented over 26 to 32 years of follow-up, encompassing 3 643 562 person-years. The association of prudent diet with colorectal cancer significantly differed by tissue *F nucleatum* status (*P* = .01 for heterogeneity); prudent diet score was associated with a lower risk of *F nucleatum*–positive cancers (*P* = .003 for trend; multivariable hazard ratio of 0.43; 95% CI, 0.25-0.72, for the highest vs the lowest prudent score quartile) but not with *F nucleatum*–negative cancers (*P* = .47 for trend, the corresponding multivariable hazard ratio of 0.95; 95% CI, 0.77-1.17). There was no significant heterogeneity between the subgroups in relation to Western dietary pattern scores.

Conclusions and Relevance Prudent diets rich in whole grains and dietary fiber are associated with a lower risk for *F nucleatum*–positive colorectal cancer but not *F nucleatum*–negative cancer, supporting a potential role for intestinal microbiota in mediating the association between diet and colorectal neoplasms.

Alterations of the human gut microbiome in liver cirrhosis

Nan Qin[1,2]*, Fengling Yang[1]*, Ang Li[1]*, Edi Prifti[3]*, Yanfei Chen[1]*, Li Shao[1,2]*, Jing Guo[1], Emmanuelle Le Chatelier[3], Jian Yao[1,2],

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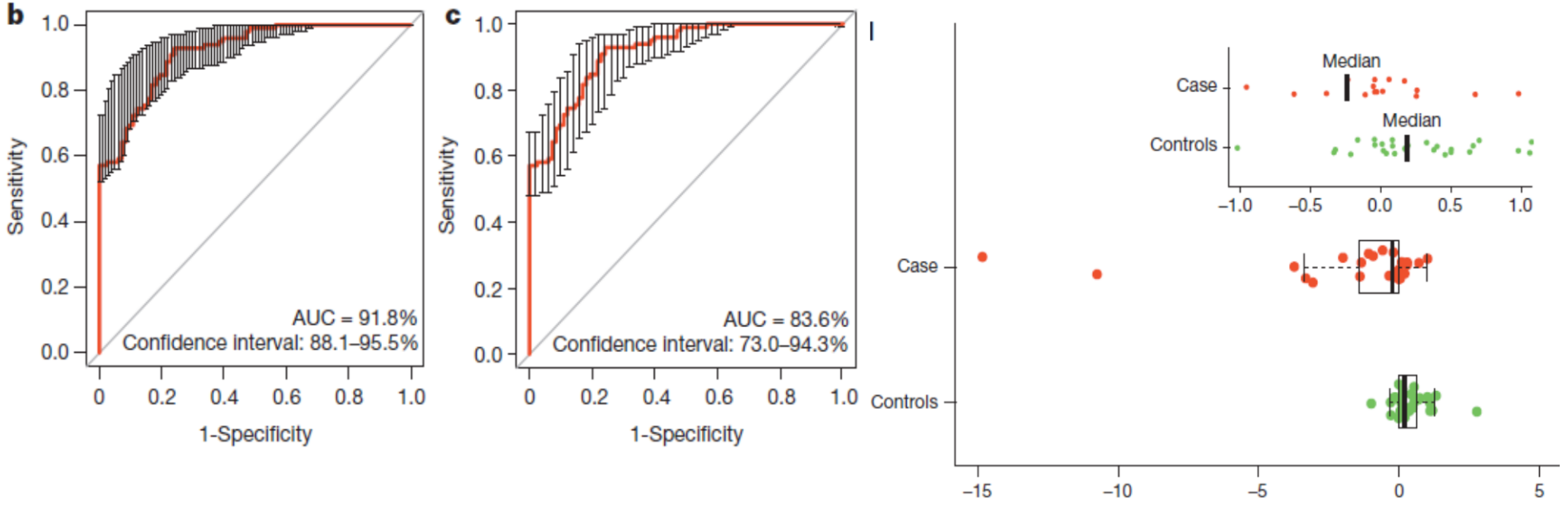
MICROBIOTA SIGNATURE OF CIRRHOSIS:

a combination of 15 microbial genes discriminates patients with liver cirrhosis from healthy individuals, with a high specificity



HEPATOLOGY

HEPATOLOGY, VOL. 00, NO. 00, 2018

Hepatocellular Carcinoma Is Associated With Gut Microbiota Profile and Inflammation in Nonalcoholic Fatty Liver Disease

Francesca Romana Ponziani,[1] Sherrie Bhoori,[2] Chiara Castelli,[3] Lorenza Putignani,[4,5] Licia Rivoltini,[3] Federica Del Chierico,[4] Maurizio Sanguinetti,[6] Daniele Morelli,[7] Francesco Paroni Sterbini,[6] Valentina Petito,[1] Sofia Reddel,[4] Riccardo Calvani,[8] Chiara Camisaschi,[3] Anna Picca,[8] Alessandra Tuccitto,[3] Antonio Gasbarrini,[1] Maurizio Pompili,[1*] and Vincenzo Mazzaferro[2*]

- The fecal microbiota of the group of patients with cirrhosis showed higher abundance of *Enterobacteriaceae* and *Streptococcus* and a reduction in *Akkermansia*.
- *Bacteroides* and *Ruminococcaceae* were increased in the HCC group, while *Bifidobacterium* was reduced.
- The results suggest that in patients with cirrhosis and NAFLD the gut microbiota profile and systemic inflammation are significantly correlated and can concur in the process of hepatocarcinogenesis.

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LEfSe analysis between patients with cirrhosis with HCC (group 1) and patients with cirrhosis without HCC (group 2). Cladogram displays the taxonomic tree of differentially abundant taxa. Histogram represents the LDA scores of bacteria with significant differential abundance between the compared groups, identified by different colors. *Features with LDA score >4.

How to modulate Gut Microbiota?

Diet and Nutritional Support

Diet composition (meat, cheese, fibers, high glicemic index, saturated fatty acids, ethanol, sweeteners…)
Caloric amount, minerals, vitamins..

Removal of predisposing conditions

Treat diabetes, endocrine, other motility disorders..
Surgery or prokinetics when indicated
Stop PPI or other antiacid, NSAIDs, antibiotic, immunosoppressant, antidepressant….

Intervention

Biotherapy (prebiotics, probiotis, symbiotics, postbiotics)

Antibiotics

Fecal Microbial Transplantation

Evidence for different FMT indications in 2018

	Metanalyses	RCTs	Open label trials	Case series/reports	Efficacy data
C. difficile infection	+++	+++	++++	++++	Outstanding
Ulcerative colitis	+	+	++	+++	Promising
Hepatic encefalopathy		+		+	Quite promising
Metabolic syndrome		+		+	Quite promising
Crohn's disease			+	+	Poor
IBS		+	+	+	Poor
Multi-resistant infections			+	+	Poor
Autism			+	+	Poor
GVHD				+	Poor

NEXT GENERATION FMT
Multi-drug resistant pathogens

Successful case series/case reports on:

- Methicillin-resistant Staphylococcus aureus (MRSA) Enterocolitis
- Vancomycin-resistant Enterococcus (VRE)
- K. pneumoniae MBL(+)
- Escherichia coli ESBL(+)

Wei et al – BMC Infect Dis 2015
Stripling et al – Open Forum Infect Dis 2015
Bilinsky et al- Arch Immunol Ther Exp 2016

One open-label trial:

- 20 participants, median of 2 strains of ARB
- FMT by nasoduodenal tube
- Complete ARB decolonization in 15 of 20 patients (75%)
- No severe adverse events

Bilinsky et al – Clin Infect Dis 2017

Conclusions

- Human microbioma study is one of the most intriguing and exciting research topics of the last years
- In the near future the association of specific microbioma types with specific disease will permit to make treatment able to restore the “good microbioma” modified by therapeutic approaches
- The challenge for Clinical Microbiology will be to set up and validate sensitive, specific, and cheap diagnostic tests that could be used in the diagnostic routine

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