Università degli Studi di Napoli Federico II
Dipartimento di Agraria
27° Workshop on the Developments in the Italian PhD Research on Food Science, Technology and Biotechnology
Portici, 13/15 September
GSICA Gruppo Scientifico Italiano di Confezionamento Alimentare
SISS Società Italiana di Scienze Sensoriali
SIMTREA Società Italiana di Microbiologia Agraria, Alimentare e Ambientale
SISTAL Società Italiana di Scienze e Tecnologie Alimentari

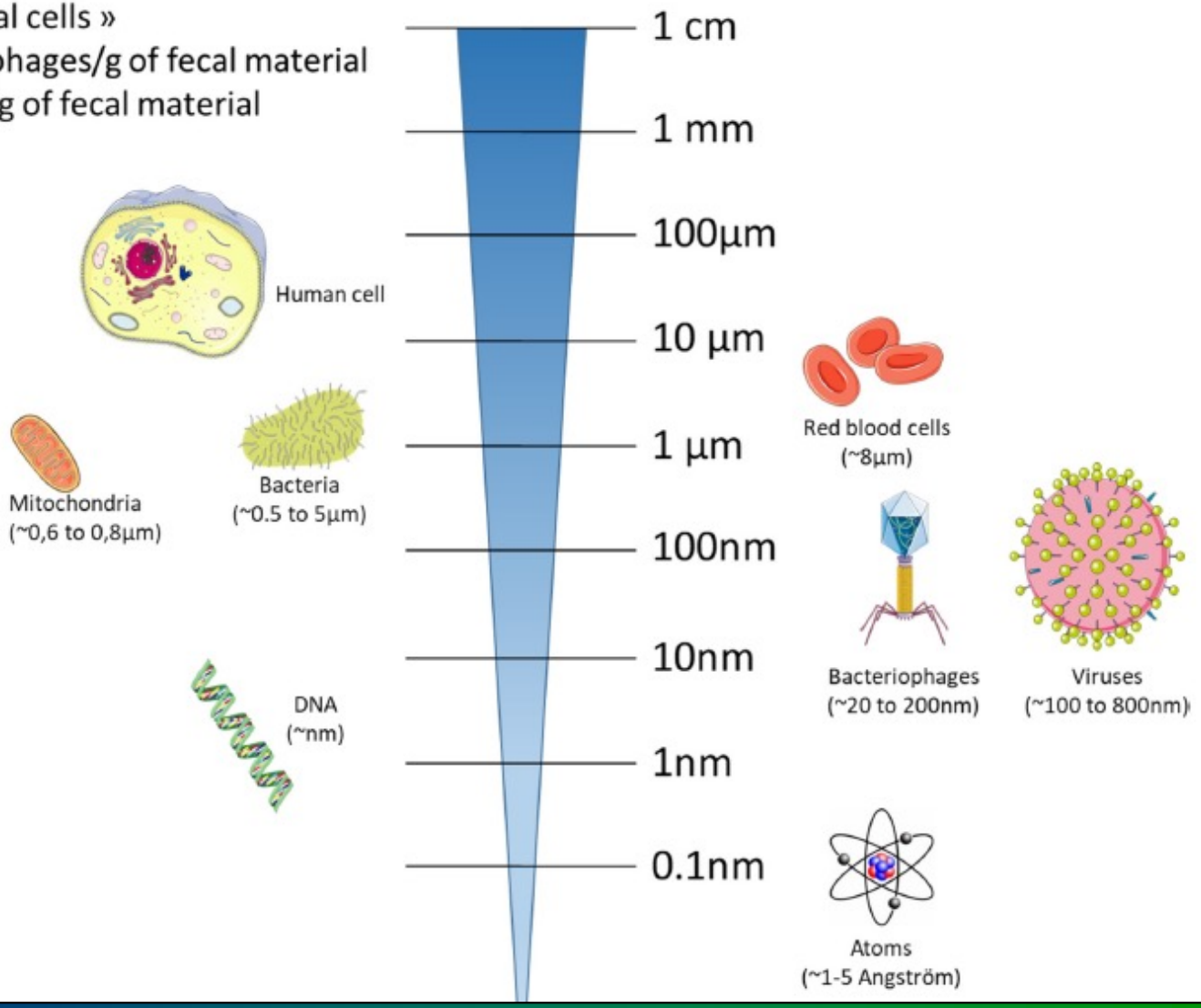
Functional foods and human gut microbiota

Prof.ssa De Angelis Maria

Relative sizes of major host cells and their components versus those of bacteria and viruses

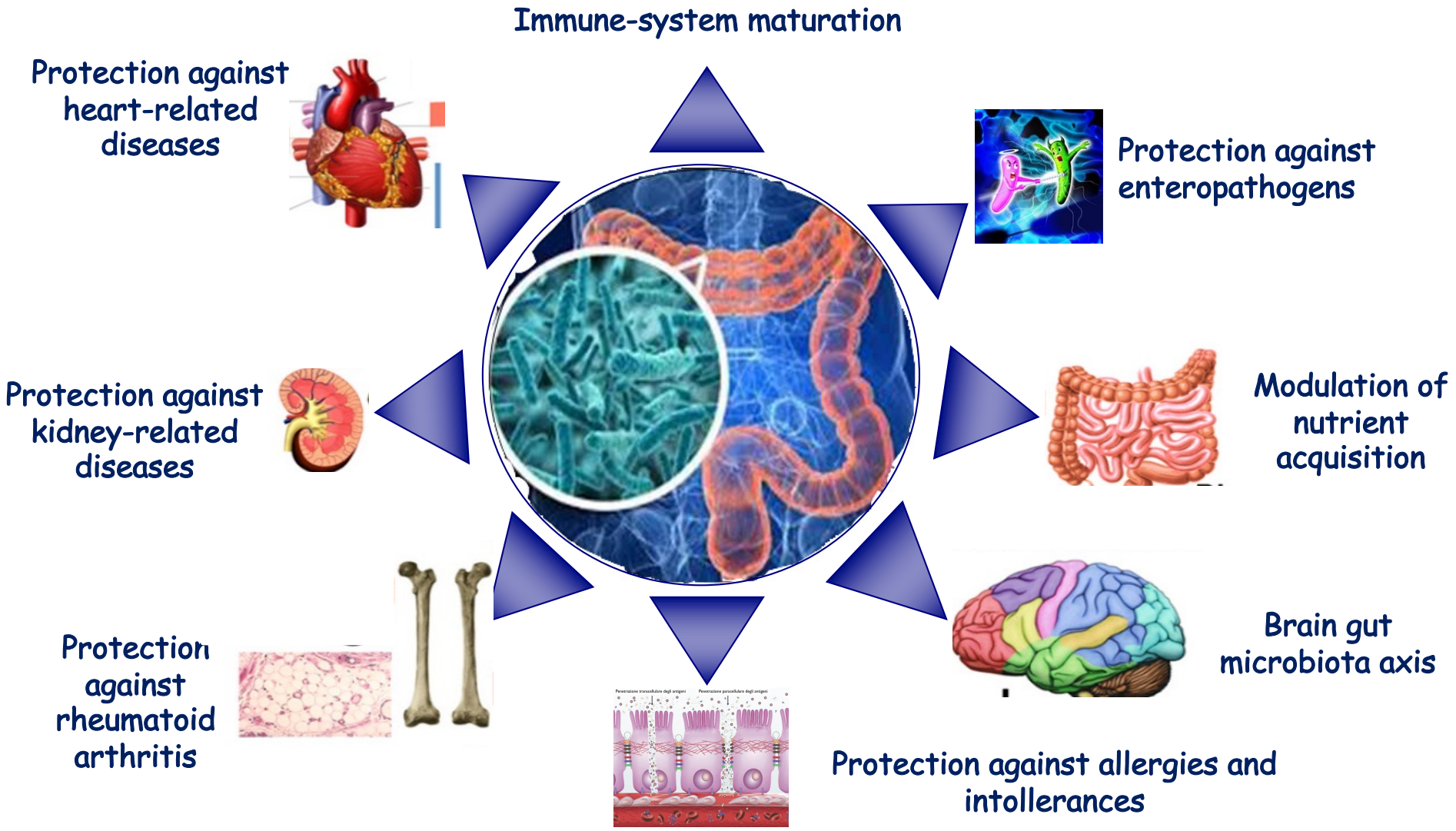
In the human body:

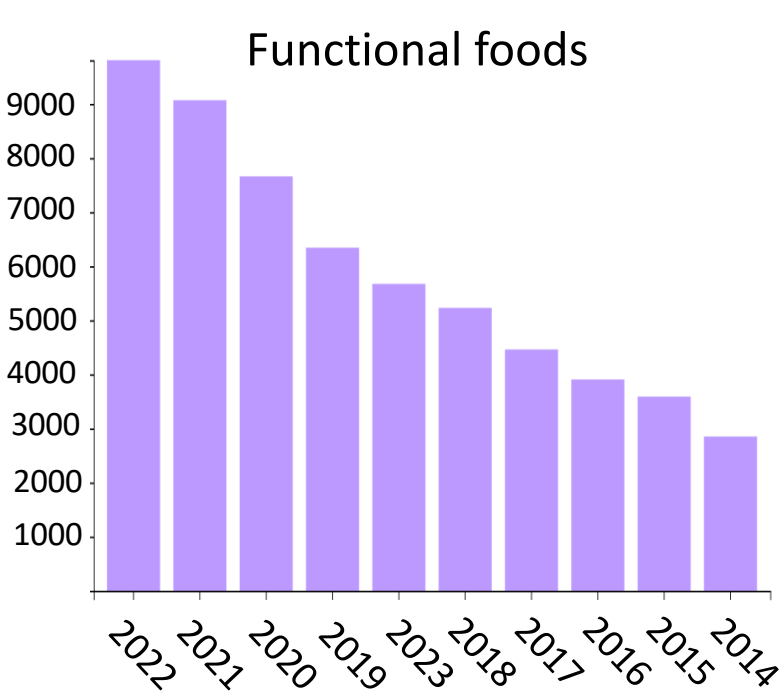
10^{13} « human cells »
10^{14} « microbial cells »
10^{12} bacteriophages/g of fecal material
10^{11} bacteria/g of fecal material

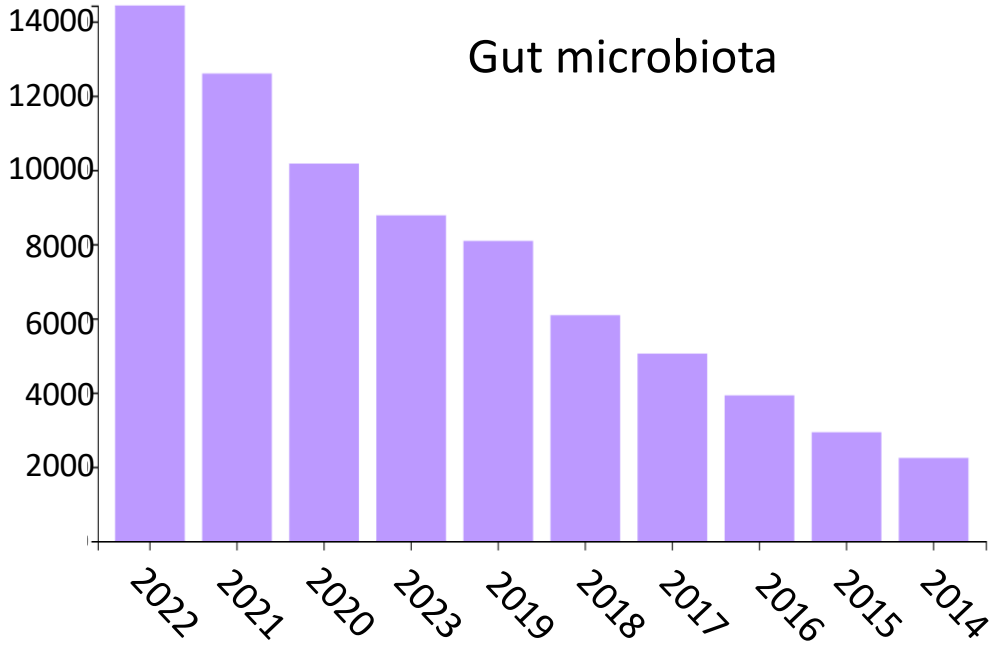


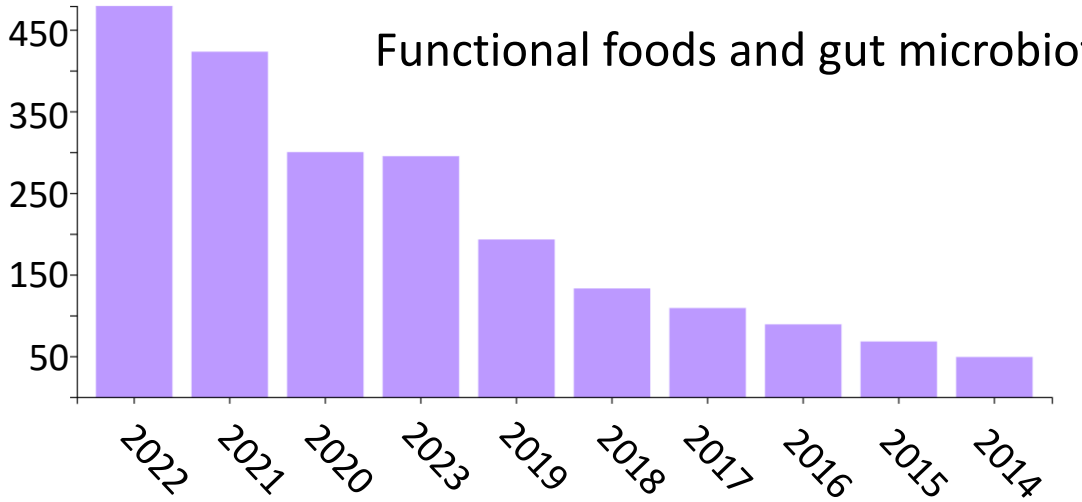
Gut microbiota and functions

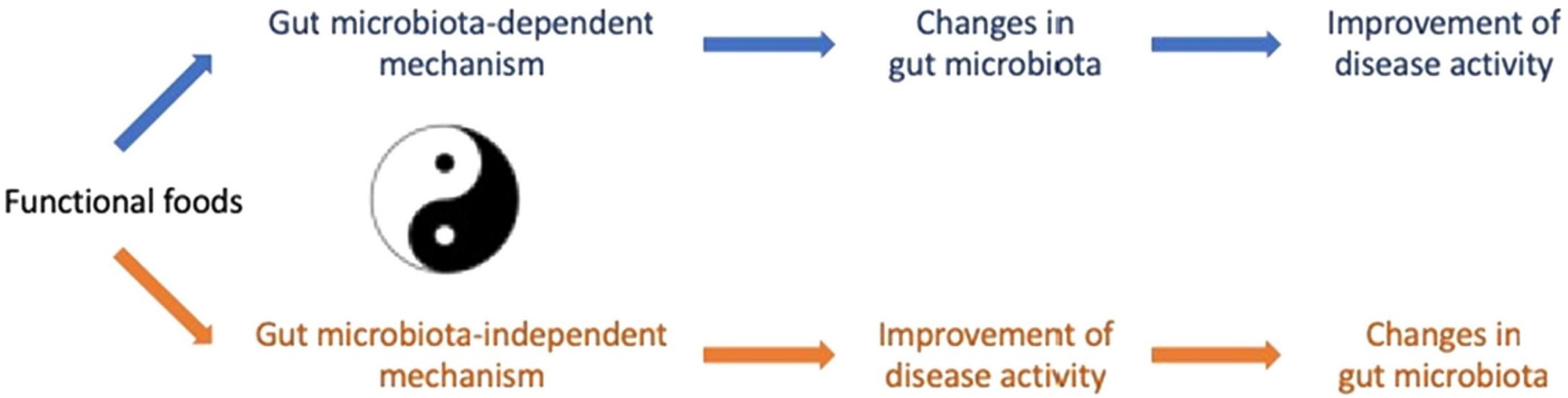
(Kelder *et al.*, 2014. *Nutrition & Diabetes*, 4:e122; Jeffery and O'Tool, 2013. *Nutrients*, 5:234-252)

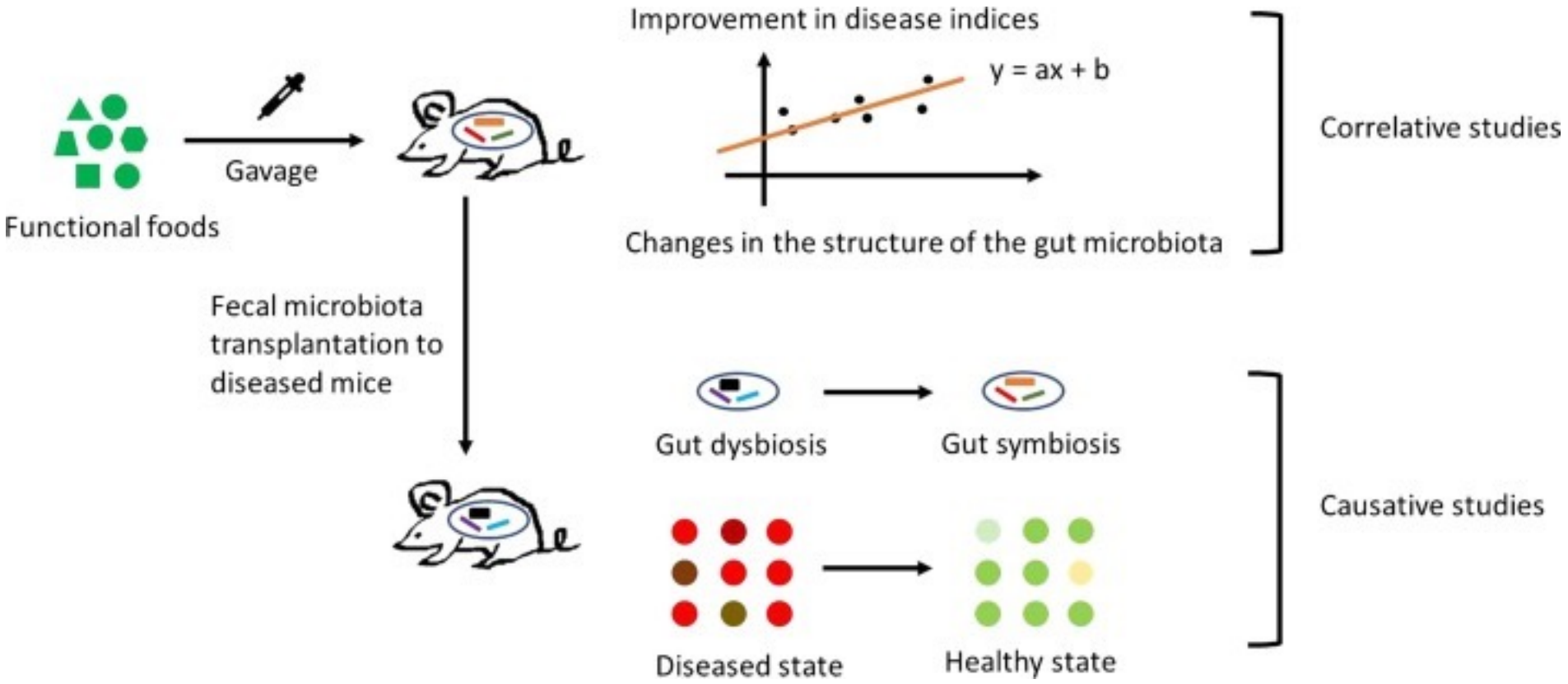



Functional foods
9000
8000
7000
6000
5000
4000
3000
2000
1000
2022
2021
2020
2019
2023
2018
2017
2016
2015
2014

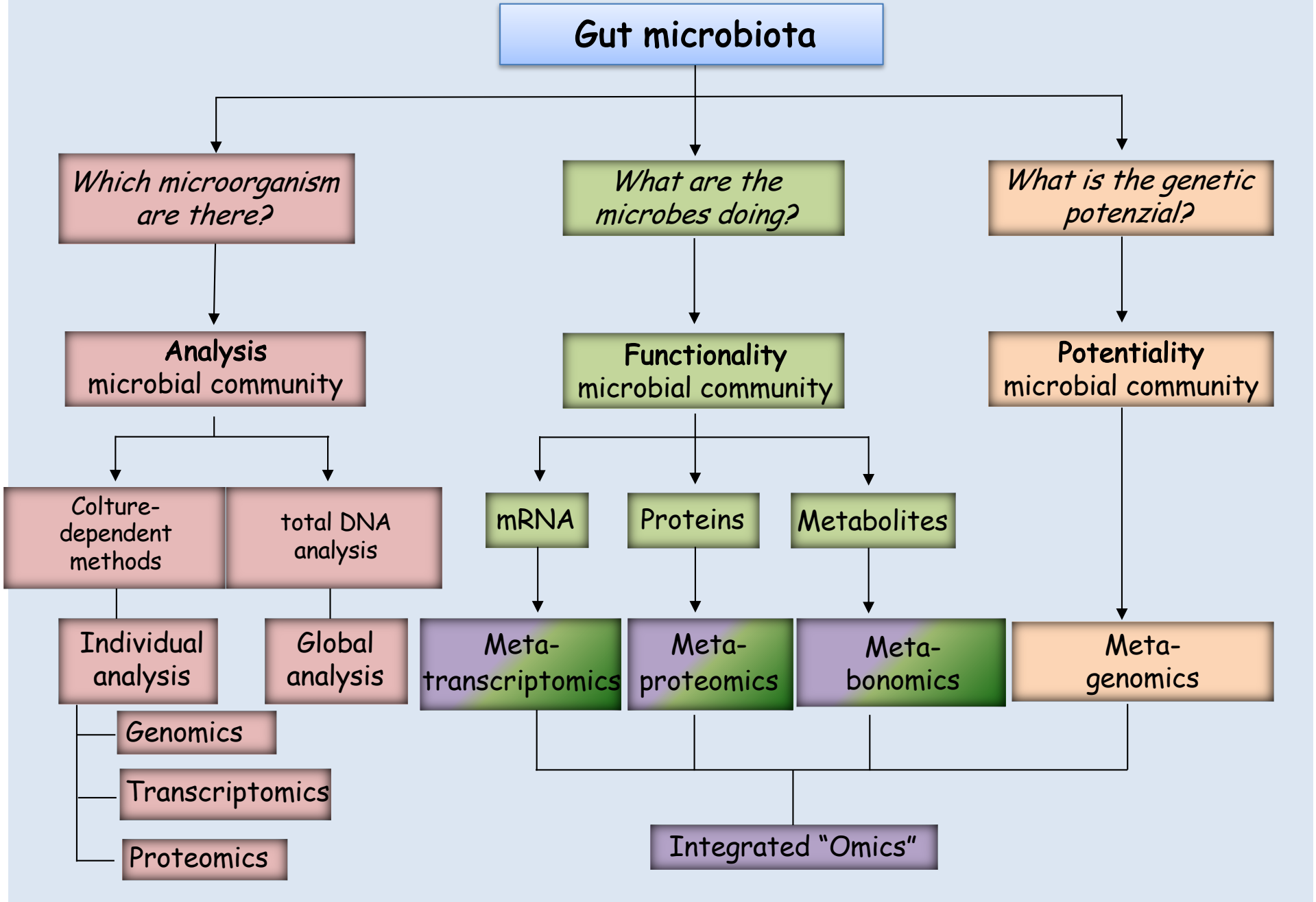

Gut microbiota
14000
12000
10000
8000
6000
4000
2000
2022
2021
2020
2023
2019
2018
2017
2016
2015
2014


Functional foods and gut microbiota
450
350
250
150
50
2022
2021
2020
2023
2019
2018
2017
2016
2015
2014

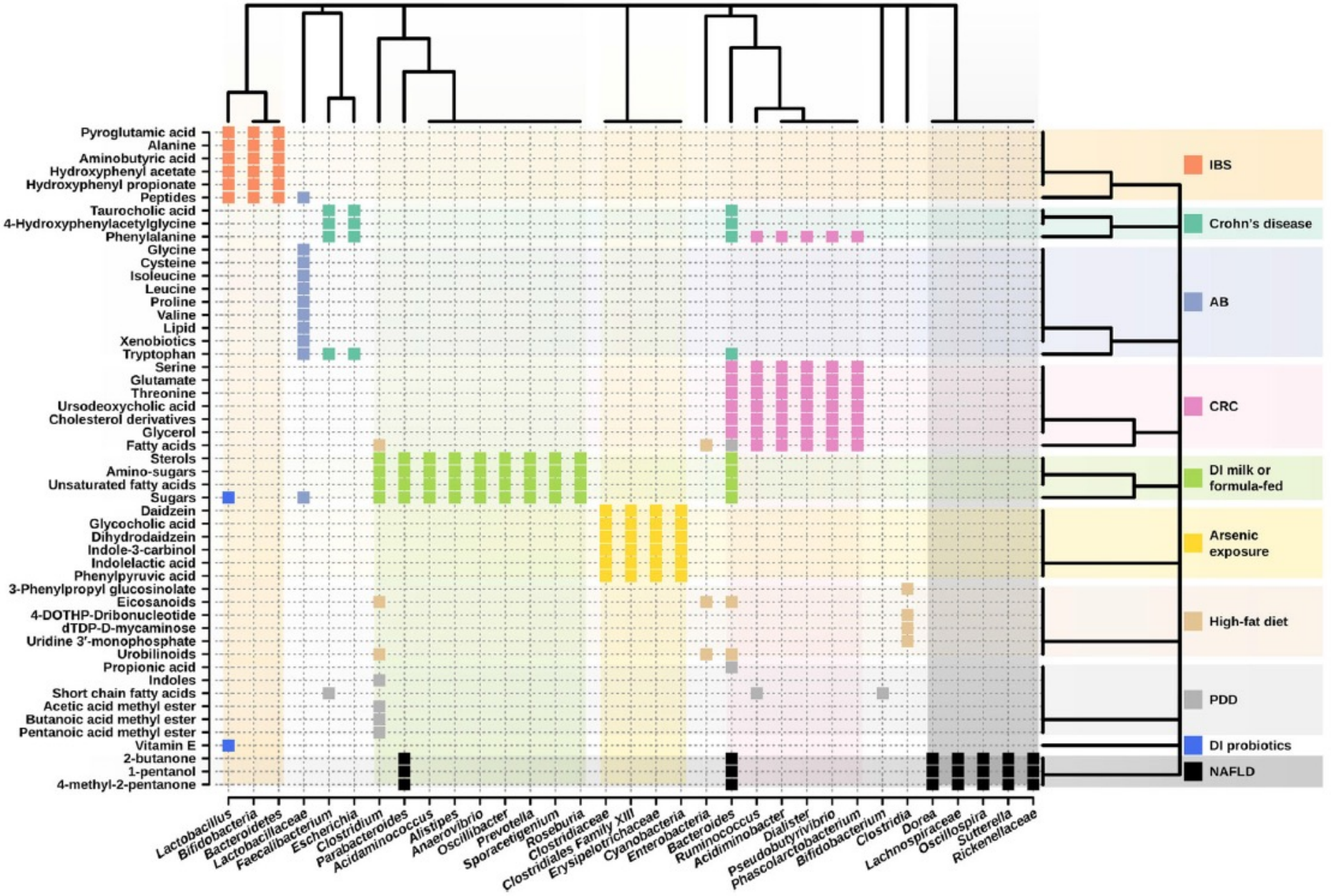

Functional foods
Gut microbiota-dependent mechanism
Changes in gut microbiota
Improvement of disease activity
Gut microbiota-independent mechanism
Improvement of disease activity
Changes in gut microbiota


Improvement in disease indices
y = ax + b
Changes in the structure of the gut microbiota
Correlative studies
Functional foods
Gavage
Fecal microbiota transplantation to diseased mice
Gut dysbiosis
Gut symbiosis
Diseased state
Healthy state
Causative studies

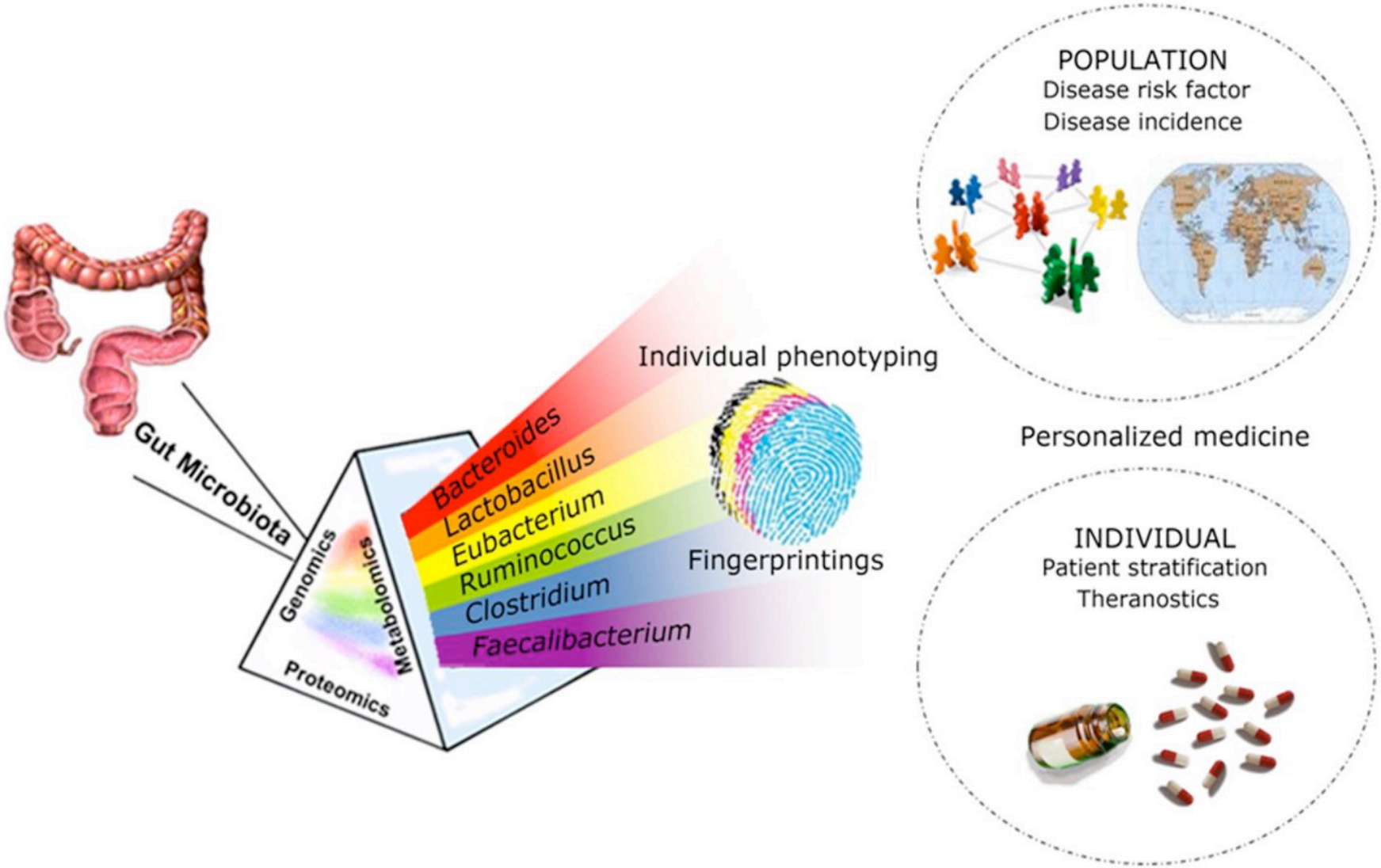
Evaluating the food and gut microbiome through meta-omics approaches



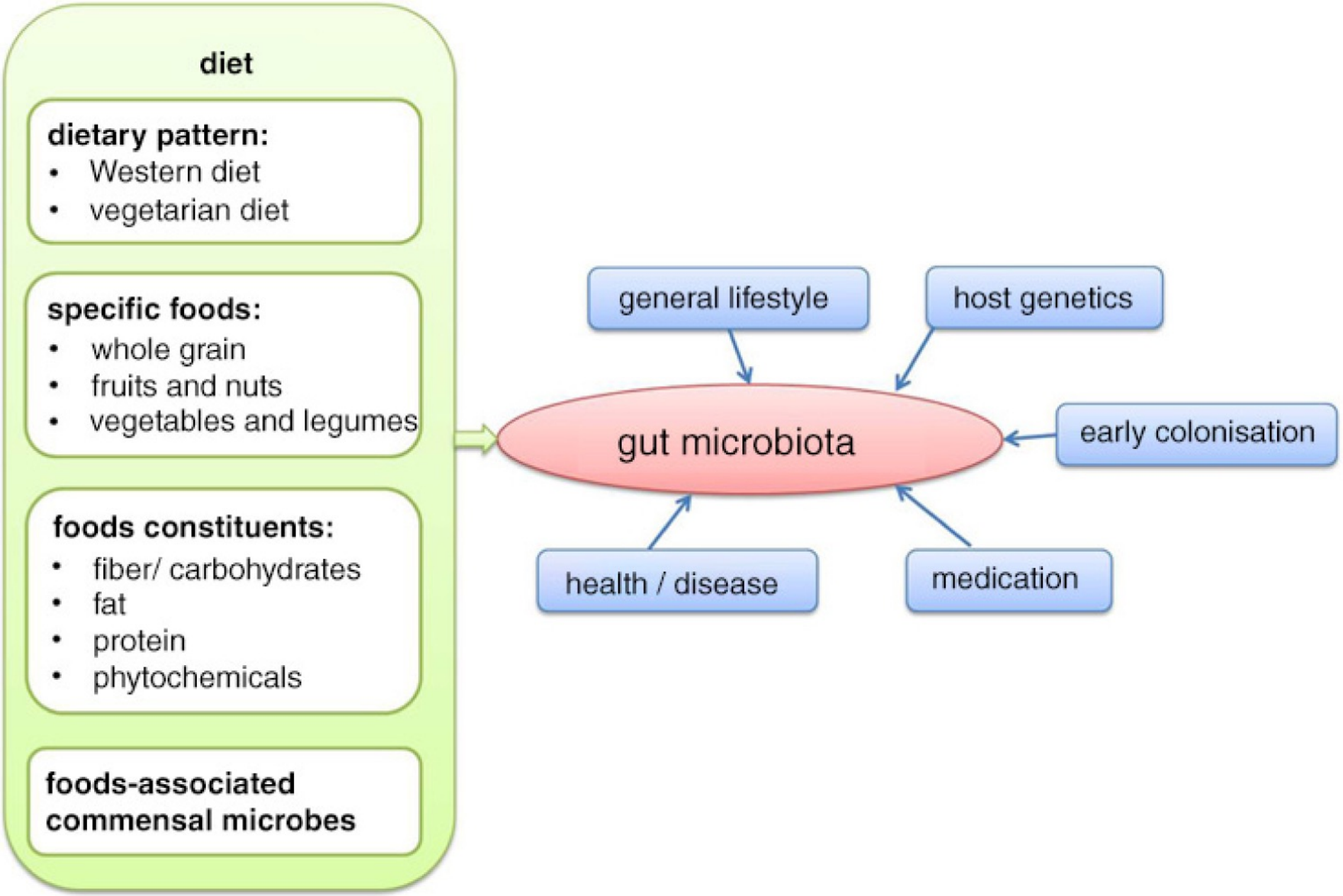
Clustering of the metabolic biomarkers and gut microbiota members



Introduction: Meta-omics approaches to study the gut microbiome



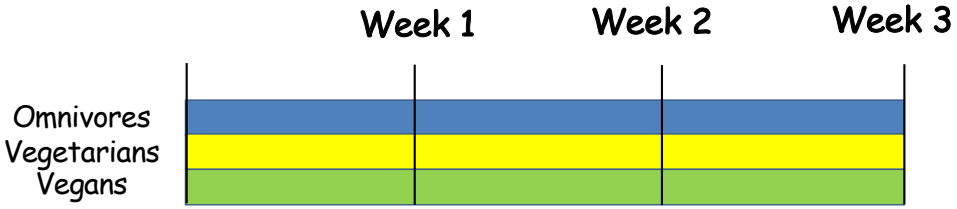
Background

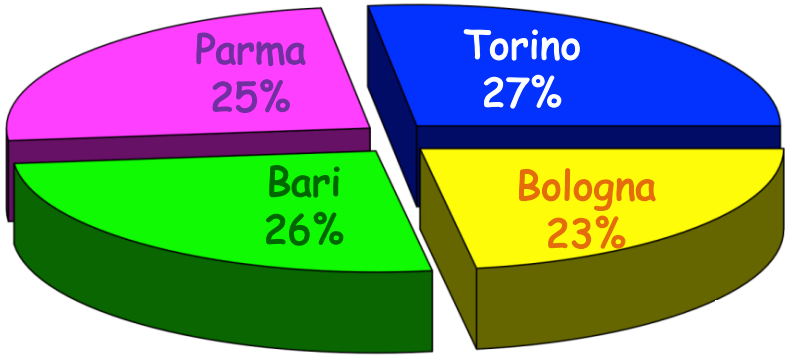

diet
dietary pattern:
• Western diet
• vegetarian diet
specific foods:
• whole grain
• fruits and nuts
• vegetables and legumes
foods constituents:
• fiber/ carbohydrates
• fat
• protein
• phytochemicals
foods-associated commensal microbes
general lifestyle
host genetics
gut microbiota
early colonisation
health / disease
medication

Ministero dell' Istruzione, dell' Università e della Ricerca
PROGRAMMI DI RICERCA SCIENTIFICA DI RILEVANTE INTERESSE NAZIONALE RICHIESTA DI COFINANZIAMENTO (D.M. 1152/ric del 27/12/2011)

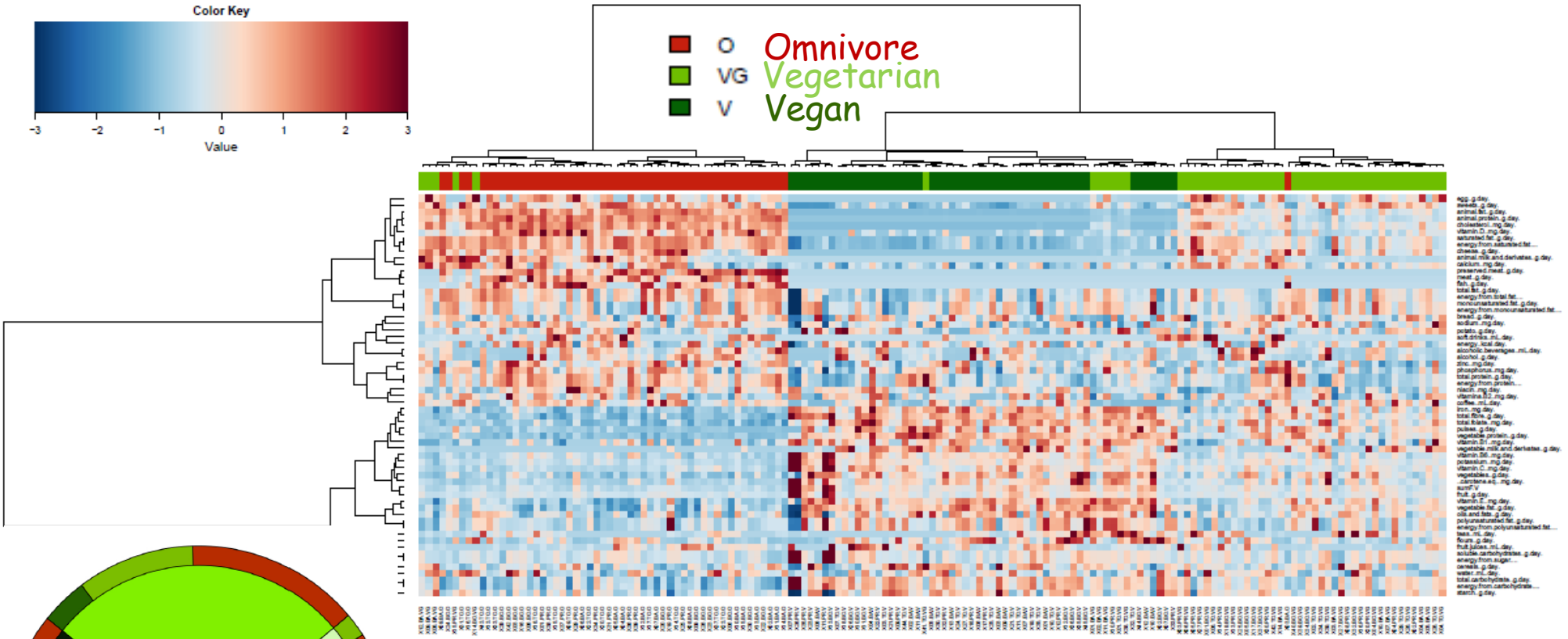
«Microorganisms in foods and in humans: study of the microbiota and the related metabolome as affected by omnivore, vegetarian or vegan diets»

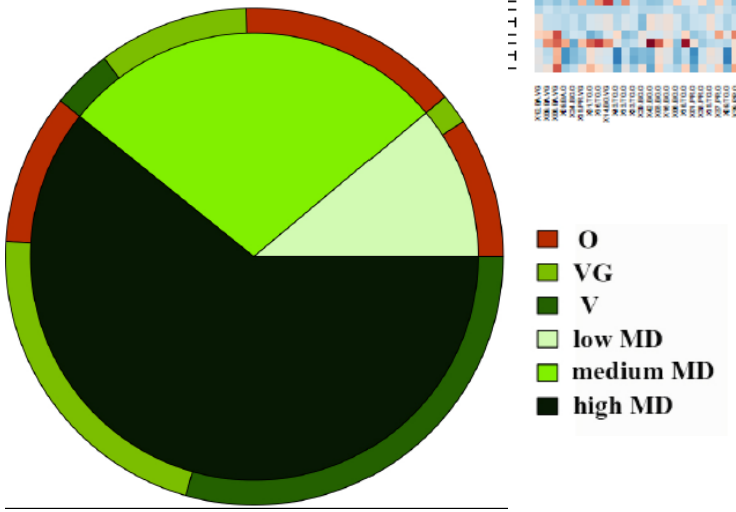
Recruitment of individuals (n = 161), administration of nutritional diaries and collection of biological samples (feces, saliva and urines)





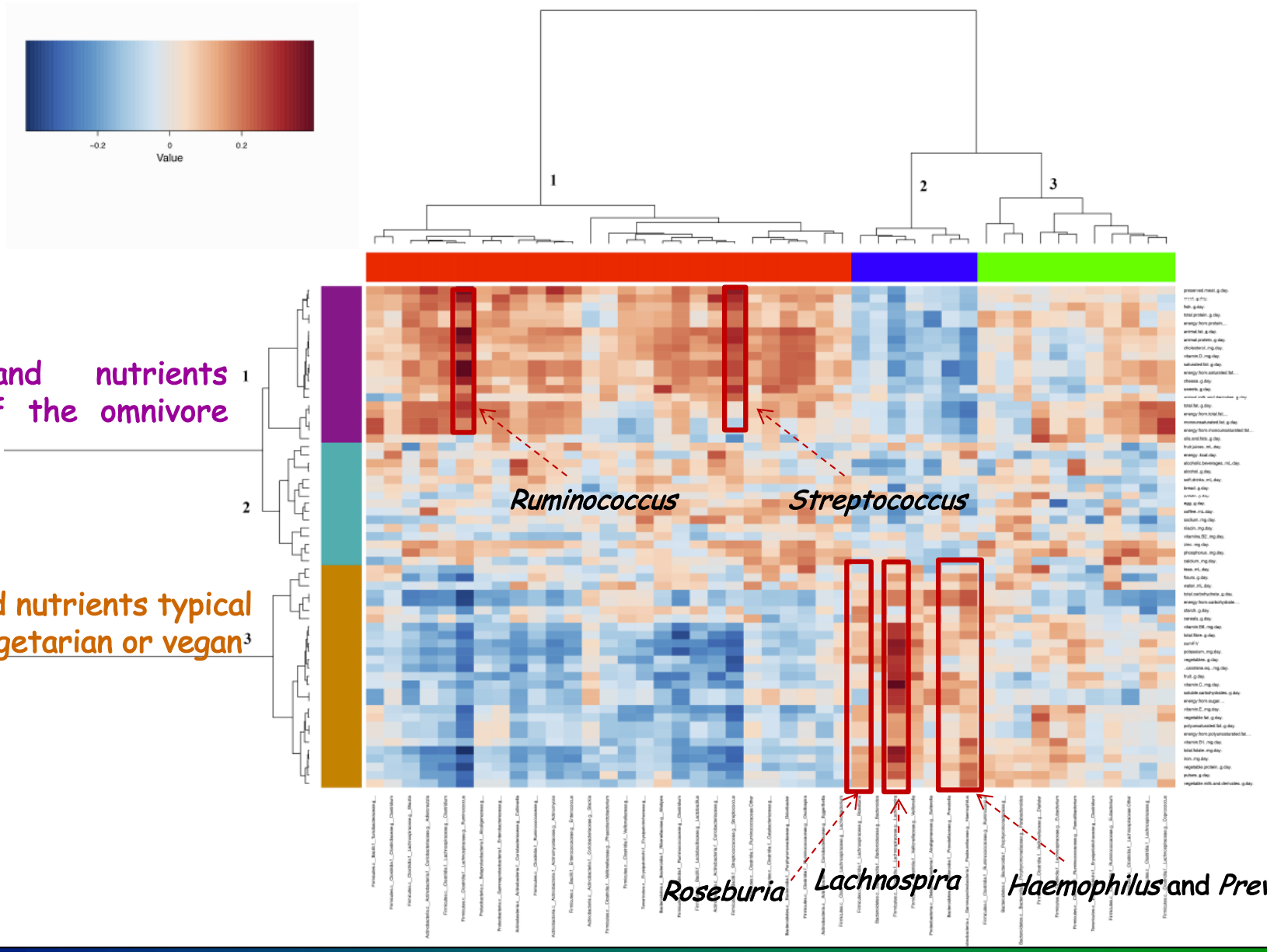
Clustering of subjects according to diet and correlating with Healthy Food Diversity index (De Filippis *et al.*, 2015. *GUT*, doi: 10.1136/gutjnl-2015-309957)

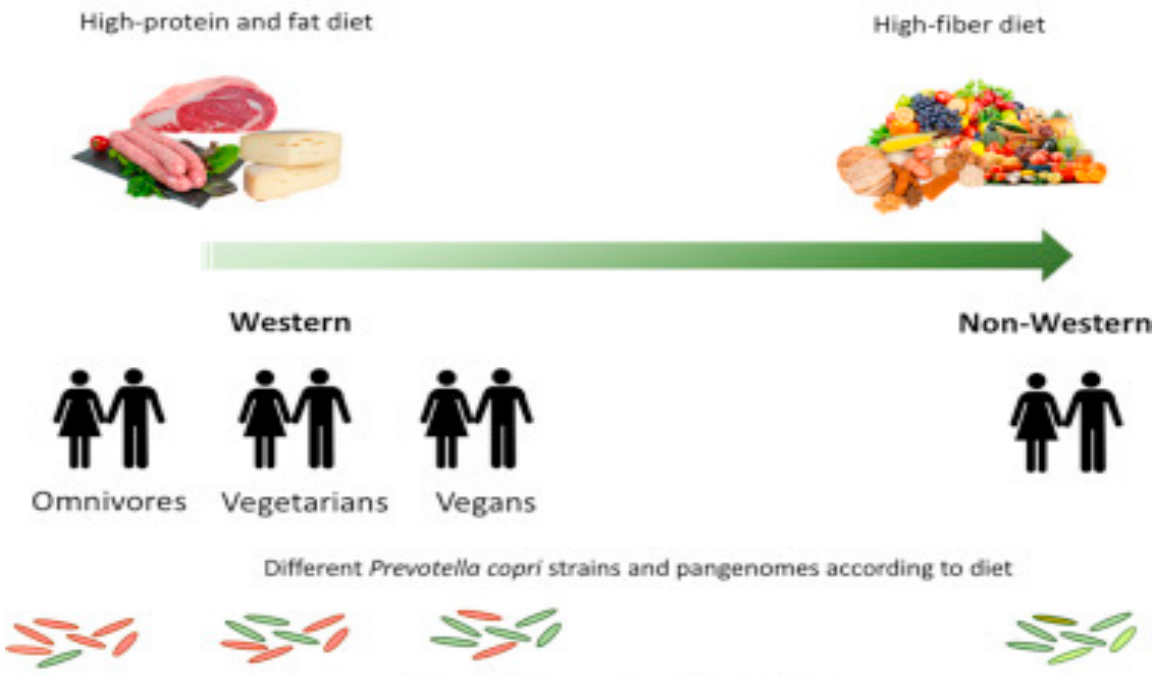


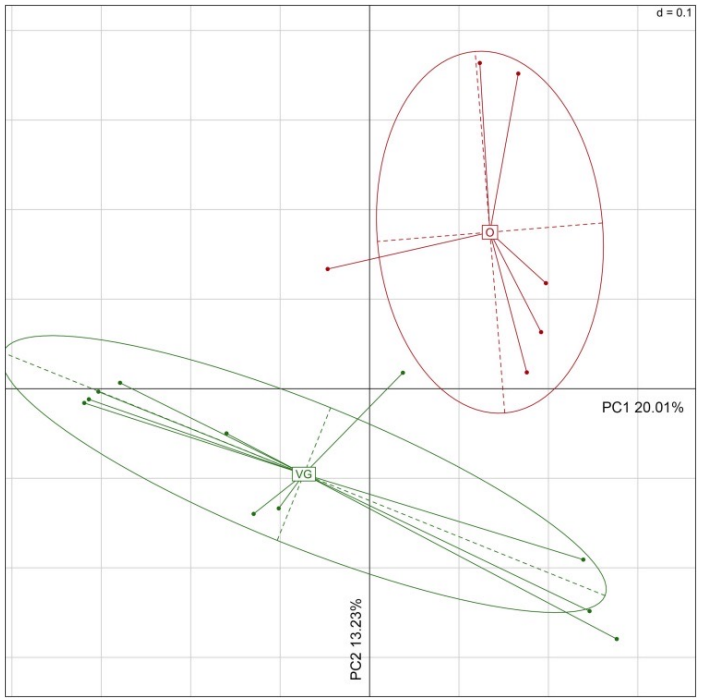


Healthy Food Diversity (HFD) index values correlated with the adherence to the MD (Spearman's rho = 0.61, P<0.00001) and were significantly higher in VG and V subjects, as well as in subjects with medium and high adherence to the MD (P<0.0001)

Microbial genera linked to intake of specific nutrients and dietary patterns







Principal Coordinates Analysis (PCoA) based on *Prevotella copri* pangenome. This analysis reveals different strains of *P. copri* that are clearly associated to omnivore (O) and vegetarian/vegan (VG) subjects.

Cell Host & Microbe

Available online 21 February 2019

In Press, Corrected Proof

Short Article

Distinct Genetic and Functional Traits of Human Intestinal *Prevotella copri* Strains Are Associated with Different Habitual Diets

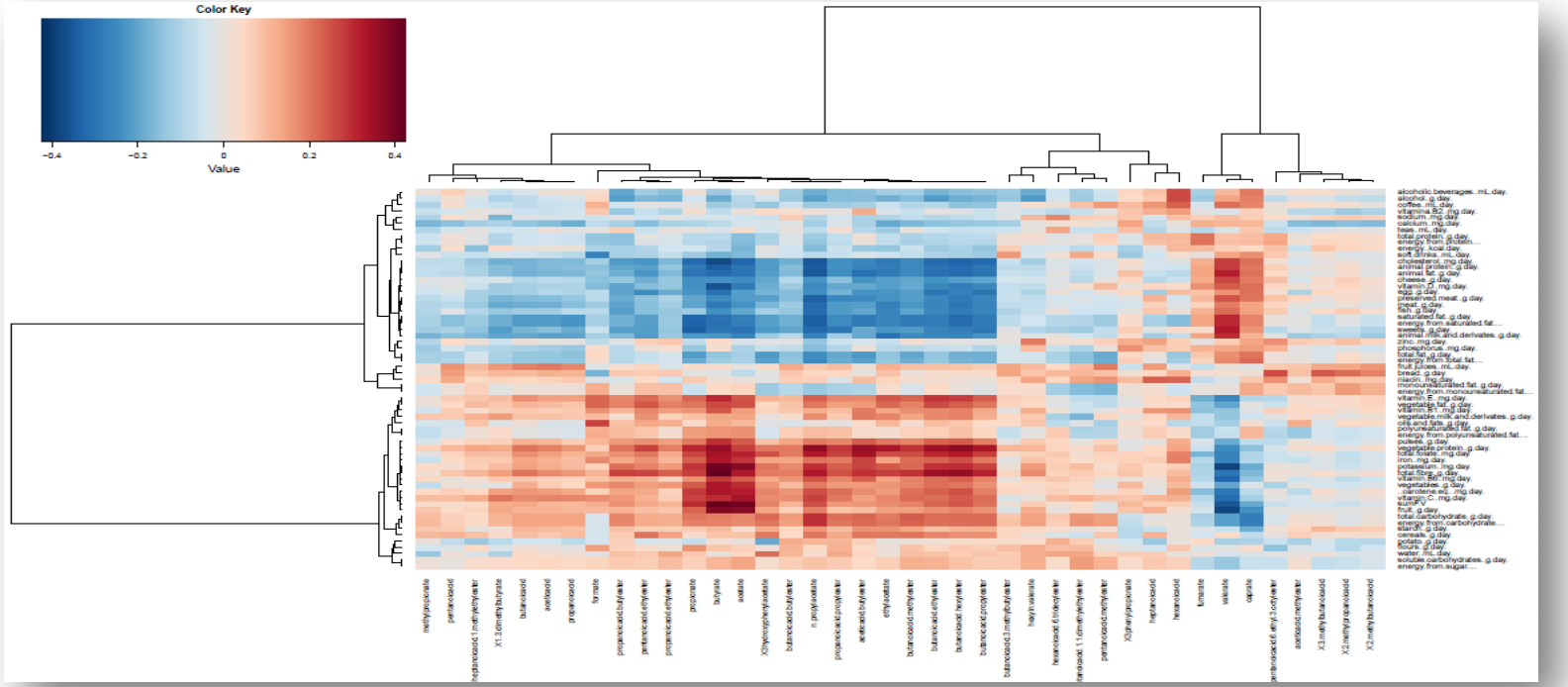
Francesca De Filippis [1, 2], Edoardo Pasolli [1, 3], Adrian Tett [3], Sonia Tarallo [4], Alessio Naccarati [4], Maria De Angelis [5], Erasmo Neviani [6], Luca Cocolin [7], Marco Gobbetti [8], Nicola Segata [3], Danilo Ercolini [1, 2, 9]

Show more

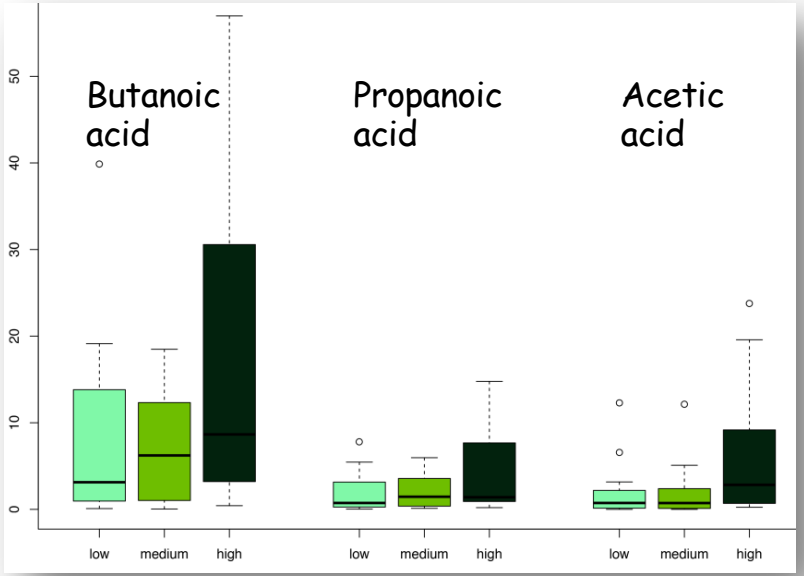
https://doi.org/10.1016/j.chom.2019.01.004

Correlations between diet, microbiota and metabolome

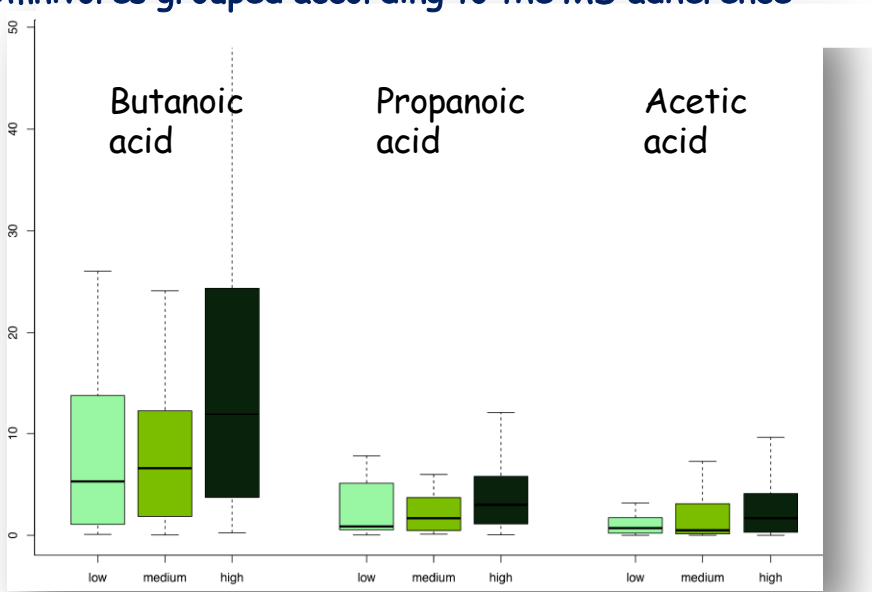
Spearman's correlations between SCFA and dietary information



All subjects grouped according to the MD adherence

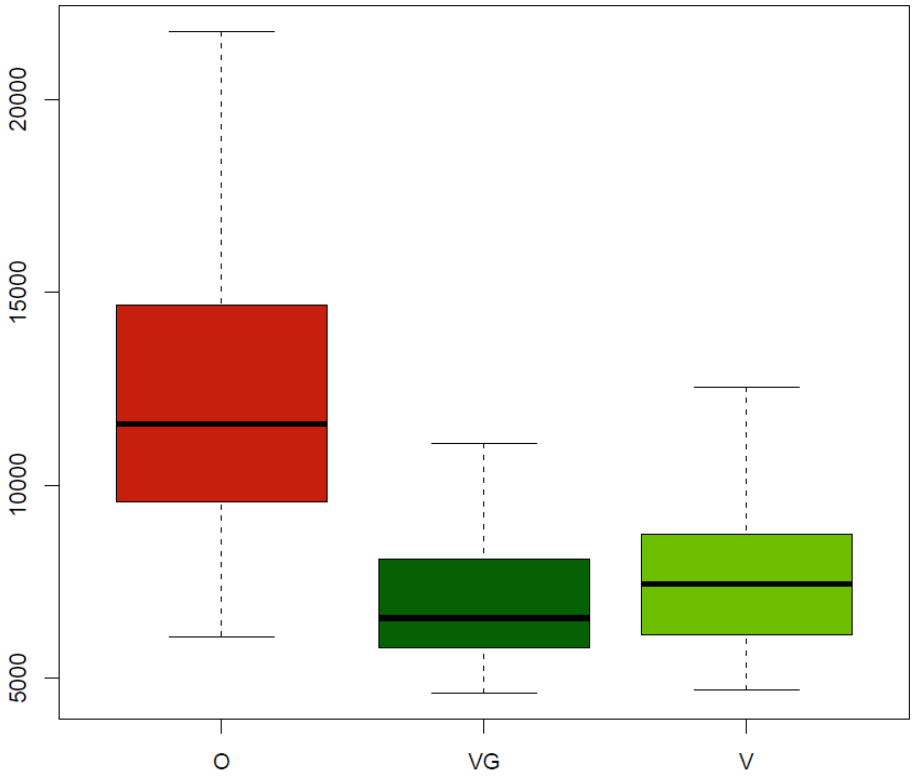


Omnivores grouped according to the MD adherence

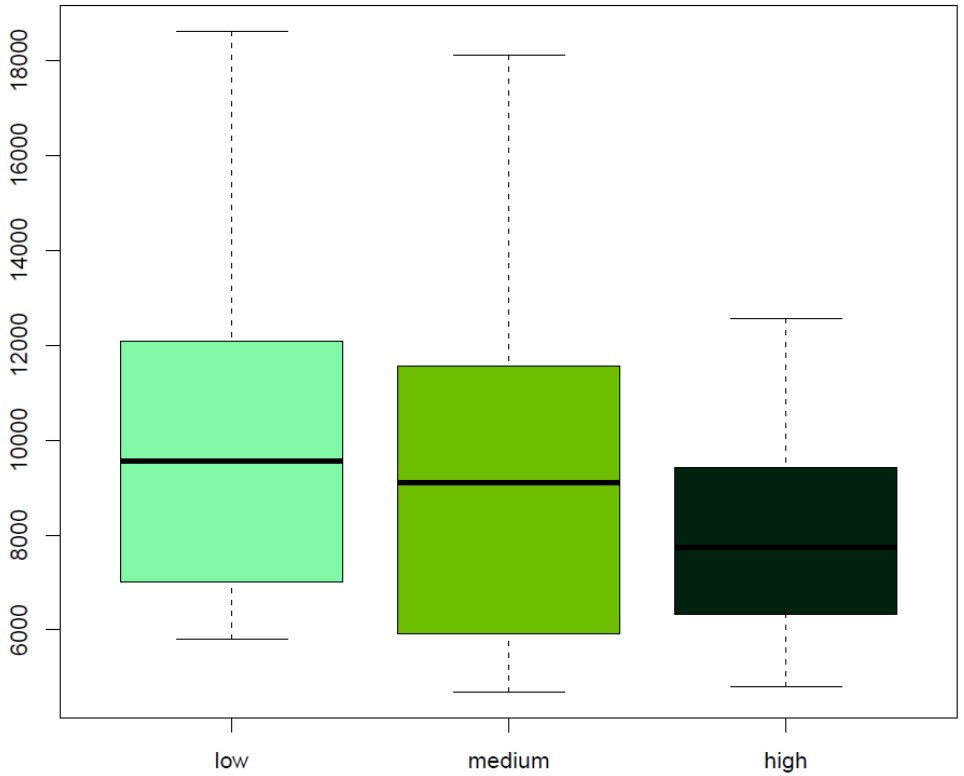


Abundance (ppm) of urinary trimethylamine oxide is associated to diet (A) and adherence to MD (B)

A



B



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SCIENTIFIC REPORTS

nature research

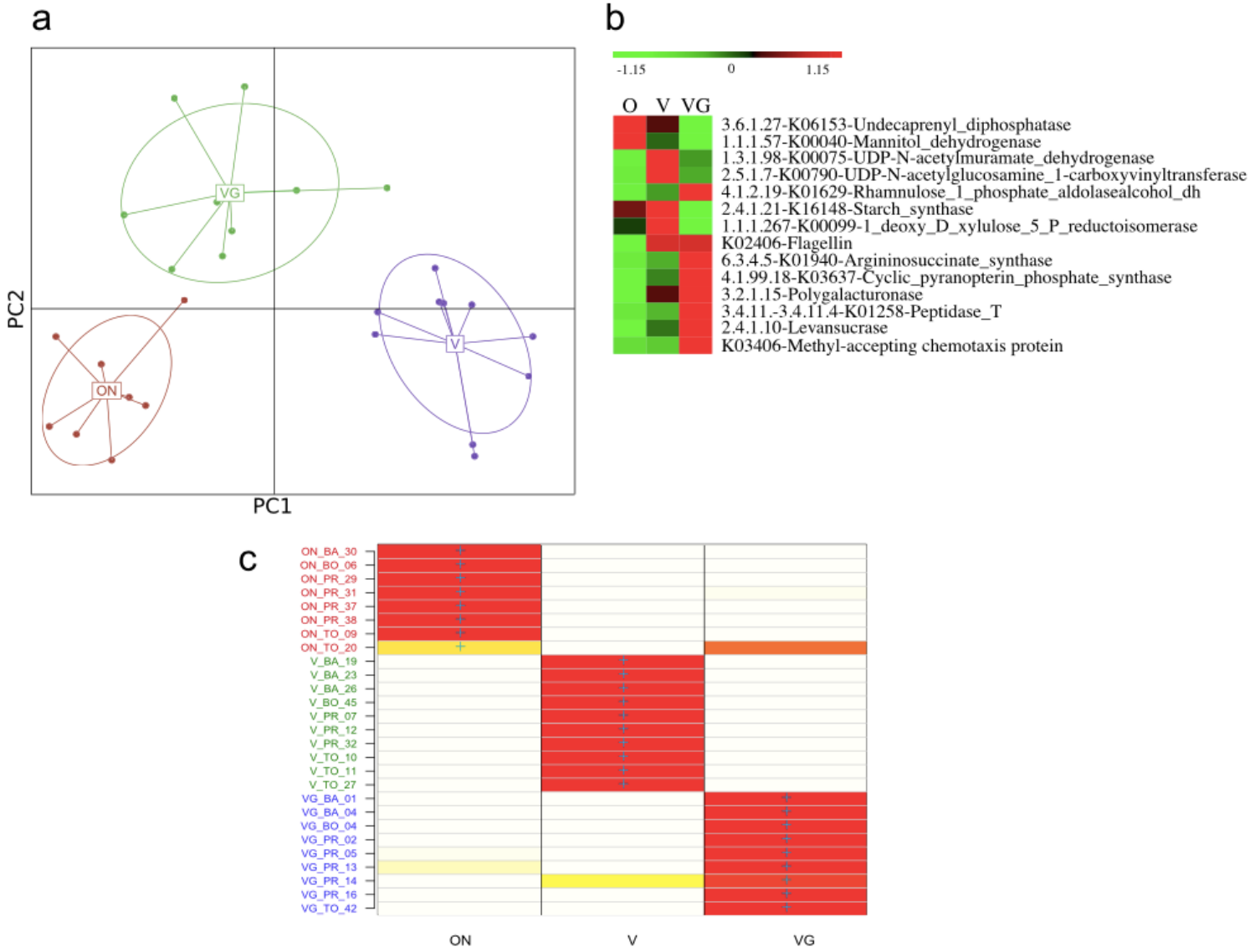
OPEN

Diet influences the functions of the human intestinal microbiome

Maria De Angelis[1], Ilario Ferrocino[2], Francesco Maria Calabrese[1,3], Francesca De Filippis[4], Noemi Cavallo[1], Sonya Siragusa[1], Simone Rampelli[5], Raffaella Di Cagno[6], Kalliopi Rantsiou[2], Lucia Vannini[7], Nicoletta Pellegrini[8], Camilla Lazzi[8], Silvia Turroni[5], Nicola Lorusso[3], Mario Ventura[3], Marcello Chieppa[9], Erasmo Neviani[8], Patrizia Brigidi[5], Paul W. O'Toole[10], Danilo Ercolini[4], Marco Gobbetti[6*] & Luca Cocolin[2]

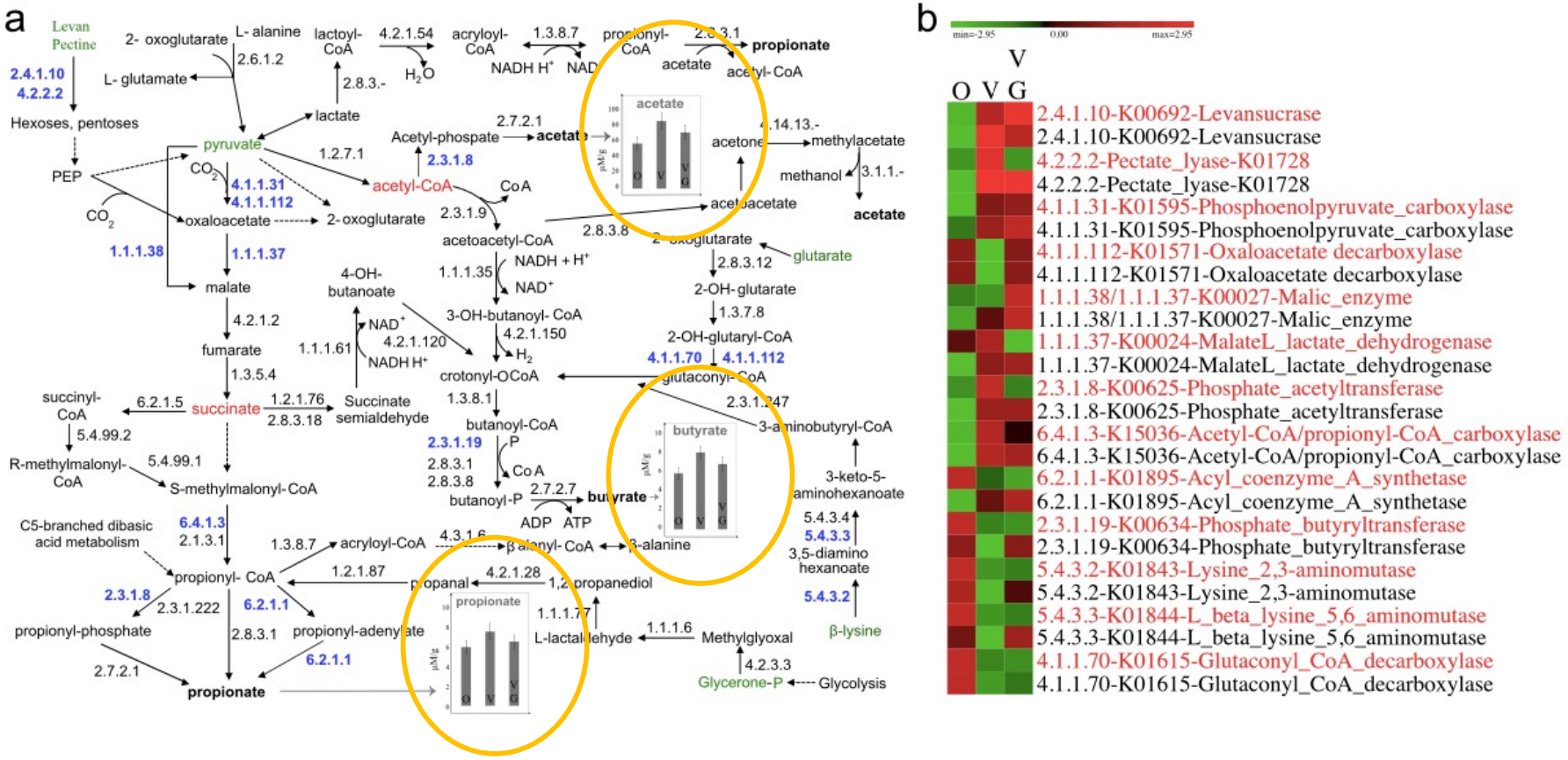
Metaproteomes associated with omnivorous, vegan and vegetarian diets

www.nature.com/scientificreports/



Diet modulates the biosynthesis of SCFAs by the intestinal microbiome

www.nature.com/scientificreports/



Diet modulates the biosynthesis of some essential amino acids

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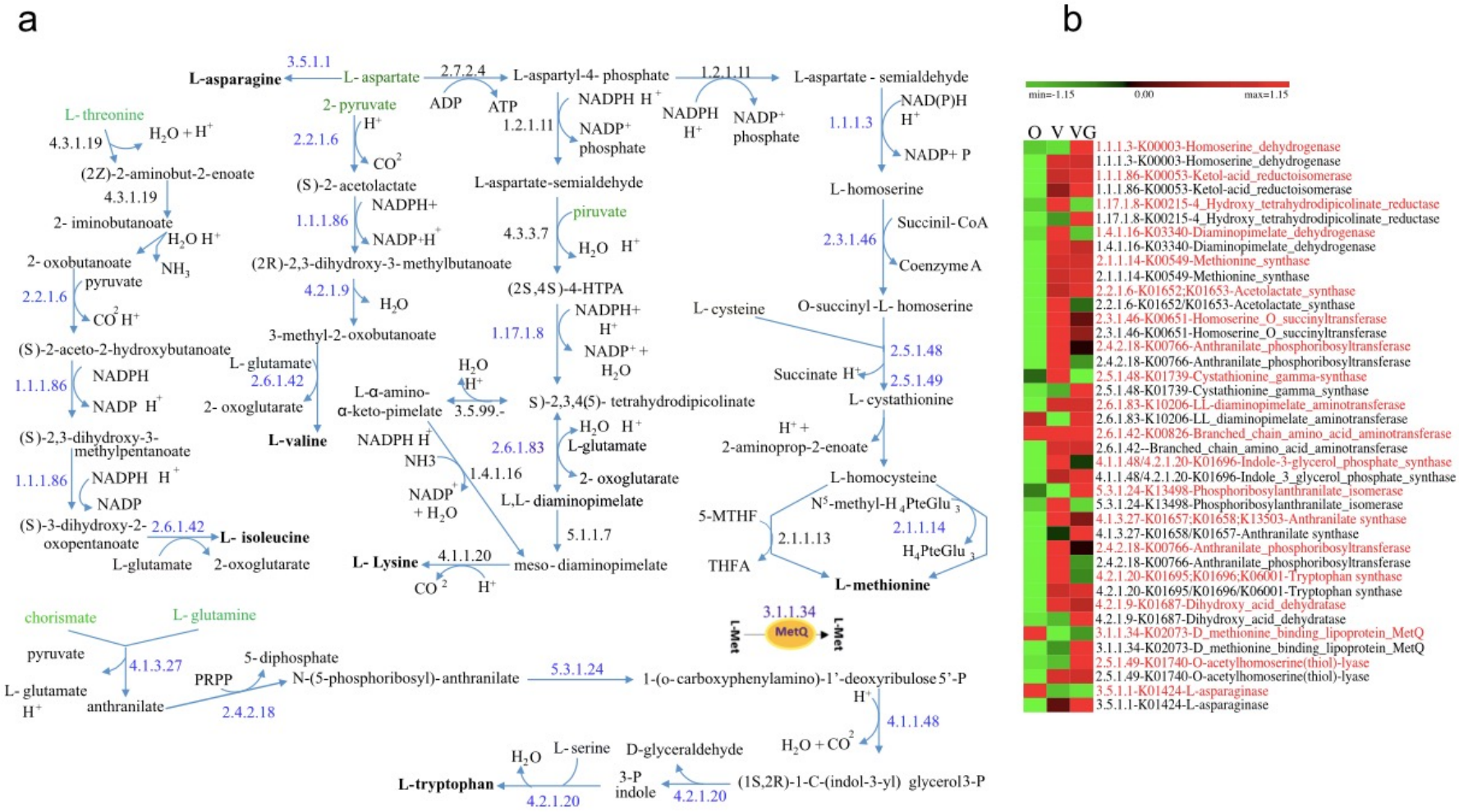
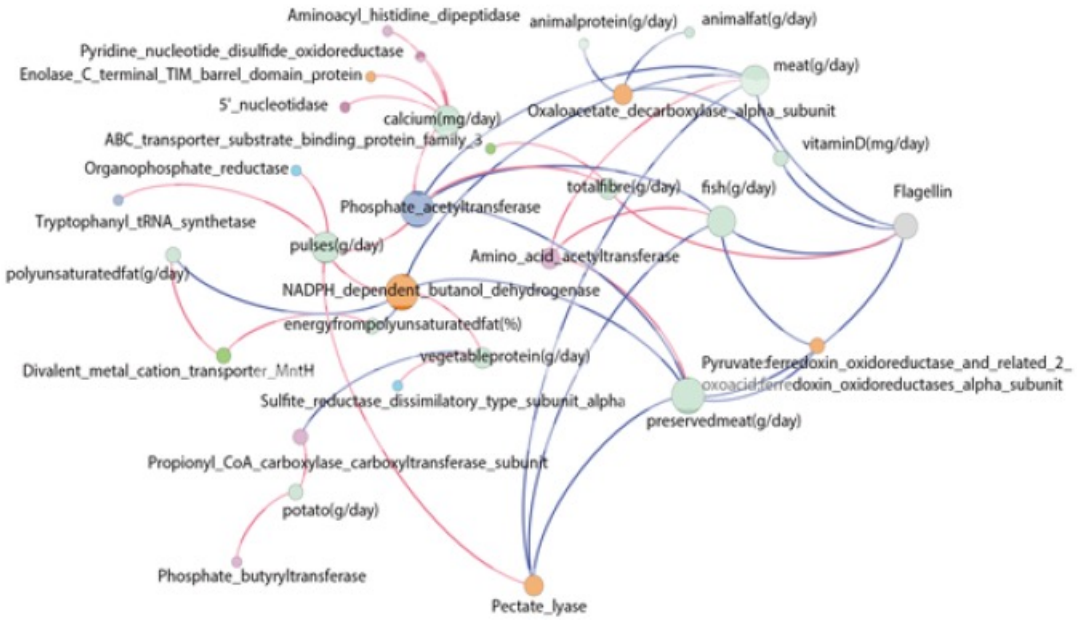
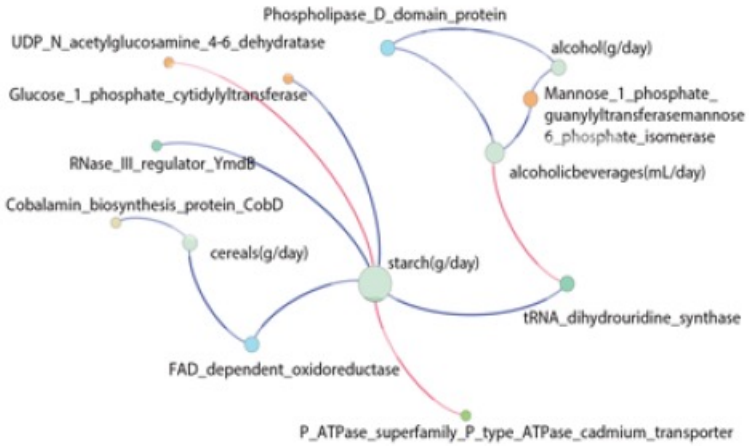
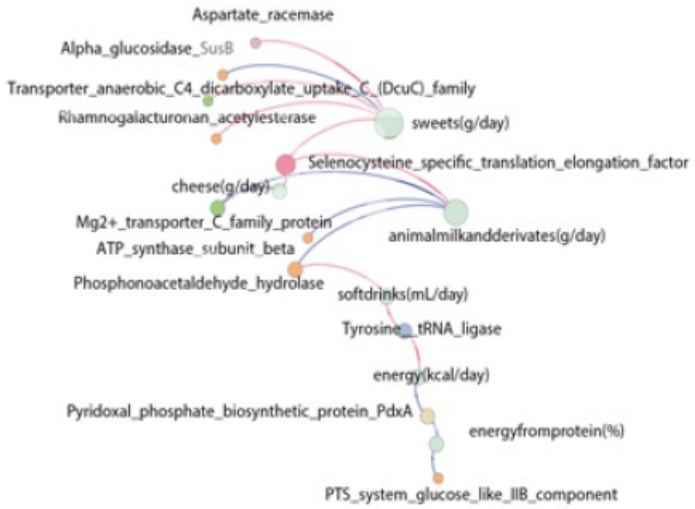
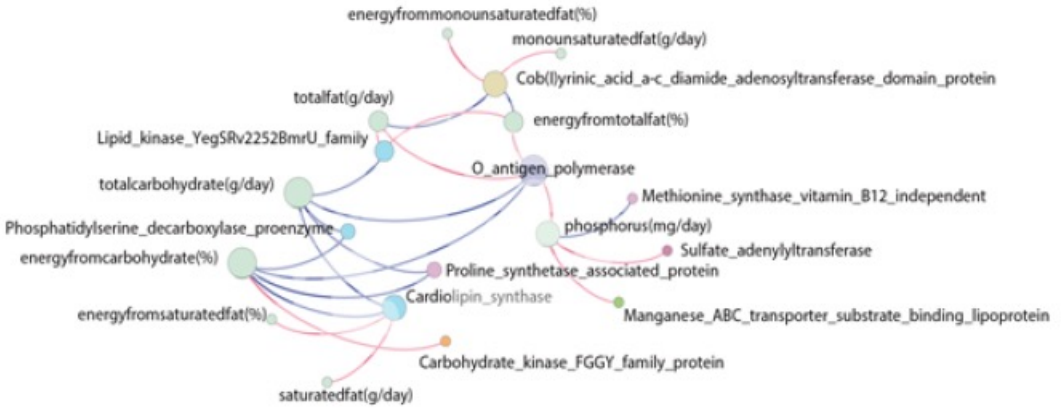


Correlation between meta-omic data

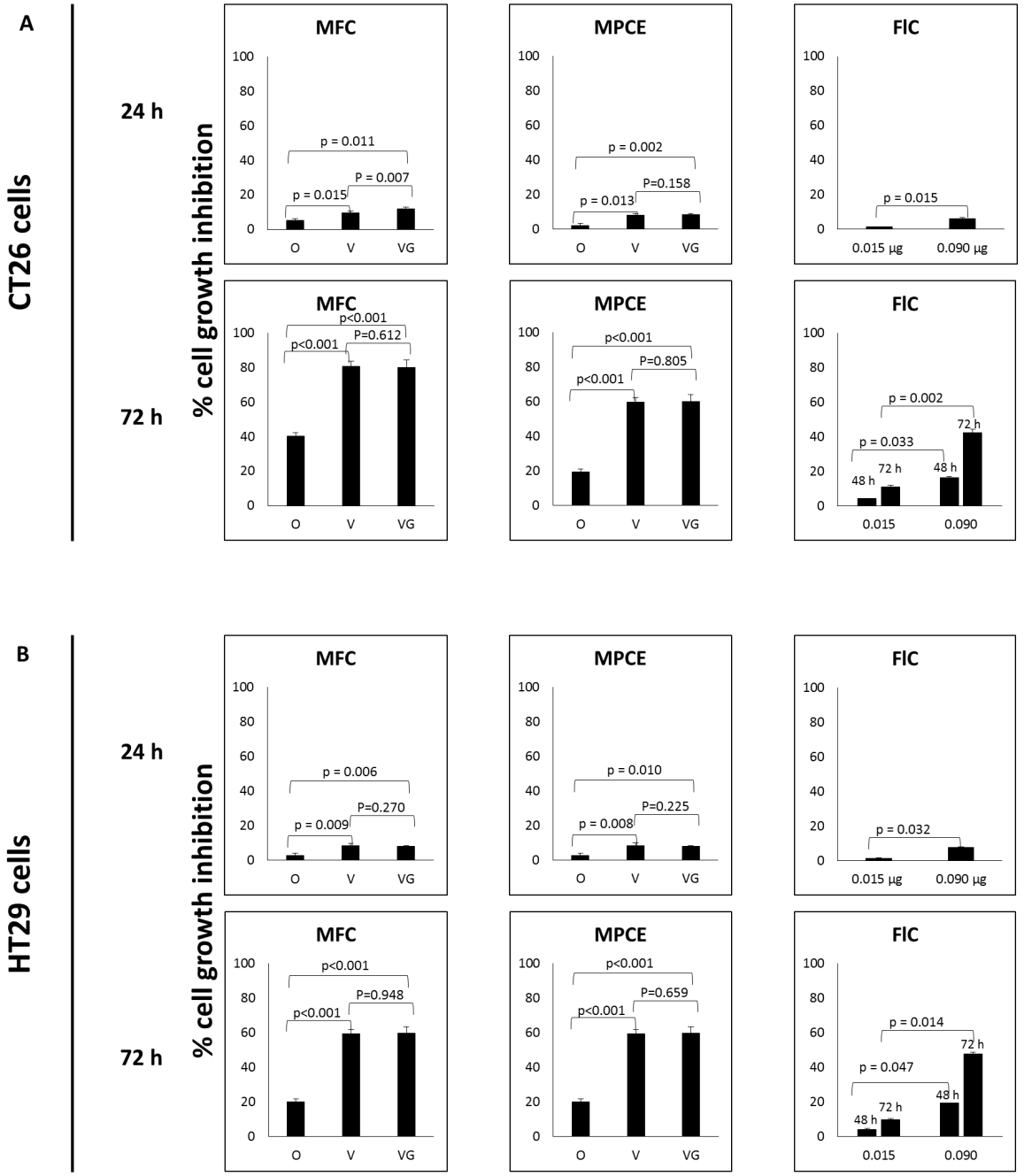




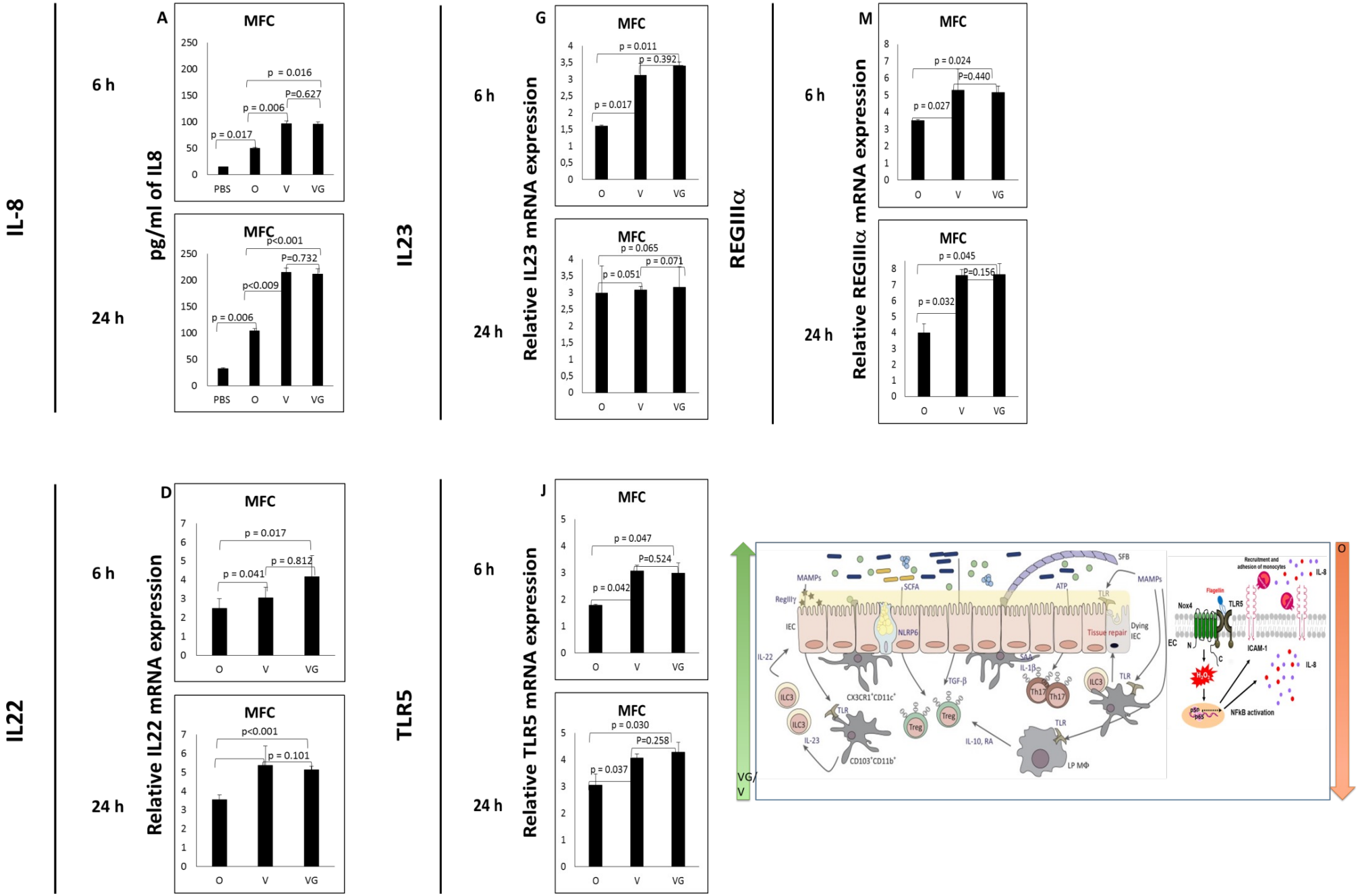




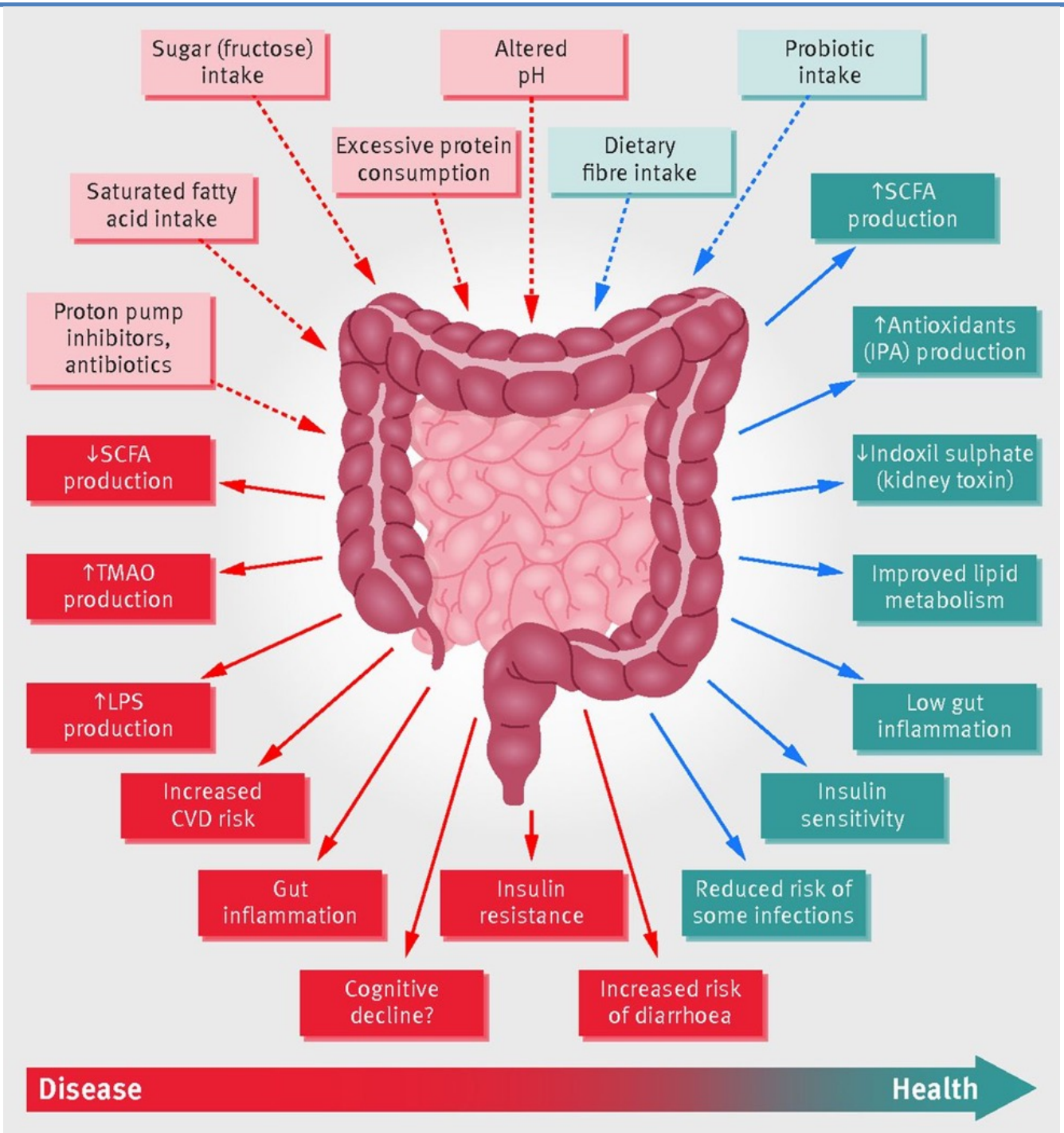
Anti-proliferative Effects of the Intestinal Microbiome in Murine CT26 and Human HT29 Colon Carcinoma Cell Lines

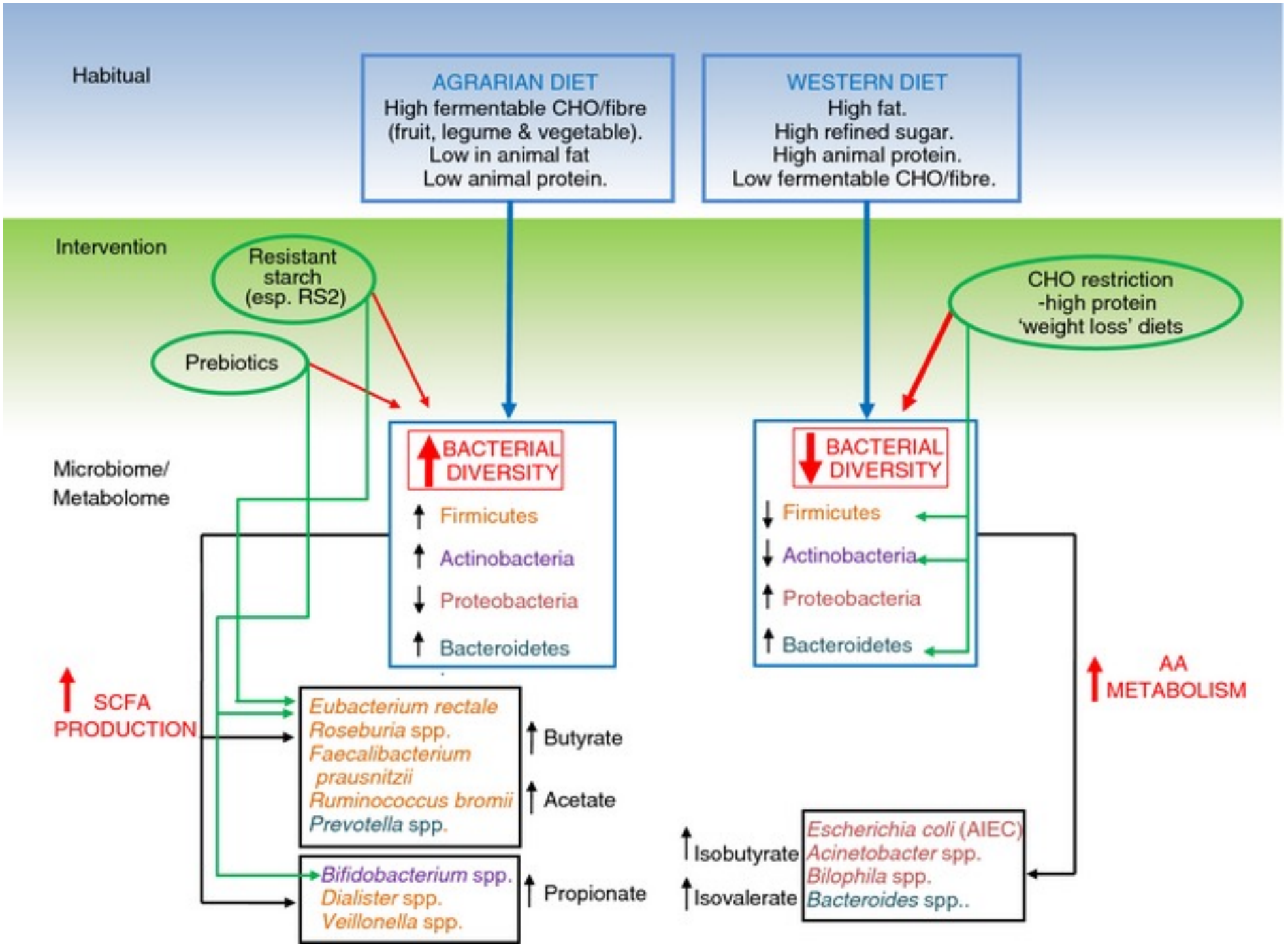


Intestinal Microbiome Increases the Expression of Interleukins, TLR-5 and Lectin RegIIIa



Functional foods, gut microbiota and human health

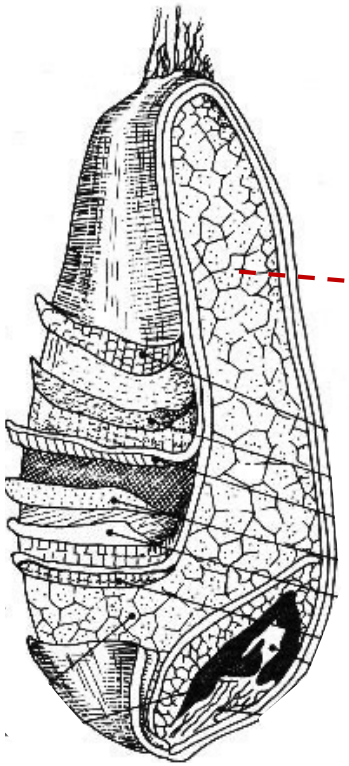


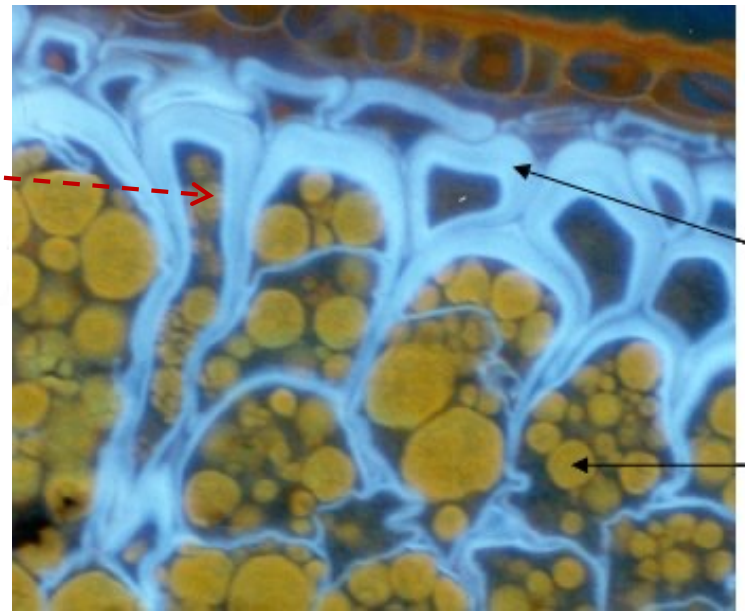

Habitual
AGRARIAN DIET
High fermentable CHO/fibre
(fruit, legume & vegetable).
Low in animal fat
Low animal protein.
WESTERN DIET
High fat.
High refined sugar.
High animal protein.
Low fermentable CHO/fibre.
Intervention
Resistant starch (esp. RS2)
Prebiotics
CHO restriction -high protein 'weight loss' diets
Microbiome/ Metabolome
BACTERIAL DIVERSITY
Firmicutes
Actinobacteria
Proteobacteria
Bacteroidetes
BACTERIAL DIVERSITY
Firmicutes
Actinobacteria
Proteobacteria
Bacteroidetes
SCFA PRODUCTION
Eubacterium rectale
Roseburia spp.
Faecalibacterium prausnitzii
Ruminococcus bromii
Prevotella spp.
Butyrate
Acetate
Bifidobacterium spp.
Dialister spp.
Veillonella spp.
Propionate
AA METABOLISM
Isobutyrate
Isovalerate
Escherichia coli (AIEC)
Acinetobacter spp.
Bilophila spp.
Bacteroides spp..

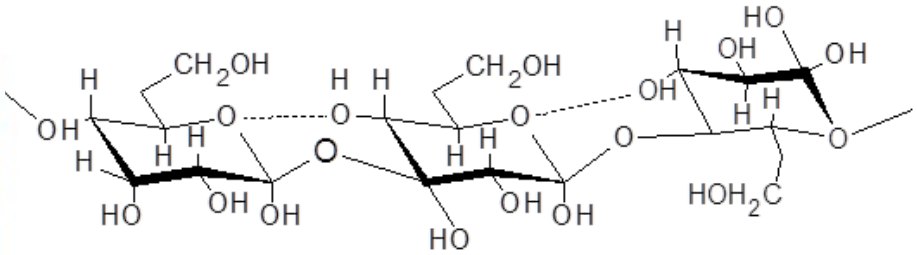
Dietary fibers (prebiotics) and microbiota

Dietary fibers are widely found in food derived from plants, such as resistant starch, pectin, oligosaccharides and inulin, most of which can be broken down by intestinal bacteria

(Eswaran *et al.*, 2013. *American Journal of Gastroenterology*, 108:718-727)







β-glucan

Starch granule

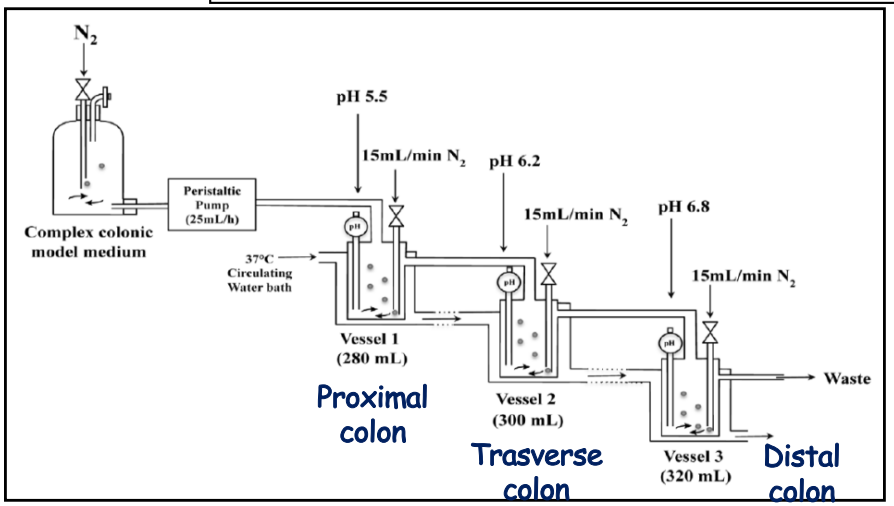
β-glucans and composition of gut microbiota

Eur J Nutr (2012) 51:693–705
DOI 10.1007/s00394-011-0248-6

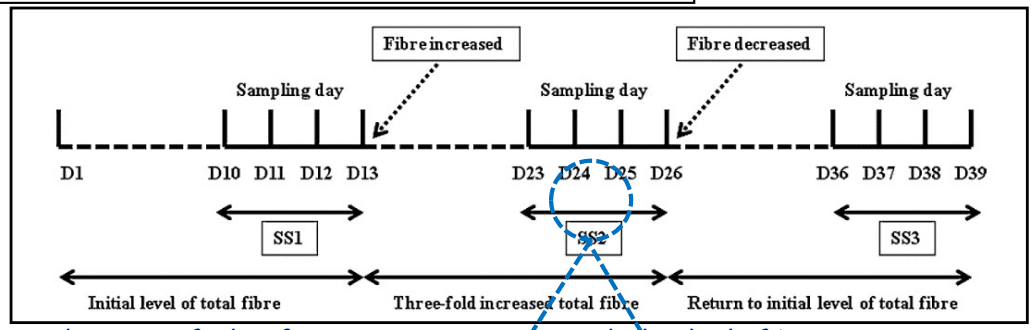
ORIGINAL CONTRIBUTION

High-level dietary fibre up-regulates colonic fermentation and relative abundance of saccharolytic bacteria within the human faecal microbiota in vitro

Qing Shen · Lu Zhao · Kieran M. Tuohy



Schematic diagram of the in vitro three-stage culture colonic model system (human colonic model).



A diagram of the fermentation course and the high-fibre treatment. Samples were taken on four consecutive days over each steady state, analysed and averaged. SS1 initial level of total fibre, SS2 threefold increased total fibre, SS3 return to initial level of total fibre

↑ *Bifidobacterium* spp.
Ruminococcus spp.
Lactobacillus-Enterococcus group
(Vessel 1, 2, 3)

↑ *Faecalibacterium prausnitzii*
Eubacterium rectale-Clostridium coccoides groups
(Vessel 1)

- *Lactobacillus-Enterococcus* group ↑; *Bifidobacterium* genus =; SCFA ↑ (Hughes *et al.*, 2008. FEMS Microbial Ecol., 64:482-493)
- Fecal total bacteria and bifidobacteria ↑ (Mårtensson *et al.*, 2005. Nutr. Res., 25:429-442)
- Significant bifidogenic effect only in subjects older than 50 years (Mitsou *et al.*, 2010. Food Res. Int., 43:1086-1092)

The European Food Safety Authority stated that: "Regular consumption of oat β-glucans can actively lower/reduce blood LDL cholesterol and total cholesterol"

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PREBIOTIC PASTA WITH BETA-GLUCANS CAN HELP DIABETICS BY INCREASING GOOD BACTERIA IN DIGESTIVE SYSTEM

Submitted by Diane Hoffman on Tue, 09/29/2015 - 06:05

Prebiotic pasta could help increase good bacteria in the gastrointestinal tract while offering an enriching experience of eating pasta. The research team noted that pasta enriched with specific type of fiber called beta-glucan can improve the concentration of 'good' bacteria and offer health benefits.

The probiotic pasta can also improve the immune system and help diabetics and patients with high cholesterol. Study subjects were analyzed by the research team for

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β-Glucan-Enriched Pasta Boosts Good Gut Bacteria, Reduces Bad Cholesterol

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Medindia » Diet & Nutrition News

Beta-Glucan-Enriched Pasta Encourages the Growth of Good Bacteria in the Gut

by Dr. Trupti Shirole on September 20, 2015 at 12:54 AM **Diet & Nutrition News** - Seleziona lingua

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Beta-glucans are special types of sugars that are found in the cell walls of certain microbes, as well as in oats and barley. They are healthy fibers that humans cannot digest, but that can be digested by some species of our gut bacteria.

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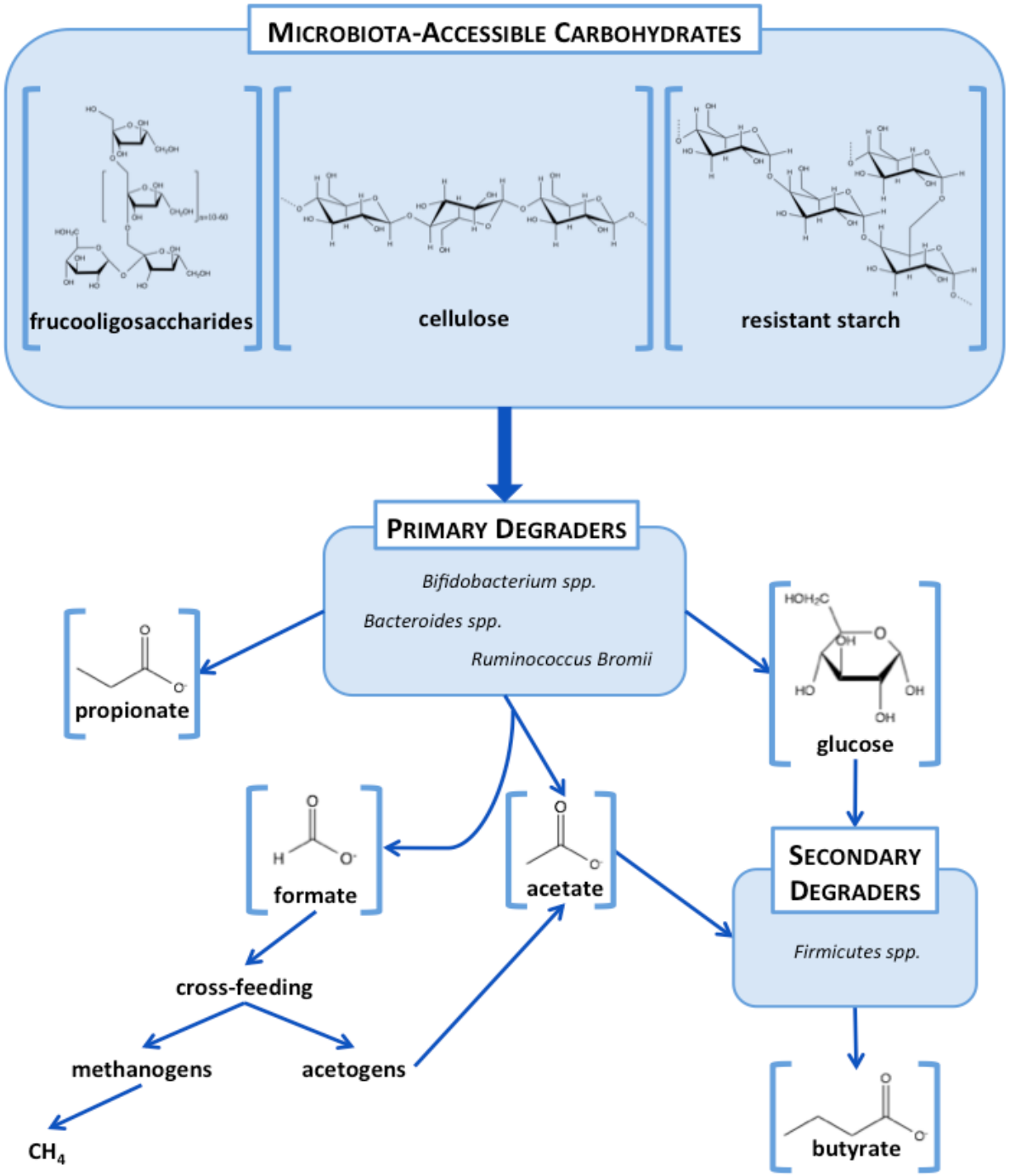
Home » Alimentazione & Benessere » Pasta arricchita con β-glucano aumenta i batteri buoni nell'intestino e riduce il colesterolo

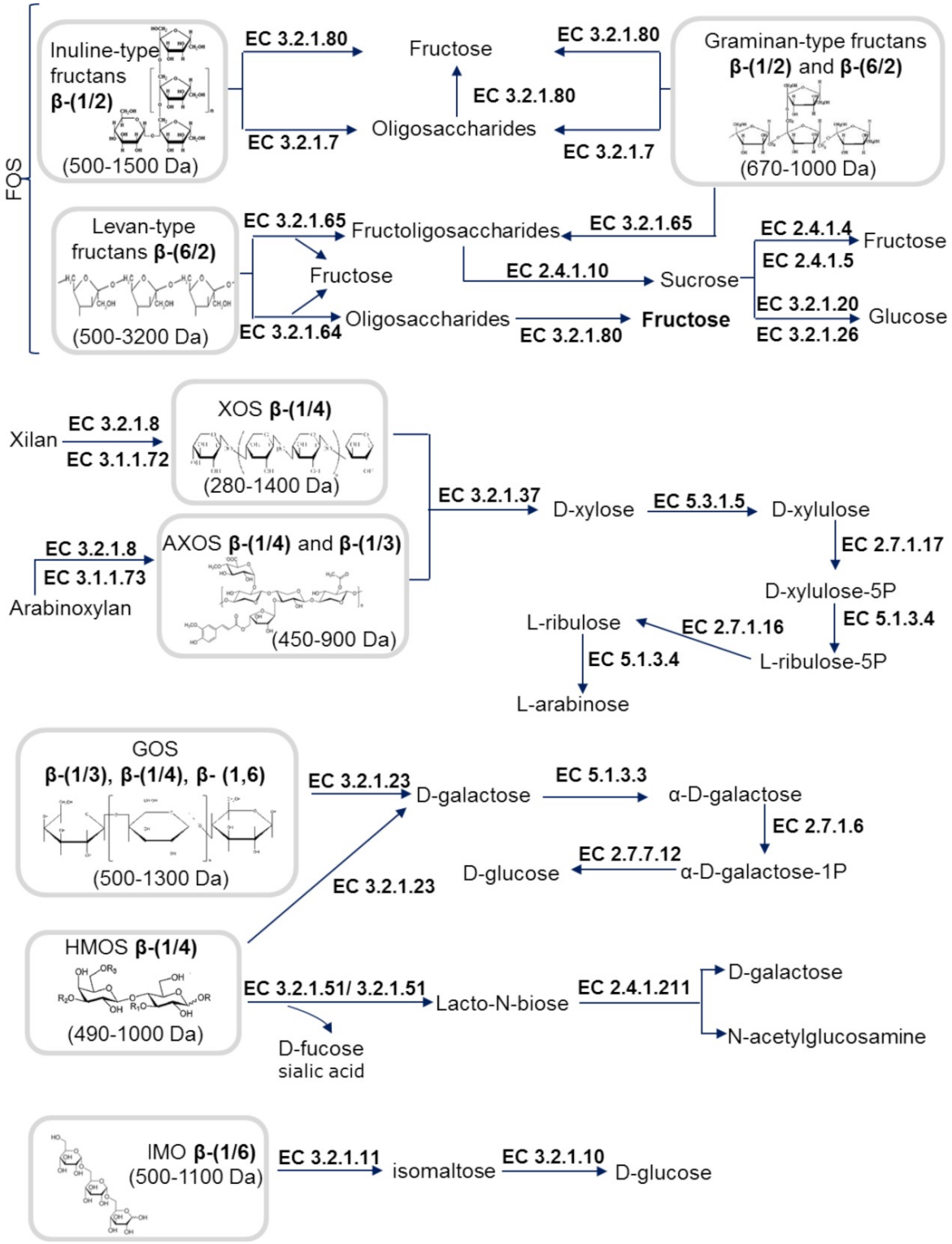
Pasta arricchita con β-glucano aumenta i batteri buoni nell'intestino e riduce il colesterolo

Le persone alimentate per due mesi con la **pasta arricchita con β-glucano** hanno mostrato un aumento delle popolazioni di batteri benefici nel loro tratto intestinale e ridotto le popolazioni di batteri non benefici. Inoltre, hanno anche dimostrato una riduzione di LDL, colesterolo cattivo. Questo lavoro è parte di un ampio sforzo per identificare potenziali prebiotici, alimenti che potrebbero favorire la crescita di batteri salutari nel tratto

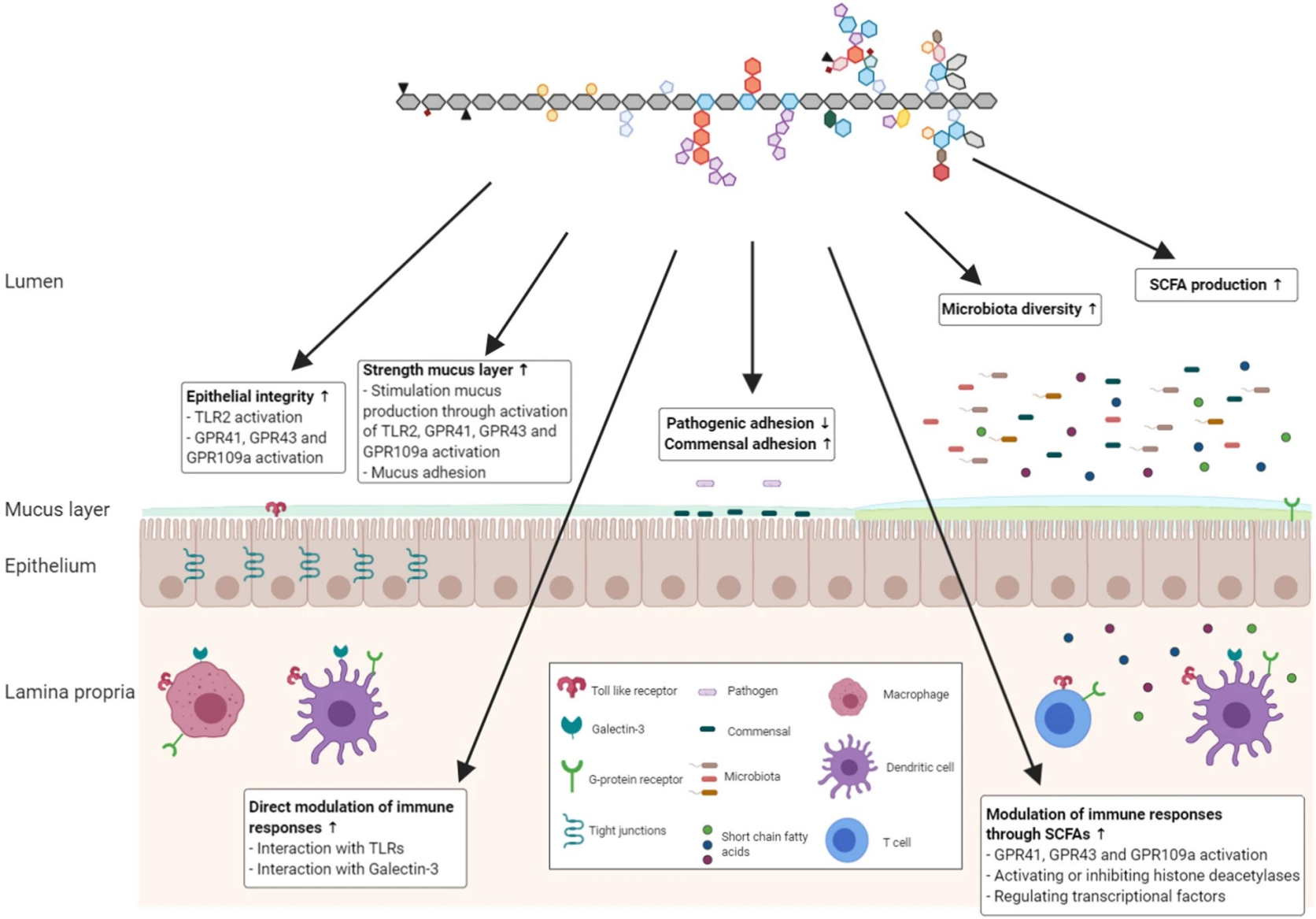
Metabolism of dietary fibers



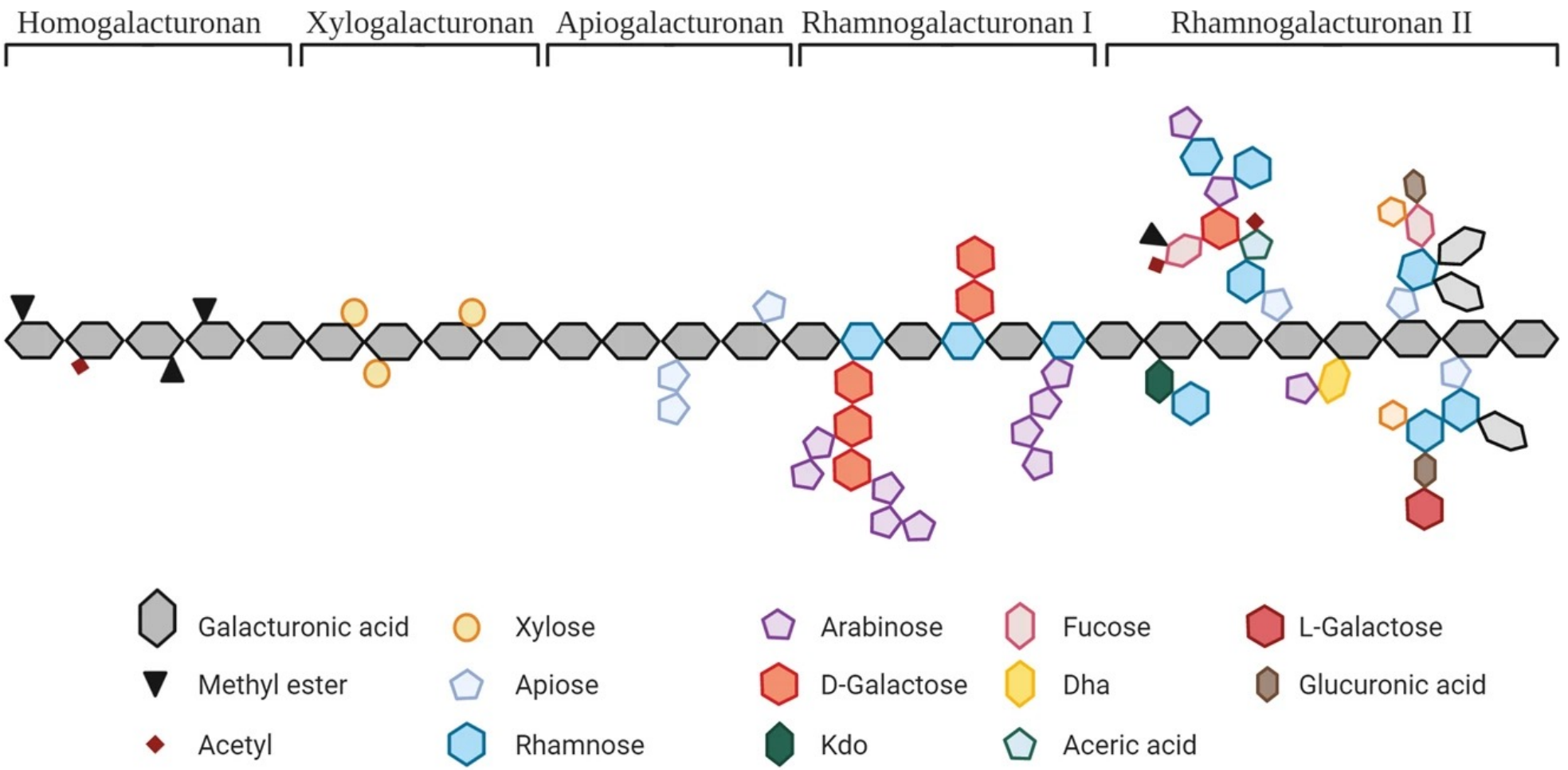
Metabolism of dietary fibers



Influence of pectins on the gastrointestinal immune barrier

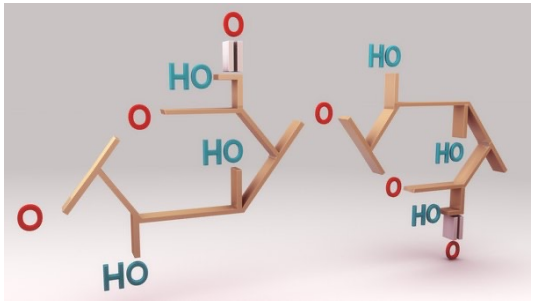


Structural characteristics of pectin molecules



Pectins can strengthen the mucus layer by goblet cells

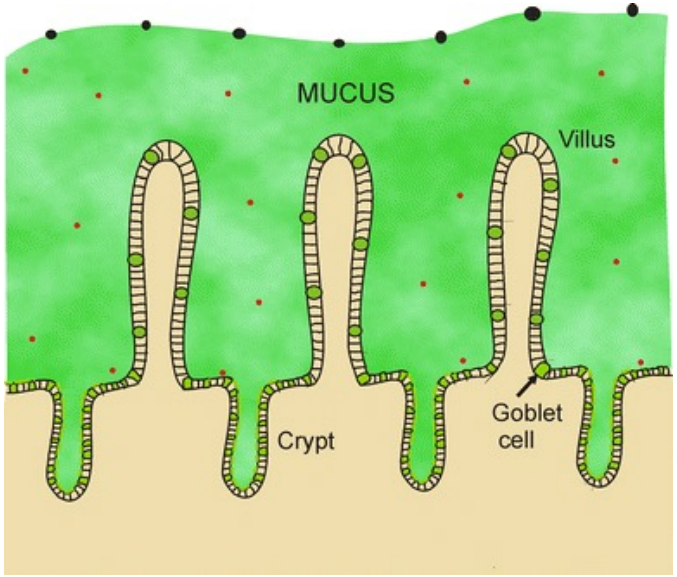
Pectins differ for the degree of methyl-esterification



pectin specific effect by:

1) activation of Goblet cells

2) mucoadhesive effect

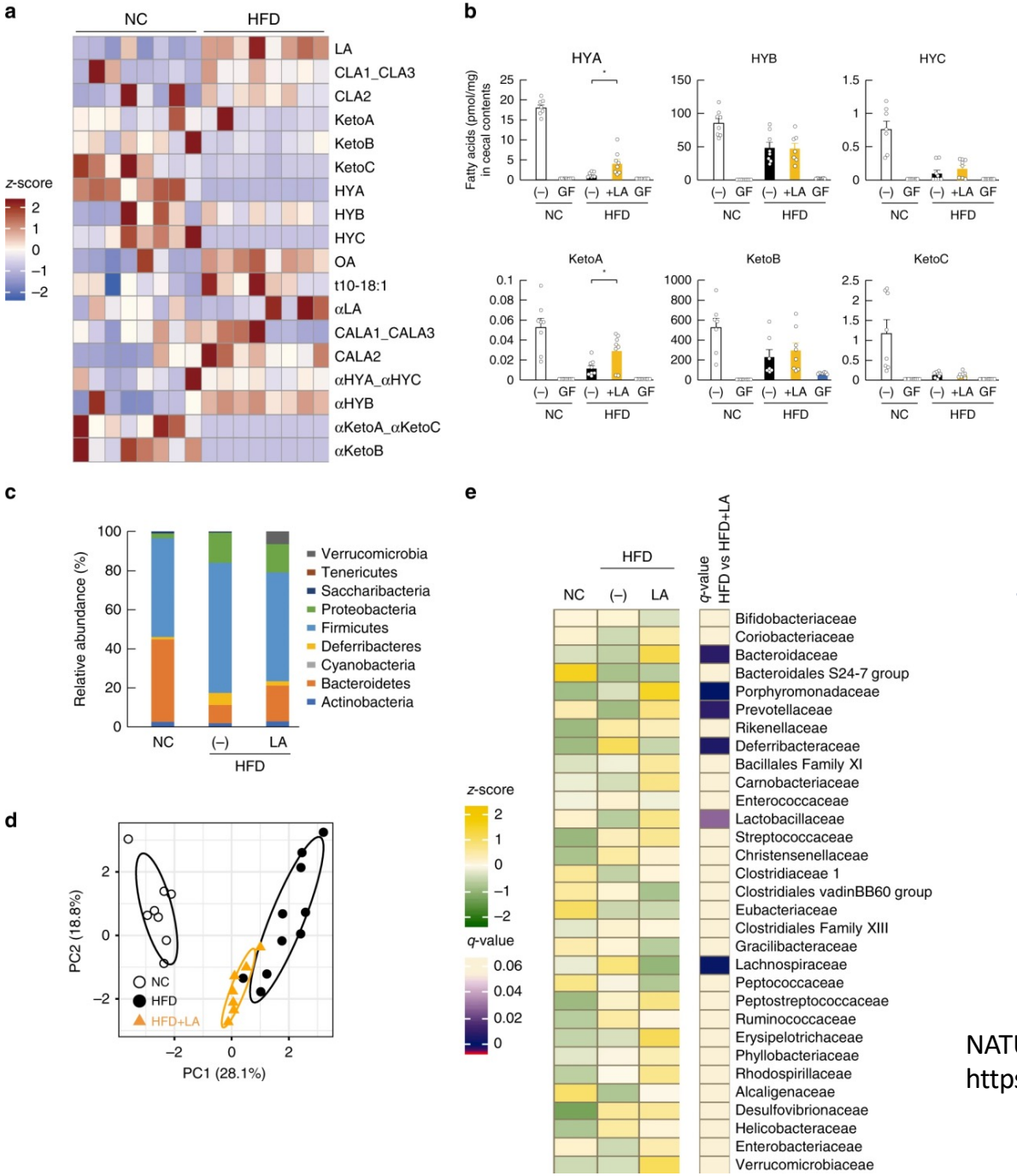


Pectins increase the abundance of beneficial intestinal microbiota that produce SCFA

SCFA in turn can induce differentiation of naïve T cells

jejunal mucus secretion

Effects of dietary PUFAs on gut microbiota composition and PUFA metabolites

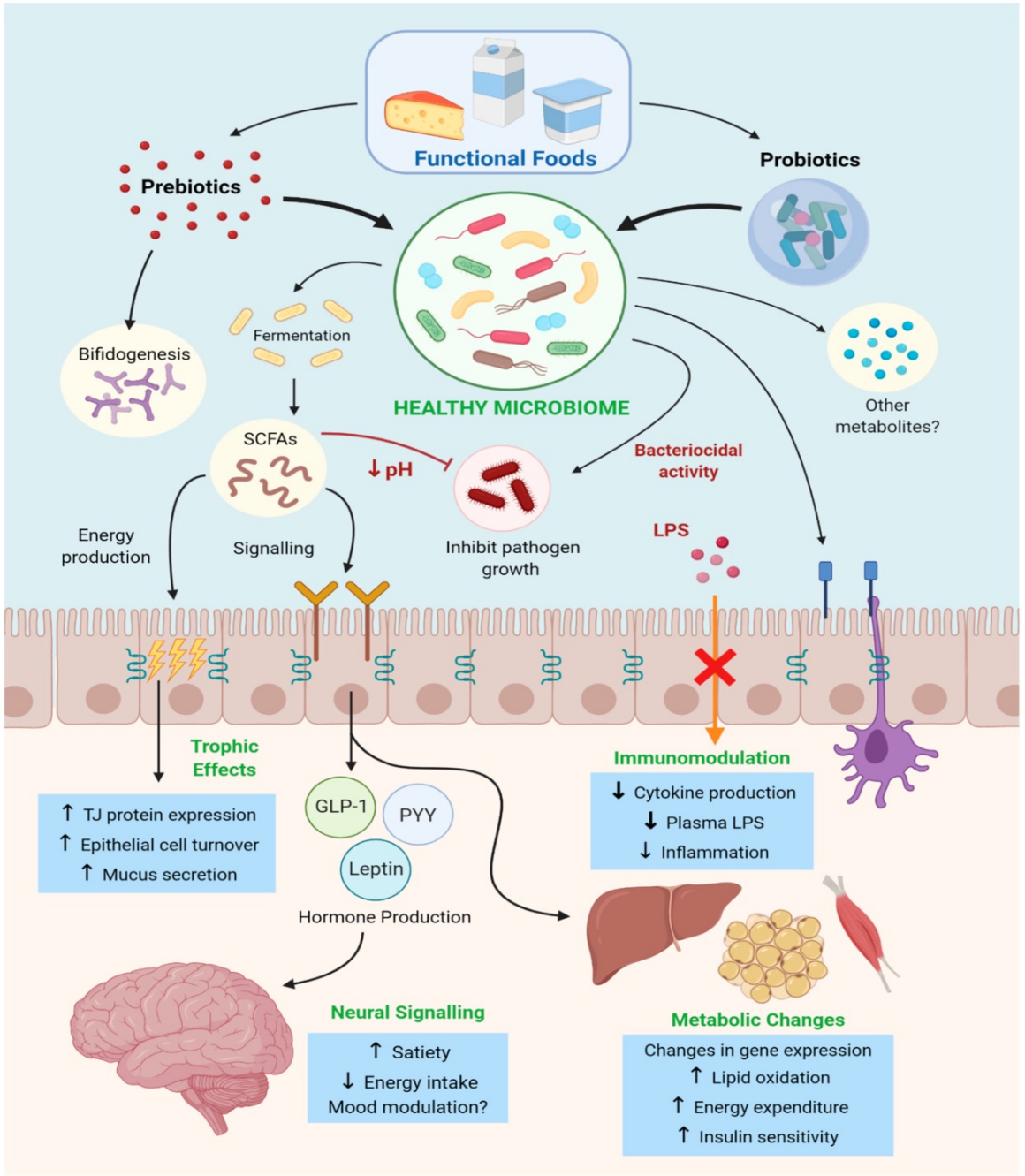


Gut microbiota conferred host resistance to HFD-induced obesity through the production of PUFA metabolites

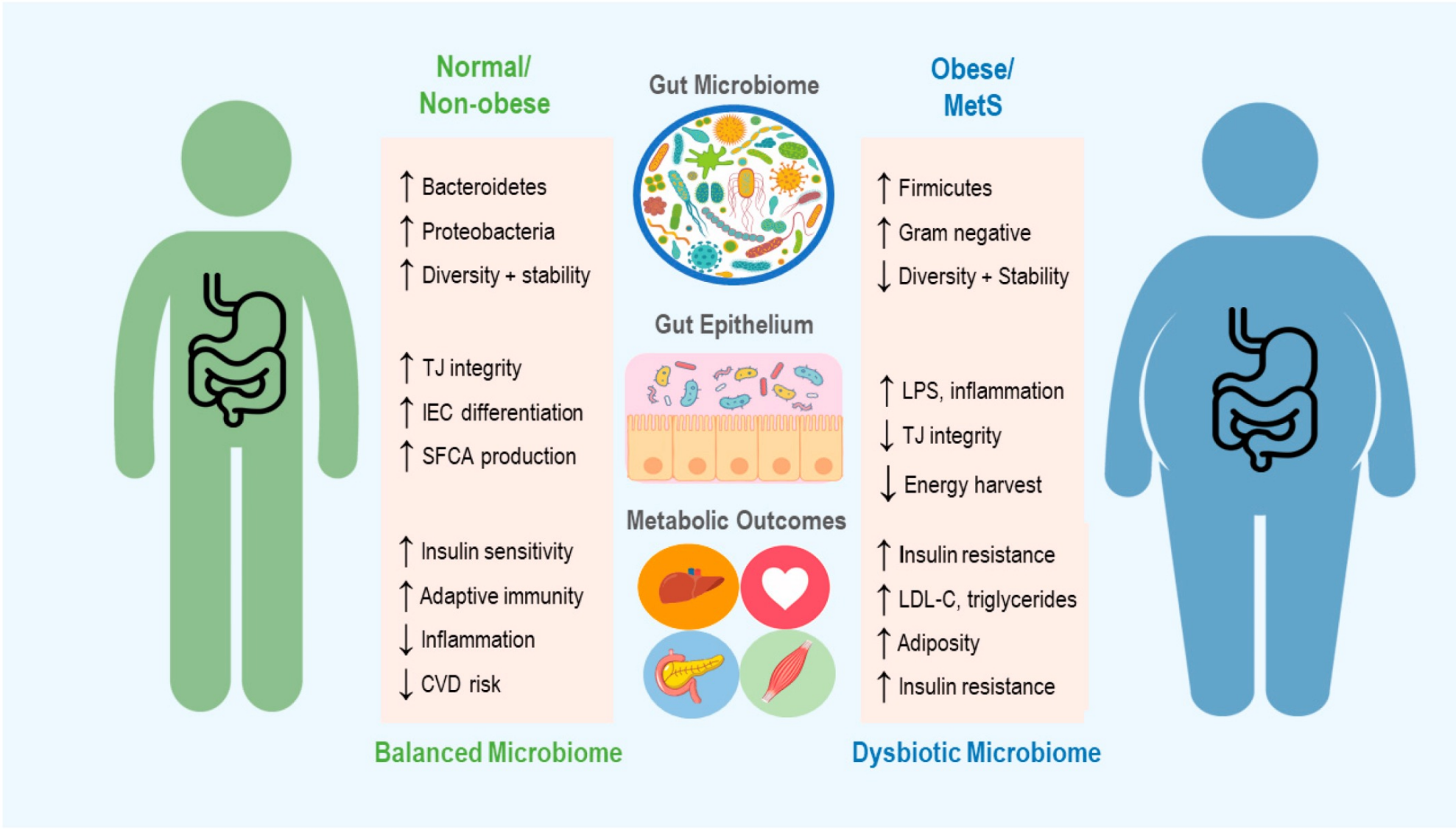
Supplementation of 10-hydroxy-*cis*-12-octadecenoic acid (HYA), an initial linoleic acid-related gut-microbial metabolite, attenuates HFD-induced obesity in mice.

NATURE COMMUNICATIONS | (2019) 10:4007 | https://doi.org/10.1038/s41467-019-11978-0

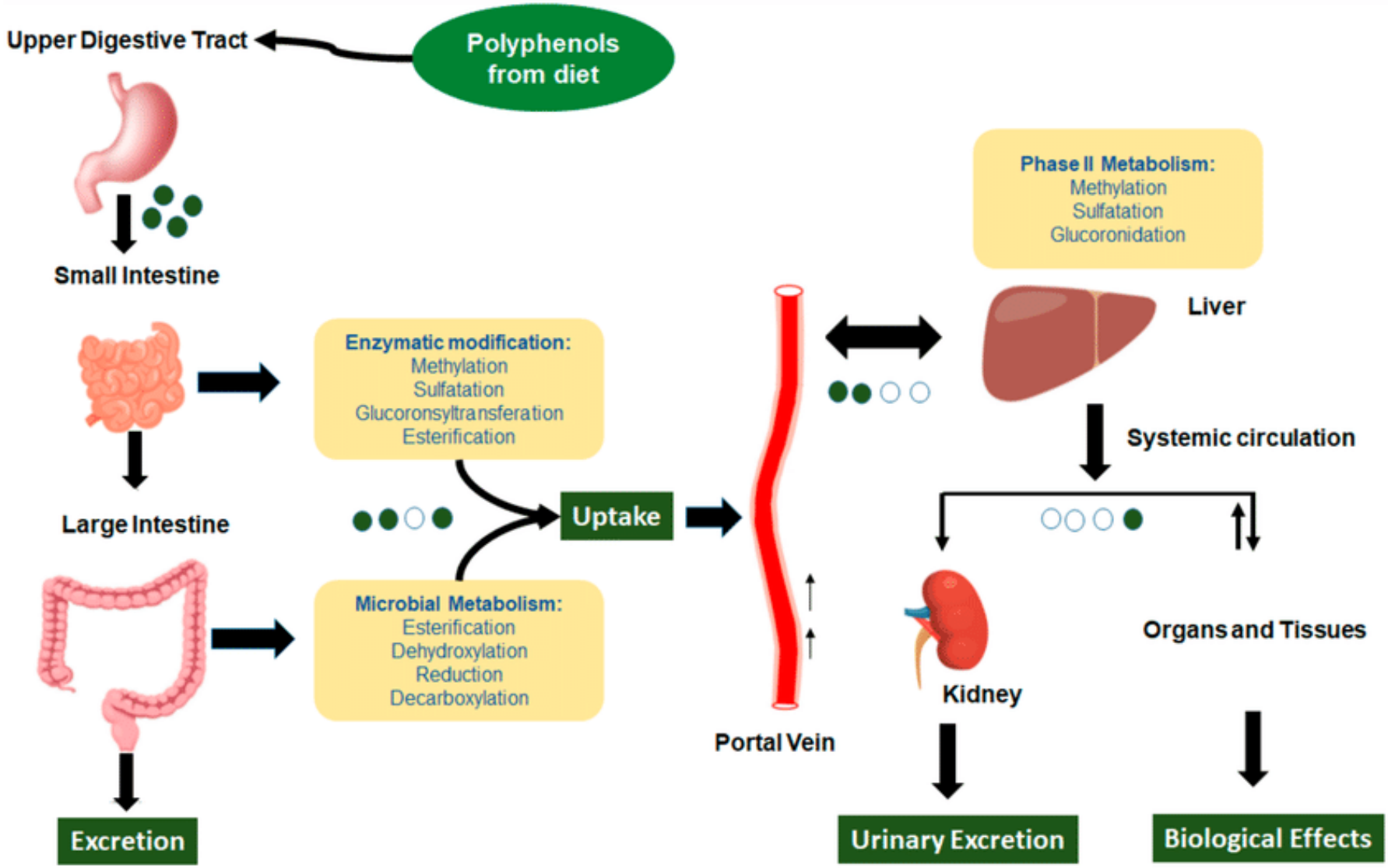
Mechanisms by which pre and probiotics initiate metabolic changes to combat development of obesity



The mechanism by which gut microbial metabolism of dietary PUFAs confers host resistance to obesity



Metabolism of dietary polyphenols



Metabolism of dietary polyphenols

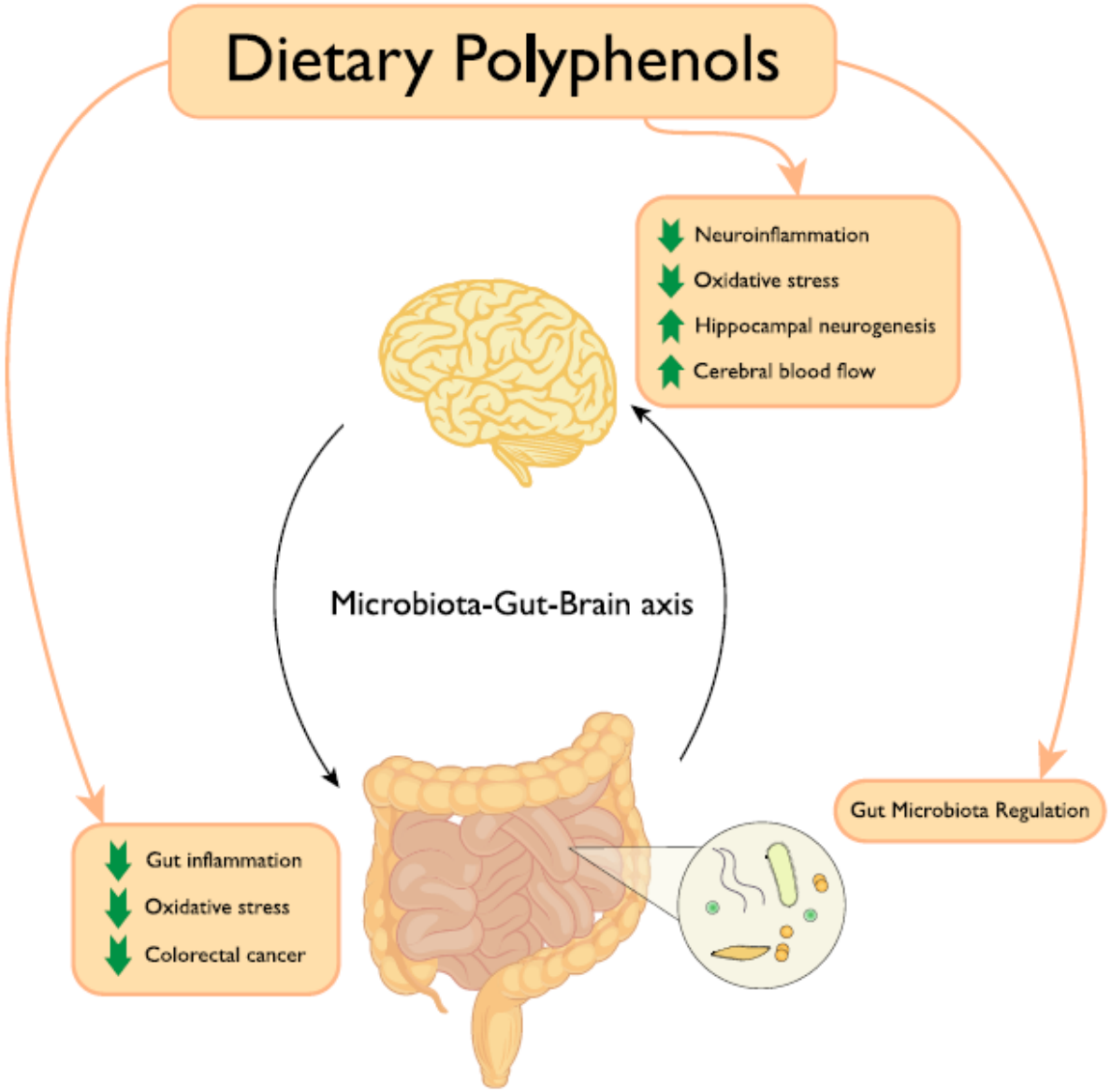
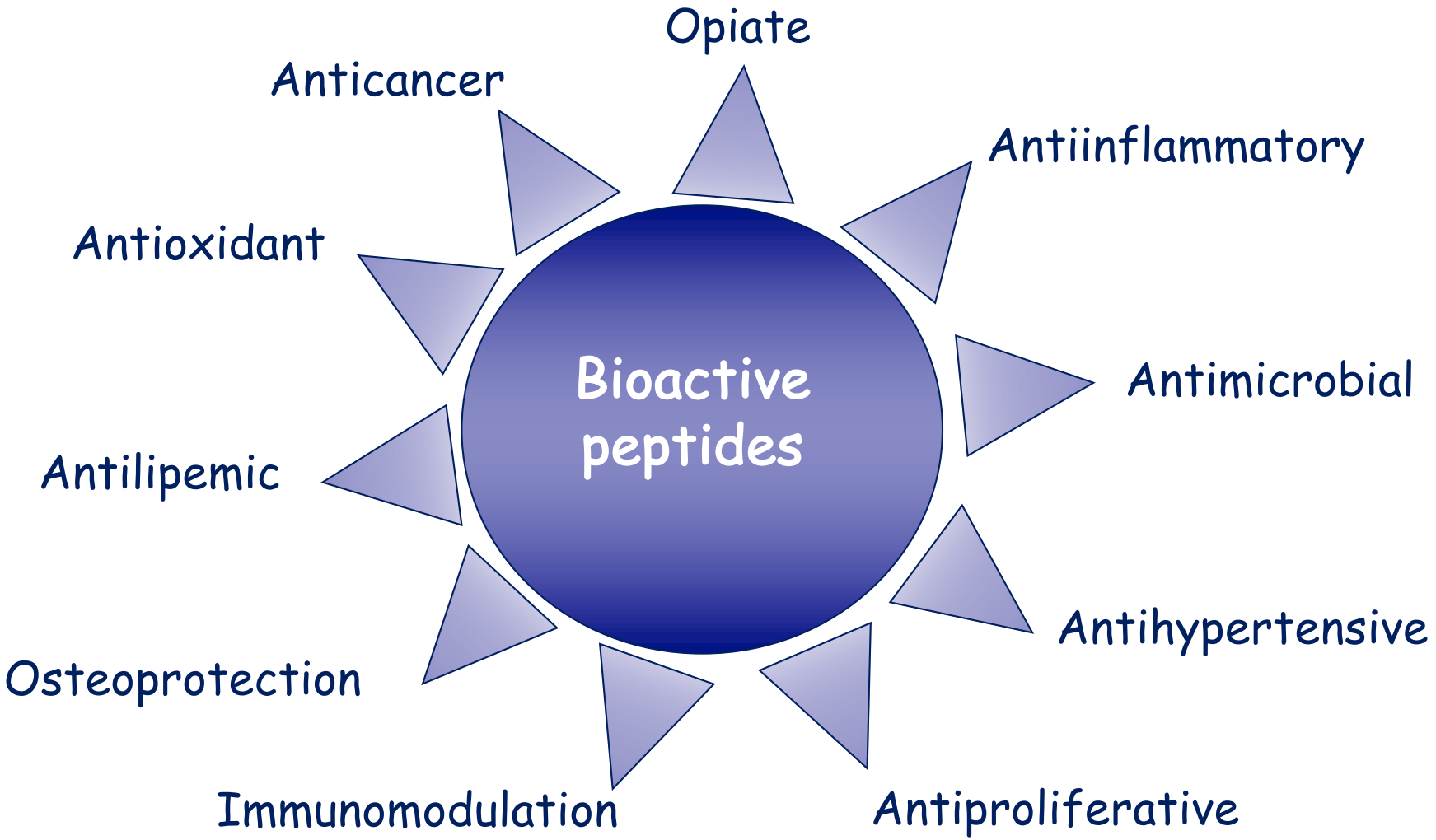
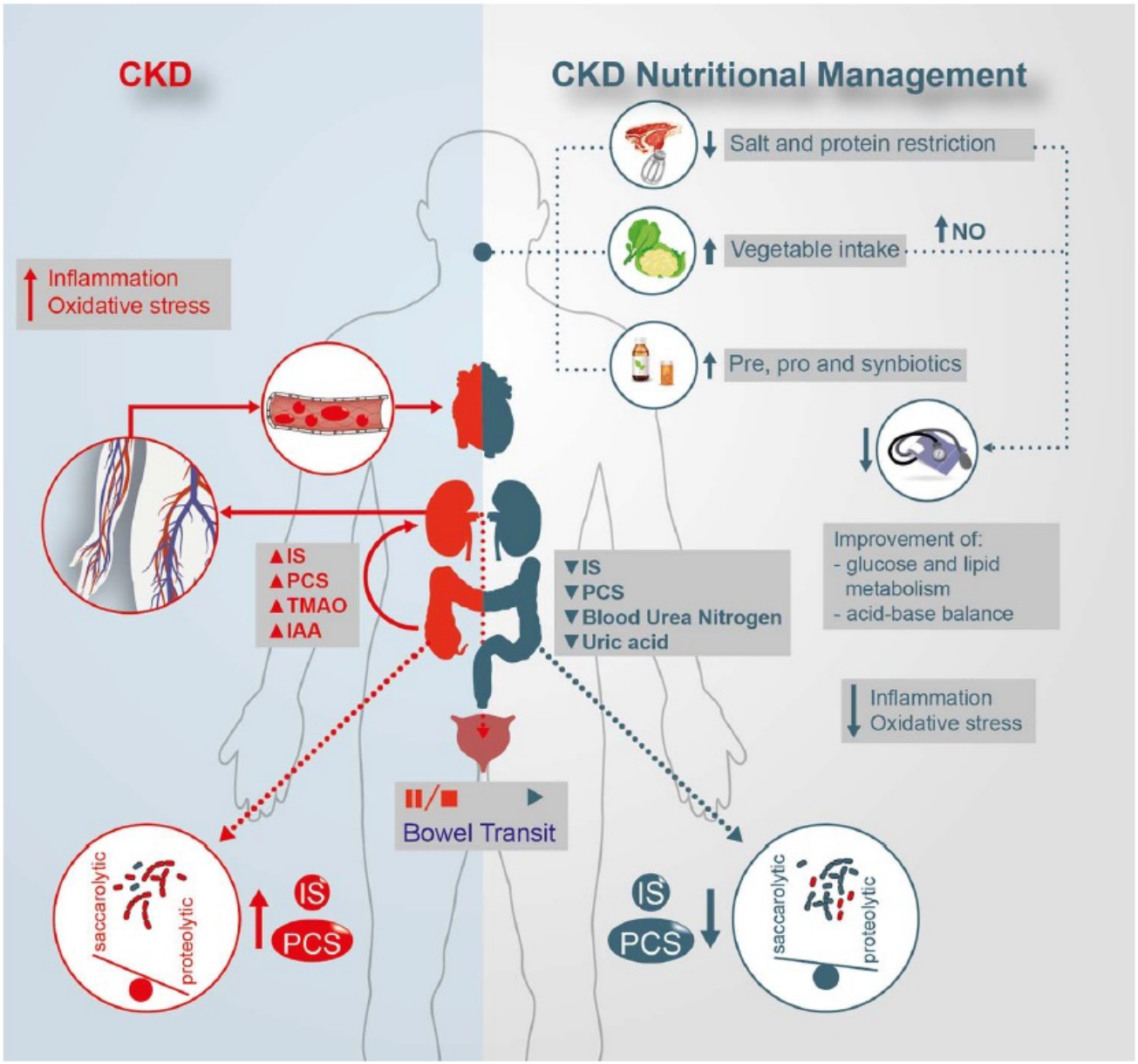


Fig. 2. Gut-brain connection regulated by dietary polyphenols - the bidirectional communication established between gut and brain is illustrated in the diagram as well as the modulation of microbiota-gut-brain axis by dietary polyphenols.

Biogenic compounds in gut: bioactivities attributed to peptides



Functional foods and gut microbiota in kidney diseases



Indoxyl sulfate (IS)
p-cresyl sulfate (PCS)
trimethylamine-N-Oxide (TMAO)
indole-3 Acetic Acid (IAA)

Dietary and gut microbiota in kidney diseases

- In chronic kidney disease (CKD) a vicious circle exists, in which proteolytic-derived microbial metabolites (p-cresol and indoxyl sulphate), represent the main circulating uremic toxins: their accumulation worsens dysbiosis and promotes CKD progression.

- Gut microbiota shaping through non-pharmacologic nutritional treatments, based on functional foods and Mediterranean Diet, represents an innovative approach in CKD, potentially restoring microbiota balance and slowing down disease progression.

Kidney & Blood Pressure Research

Kidney Blood Press Res 2014;39:114-123
DOI: 10.1159/000355785
Published online: July 29, 2014
Accepted: April 11, 2014
1423-0143/14/0393-0114$39.50/0

Review

What Would You Like to Eat, Mr CKD Microbiota? A Mediterranean Diet, please!

Eustacchio Montemurno[a] Carmela Cosola[b] Giuseppe Dalfino[b]
Giuseppe Daidone[c] Maria De Angelis[d] Marco Gobbetti[d] Loreto Gesualdo[a]

A low-sodium bread improves the adherence to a low-sodium diet in hypertensive subjects

- Direct relationship between salt intake and blood pressure which is the first cause of mortality and the second of morbidity worldwide

Why it is hard to reduce salt in diets?

Distribution of salt in Western diets:
-15% table salt
-5% naturally present in food
-80% processed food

Randomized controlled multi-center pilot trial (*ClinicalTrials.gov identifier nr. NCT03127553*)

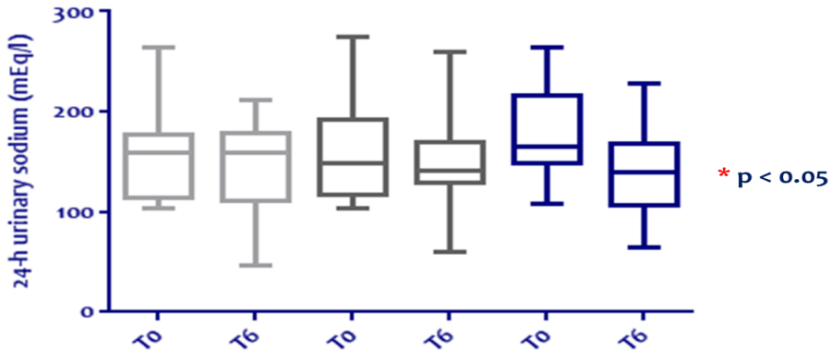
Enrollment= 57 patients

A. Free diet (with standard Altamura bread (750 mg Na/100g)

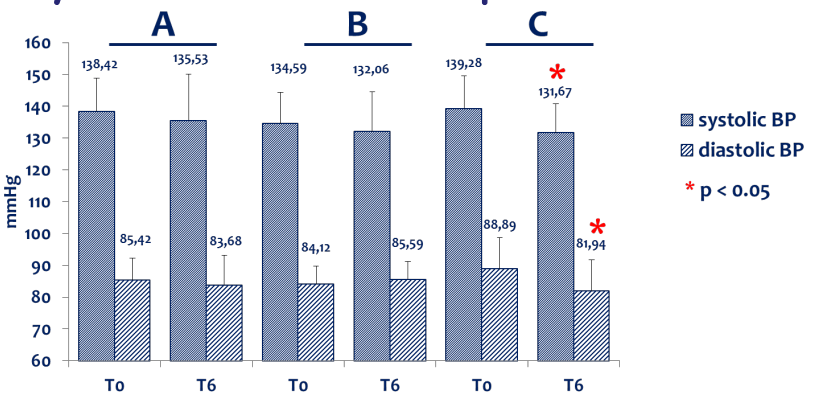
B. Low-sodium (2300 mg Na/die) diet using Altamura bread (750 mg Na/100g)

C. Low-sodium (2300 mg Na/die) diet with **low-sodium "PANdelCUORE" Altamura bread (280 mg Na/100g)**

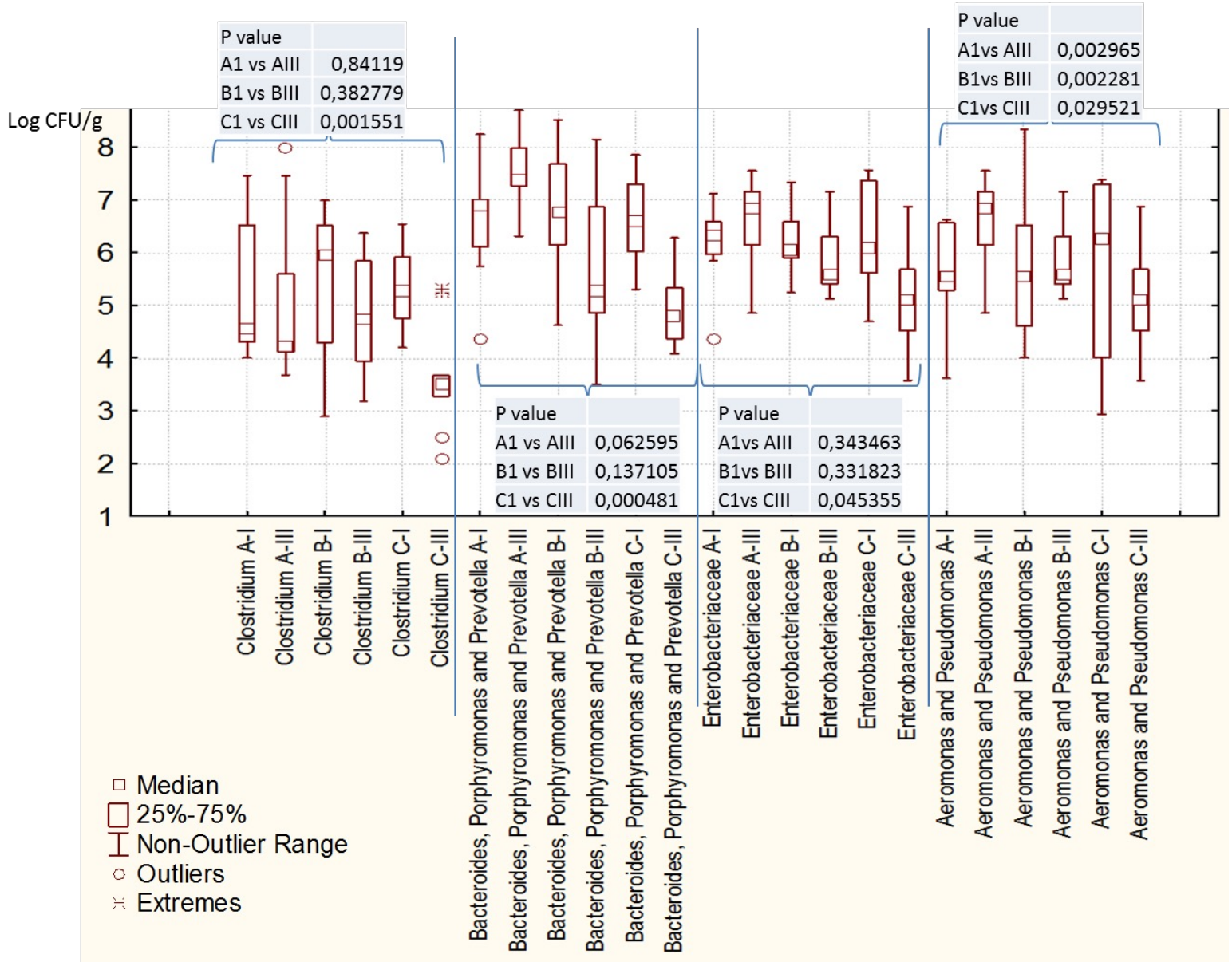
Sodium excretion as a measure of adherence



Systolic and diastolic pressure



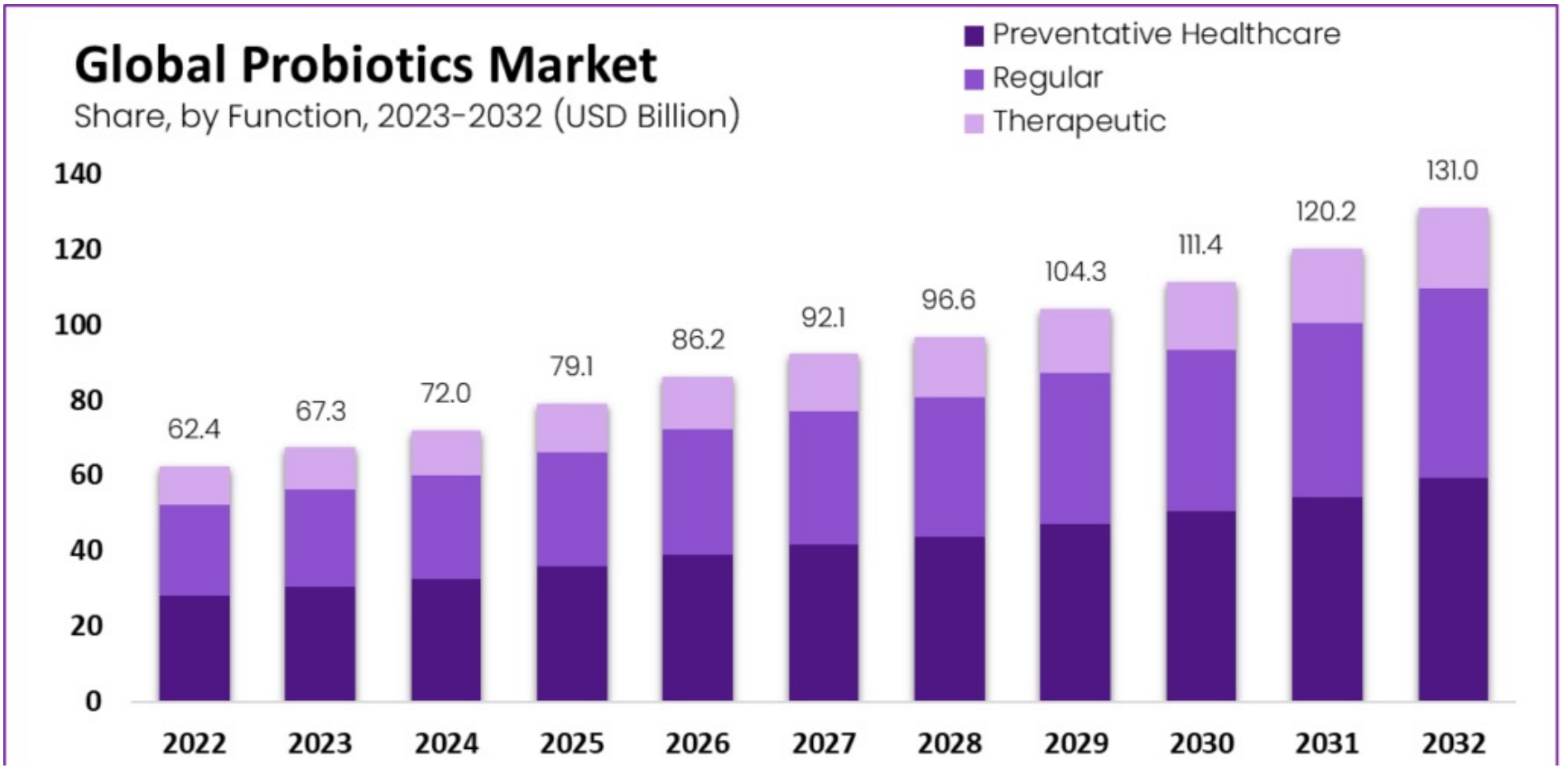
A low-sodium bread affects the gut microbiota in hypertensive subjects



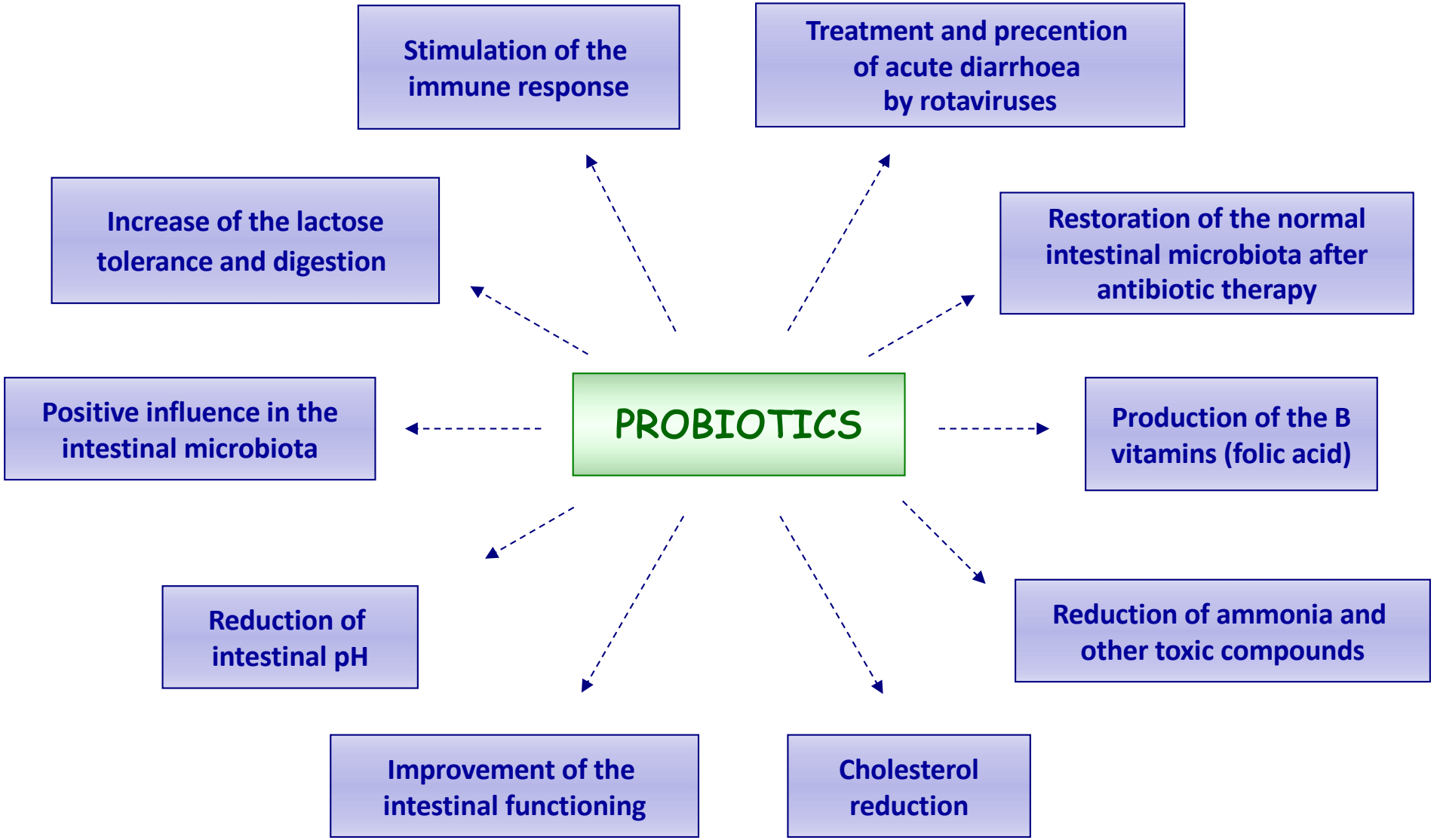
Probiotics

Probiotic Market Size is Expected to Reach USD 131 Billions by 2032

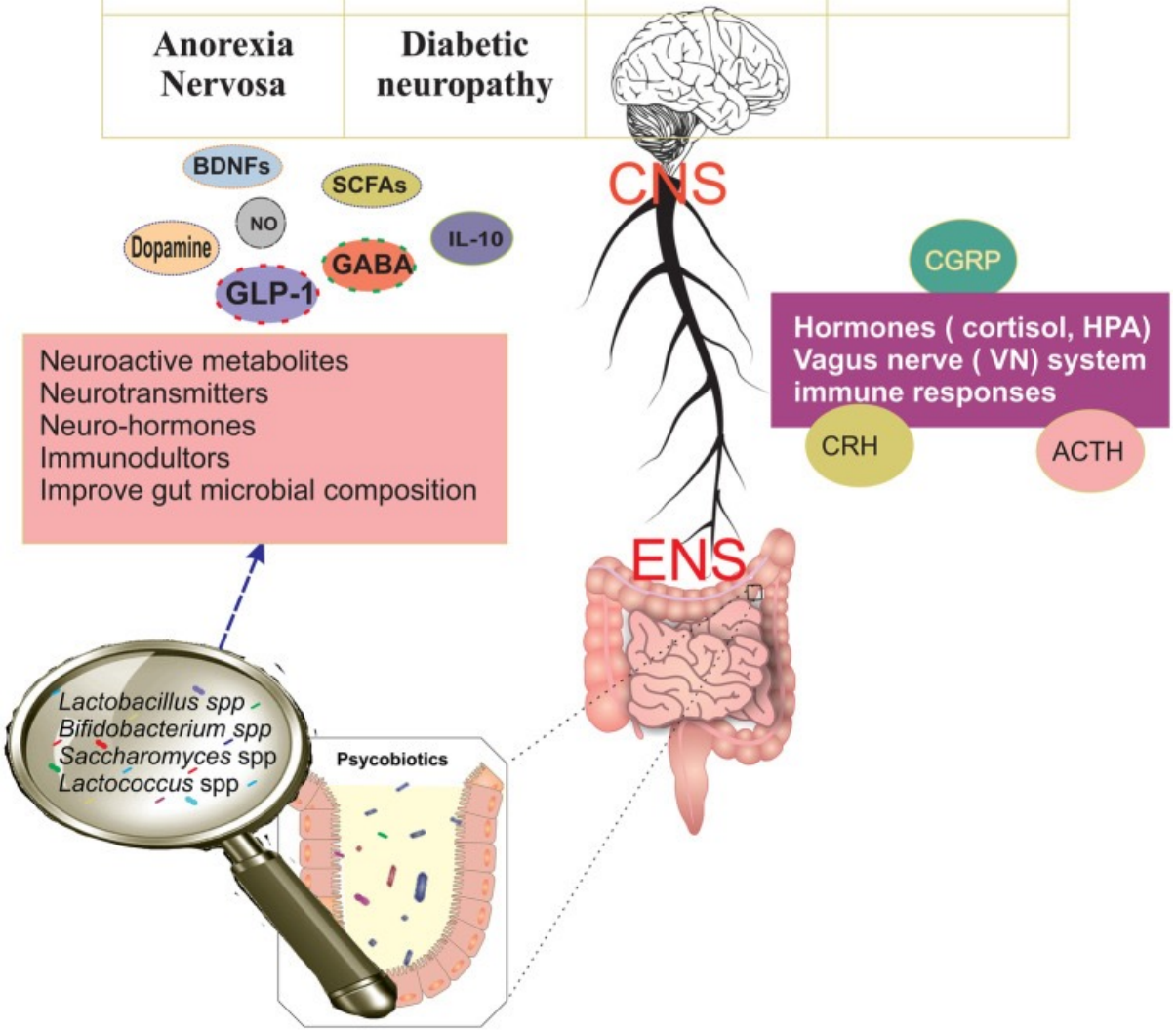
PROBIOTICS aquired the role of functional food ingredient and more than 1000 products are nowadays on the market.

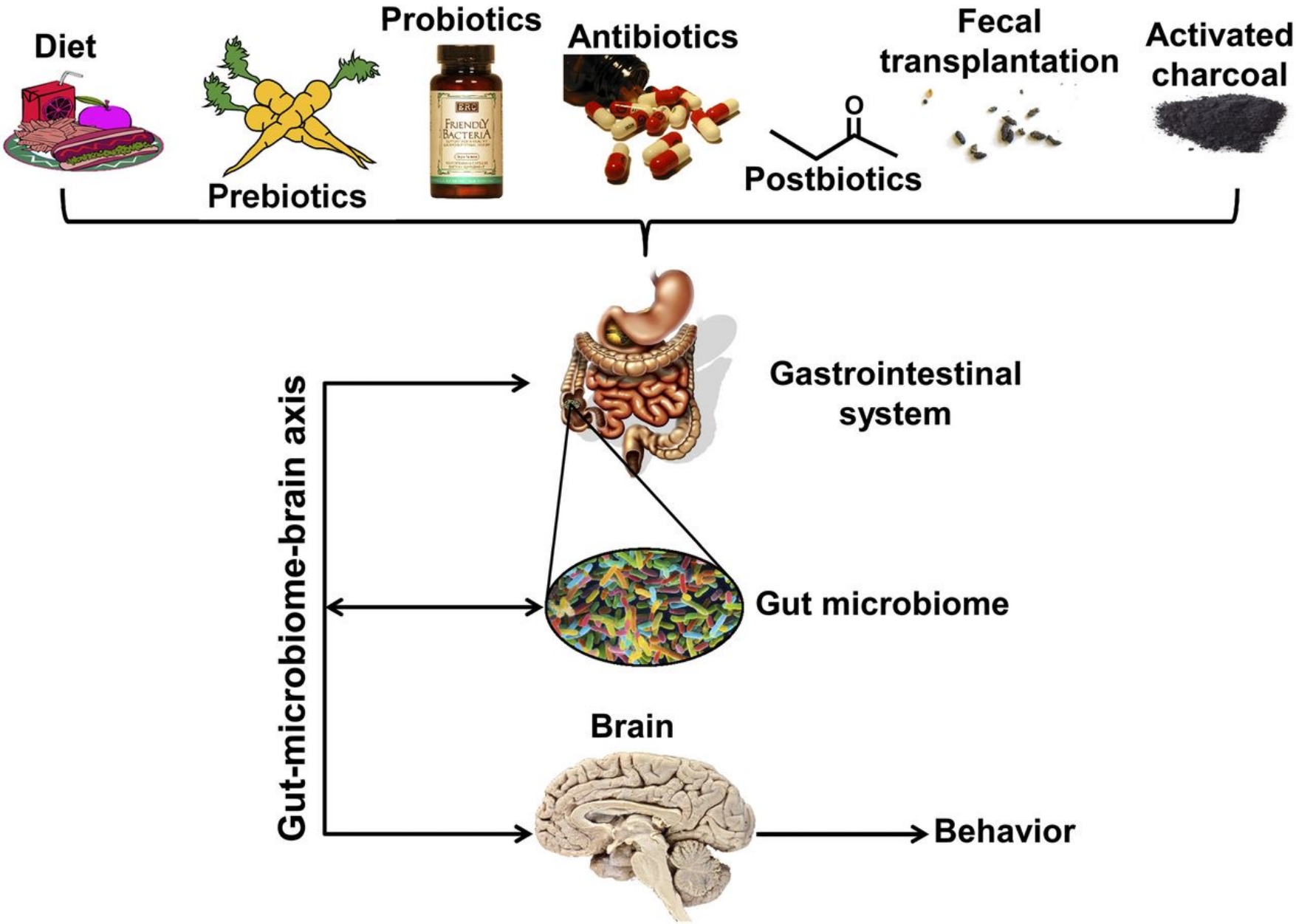


Probiotic effect



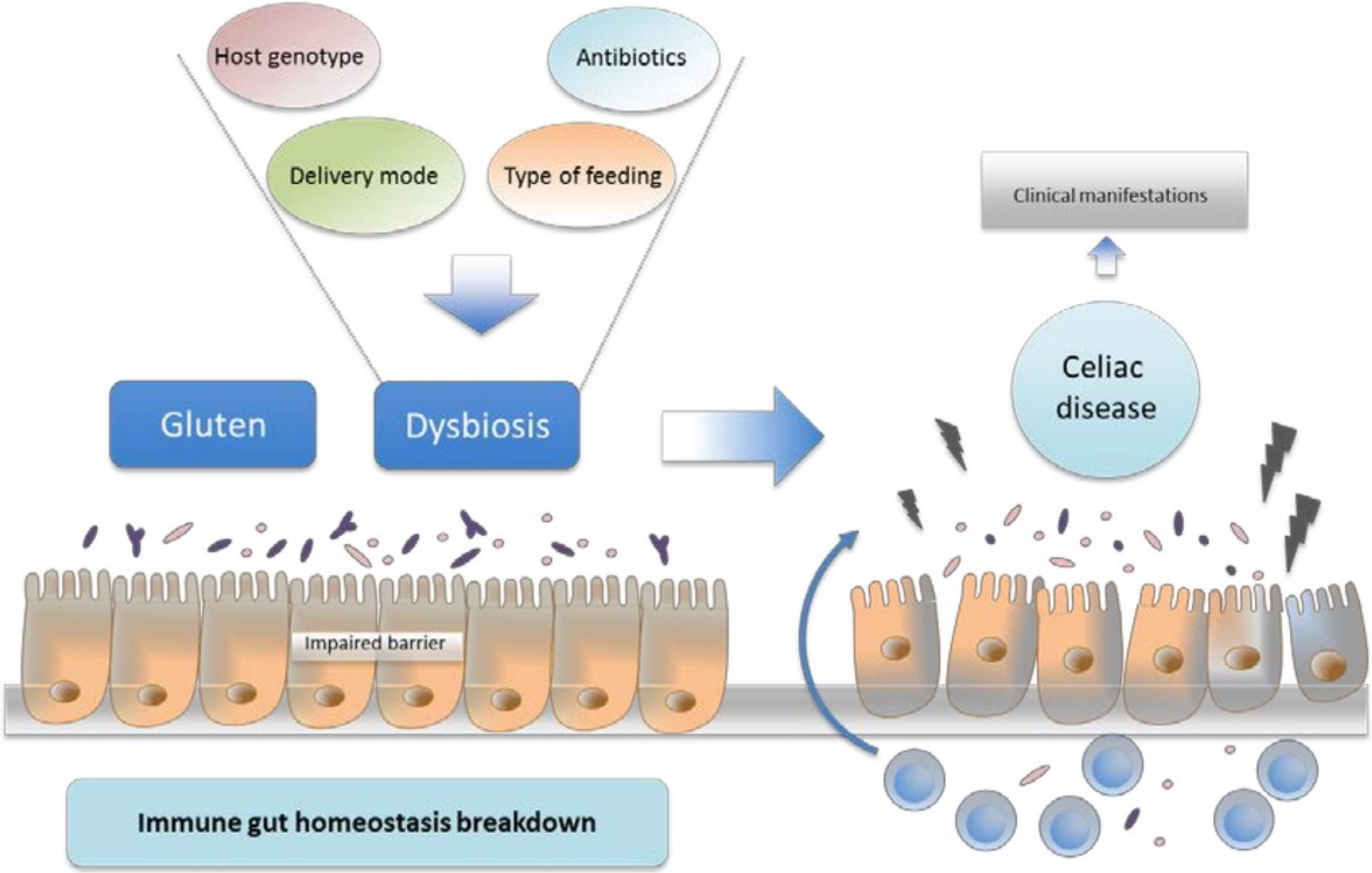
Alzheimer's disease	Parkinson`s diseases	Multiple sclerosis	Autism Spectrum
Depression	anxiety	Insomnia	Schizophrenia
Anorexia Nervosa	Diabetic neuropathy		




Diet
Prebiotics
Probiotics
Antibiotics
Postbiotics
Fecal transplantation
Activated charcoal
Gut-microbiome-brain axis
Gastrointestinal system
Gut microbiome
Brain
Behavior

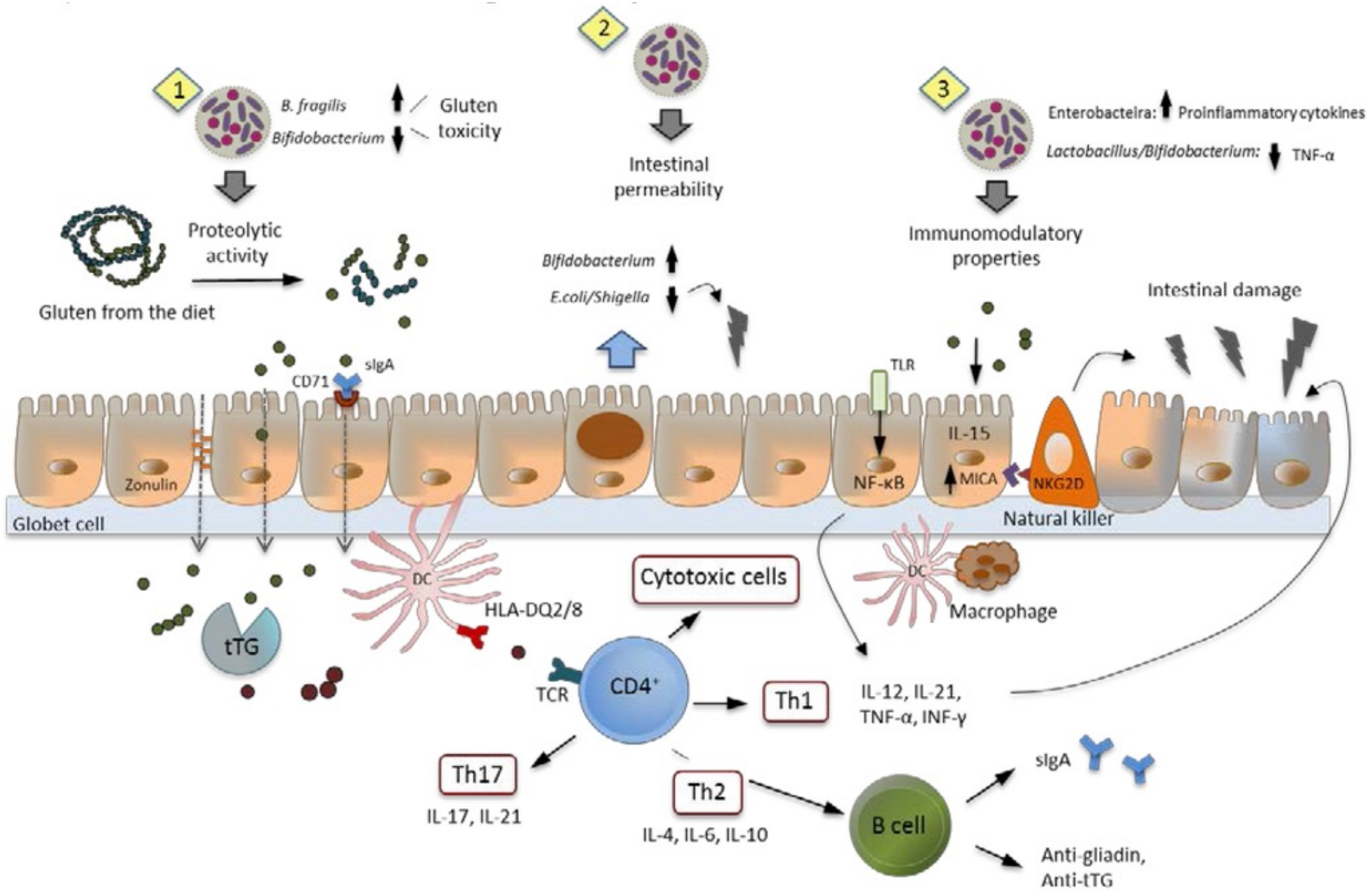
- Dietary implementation with probiotics/prebiotics to restore some microbial gaps (e.g. lattobacilli and bifidobatteri) could represents an alternative strategy to the treatment of intestinal dysbiosis in Neurological Disorders (AD and PDD-NOS).

Celiac disease, functional foods and gut microbiota



Microbiota and Celiac Disease: Cause, Consequence or Co-Evolut

Cenit et al., 2015. *Nutrients*, 7, 6900-6923; doi:10.3390/nu7085314



Probiotics as a promising alternative for gluten detoxification

Three main mechanisms are evoked:

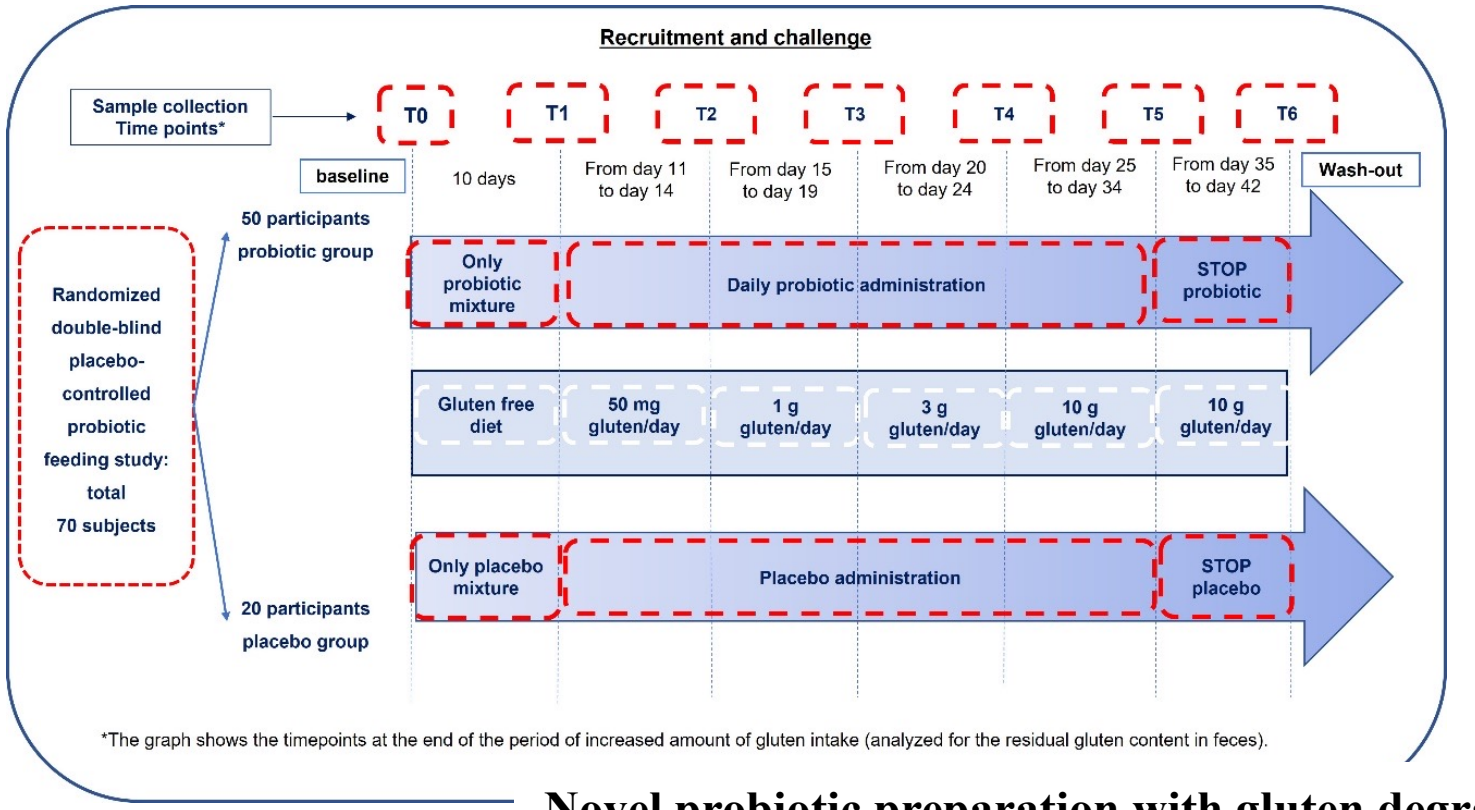
1. hydrolysis of gluten into small non-immunogenic polypeptides;

2. limited access of immunogenic polypeptides to the lamina propria and reduced epithelial permeability;

3. maintenance of the gut microbiota homeostasis, with regulation of both internal and adaptive immune systems

Probiotics as a promising alternative for gluten detoxification

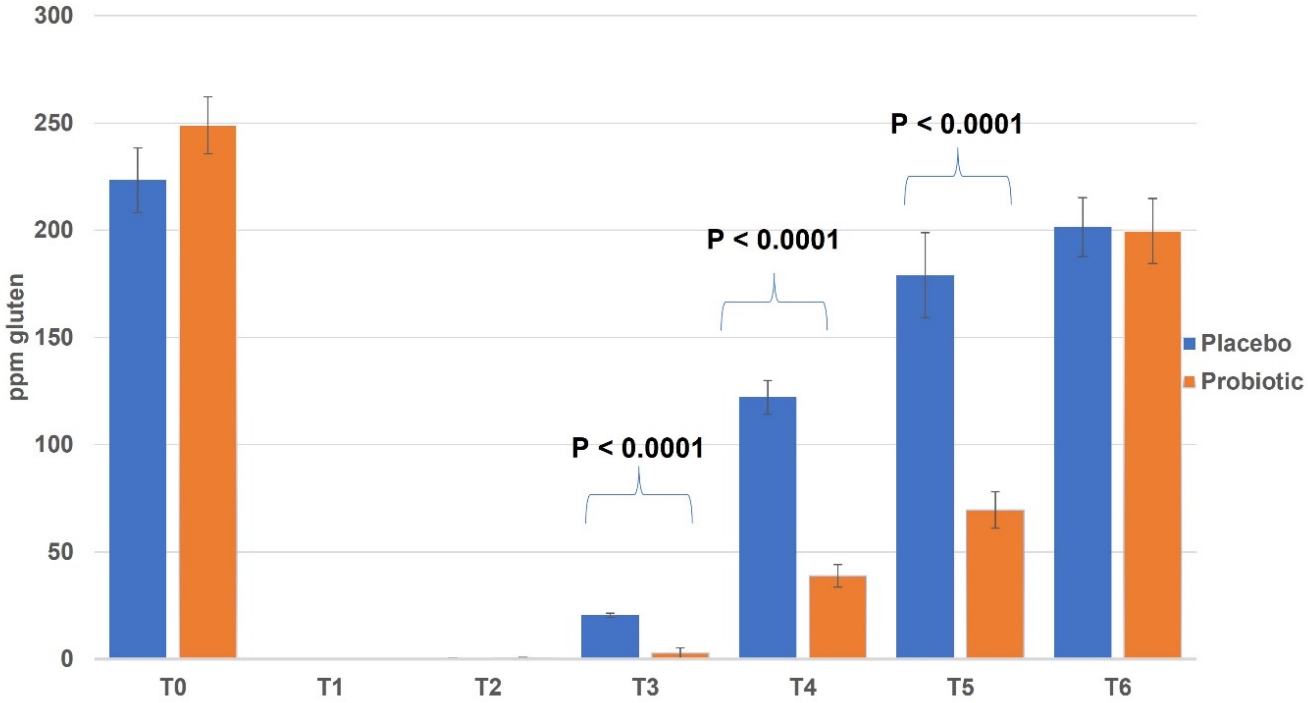
Results from a recent in vivo trial showed how 32 days of probiotics treatment enhanced gluten digestion and promotes gut microbiota functionality in GFD



Novel probiotic preparation with gluten degrading activity and gut microbiota modulating effect

Olga Nikoloudaki[1], Giuseppe Celano[2], Andrea Polo[1], Claudia Cappello[1], Lena Granehäll[1], Alice Costantini[1], Mirco Vacca[2], Bodo Speckmann[3], Raffaella Di Cagno[1*], Maria De Angelis[2], Marco Gobbetti[1]

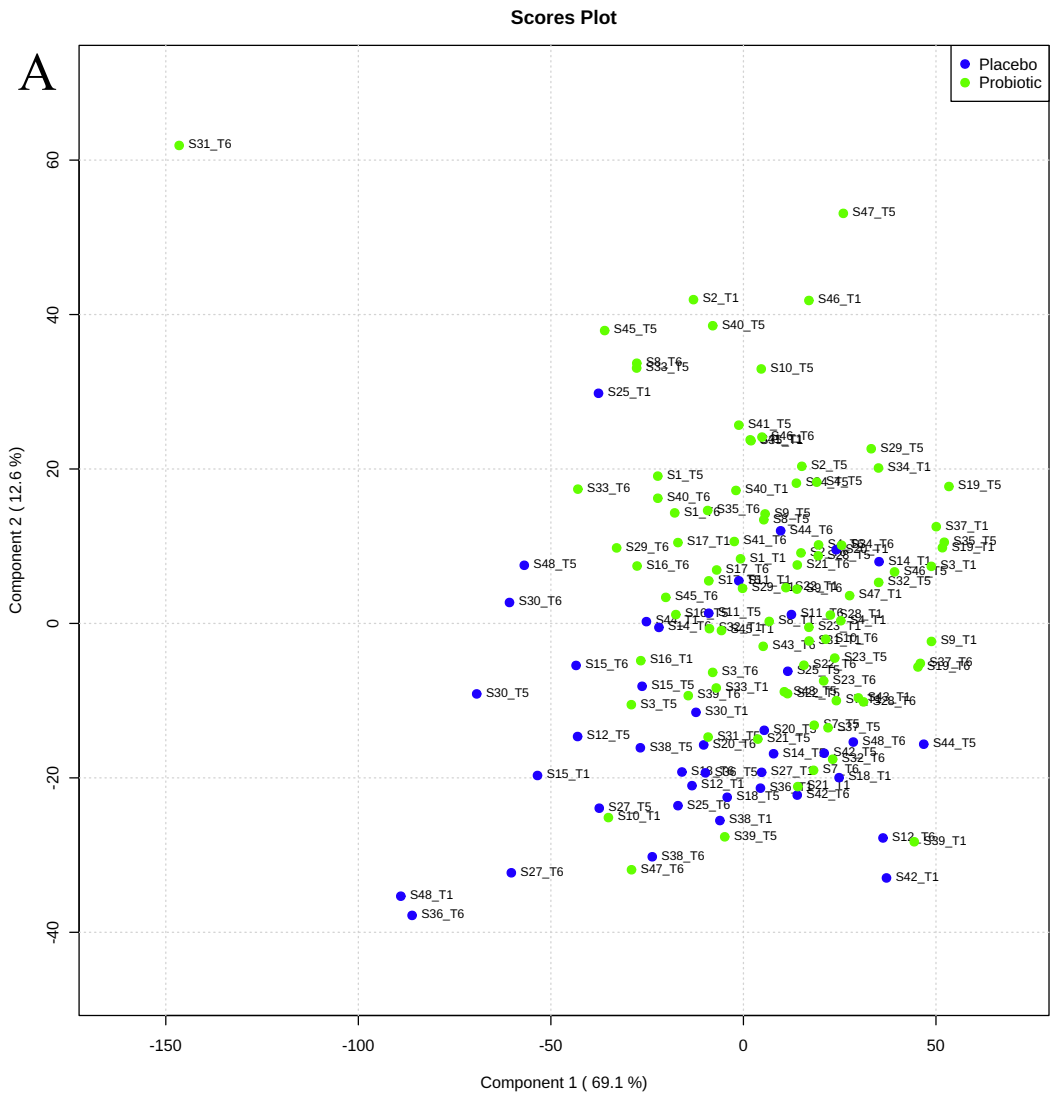
Novel probiotic preparation with gluten degrading activity and gut microbiota modulating effect

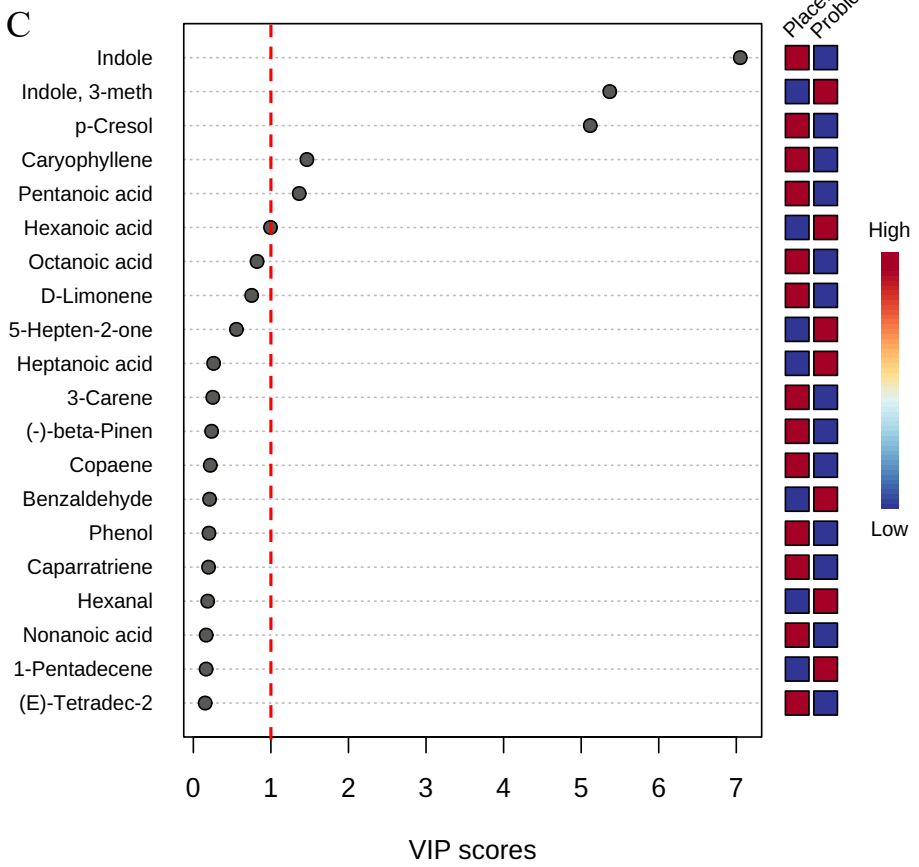


Average gluten concentrations (ppm) in fecal samples of participants belonging to the placebo (n=20; blue colour bar) and probiotic group (n=50; orange colour bar). All enrolled participant were strictly adherent to MD.

Probiotics as a promising alternative for gluten detoxification

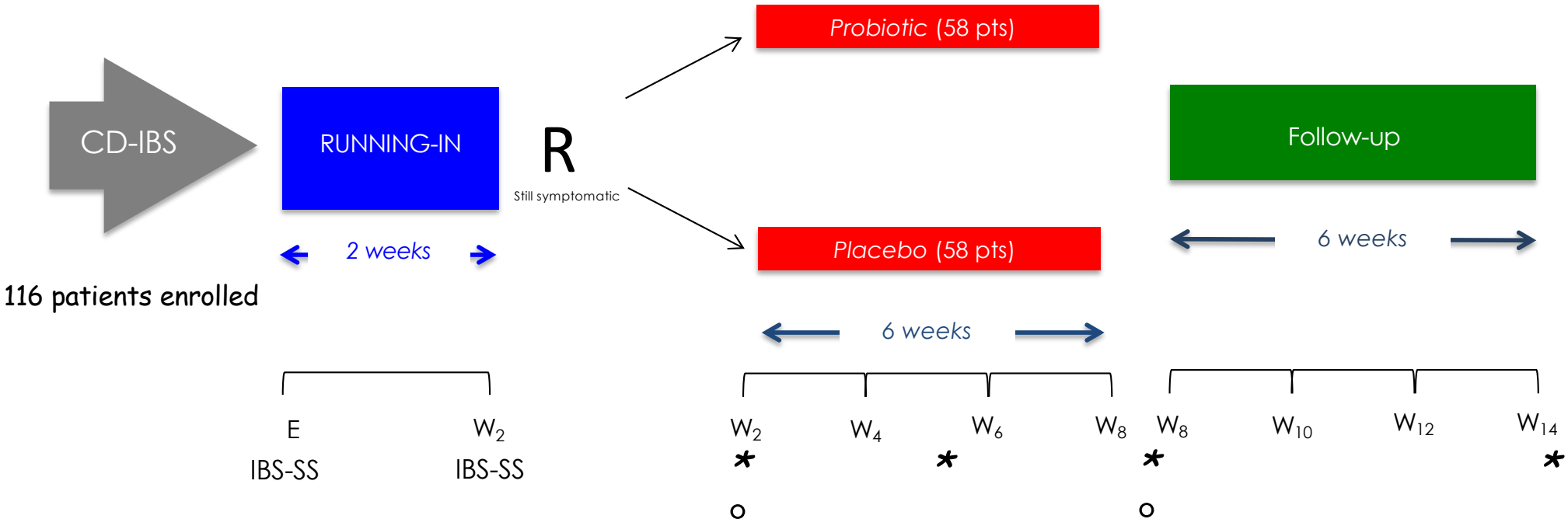
Partial least squares-discriminant analysis (PLS-DA) based on volatile compounds (VOCs) abundance normalized matrix.





Skatole (3-methyl-indole) and hexanoic acid were higher in probiotic group, while indole, p-cresol, caryophyllene and pentanoic acid were increased in placebo group

Clinical and Microbiological Effect of a Multispecies Probiotic Supplementation in Celiac Patients With Persistent IBS-type Symptoms



* IBS severity score (IBS-SS) assessed by VAS

* Gastrointestinal Symptom Rating Scale (GSRS)

* Bristol Stool Chart (BSC)

* IBS Quality of Life (I-QOL)

* Symptom Check List (SL-90)

* Hospital Anxiety & Depression Scale (HADS)

o Urine - stools

Probiotic mixture:

Lactobacillus plantarum CECT 4528

Lactobacillus casei 101/37 LMG P-17504

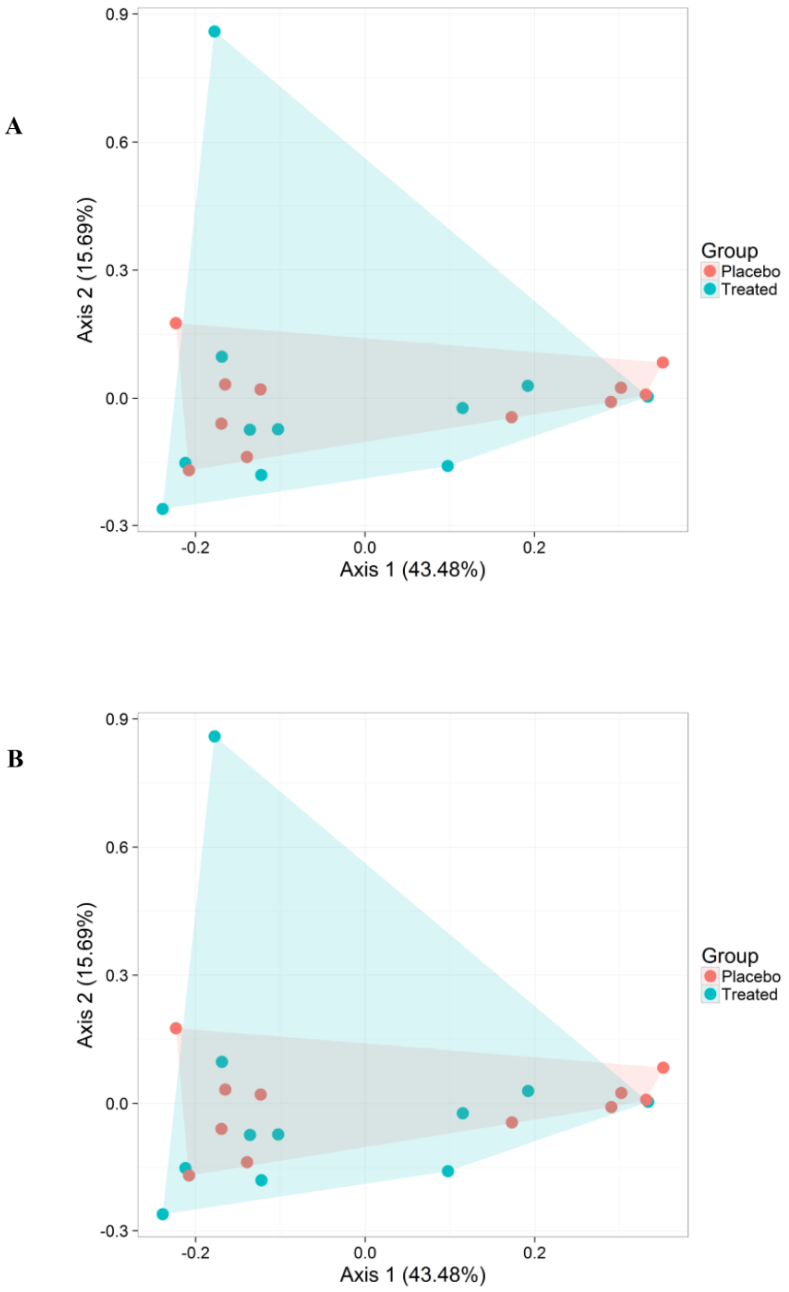
Bifidobacterium breve Bbr8 LMG P-17501

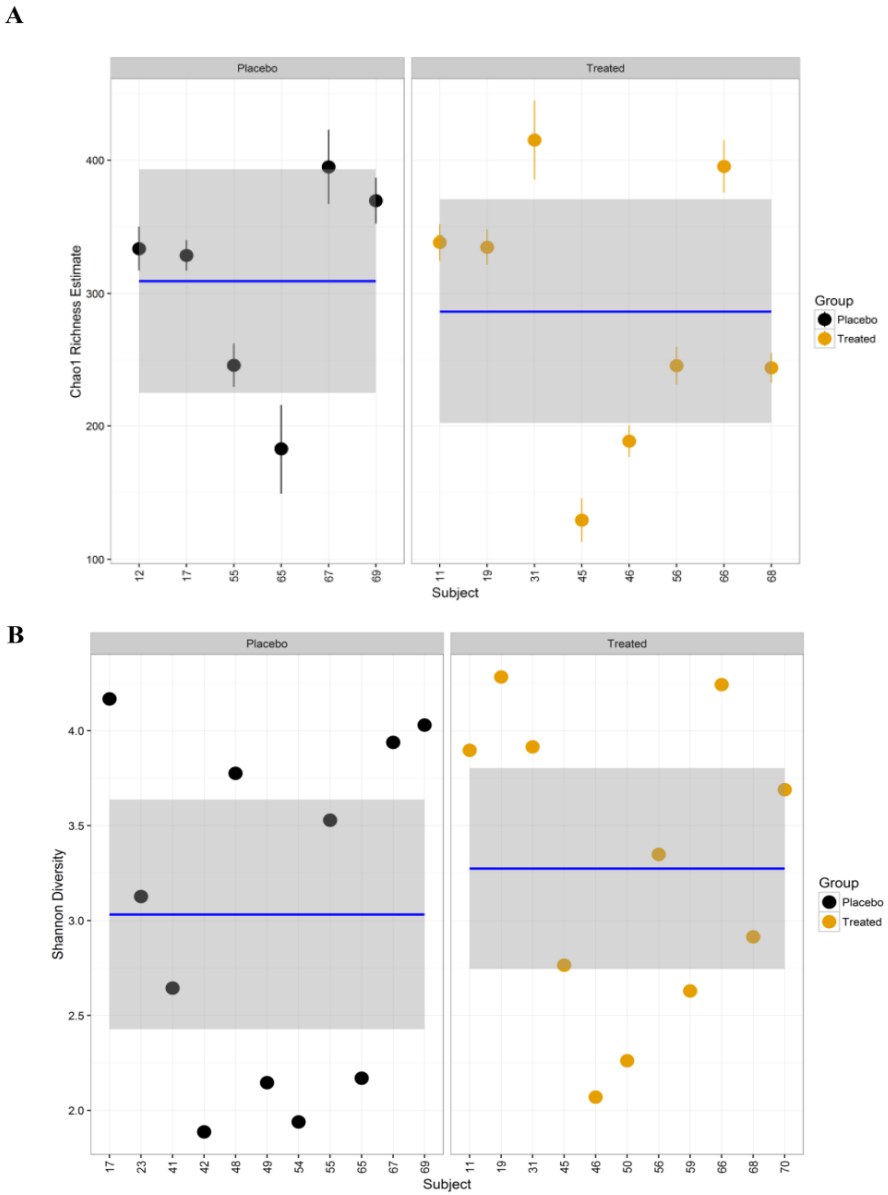
Bifidobacterium breve Bl10 LMG P-17500

Bifidobacterium animalis (Subsp. lactis) LMG P-17502

ClinicalTrials.gov Identifier: NCT01699191

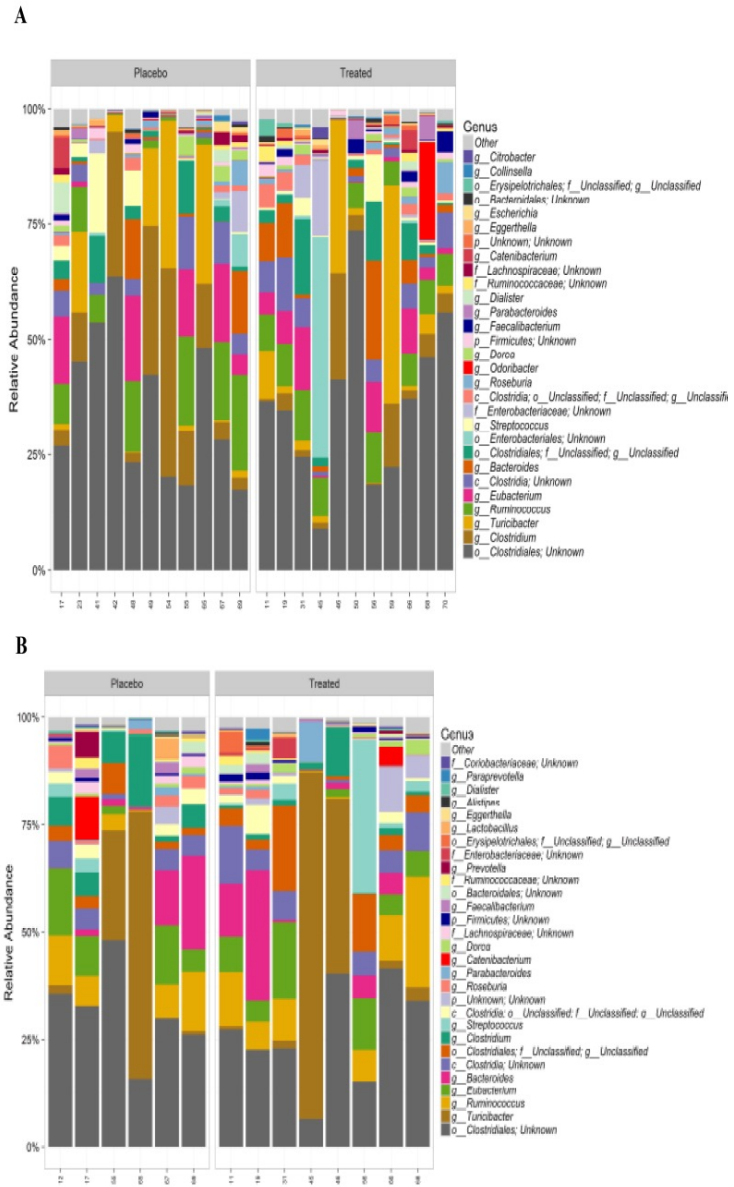
Microbiome in CD with Persistent IBS-type Symptoms

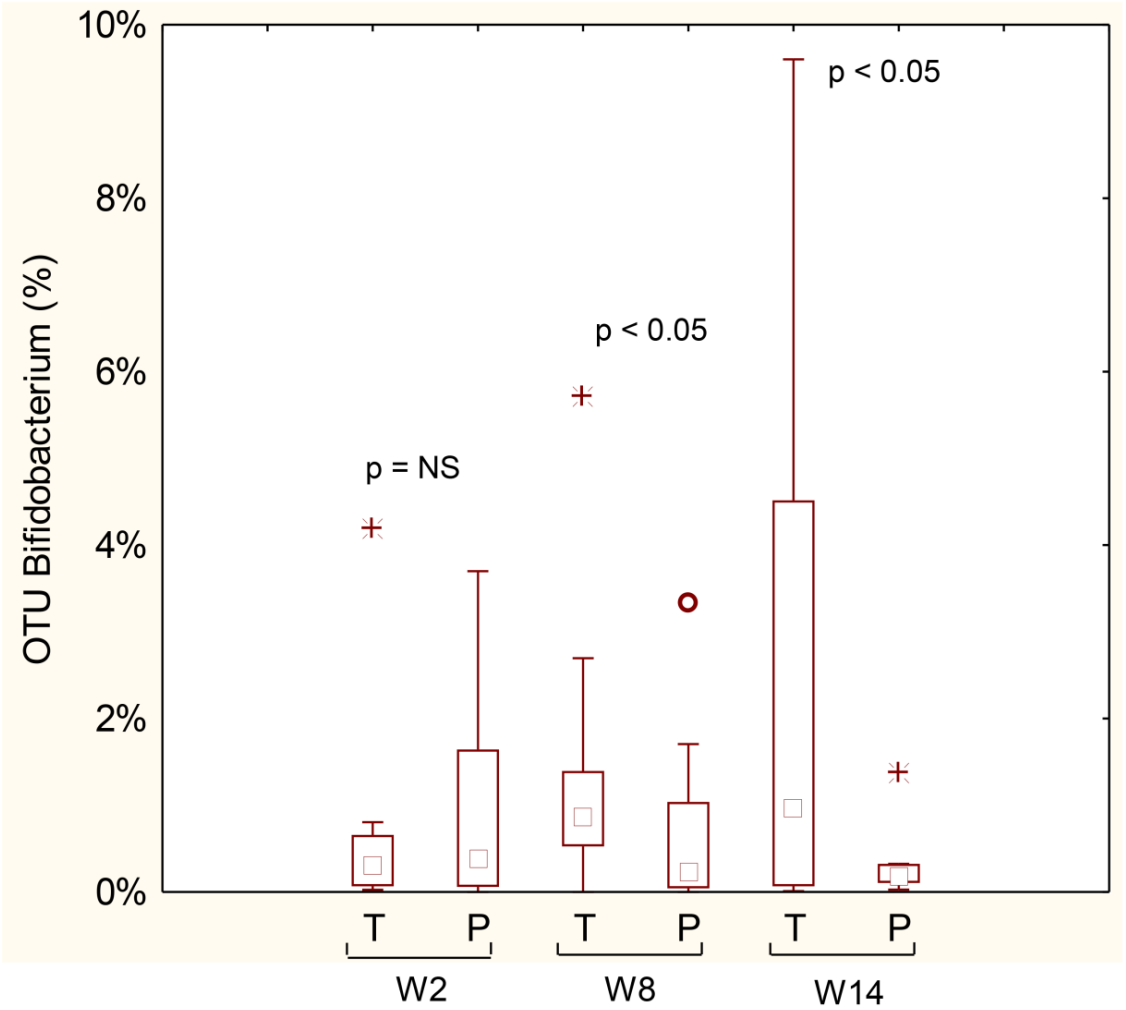




Patent N. 0001425900

Microbiome in CD with Persistent IBS-type Symptoms





Patent N. 0001425900

Probiotics improve the clinical scores

	Probiotics (n = 54)	Placebo (n = 55)	*P*
Age (y)*	43.3 (18.8-62.2)	44.6 (19.3-63.4)	NS
Male/female	6/35	9/46	NS
BMI (kg/m^2)	22.8 ± 3.5	23.4 ± 2.9	NS
Positive EMA	0	0	NS
TTG-IgA (IU/mL)*†	0.8 (0-1.2)	0.5 (0-2.1)	NS
SGA of relief	6.1 ± 2.4 (95% CI, 4.6-7.1)	6.3 ± 1.7 (95% CI, 5.5-6.5)	NS
Duration of GFD (y)*	6.8 (2.6-16.7)	7.4 (3.5-17.5)	NS
IBS-SSS	295 ± 84.9 (95% CI, 269-320)	237.6 ± 86.5 (95% CI, 211-263)	0.01
GSRS	18.7 ± 5.8 (95% CI, 14.6-26.1)	14.9 ± 5.1 (95% CI, 13.4-27.5)	0.02
Bristol Stool Charts	2.6 ± 1.2	2 ± 1.5	NS
IBS-QOL	33.7 ± 17 (95% CI, 28.6-38.9)	31.5 ± 19.3 (95% CI, 25.7-37.2)	NS

*Median (range).

†TTG-IgA normal value < 10 IU/mL.

CI indicates confidence interval; GFD, gluten-free diet; GSRS, Gastrointestinal Symptom Rating Scale; IBS-QOL, Irritable Bowel Syndrome Quality of Life; IBS-SSS, Irritable Bowel Syndrome Severity Scoring System; NS, not significant; tTG-IgA, tissue transglutaminase immunoglobulin-A.

Patent N. 0001425900

Probiotic containing diet, celiac disease and gut microbiota

- Dietary fibers and probiotics may offer a potential treatment to improve the microbiota and metabolome of celiac and IBS subjects.

Thanks !