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# Il ruolo della cucina e della chetosi sulla funzione del microbiota intestinale

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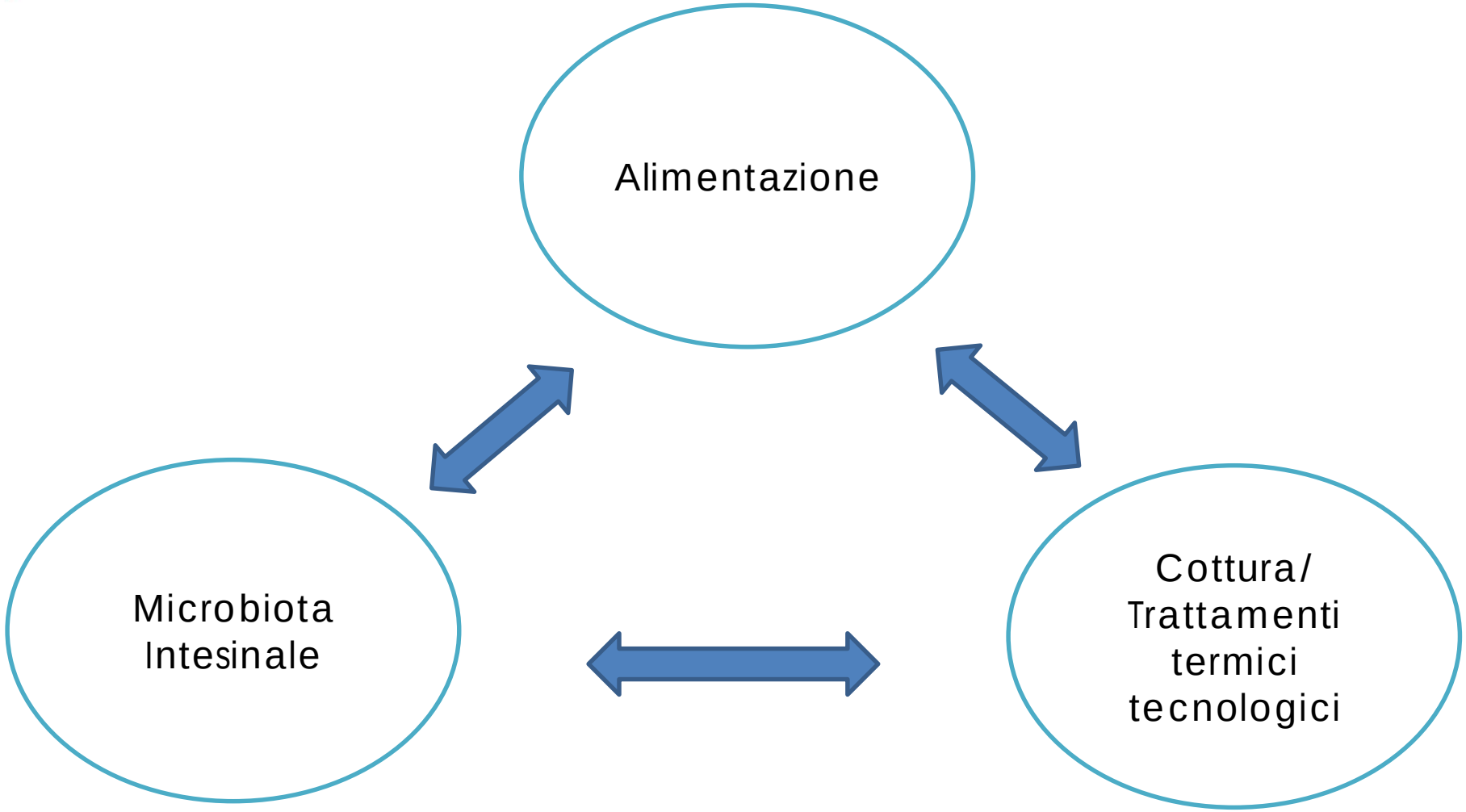
Alimentazione
Microbiota Intesinale
Cottura/ Trattamenti termici tecnologici

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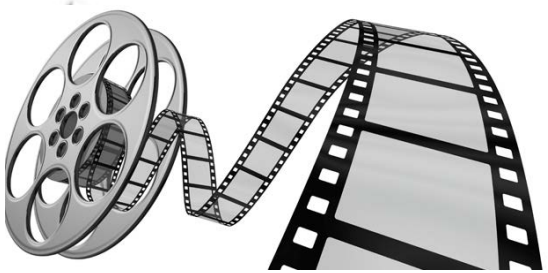
# MICROBIOTA! Chi era costui?

Il **microbiota** è l'insieme dei microorganismi (**virus, funghi, batteri**) che popolano, con diversa densità e "demografia" il tratto digerente, le mucose, l'epitelio, etc.

- **I funghi costituiscono il micobioma** e comprendono, ad esempio, *Candida*, e *Saccharomyces*
- Hanno un ruolo importante grazie alle complesse interazioni funghi-batteri, funghi-funghi e funghi-ospite, che influenzano la salute e, in alcuni casi, le malattie dell'ospite.

- **I virus costituiscono il viroma.** Nelle feci umane si ritiene siano presenti anche $10^9$ particelle virus-simil per grammo. I batteriofagi sono i virus enterici prevalenti. Si ritiene che i virus influenzino lo stato di salute dell'ospite interferendo con la struttura della comunità e della funzione batterica.



*microorganisms* MDPI

*Review*

# What is the Healthy Gut Microbiota Composition? A Changing Ecosystem across Age, Environment, Diet, and Diseases

Emanuele Rinninella [1,2,*], Pauline Raoul [2], Marco Cintoni [3], Francesco Franceschi [4,5], Giacinto Abele Donato Miggiano [1,2], Antonio Gasbarrini [2,6] and Maria Cristina Mele [1,2]

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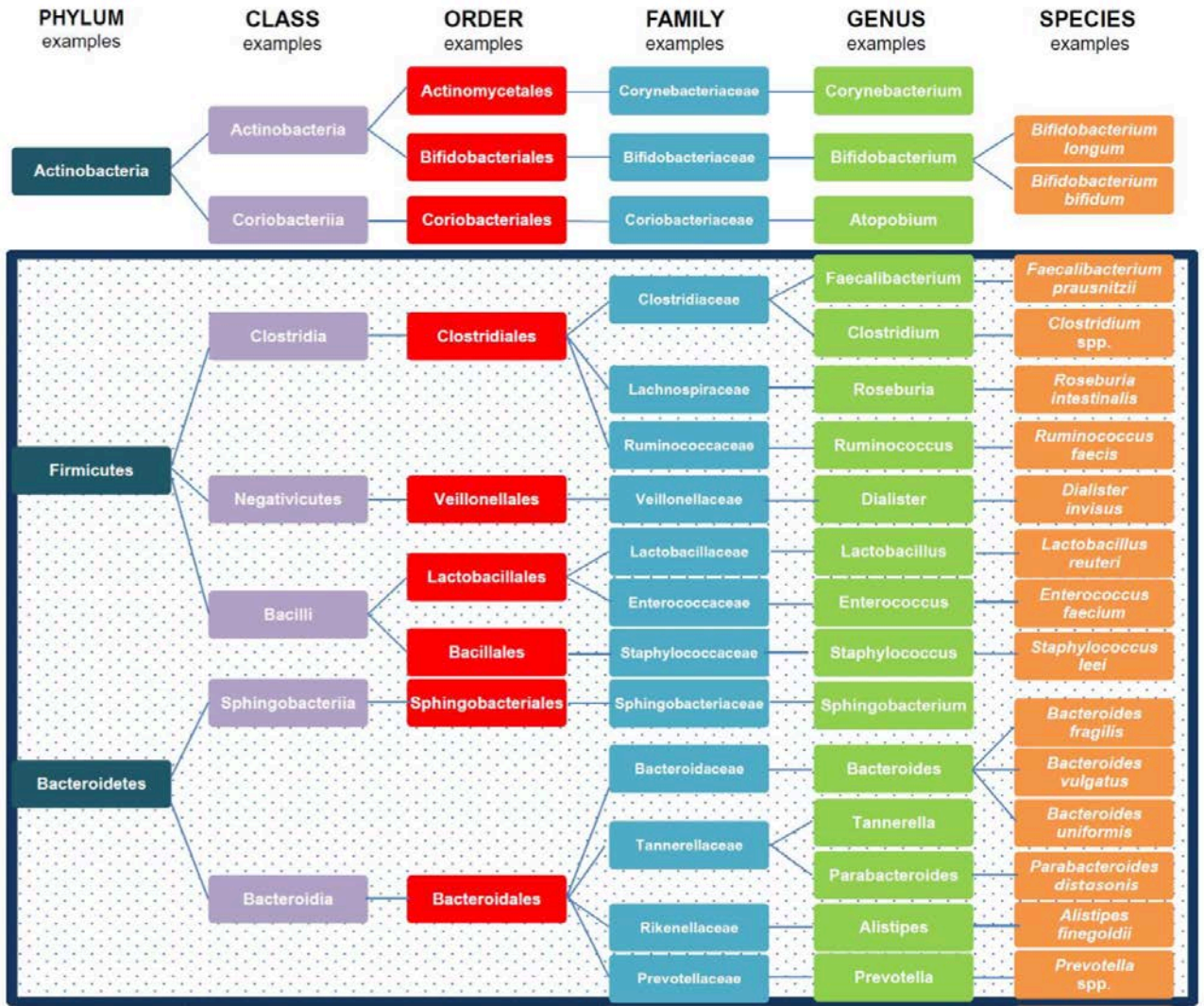


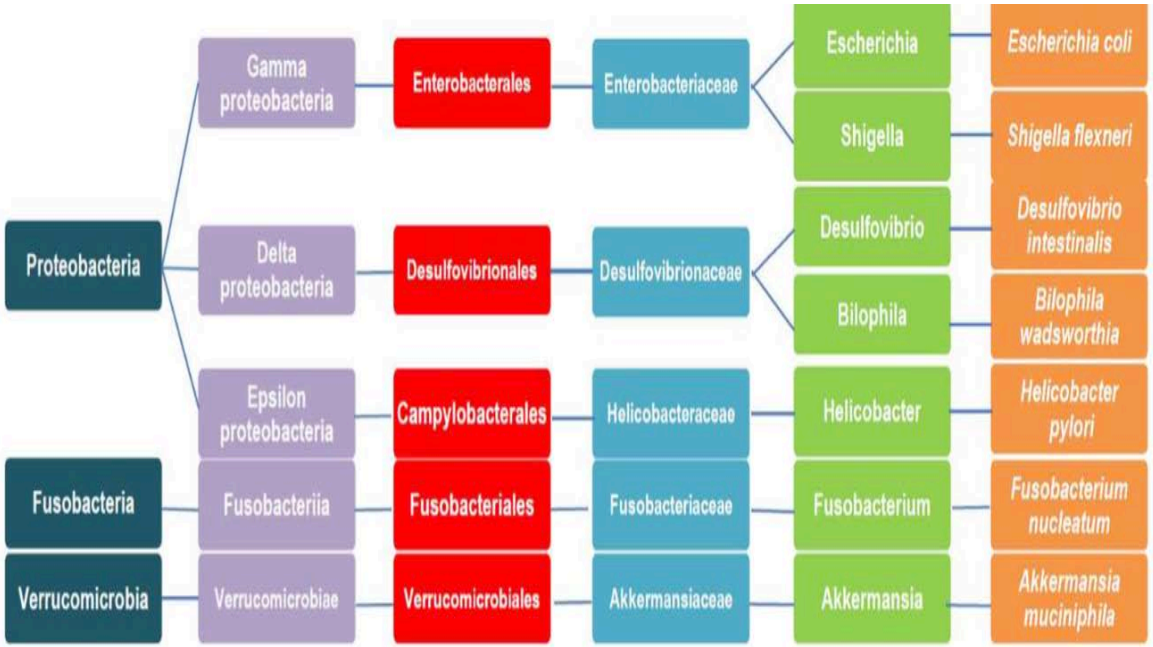

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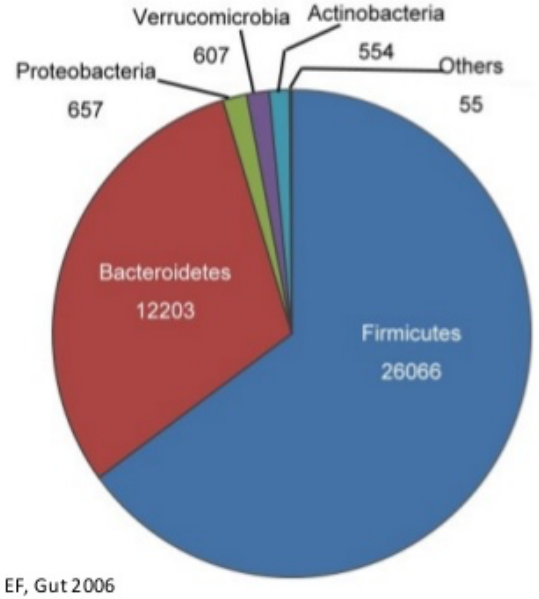
# The gut microbiota in human energy homeostasis and obesity

**Michael Rosenbaum**[1], **Rob Knight**[2], and **Rudolph L. Leibel**[1]

Michael Rosenbaum: mr475@cumc.columbia.edu

| Phylum | % Microbiome | Genus or species | Relevant function | Sources | Refs |
|---|---|---|---|---|---|
| Major phyla (>1% of most individuals) | | | | | |
| Firmicutes | ~60–65% | *Clostridium* *Eubacterium* *Faecalibacterium* *Lactobacilli* *Roseburia* *Ruminococcus* | Some species ferment fiber into butyrate; other functions range from symbionts to pathogens Butyrate production | | [5,6,9,28,81,82] |
| Bacteroidetes | ~20–25% | *Alistipes* *Bacteroides* | Polysaccharide degradation | Increased in protein-rich, high-meat diets | [5,6,8,9,16,81–84] |
| | | *Parabacteroides* *Prophyromonas* *Prevotella* | Some species ferment fiber into butyrate | Increased in grain rich high-fiber diets | |
| Proteobacteria | –5–10% | *E. coli* | | | [5,6,9,81,82] |
| Actinobacteria | –3% | *Bifidobacterium* *colinsella* | Vitamin biosynthesis | Common probiotic | [5,6,9,81,82] |
| Minor phyla (<1% of most individuals) | | | | | |
| Archaea | <1% | *Methanobrevibacter* *Methanosphaera* | Both convert hydrogen gas to methane (methanogens) | | [85,86] |
| Deferribacteres | <1% | | Degrade iron | Increased in gastrointestinal bleeding | [8,16,83,84] |
| Fusobacteria | <1% | *Fusobacterium* *nucleatum* | Proinflammatory colonic tumorigenic factor | Increased in high-meat diets | [16,87,88] |
| Melainabacteria | <1% | | Synthesize vitamins B and K, ferment carbohydrate into ethanol, lactate, and formate | Increased in high-plant diets, present in groundwater | [16,28,89] |
| Spirochaetes | <1% | Predominantly *Treponema* | | More common in rural communities and in high-fiber diets | [16,30] |
| Verrucomicrobia | <1% | *Akkermansia* *muciniphila* | Degrade mucin, diminish inflammation, and increase gut butyrate and mucus layer thickness | | [90] |

## HUMAN GUT MICROBIOTA



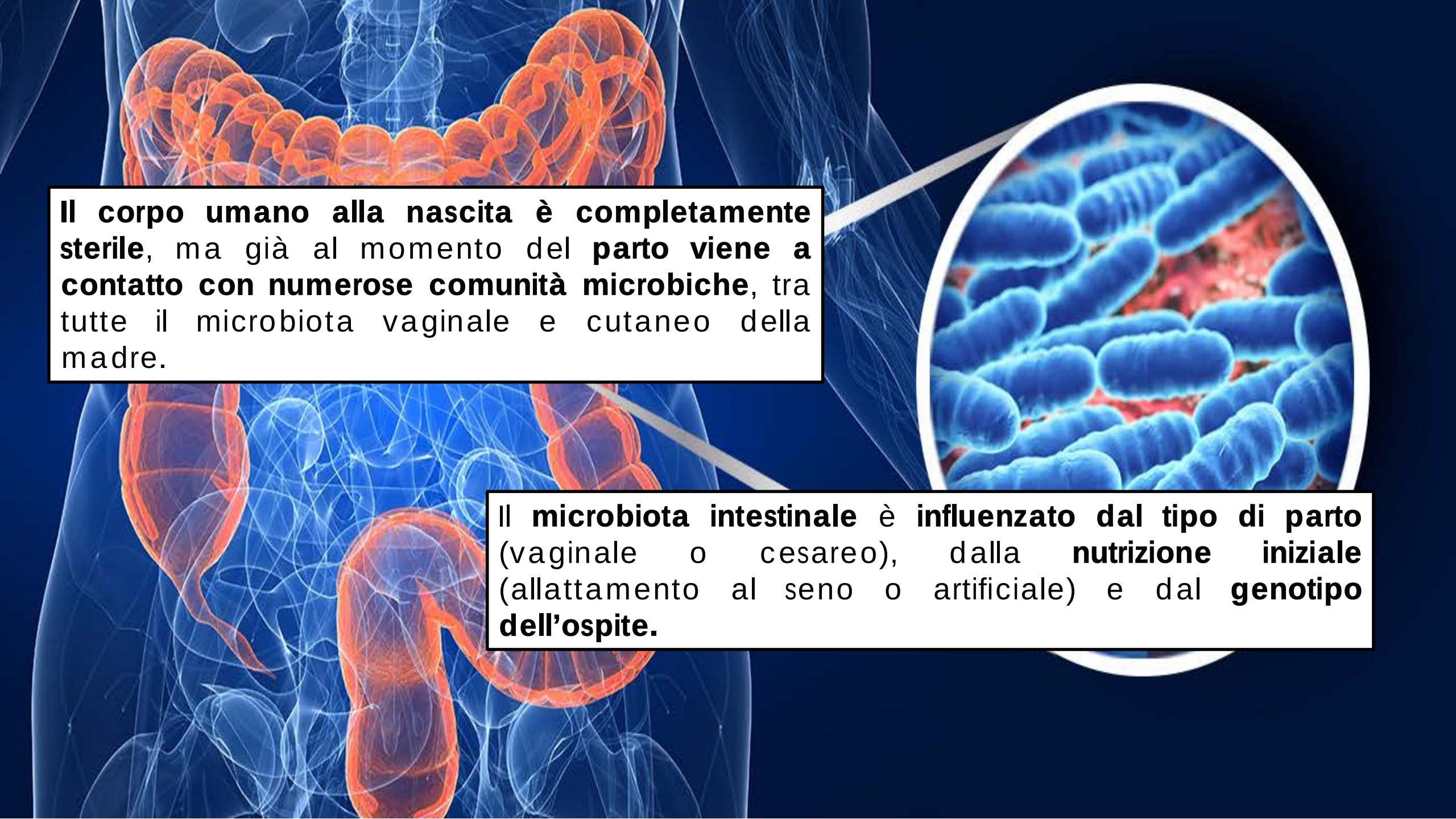

Verdu EF, Gut 2006
Gwee KA, Gut 2003

> 90% 2 ceppi dominanti (***Bacteroidetes, Firmicutes***)

< 10% 5 sub-dominanti ceppi (***Actinobacteria, Proteobacteria, Fusobacteria, Cyanobacteria*** and ***Verrucomicrobia***)

1000-1200 "filotipi"

50-80% Firmicutes dominanti **Clostridium cluster IV e XIVa**



**Il corpo umano alla nascita è completamente sterile**, ma già al momento del **parto viene a contatto con numerose comunità microbiche**, tra tutte il microbiota vaginale e cutaneo della madre.

Il **microbiota intestinale** è **influenzato dal tipo di parto** (vaginale o cesareo), dalla **nutrizione iniziale** (allattamento al seno o artificiale) e dal **genotipo dell'ospite.**

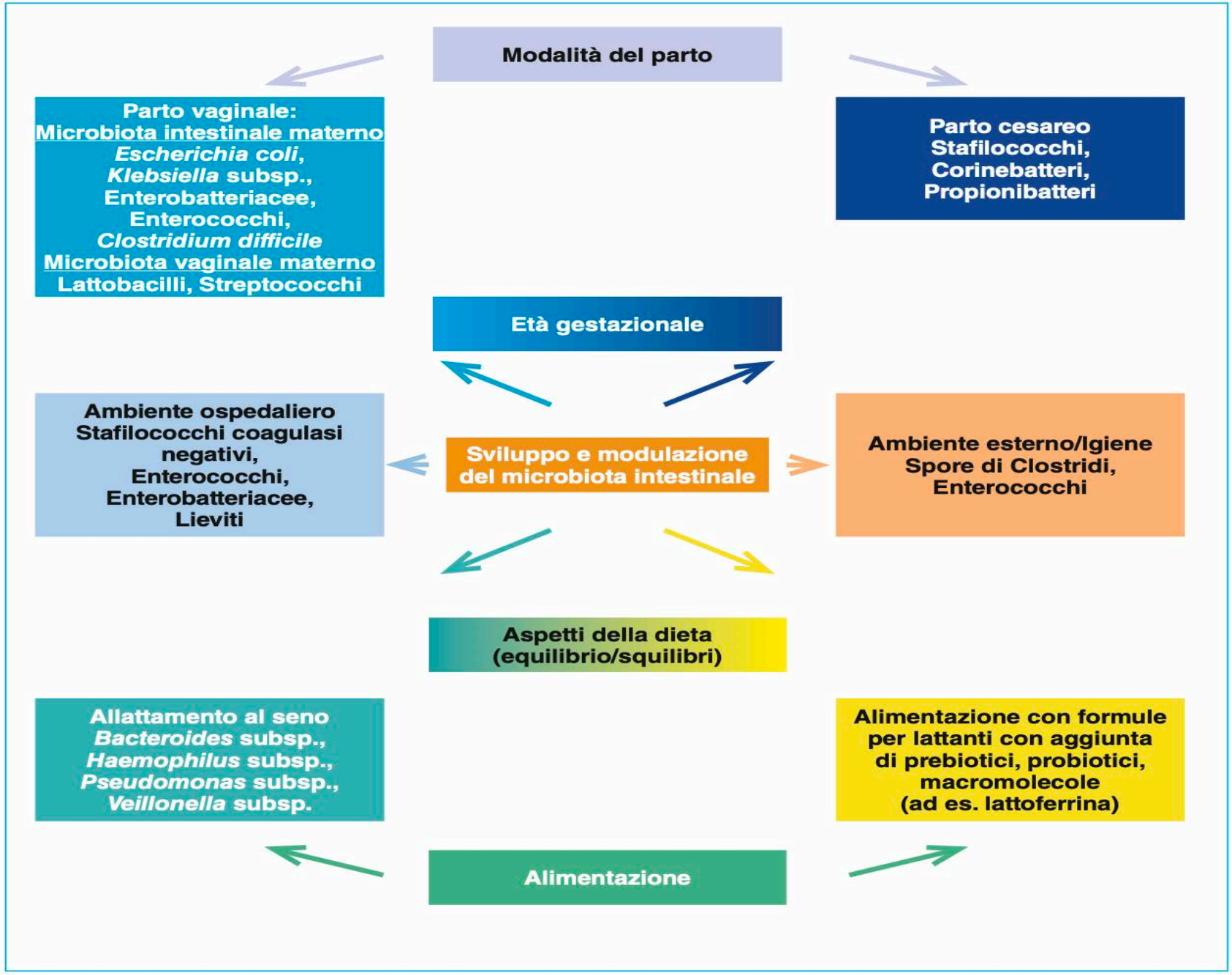



**FIGURA 1.** Principali determinanti del microbiota intestinale del bambino (da Putignani et al., 2014, mod.).

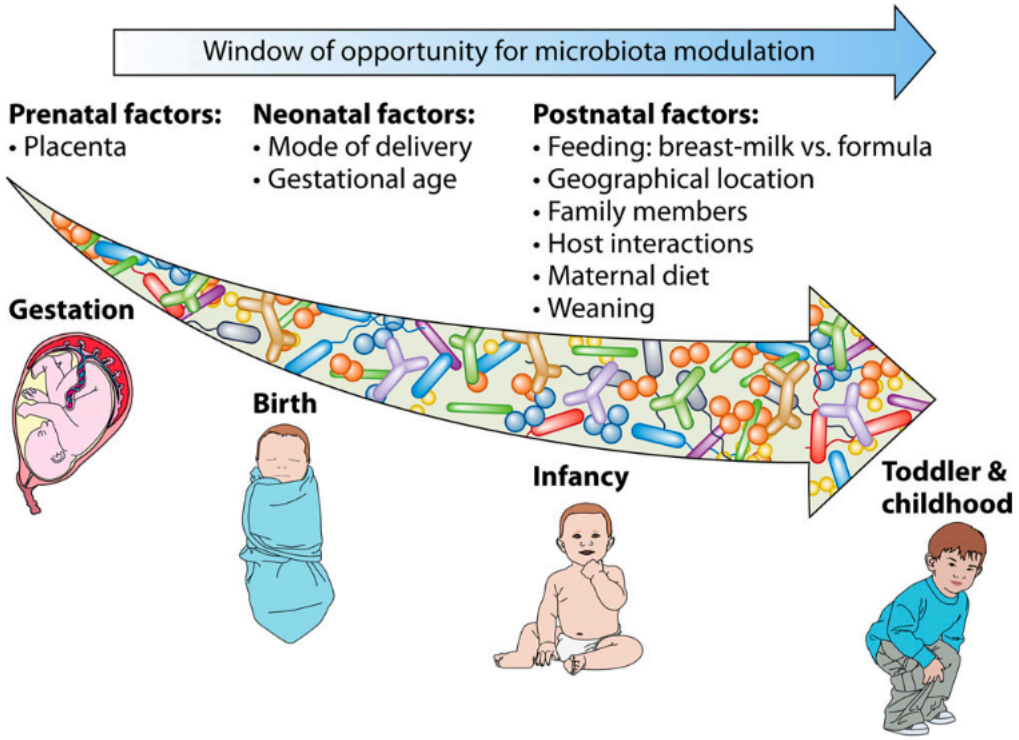



**FIG 3** Window of opportunity for microbiota modulation from gestation to childhood. The schematic representation shows a list of prenatal, neonatal, and postnatal factors that contribute to the bacterial gut composition in infants.

# The First Microbial Colonizers of the Human Gut: Composition, Activities, and Health Implications of the Infant Gut Microbiota

Christian Milani,[a] Sabrina Duranti,[a] Francesca Bottacini,[b] Eoghan Casey,[b] Francesca Turroni,[a,c] Jennifer Mahony,[b] Clara Belzer,[d] Susana Delgado Palacio,[e] Silvia Arboleya Montes,[e] Leonardo Mancabelli,[a] Gabriele Andrea Lugli,[a] Juan Miguel Rodriguez,[f] Lars Bode,[g] Willem de Vos,[d,h] Miguel Gueimonde,[e] Abelardo Margolles,[e] Douwe van Sinderen,[b] Marco Ventura[a,c]

The infant gut microbiota is characterized by a **high degree of instability, only reaching a state similar to that of adults by 2–3 years of age**; consistent with the establishment of a varied solid food diet. The diet-related factors influencing the development of the infant gut microbiome include whether the child is breast or formula-fed as well as how and when solid foods are introduced.

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*Review*

# Precision Nutrition and the Microbiome, Part I: Current State of the Science

Susan Mills [1], Catherine Stanton [2], Jonathan A. Lane [3], Graeme J. Smith [3,*] and R. Paul Ross [1,*]

- **Ageing has a significant impact on the gut microbiota** with dramatic compositional and functional changes observed in the elderly microbiota (in general >65 years)
- In general, the *elderly microbiota* has been characterised by a **decline in microbial diversity,** an **increase in the abundance of opportunistic pathogens** and **a decrease in species associated with short chain fatty acid (SCFA) production**, in particular butyrate
- A study investigating the semi-supercentarian microbiota (105–109 years old) revealed not only a decrease in saccharolytic butyrate producers (*Faecalibacterium*, *Coprococcus*, *Roseburia*) and an increase in potential opportunistic bacteria, as expected, but also **an enrichment and/or higher prevalence in health associated bacterial groups, including *Akkermansia*, *Bifidobacterium* and *Christensenellaceae*.**

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DOI: 10.3748/wjg.v21.i29.8787

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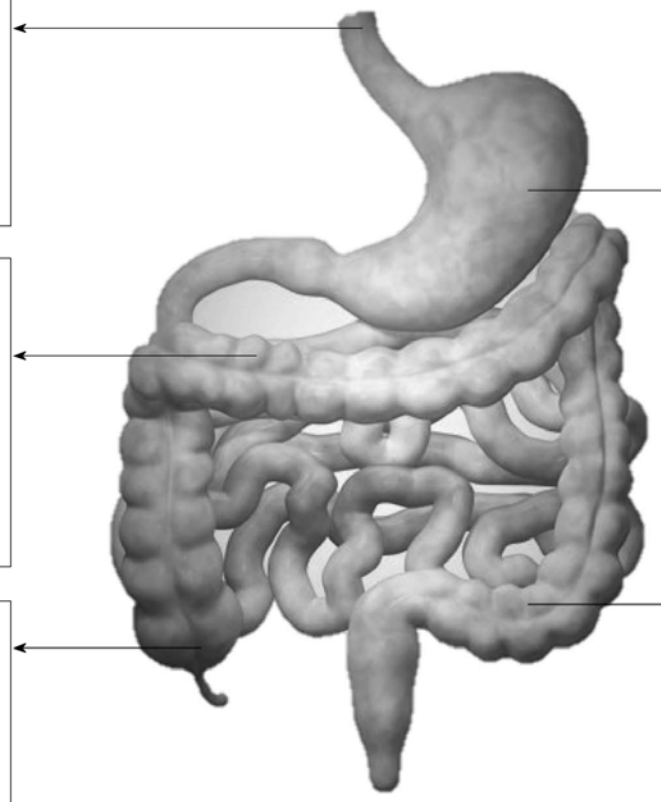
REVIEW

# Role of the normal gut microbiota

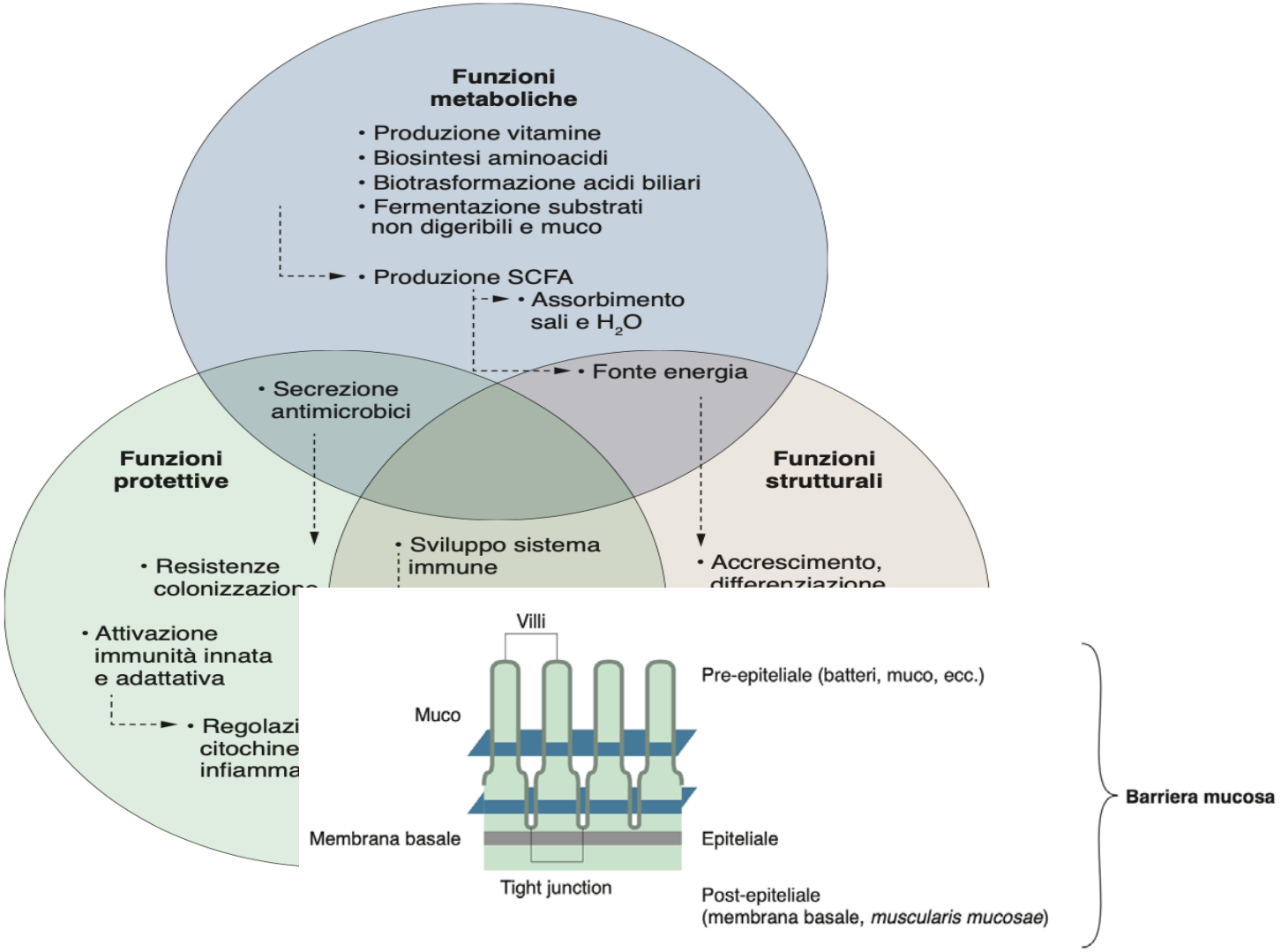
Sai Manasa Jandhyala, Rupjyoti Talukdar, Chivkula Subramanyam, Harish Vuyyuru, Mitnala Sasikala, D Nageshwar Reddy



# FUNZIONI DEL MICROBIOTA

The normal gut microbiota imparts specific function in

- host nutrient metabolism,
- xenobiotic and drug metabolism,
- maintenance of structural integrity of the gut mucosal barrier,
- immunomodulation,
- protection against pathogens.



# FUNZIONI METABOLICHE DEL MICROBIOTA

Synthesis of **vitamin K** and several components of **vitamin B** is a major metabolic function of the gut microbiota.

Members of genus *Bacteroides* have been shown to **synthesize conjugated linoleic acid (CLA)** that is known to be antidiabetic, antiatherogenic, antiobesogenic, hypolipidemic and have immunomodulatory properties

The gut microbiota largely derives their nutrients from dietary carbohydrates.

**Fermentation of the carbohydrates** that escaped proximal digestion and indigestible oligosaccharides by colonic organisms such as *Bacteroides, Roseburia, Bifidobacterium, Fecalibacterium,* and *Enterobacteria* **result in the synthesis of short chain fatty acids (SCFA**) which are rich sources of energy for the host.

## Il microbiota intestinale

LUCIO CAPURSO[1]

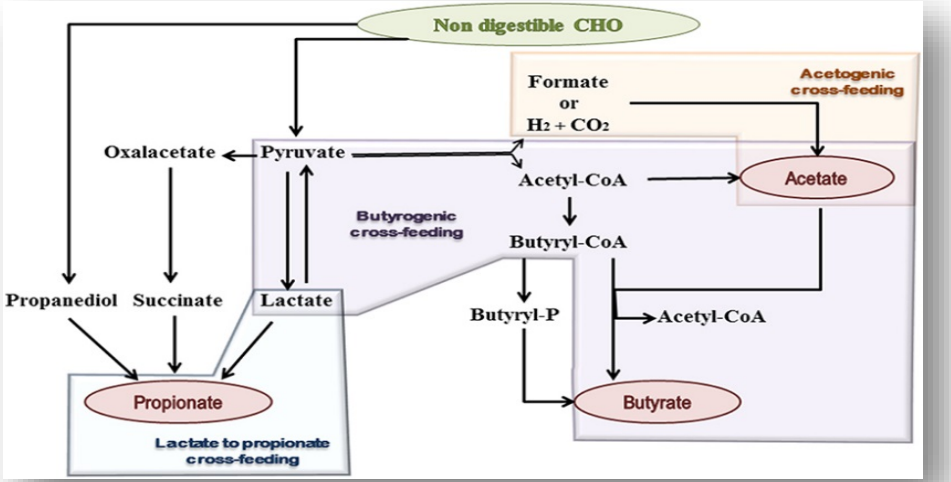
**Tabella 2.**

| Vitamina | Batteri |
|---|---|
| Vitamina K | *Escherichia coli* |
| Folati | *Bifidobacterium bifidum*<br>*Bifidobacterium longum subsp. infantis* |
| Riboflavina | *Bacillus subtilis Escherichia coli* |
| Cobalamina | *Lactobacillus reuteri CRL1098* |
| Niacina<br>Piridossina | *Strepto-coccus thermophilus ST5*<br>*Lactobacillus helveticus R0052*<br>*Bifidobacterium longum R0175* |

Carboidrati non-digeribili vengono metabolizzati dalla flora batterica

- grande varietà di reazioni e di pathway metabolici
- principali prodotti **della fermentazione dei carboidrati:**

**acidi grassi a catena corta (SCFA**, Short Chain Fatty Acids) *(Goncalves P. et al., 2018)*




**acido acetico**

- riassorbito dalla parete intestinale
- riversato nel circolo periferico
  e utilizzato come substrato energetico da vari tessuti tra cui tessuto adiposo per la lipogenesi

**acido propionico**, riassorbito a livello intestinale, utilizzato dal fegato come substrato gluconeogenico.

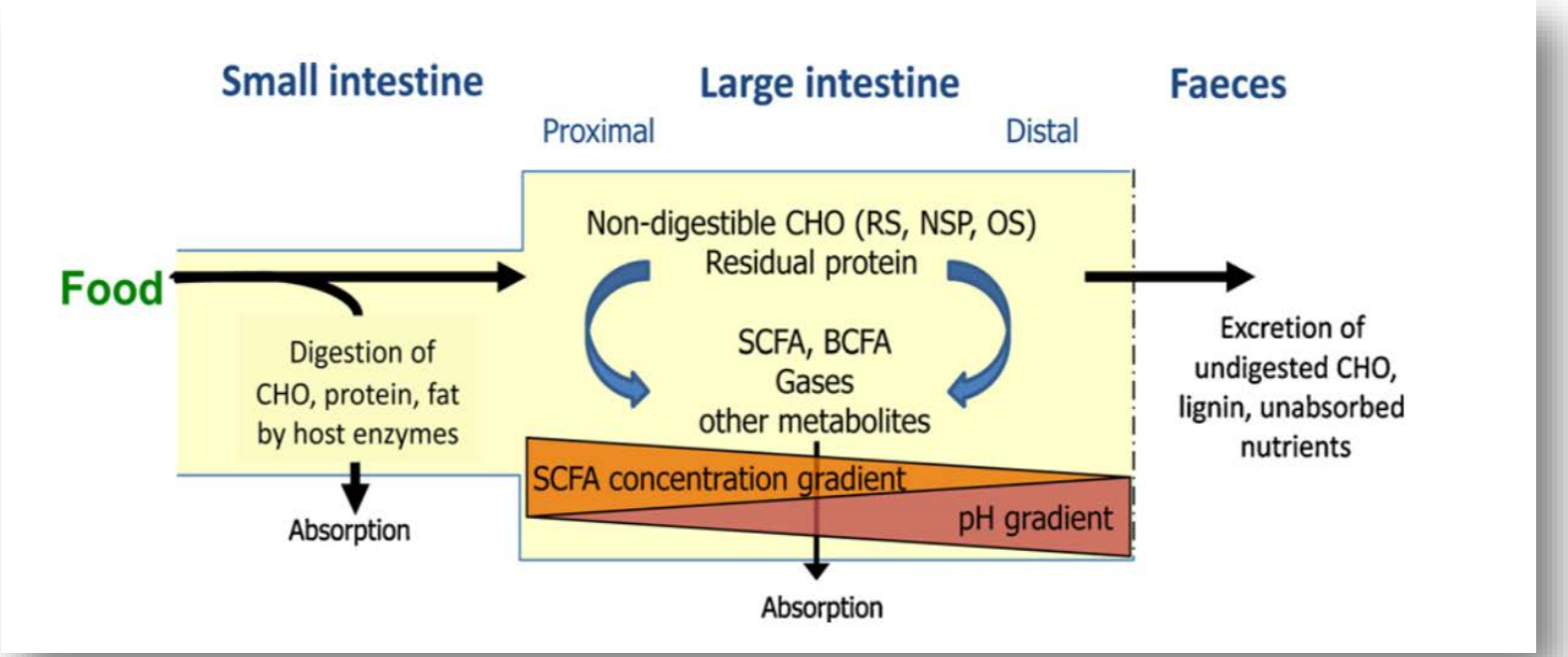
**acido butirrico**, fonte energetica per le stesse cellule intestinali

Il **colon** è un ambiente povero di zuccheri semplici quali mono- e disaccaridi, ma sono invece **presenti oligo- e polisaccaridi** che resistono all'idrolisi da parte delle idrolasi dell'ospite tra cui:

amido (5-20% dell'amido ingerito raggiunge il colon inalterato ed è fermentato in questa sede)
galatto-oligossaridi (GOS) e frutto-oligosaccaridi (FOS), es. inulina
oligosaccaridi delle leguminose (raffinosio e stachiosio),
pectine, gomme, mucillagini e alcune emicellulose

- La microflora è in grado di **influenzare il bilancio energetico** dell'organismo ospite
  - studi su animali germ-free (Hooper et al 2002).

- I batteri intestinali traggono l'energia necessaria attraverso il metabolismo di zuccheri (fermentazione).



Hindawi Publishing Corporation
Journal of Obesity
Volume 2012, Article ID 879151, 14 pages
doi:10.1155/2012/879151

*Review Article*

**Is the Gut Microbiota a New Factor Contributing to Obesity and Its Metabolic Disorders?**

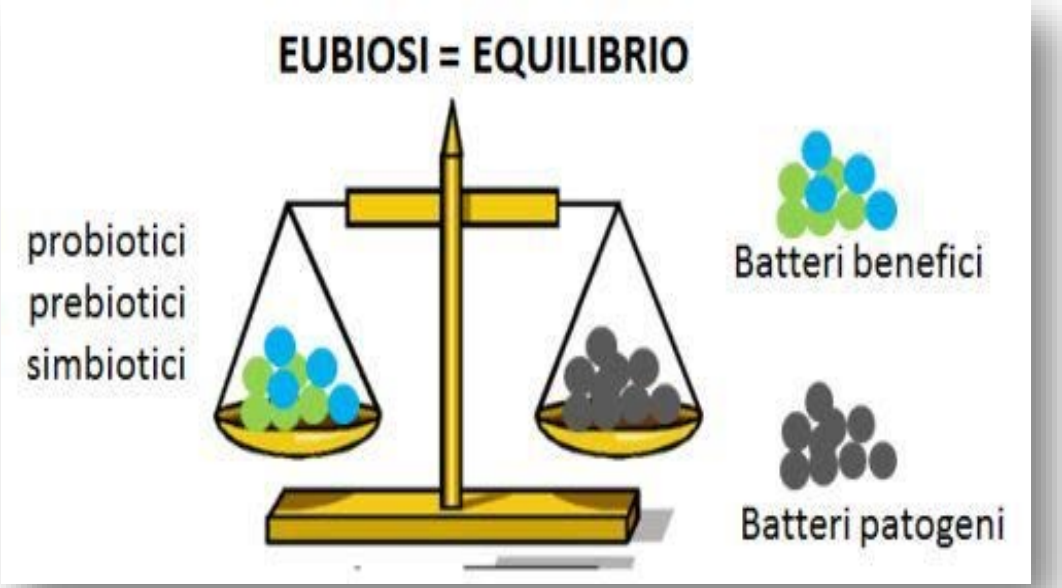
**Kristina Harris,[1] Amira Kassis,[2] Geneviève Major,[2] and Chieh J. Chou[2]**

Another mechanism by which the gut microbiota affects body weight is by **increasing energy harvesting from dietary fibers**.
The intestinal microbiota **breaks down indigestible polysaccharides** (i.e., fiber) to short-chain fatty acids (SCFAs) providing 80 to 200 kcal per day or about 4–10% of daily energy intake in normal adults.

# Eubiosis and dysbiosis: the two sides of the microbiota

Valerio Iebba[1], Valentina Totino[1], Antonella Gagliardi[1], Floriana Santangelo[1], Fatima Cacciotti[1], Maria Trancassini[1], Carlo Mancini[1], Clelia Cicerone[2], Enrico Corazziari[2], Fabrizio Pantanella[1], Serena Schippa[1]

In circostanze normali, si ha **equilibrio**, noto come **eubiosi**, nella composizione e nella quantità di microbi intestinali.




Variazioni del microbiota intestinale (ad es. modifica della quantità o del tratto intestinale in cui risiedono) → possibili cambiamenti estremi (es. proliferazione di patogeni o promozione del trasferimento di un determinato ceppo batterico in un altro tratto intestinale, determinando **disbiosi**)

Contributo a comparsa o sviluppo di una varietà di **malattie**

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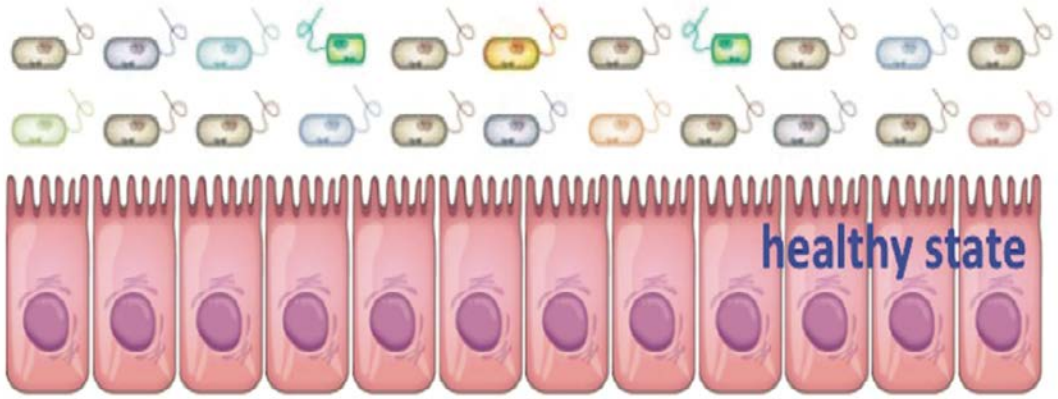
## EUBIOSI

- diverse commensal microbiota
- 90% *Firmicutes* and *Bacteroidetes*
- enhanced SCFAs production
- no over inflammation
- intact mucosal barrier




## DISBIOSI

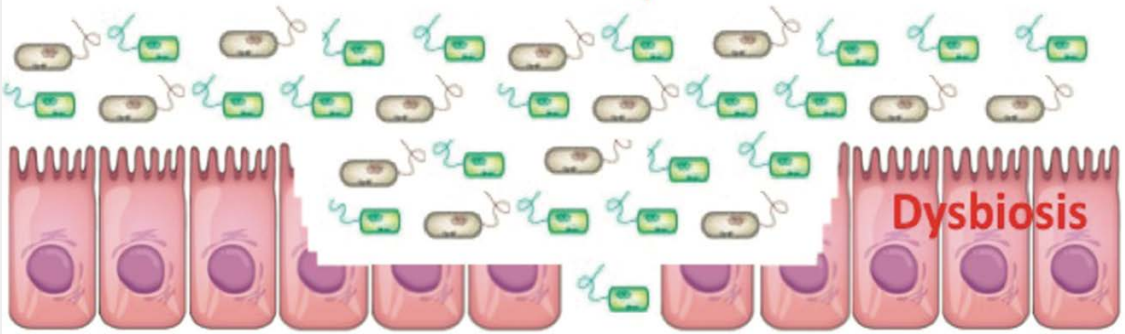
- reduced microbiota diversity
- increase in opportunistic pathogens
- reduced *Firmicutes* and *Bacteroidetes*
- reduced SCFAs production
- intestinal inflammation
- disrupted mucosal barrier

**Generation of Dysbiosis**

host genetic factors

environmental factors

infections



# PERDITA DELL'EUBIOSI

Perdita numerica di batteri benefici

*Overgrowth* di batteri potenzialmente patogeni

Alterazione nella localizzazione delle specie batteriche

Perdita **alfa diversità** e **beta diversità**

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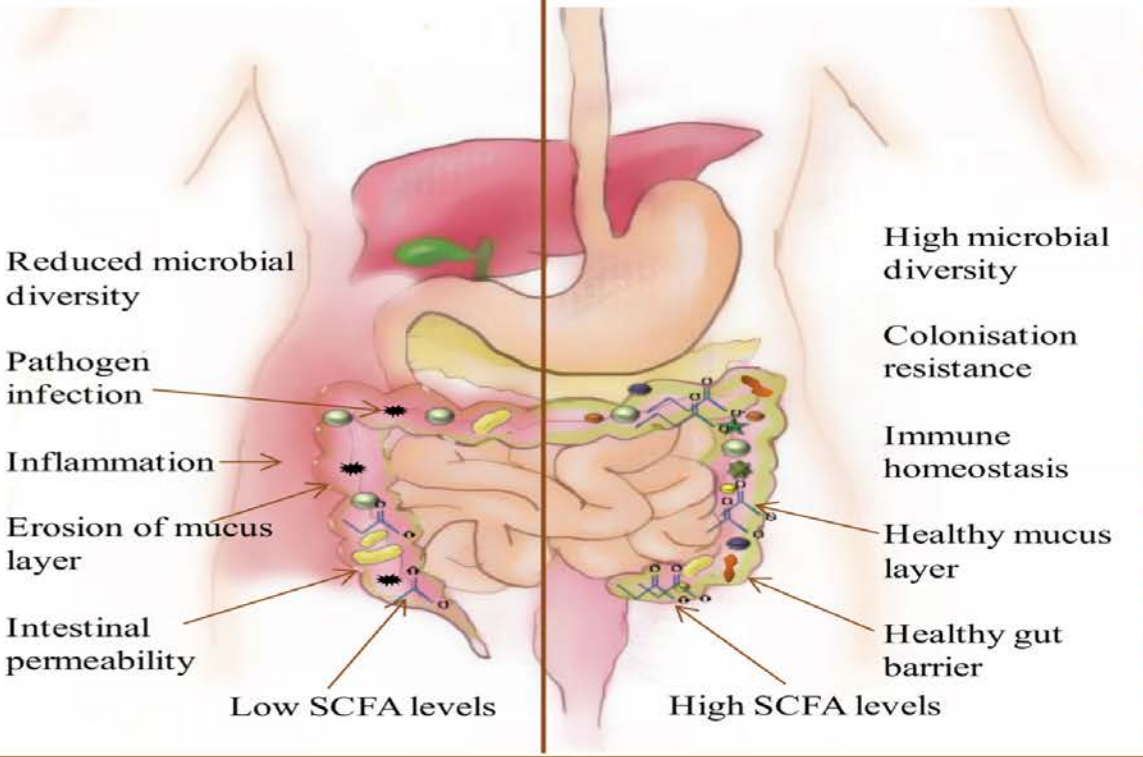
*Review*

# Precision Nutrition and the Microbiome, Part I: Current State of the Science

**Susan Mills [1], Catherine Stanton [2], Jonathan A. Lane [3], Graeme J. Smith [3,*] and R. Paul Ross [1,*]**

| Poor Quality Diet | Consequences | Healthy Diet |
|---|---|---|
| Predominant foods<br>▪Animal-derived protein (meat & processed meat)<br>▪Saturated fats<br>▪Refined grains<br>▪Sugar<br>▪Salt<br>▪Alcohol<br>▪Corn-derived fructose |  | Predominant foods<br>▪Fruits<br>▪Vegetables<br>▪Fibre<br>▪Plant-derived protein<br>▪MUFAs<br>▪n-3 PUFAs |

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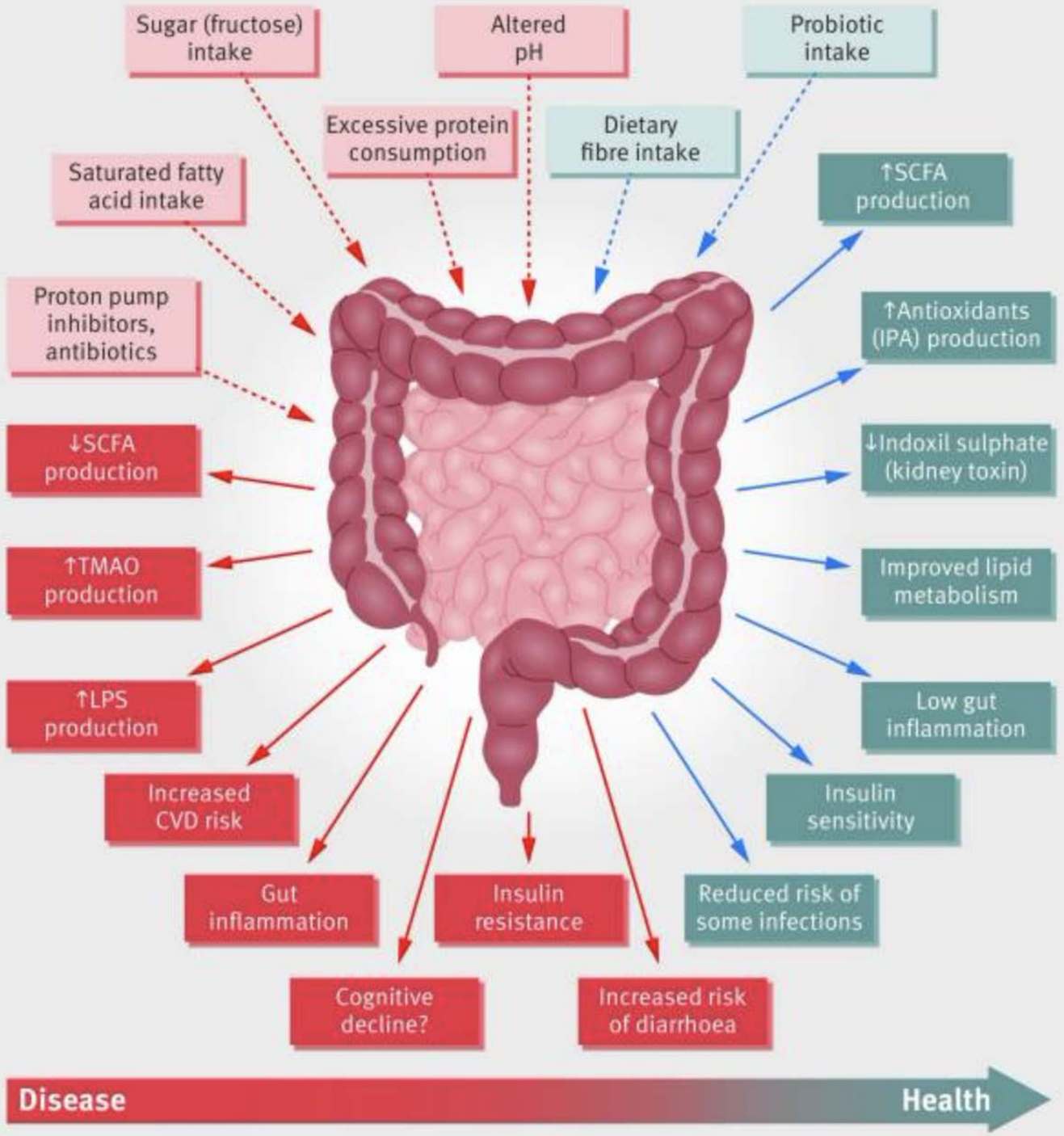
# Role of the gut microbiota in nutrition and health

Ana M Valdes, associate professor,[1,2] Jens Walter, CAIP chair for nutrition, microbes, and gastrointestinal health,[3] Eran Segal, professor,[4] and Tim D Spector, professor[5]



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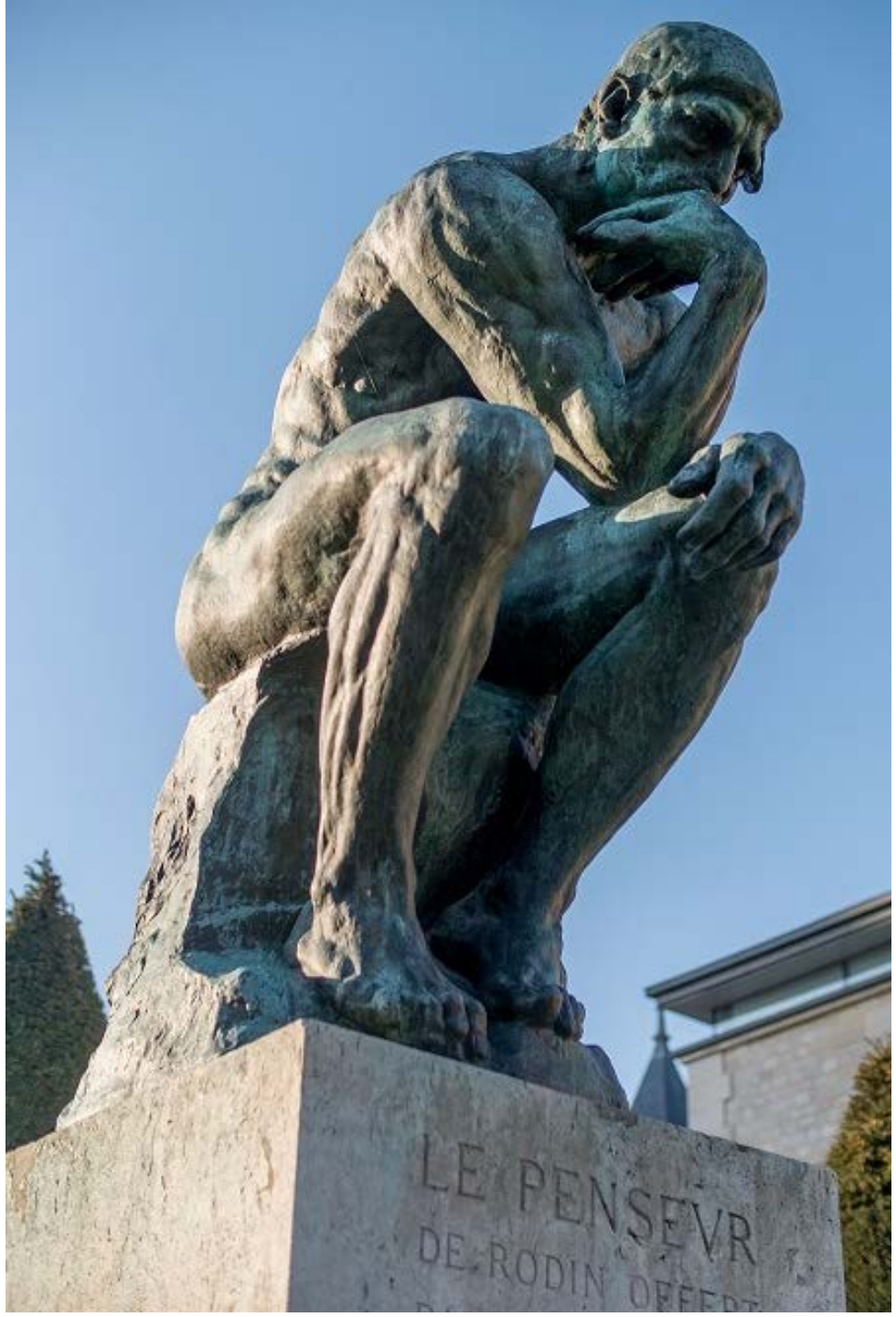
# ESISTE UNA RELAZIONE TRA OBESITA' E MICROBIOTA?



REVIEW

Microbiota modulation by eating patterns and diet composition: impact on food intake

**Elizabeth Klingbeil and Claire B. de La Serre**
*Foods and Nutrition, University of Georgia, Athens, Georgia*

Submitted 6 February 2018; accepted in final form 29 August 2018

**Obesity** in humans and animal models **is characterized by abnormal gut microbiota composition, or dysbiosis**

Microbiota composition is heavily influenced by the environment, especially the diet.

The effects of dietary fat consumption on microbiota composition have been determined in different models. The "high-fat diet (HFD)/ obese-type" microbiota **is characterized by**

an increased *Firmicutes/Bacteriodetes* ratio,
a decreased bacterial diversity
an increased proinflammatory potential.

This proinflammatory potential is associated with **increased gut permeability** and **elevated circulating levels of LPS**, a condition known as metabolic endotoxemia. Metabolic endotoxemia is a state of chronic low-grade inflammation and appears to be sufficient to promote food intake and weight gain

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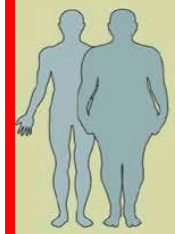
**Obesity**



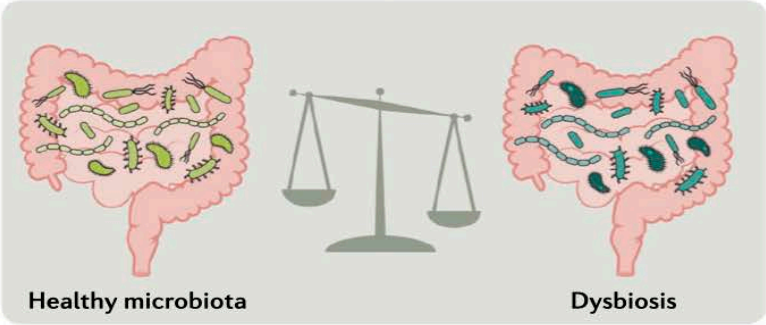
**Taxa features**
- ↓ Bacteroidetes to Firmicutes ratio
- ↓ *Akkermansia muciniphila*
- ↓ *Bacteroides thetaiotaomicron*
- ↓ *Clostridium histolyticum*
- ↓ *Clostridium coccoides*
- ↑ *Dorea longicatena*
- ↑ *Eubacterium ventriosum*
- ↓ *Faecalibacterium prausnitzii*
- ↓ *Methanobrevibacter smithii*
- ↑ *Roseburia intestinalis*
- ↑ *Ruminococcus gnavus*
- ↑ *Ruminococcus torques*

**Function features**
- ↑ LGC: degradation of β-glucuronide and aromatic amino acids
- ↑ HGC: production of organic acids and $H_2$
- ↑ Phosphotransferase system
- ↓ Glycosaminoglycan degradation
- ↑ Glutamine or glutamate transport system
- ↑ Phenylalanine, tyrosine and tryptophan biosynthesis
- ↓ Valine, leucine and isoleucine degradation
- ↓ Superoxide reductase

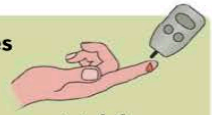
**Malnutrition**

**Taxa features**
- ↓ Anaerobes to facultative anaerobes ratio
- ↓ *Bifidobacterium longum*
- ↓ *Bifidobacterium pseudolongum*

**Function features**
- ↓ Lantibiotics production
- ↓ Energy harvest
- ↓ Immune protection
- ↓ Vitamin biosynthesis
- ↑ Pathogenic factors



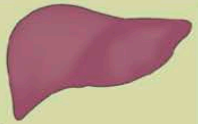

**Type 2 diabetes**



**Taxa features**
- ↓ *Akkermansia muciniphila*
- ↑ *Bacteroides vulgatus*
- ↑ *Clostridium clostridioforme*
- ↑ *Clostridium hathewayi*
- ↓ *Clostridiales* sp. SS3/4
- ↑ *Prevotella copri*

**Function features**
- ↑ Membrane transport of sugars
- ↑ BCAA transport
- ↓ SCFA production
- ↓ Metabolism of cofactors and vitamins

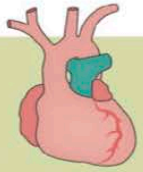
**Metabolic liver disease**



**Taxa features**
- ↓ *Coprococcus comes*
- ↓ *Faecalibacterium prausnitzii*
- ↑ *Klebsiella pneumoniae*
- ↑ *Streptococcus anginosus*
- ↑ *Veillonella atypica*

**Function features**
- ↑ Oxidative damage
- ↑ γ-Aminobutyric acid biosynthesis
- ↓ Haem biosynthesis
- ↑ Dentrification
- ↑ Ethanol production
- ↑ Lipopolysaccharide and peptidoglycan biosynthesis
- ↑ BCAAs and AAA biosynthesis

**Cardio-metabolic disease**



**Taxa features**
- ↓ *Enterobacter aerogenes*
- ↓ *Escherichia coli*
- ↑ *Faecalibacterium prausnitzii*
- ↑ *Klebsiella* spp.
- ↑ *Ruminococcus gnavus*
- ↑ *Streptococcus* spp.

**Function features**
- ↓ Activities of SCFAs
- ↑ TMA lysases
- ↑ Phosphotransferase system
- ↓ Vitamin metabolism
- ↑ Lipopolysaccharide biosynthesis
- ↑ Tryptophan production
- ↓ SCFA metabolism
- ↓ Butyrate production

# Early differences in fecal microbiota composition in children may predict overweight[1–3]

*Marko Kalliomäki, Maria Carmen Collado, Seppo Salminen, and Erika Isolauri*

- Celebre studio finlandese, condotto congelando campioni fecali di 49 neonati, che sono stati seguiti nel tempo.

  I 25 bambini che a sei anni erano sovrappeso o obesi, presentavano già alla nascita un microbiota differente da quello dei soggetti che alla stessa età risultavano normopeso: suggerendo che tali modificazioni del microbiota, che precedono la comparsa dell'eccesso ponderale, possano esserne almeno in parte causalmente responsabili (Kalliomäki et al., 2008).

- Tra i meccanismi proposti per spiegare questo possibile effetto del microbiota nello sviluppo (o nel controllo) dell'eccesso ponderale, spiccano:

✓ **l'eccessivo deposito di energia nell'organismo,**

✓ i più **alti livelli** di **acidi grassi a corta catena** promotori della adipogenesi,

✓ la **sovraespressione di geni correlati all'obesità**

✓ l'**aumentata produzione di lipopolisaccaride** da parte del microbiota, che causa obesità e infiammazione (Chen et al., 2014).

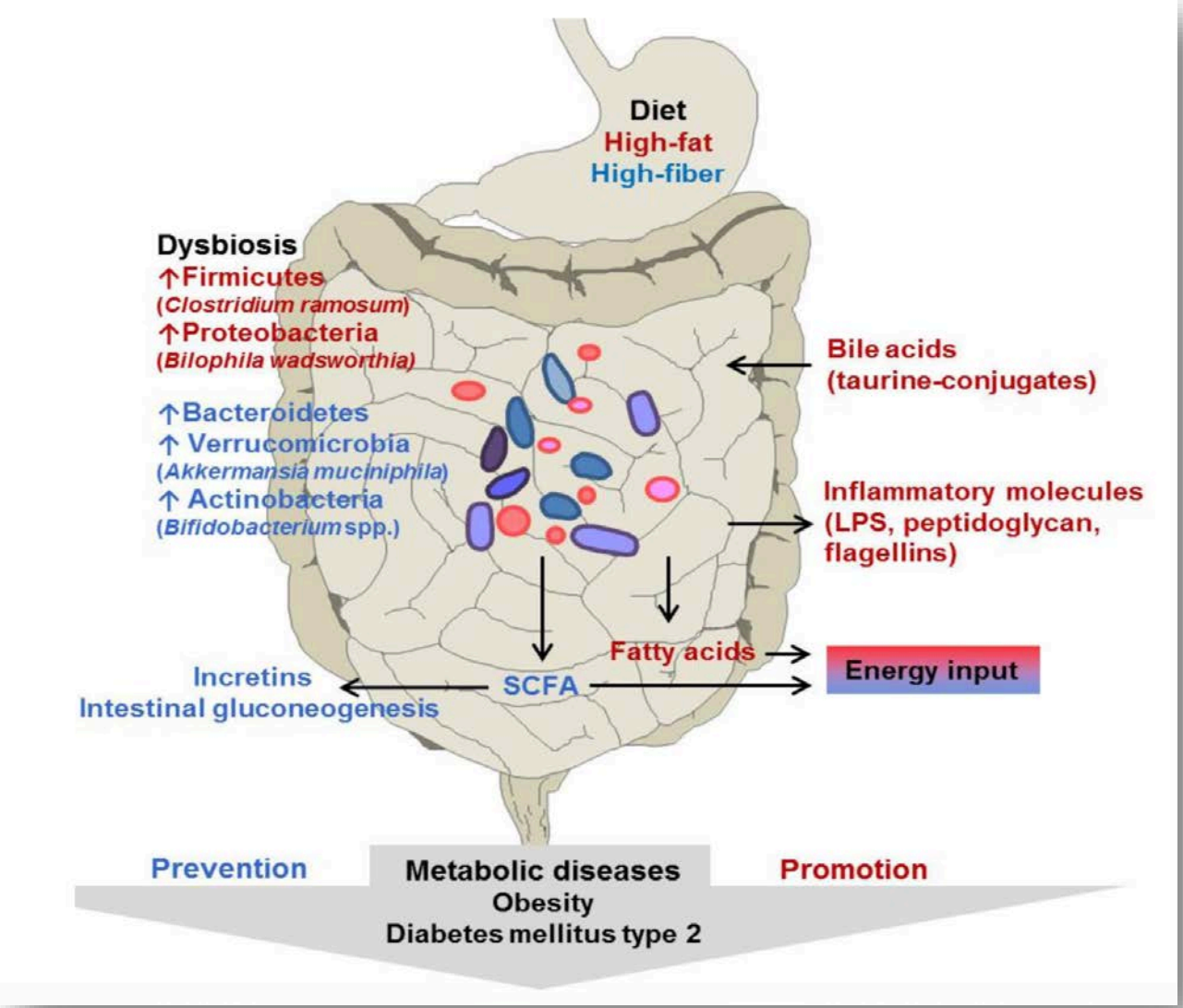
KDA Ketogenic Diet ACADEMY
nutrients
SINut Società Italiana di Nutraceutica

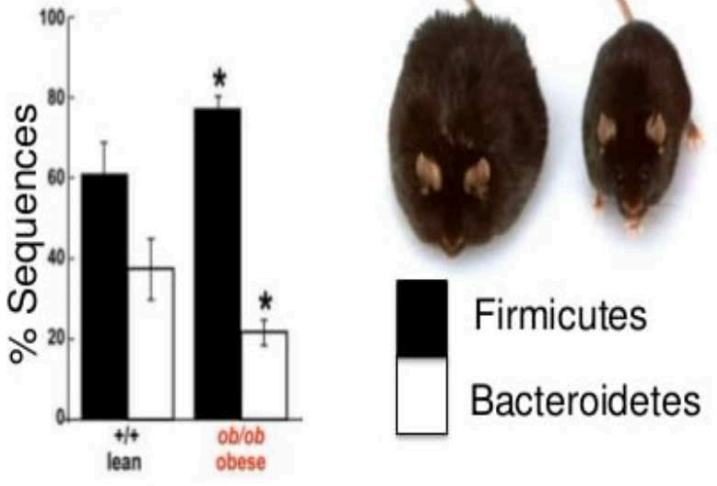
*Review*

# The Intestinal Microbiota in Metabolic Disease

Anni Woting * and Michael Blaut

**Livelli di SCFA fecali più alti nei pazienti sovrappeso e obesi rispetto ai soggetti magri**
(improbabile conseguenza di ridotto assorbimento SCFA nel colon o un maggiore apporto di fibre alimentari nei soggetti obesi/sovrappeso)
**Le attività metaboliche della flora intestinale "facilitano" l'estrazione di calorie dagli alimenti agevolando l'accumulo di sostanze, quali acidi grassi, nel tessuto adiposo.**






Ley *et al.*, PNAS 102: 11070-5 (2006)

**Microbiota di topo obeso** ha maggiore capacità di estrapolare energia dalla dieta
- Fermentazione di componenti alimentari non digeriti da parte dei batteri intestinali → aumento SCFA (importante fonte di energia per l'ospite)
- Soggetti sovrappeso/obesi con disturbi metabolici: percentuale maggiore di batteri appartenenti a Eubacterium rectale-Clostridium coccoides con efficiente estrapolazione di energia dai nutrienti nel intestino, rispetto a soggetti normopeso *(Schwiertz et al.)*

In male rodents, **HFD-driven changes in microbiota composition include** an **increase in the *Firmicutes-Bacteriodetes* ratio** ⟶ increase in *Erysipelotrichales* and *Clostridiales* abundances, two orders belonging to the phylum *Firmicutes*.

HFD consumption has also been reported to increase *Proteobacteria* abundance:

*Proteobacteria* are gram-negative, LPS- carrying, proinflammatory bacteria.

Bacterial products such as LPS can activate pattern recognition receptors, e.g., Toll-like receptors (TLR)

HFD consumption has also been reported to decrease the abundance of *Bifidobacteria*.

HFD feeding leads to a decrease in *Akkermansia* abundance

# Changes in Gut Microbiota Control Metabolic Endotoxemia-Induced Inflammation in High-Fat Diet–Induced Obesity and Diabetes in Mice

Patrice D. Cani,[1,2] Rodrigo Bibiloni,[3] Claude Knauf,[2] Aurélie Waget,[2] Audrey M. Neyrinck,[1] Nathalie M. Delzenne[1], and Rémy Burcelin[2]

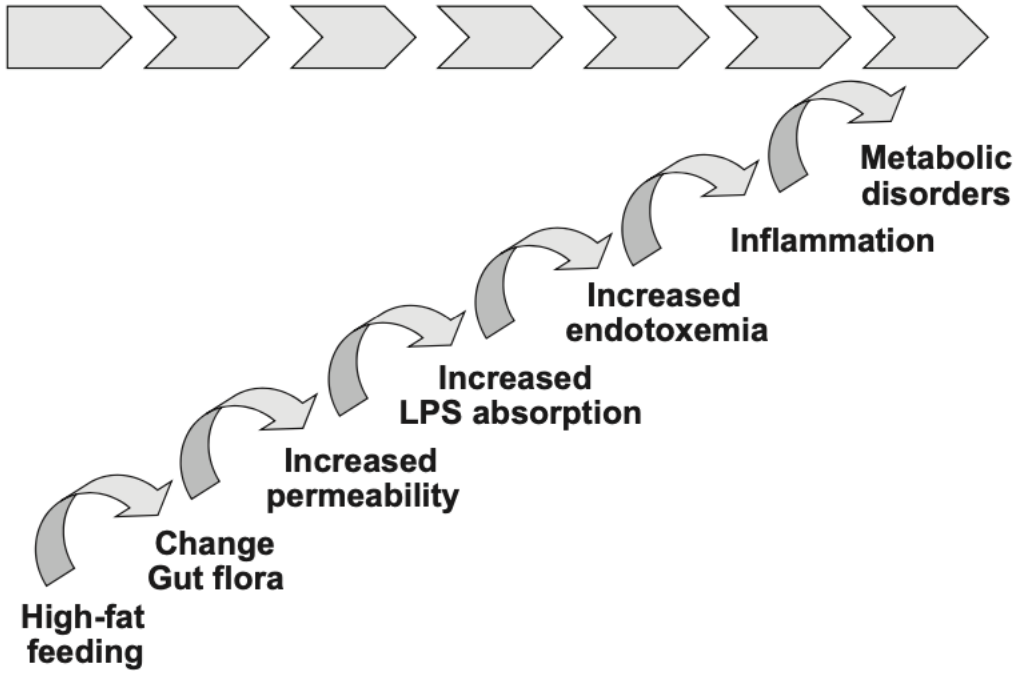



FIG. 8. Hypothesis for bacteria-induced metabolic disease. On excessive high-fat feeding, intestinal microflora changes. This is associated with an increased intestinal permeability. Consequently, endotoxemia increases and triggers inflammation and metabolic disorders.

**HHS Public Access**
Author manuscript
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**Influence of High-Fat-Diet on Gut Microbiota: A Driving Force for Chronic Disease Risk**

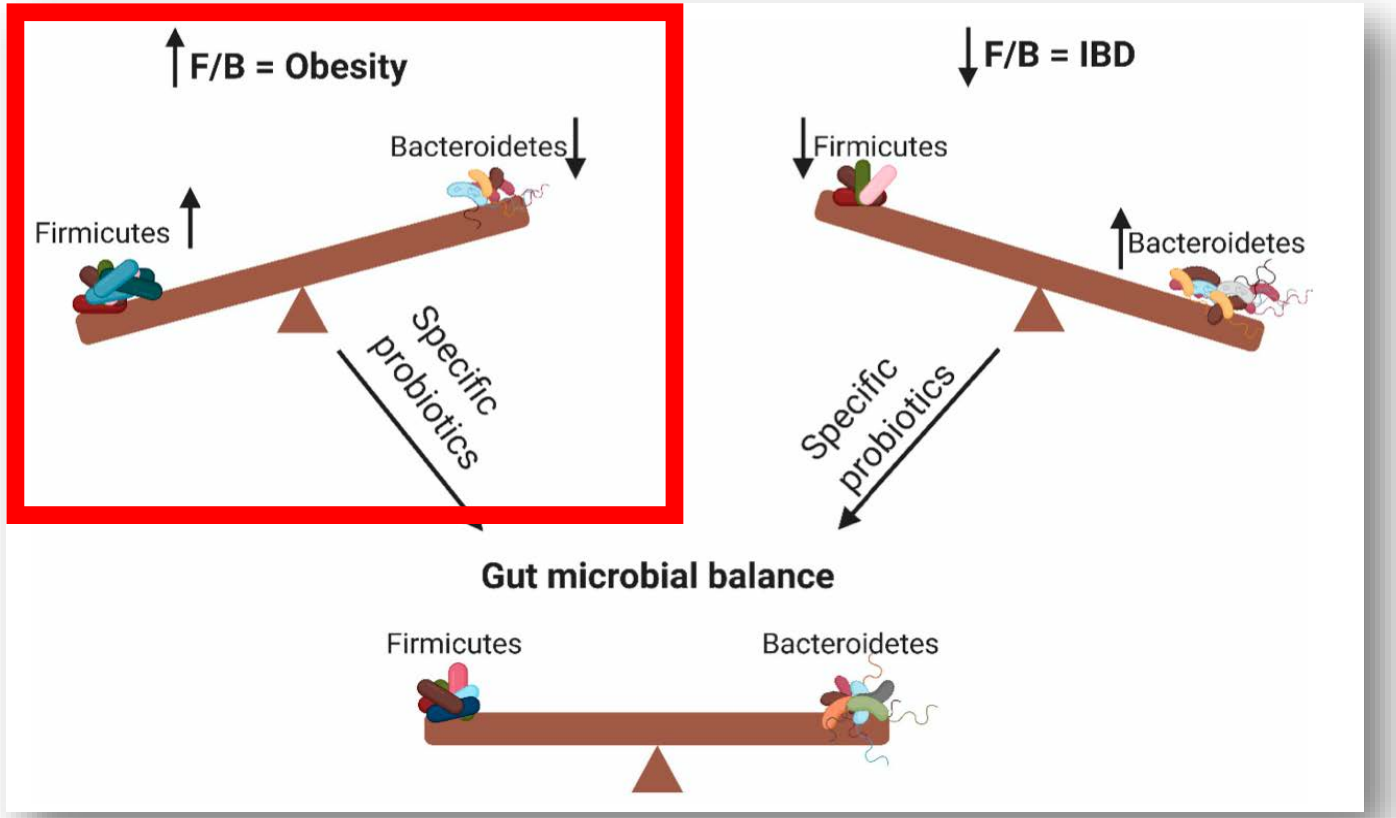
**E. Angela Murphy**[1], **Kandy T. Velazquez**[1], and **Kyle M. Herbert**[1]

- Eccessivo consumo HFD (High Fat Diet): contributo a epidemia di obesità.
- Meccanismi più complessi del semplice concetto di bilancio energetico
- Alterazioni indotte da HFD nel microbiota intestinale nell'epidemia di obesità
- Consumo di HFD → diminuzione Bacteroidetes e aumento dei Firmicutes.

Potenziali meccanismi:

1) **migliore capacità di «estrapolare» energia e stoccarla**
2) **maggiore permeabilità intestinale e infiammazione**

Studi in **pazienti obesi**:
prima di dieta ipocalorica povera di grassi e carboidrati: **elevati livelli Firmicutes** (specializzati nella degradazione di polisaccaridi indigeribili)
**<u>Al termine della dieta: aumento Bacteroidetes</u>**, dal 3% al 15 %.



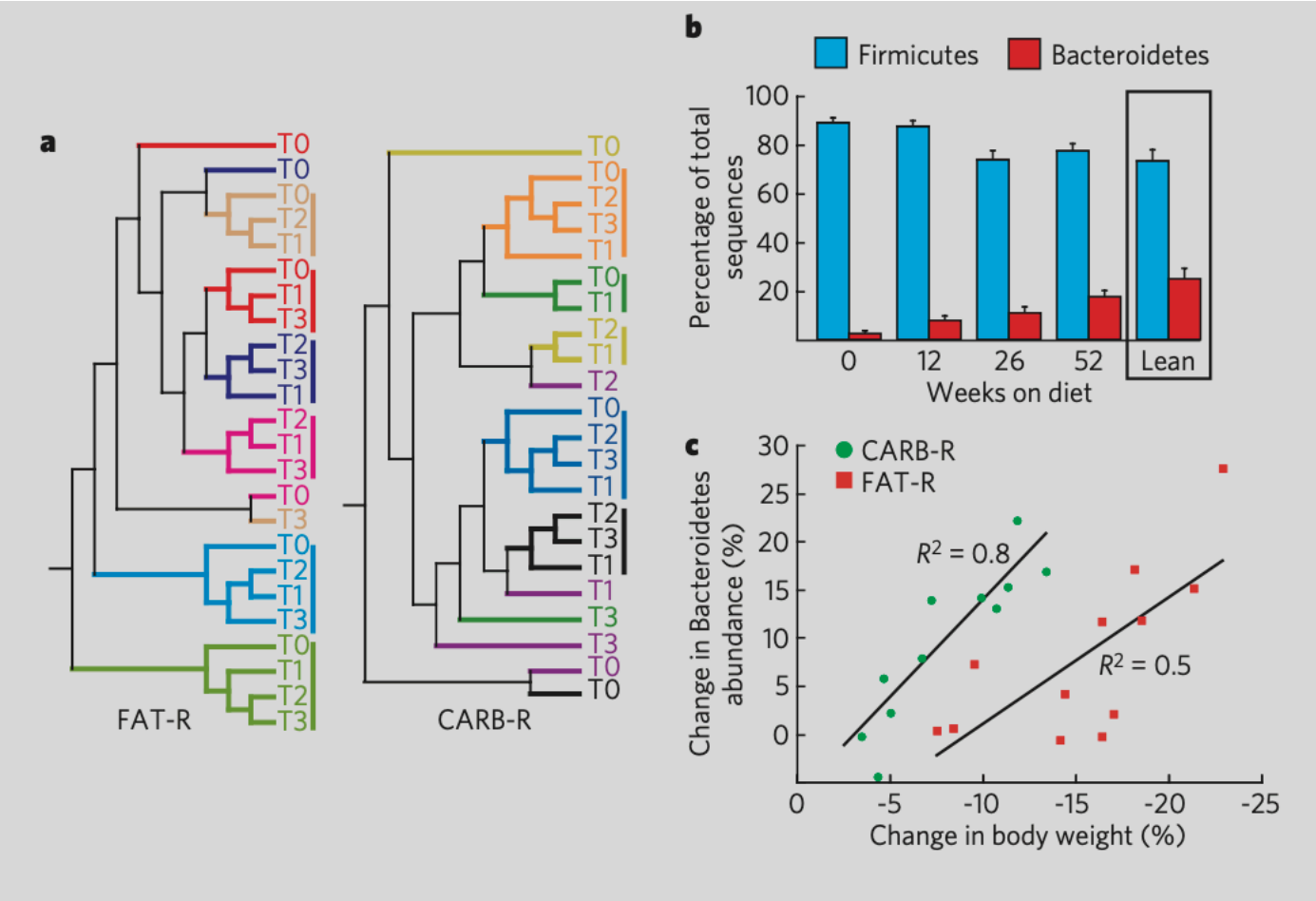
MICROBIAL ECOLOGY

# Human gut microbes associated with obesity

To investigate the relation between gut microbial ecology and body fat in humans, we studied **12 obese people**, who were randomly assigned to either **a fat-restricted (FAT-R)** or to **a carbohydrate-restricted (CARB-R)** low- calorie diet.

Before diet therapy, obese people had fewer Bacteroidetes ($P<0.001$) and more Firmicutes ($P=0.002$) than did lean controls (Fig. 1b).

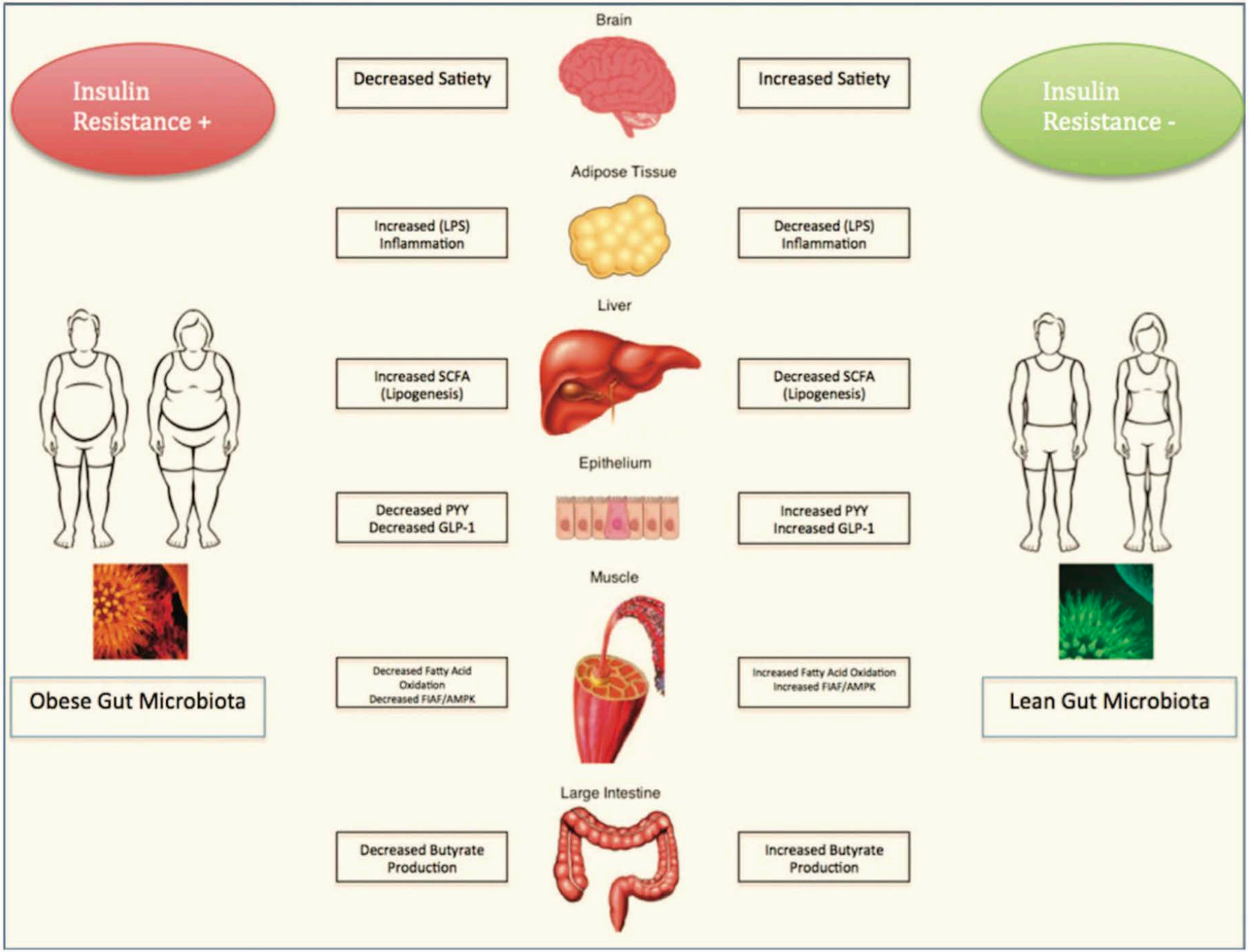
Over time, the relative abundance of Bacteroidetes increased ($P<0.001$) and the abundance of Firmicutes decreased ($P=0.002$), **irrespective of diet type.**



KDA
Ketogenic Diet
ACADEMY

# The Influence of the Gut Microbiome on Obesity, Metabolic Syndrome and Gastrointestinal Disease

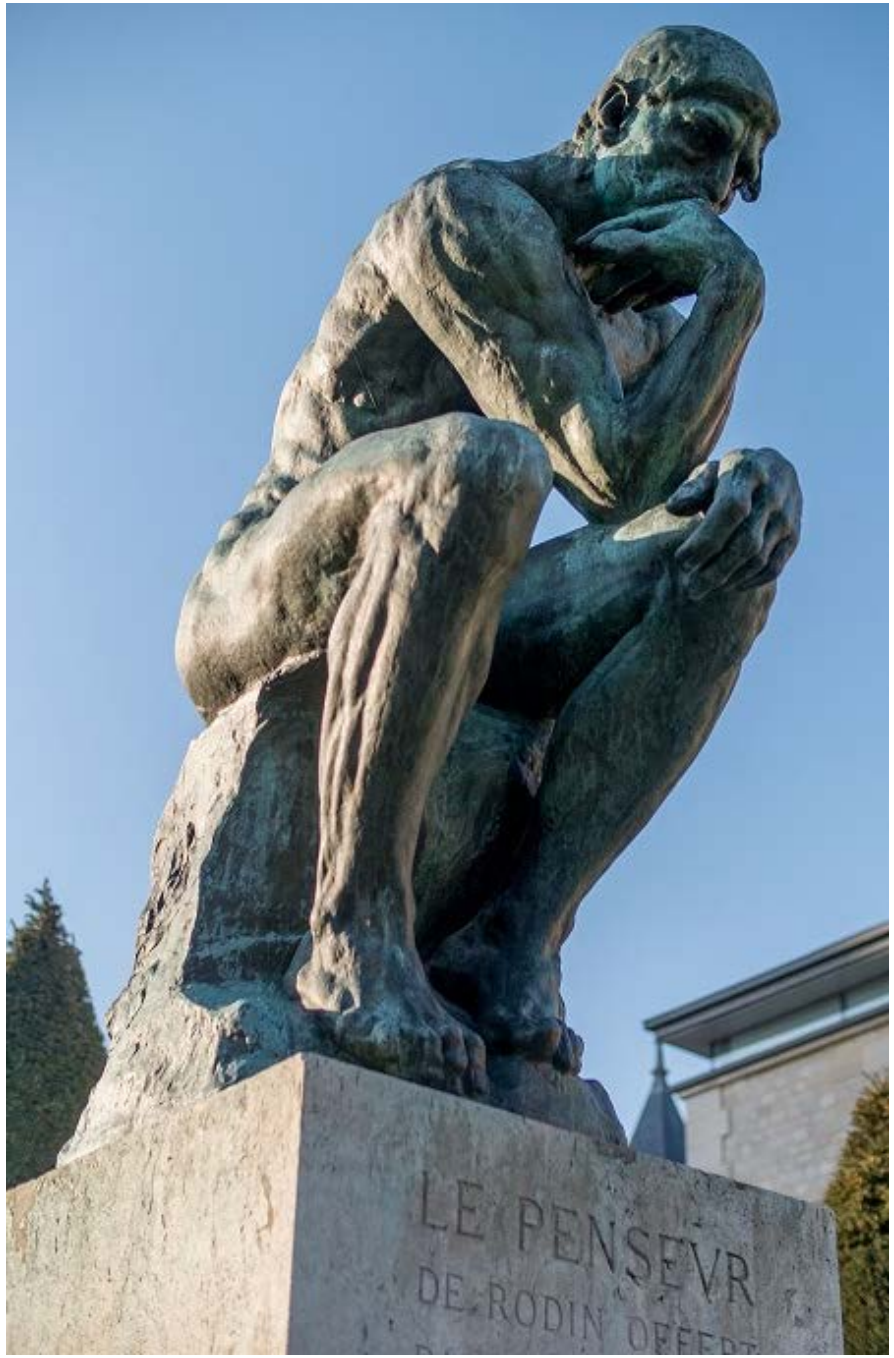
Parth J. Parekh, MD[1], Luis A. Balart, MD, MACG[1] and David A. Johnson, MD, MACG, FASGE[2]



KDA Ketogenic Diet ACADEMY

SINut Società Italiana di Nutraceutica

# CHE RELAZIONE ESISTE TRA ALIMENTAZIONE E MICROBIOTA?



European Review for Medical and Pharmacological Sciences 2016; 20: 4742-4749

# The role of diet on gut microbiota composition

S. BIBBÒ[1,2], G. IANIRO[1], V. GIORGIO[3], F. SCALDAFERRI[1], L. MASUCCI[4], A. GASBARRINI[1], G. CAMMAROTA[1]

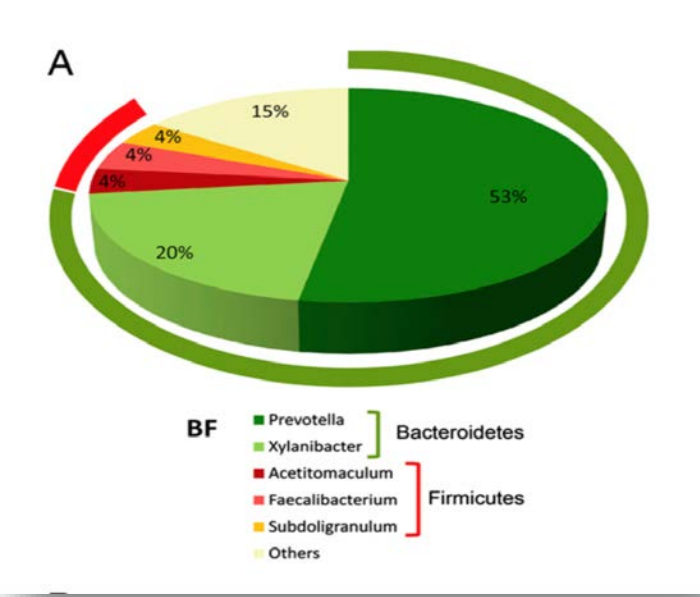
Diet is known to have a strong influence on the composition of intestinal microbiota.
To confirm this hypothesis, some researchers sequenced **oral microbiota** from skeleton teeth of people who lived over the various eras ⟶ They showed that the most significant changes in human gut microbiota had occurred during **two socio-dietary breakthroughs over the human history**:

1. the passage from the hunter-gatherer Paleolithic era to the farming Neolithic era (10000 years ago), with a diet rich in carbohydrates
2. the beginning of the industrialized period, characterized by processed flour and sugar diet (about two centuries ago)

# Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa

Scopo studio (2010): comparare microbiota intestinale di bambini provenienti da aree geografiche diverse:

- 14 bambini età 1-6 anni che vivono in un **villaggio dell'Africa rurale** (ambiente con caratteristiche insediamenti ad agricoltura di sussistenza dell'età Neolitica - Burkina Faso);
- 15 bambini pari età **Europa occidentale**, sottoposti ad alimentazione Occidentale (ambiente industrializzato).



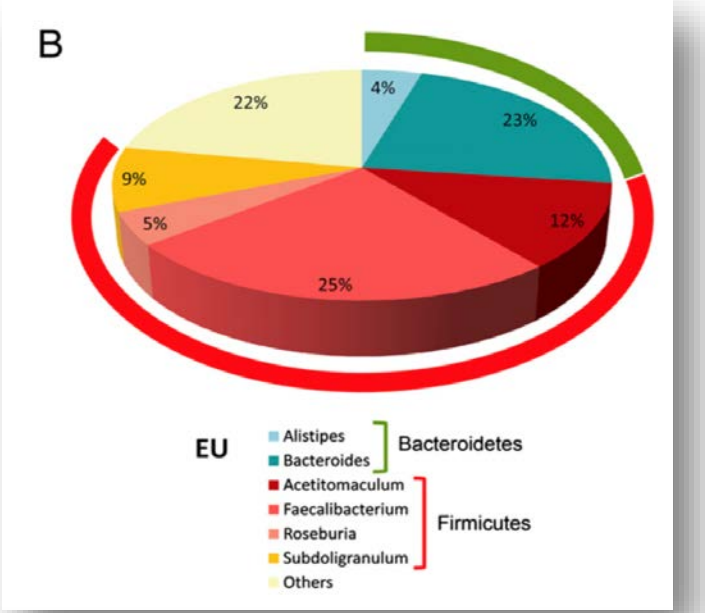




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**Table S2. Total daily food intake in terms of protein, fat, carbohydrate and fiber in relation to the average of maximum quantity ingested per day relative to BF children**

| Dish component° | Daily Q* (g) | Food energy (kcal) | Moisture (%) | Protein (g) | Fat (g) | Carbohydrate (including fiber) (g) | Fiber (g) |
|---|---|---|---|---|---|---|---|
| 1–2 y old | | | | | | | |
| Cereals and starchy component (millet, sorghum) | 120.0 | 344.1 | 34.3 | 7.1 | 2.7 | 73.2 | 0.8 |
| Legumes (black-eyed peas, Niebè) | 40.0 | 168.0 | 2.8 | 19.0 | 9.2 | 6.3 | 4.3 |
| Vegetables (Nerè) | 50.0 | 46.0 | 39.3 | 2.8 | 3.2 | 3.6 | 0.5 |
| Fruit (mango, papaya) | 90.0 | 33.8 | 80.1 | 0.6 | 0.1 | 8.6 | 4.4 |
| Milk (breast milk) | 120.0 | 80.4 | 103.8 | 1.3 | 3.7 | 10.9 | 0.0 |
| Total daily food intake | 420.0 | 672.2 | 260.3 | 30.9 | 18.9 | 102.6 | 10.0 |
| 2–6 y old | | | | | | | |
| Cereals and starchy component (millet, sorghum) | 170.0 | 495.4 | 46.4 | 10.1 | 4.1 | 105.5 | 1.1 |
| Legumes (black-eyed peas, Niebè) | 70.0 | 267.4 | 6.0 | 25.8 | 8.5 | 26.3 | 6.2 |
| Vegetables (Nerè) | 60.0 | 55.2 | 47.1 | 3.4 | 3.8 | 4.3 | 0.6 |
| Fruit (mango, papaya) | 130.0 | 48.8 | 115.7 | 0.9 | 0.2 | 12.5 | 6.4 |
| Fat (Karitè butter) | 15.0 | 129.3 | 0.2 | 0.0 | 14.7 | 0.1 | 0.0 |
| Total daily food intake | 445.0 | 996.1 | 215.4 | 40.2 | 31.2 | 148.6 | 14.2 |

°Nutritional composition of foods is available at http://www.fao.org/docrep/003/x6877e/X6877E00.htm.
*Average of maximum quantity ingested per child per day.

**Table S3. Total daily food intake in terms of protein, fat, carbohydrate and fiber in relation to the average of maximum quantity ingested per day relative to EU children**

| Dish component° | Daily Q* (g) | Food energy (kcal) | Moisture (%) | Protein (g) | Fat (g) | Carbohydrate (including fiber) (g) | Fiber (g) |
|---|---|---|---|---|---|---|---|
| 1–2 y old | | | | | | | |
| Cereals and starchy component (bread, biscuits, pasta, rice) | 130.0 | 266.3 | 35.0 | 8.6 | 2.9 | 107.5 | 1.6 |
| Vegetables (carrot, potato, tomato, zucchini) | 100.0 | 56.6 | 82.5 | 2.2 | 1.3 | 20.7 | 1.8 |
| Fruit (apple, pear, banana) | 100.0 | 50.2 | 83.0 | 0.7 | 0.2 | 26.5 | 2.2 |
| Milk (breast milk) | 300.0 | 210.0 | 262.5 | 3.0 | 13.2 | 20.7 | 0.0 |
| Milk derivatives (parmesan, mozzarella, yogurt) | 100.0 | 158.4 | 74.2 | 8.0 | 13.8 | 4.6 | 0.0 |
| Meat (chicken, beef), fish (cod, sole) | 80.0 | 132.2 | 53.0 | 19.3 | 4.8 | 6.0 | 0.0 |
| Oil (extra virgin olive oil) | 20.0 | 179.8 | 0.0 | 0.0 | 20.0 | 0.0 | 0.0 |
| Honey | 5.0 | 15.2 | 0.9 | 0.0 | 0.0 | 4.0 | 0.0 |
| Total daily food intake | 835.0 | 1068.7 | 591.1 | 41.9 | 56.1 | 190.0 | 5.6 |
| 2–6 y old | | | | | | | |
| Cereals and starchy component (bread, biscuits, pasta, rice) | 160.0 | 375.0 | 68.0 | 9.7 | 4.9 | 152.4 | 3.5 |
| Legumes (beans, peas) | 20.0 | 10.9 | 15.4 | 1.2 | 0.1 | 3.7 | 0.9 |
| Vegetables (carrot, potato, tomato, zucchini) | 100.0 | 50.9 | 82.3 | 2.3 | 1.1 | 18.4 | 1.6 |
| Fruit (apple, pear, banana) | 140.0 | 83.5 | 114.9 | 1.1 | 0.3 | 43.0 | 2.4 |
| Milk (cow's milk) | 140.0 | 64.4 | 125.3 | 4.5 | 2.2 | 14.3 | 0.0 |
| Milk derivatives (parmesan, mozzarella, yogurt) | 150.0 | 250.3 | 106.8 | 16.8 | 19.9 | 6.5 | 0.0 |
| Meat (chicken, beef), fish (cod, sole) | 120.0 | 157.7 | 83.9 | 26.0 | 4.6 | 6.2 | 0.0 |
| Egg | 30.0 | 91.1 | 16.9 | 2.9 | 8.7 | 0.4 | 0.0 |
| Oil and fats (extra-virgin olive oil, butter) | 25.0 | 210.7 | 1.4 | 0.1 | 23.3 | 0.2 | 0.0 |
| Sugar | 10.0 | 38.7 | 0.0 | 0.0 | 0.0 | 10.0 | 0.0 |
| Snacks | 30.0 | 179.6 | 18.8 | 2.2 | 8.7 | 34.9 | 0.0 |
| Total daily food intake | 925.0 | 1512.7 | 633.6 | 66.7 | 73.9 | 290.0 | 8.4 |

KDA Ketogenic Diet ACADEMY

Singh et al. J Transl Med (2017) 15:73
DOI 10.1186/s12967-017-1175-y

Journal of Translational Medicine

REVIEW Open Access

# Influence of diet on the gut microbiome and implications for human health

Rasnik K. Singh[1], Hsin-Wen Chang[2], Di Yan[2], Kristina M. Lee[2], Derya Ucmak[2], Kirsten Wong[2], Michael Abrouk[3], Benjamin Farahnik[4], Mio Nakamura[2], Tian Hao Zhu[5], Tina Bhutani[2] and Wilson Liao[2*]

**Table 1 Overview of select gut bacterial genera and species commonly affected by diet**

| Bacteria | Basic features | Associated physiologic changes | Associated disease states | References |
|---|---|---|---|---|
| *Bifidobacterium* spp. | Gram positive obligate anaerobe branched; nonmotile | SCFA production; improve gut mucosal barrier; lower intestinal LPS levels | Reduced abundance in obesity | [166, 167] |
| *Lactobacillus* spp. | Gram positive facultative anaerobe rod-shaped | SCFA production; anti-inflammatory and anti-cancer activities | Attenuate IBD | [168, 169] |
| *Bacteroides* spp. | Gram negative obligate anaerobe rod-shaped; variable motility | Activate CD4 + T cells | Increased abundance in IBD | [170–173] |
| *Alistipes* spp. | Gram negative obligate anaerobe rod-shaped; bile-resistant and pigment-producing[a] | | Reported in tissue from acute appendicitis and perirectal and brain abscesses | [174] |
| *Bilophila* spp. | Gram negative obligate anaerobe urease-positive, bile resistant, catalase-positive | Promote pro-inflammatory $T_H1$ immunity | B. wadsworthia observed in colitis, perforated and gangrenous appendicitis, liver and soft tissue abscesses, cholecystitis, FG, empyema, osteomyelitis, and HS | [175, 176] |
| *Clostridium* spp. | Gram positive obligate anaerobe rod-shaped; spore-forming | Promote generation of $T_H17$ cells | Several spp. are pathogenic causing tetanus, botulism, gas gangrene, or pseudomembranous colitis | [177, 178] |
| *Roseburia* spp. | Gram variable obligate anaerobe curved rod-shaped; motile | SCFA production | Reduced abundance in IBD | [179] |
| *Eubacterium* spp. | Gram positive obligate anaerobe rod-shaped | SCFA production; form beneficial phenolic acids | Reduced abundance in IBD | [180, 181] |
| *Enterococcus* spp. | Gram positive facultative anaerobe cocci | | Several spp. are pathogenic causing UTI, endocarditis, or bacteremia | [182] |
| *Faecalibacterium prausnitzii* | Gram positive obligate anaerobe rod-shaped; nonmotile | SCFA production; anti-inflammatory effects | Reduced abundance in IBD and obesity | [183, 184] |
| *Akkermansia muciniphila* | Gram negative obligate anaerobe oval-shaped; nonmotile | Anti-inflammatory effects | Reduced abundance in IBD, obesity, and psoriatic arthritis | [53, 133, 185] |
| *Escherichia coli* | Gram negative facultative anaerobe rod-shaped | TLR-activation | Increased abundance in IBD gastroenteritis, UTI, and meningitis | [186–188] |
| *Helicobacter pylori* | Gram negative microaerophilic helix-shaped; motile | | Gastritis; ulcers; MALT cancers | [189, 190] |
| *Streptococcus* spp. | Gram positive facultative anaerobe cocci | | Some spp. are pathogenic causing meningitis, pneumonia, and endocarditis | [191] |

*spp* species, *SCFA* short chain fatty acid, *LPS* lipopolysaccharide, *IBD* inflammatory bowel disease, $T_H$ T helper, *FG* Fournier's gangrene, *HS* hidradenitis suppurativa, *UTI* urinary tract infection(s), *TLR* toll-like receptor, *MALT* mucosa-associated lymphoid tissue

[a] *A. putredinis* does not produce pigment and is susceptible to bile

Protein

**Table 2 Effects of protein on gut microbiota**

| | Microbial diversity | *Bifidobacteria* | *Lactobacilli* | *Bacteroides* | *Alistipes* | *Bilophila* | *Clostridia* | *Roseburia* | *Eubacterium Rectale* | References |
|---|---|---|---|---|---|---|---|---|---|---|
| Animal protein | ↑ | ↑↓ | | ↑↓ | ↑ | ↑ | ↑ | ↓ | ↑↓ | [13, 29–35, 38–40] |
| Whey protein extract | ↑ | ↑ | ↑ | ↓ | | | ↓ | | | [32, 33] |
| Pea protein extract | ↑ | ↑ | ↑ | | | | | | | [31] |

Arrow thickness corresponds to relative number of studies supporting the relationship

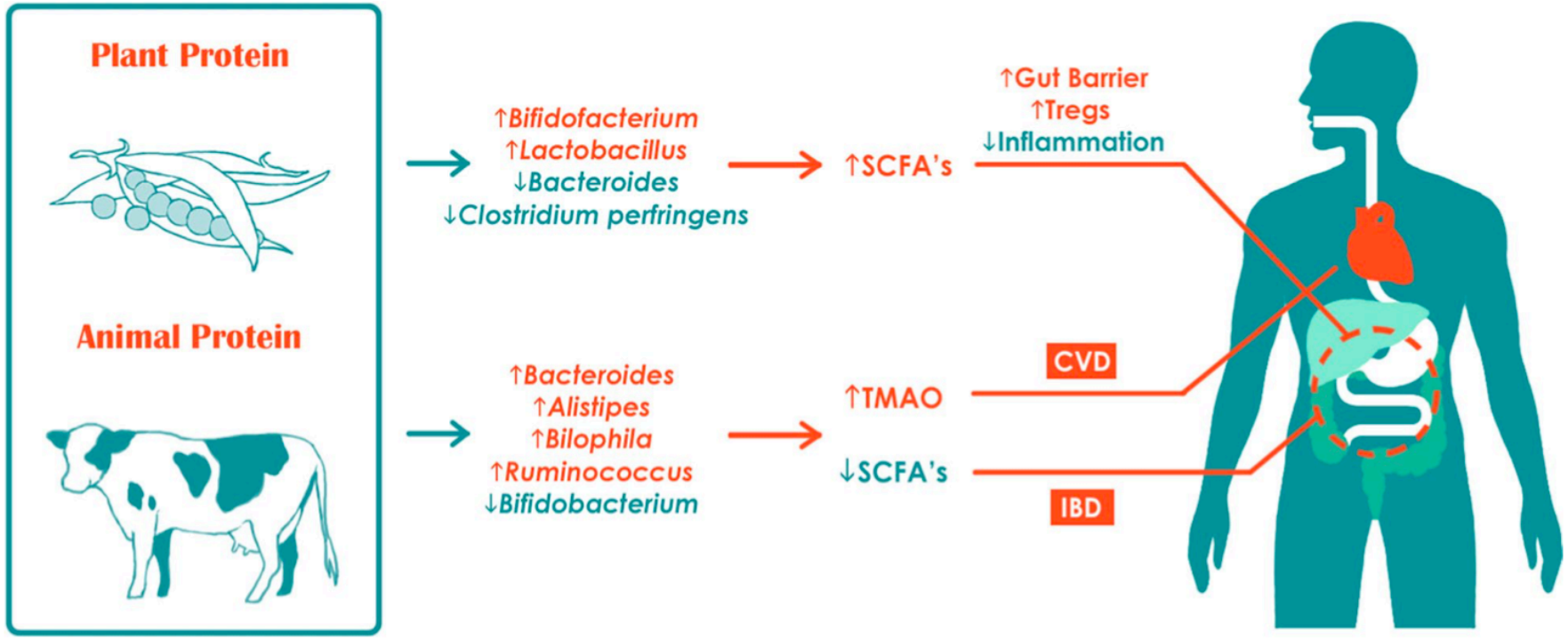



**Fig. 2** Impact of dietary protein on intestinal microbiota and health outcomes. *SCFA's* short chain fatty acids, *TMAO* trimethylamine N-oxide, *Tregs* T regulatory cells, *CVD* cardiovascular disease; *IBD* inflammatory bowel disease

KD Ketogenic ACADE

Fat

Vut a di Nutraceutica

**Table 3 Effects of fats on gut microbiota**

| | Lactic acid bacteria[a] | *Bifidobacteria* | *Clostridiales* | *Bacteroides* | *Bilophila* | *Faecalibacterium prausnitzii* | *Akkermansia muciniphila* | References |
|---|---|---|---|---|---|---|---|---|
| High fat | ↓ | | ↑ | ↑ | | | | [30, 49, 51, 52] |
| Low fat | | ↑ | | | | | | [49] |
| High saturated fat | | | | ↑ | ↑ | ↑ | | [26, 49] |
| High unsaturated fat | ↑ | ↑ | | | | | ↑ | [45, 49, 50] |

[a] Lactic acid bacteria include Lactobacillus and Streptococcus

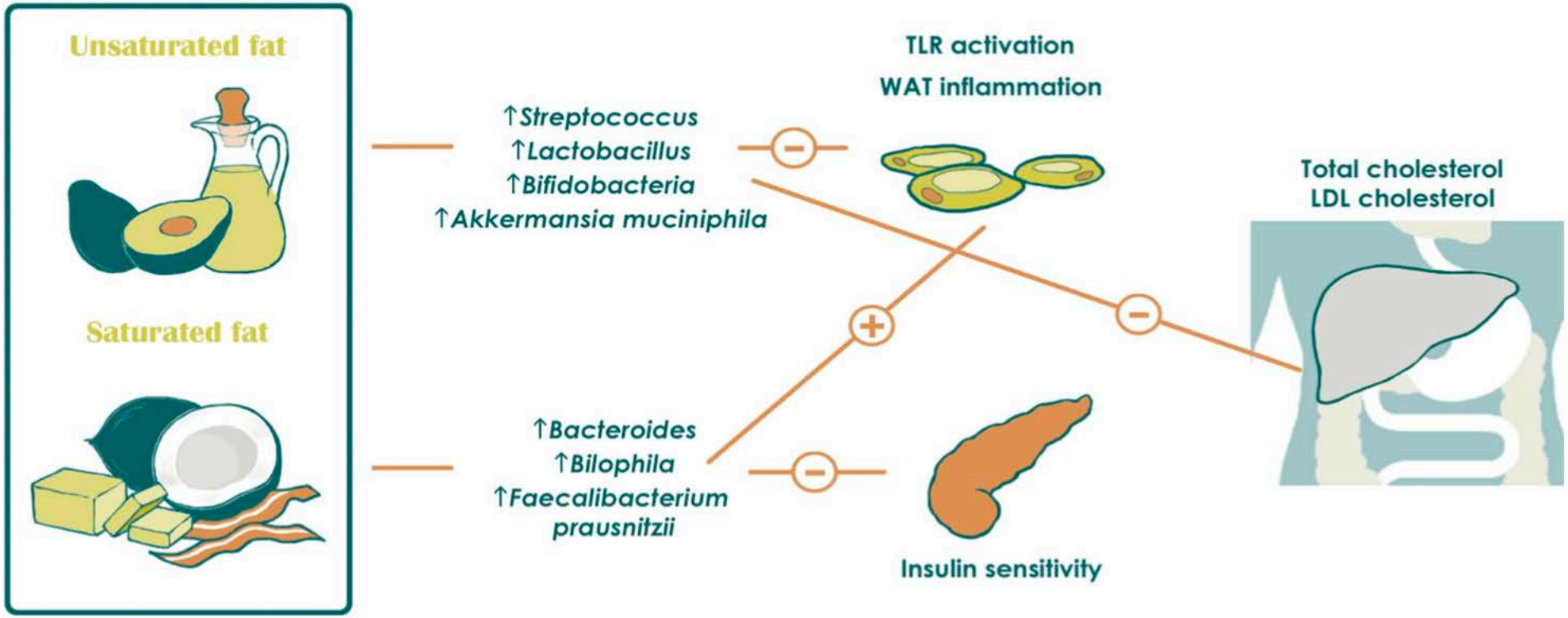



**Fig. 3** Impact of dietary fats on intestinal microbiota and host metabolism. *TLR* toll-like receptor, *WAT* white adipose tissue, *LDL* low-density lipoprotein

A proposito di OLIO EVO…

**Extra-virgin olive oil and the gut-brain axis: influence on gut microbiota, mucosal immunity, and cardiometabolic and cognitive health**

Jasmine F. Millman, Shiki Okamoto, Taiki Teruya, Tsugumi Uema, Shinya Ikematsu, Michio Shimabukuro, and Hiroaki Masuzaki

In rodents, **consumption of EVOO increased a-diversity**, a measure of species richness, as well as **b-diversity**, a measure of the differences in composition between samples, compared with controls.

These results are associated with favorable effects on metabolic health, because reduced microbial diversity is associated with increased chronic inflammation and subsequent development of metabolic diseases. Extra-virgin olive oil ingestion in rodents also can promote the growth of certain types of beneficial bacteria including species of Lactobacillus, Bifidobacterium.

In additionally, EVOO has demonstrated antibacterial and bacteriostatic effects against bacteria such as those in the Desulfovibrionaceae, a family of opportunistic pathogens associated with obesity and inflammation.

The ability of EVOO to act as both a prebiotic, stimulating the growth of beneficial bacteria, and an antibacterial, suppressing the growth of pathogenic bacteria, is likely attributable to the array of phenolic compounds EVOO contains.

Sugar

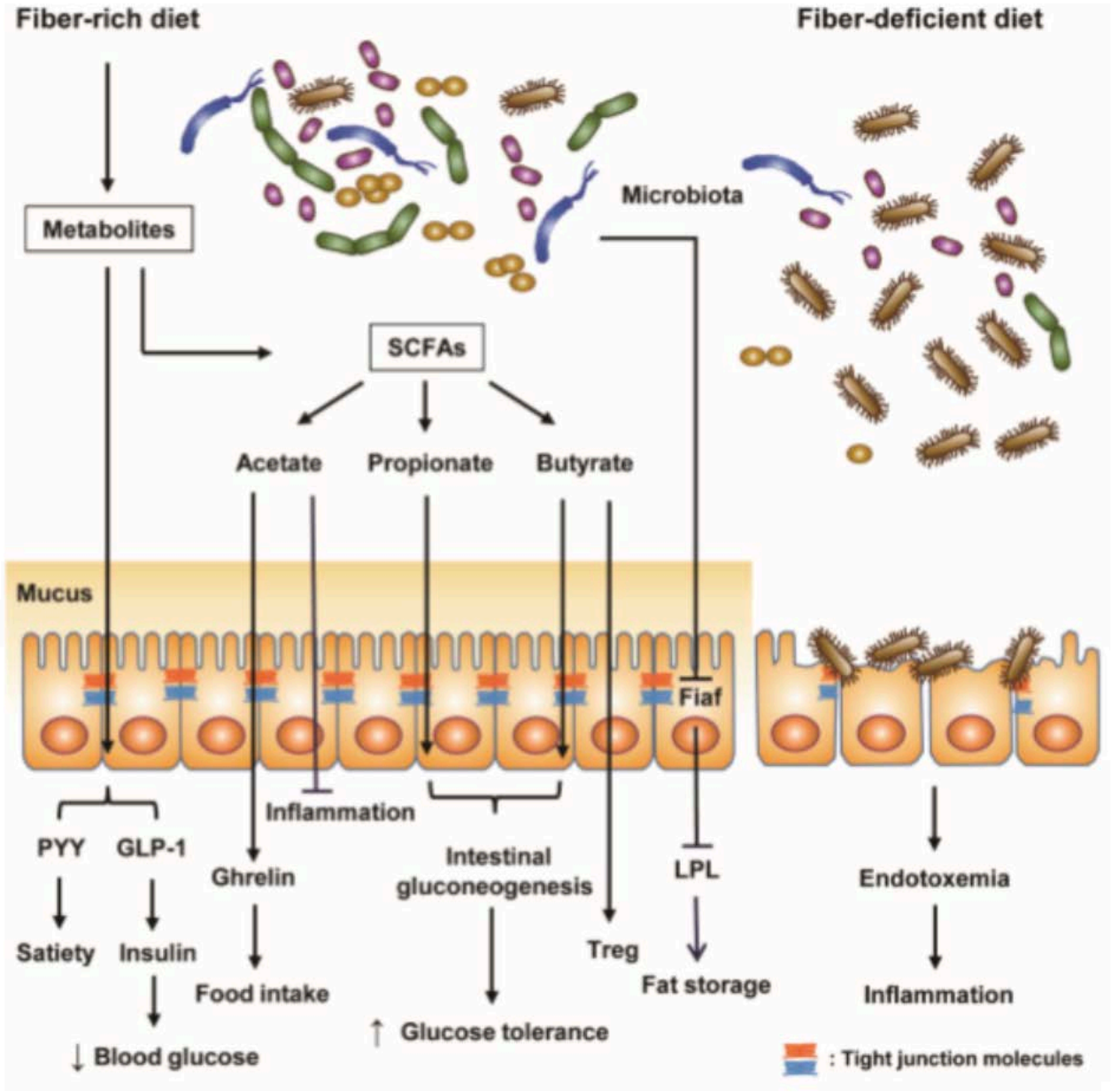
There is accumulating evidence showing that **high amounts of dietary sugar** (fructose or sucrose) **can rapidly alter the gut microbiota**.

In male rats, consumption of a diet containing 17% fructose leads to a **significant decrease in microbial diversity** within a week of diet onset.

A high-sugar diet (HSD) induces changes in microbiota composition that are comparable to those of a HFD: an increase in the *Firmicutes-to-Bacteriodetes* ratio and a significant decrease in *Bacilli* abundance.

Male rats fed a HSD display an increase in liver fat deposition associated with increases in the abundance of *Clostridia*, particularly the families *Ruminococcaceae* and *Lachnospiraceae*, which had been linked to fat accumulation

# Fiber

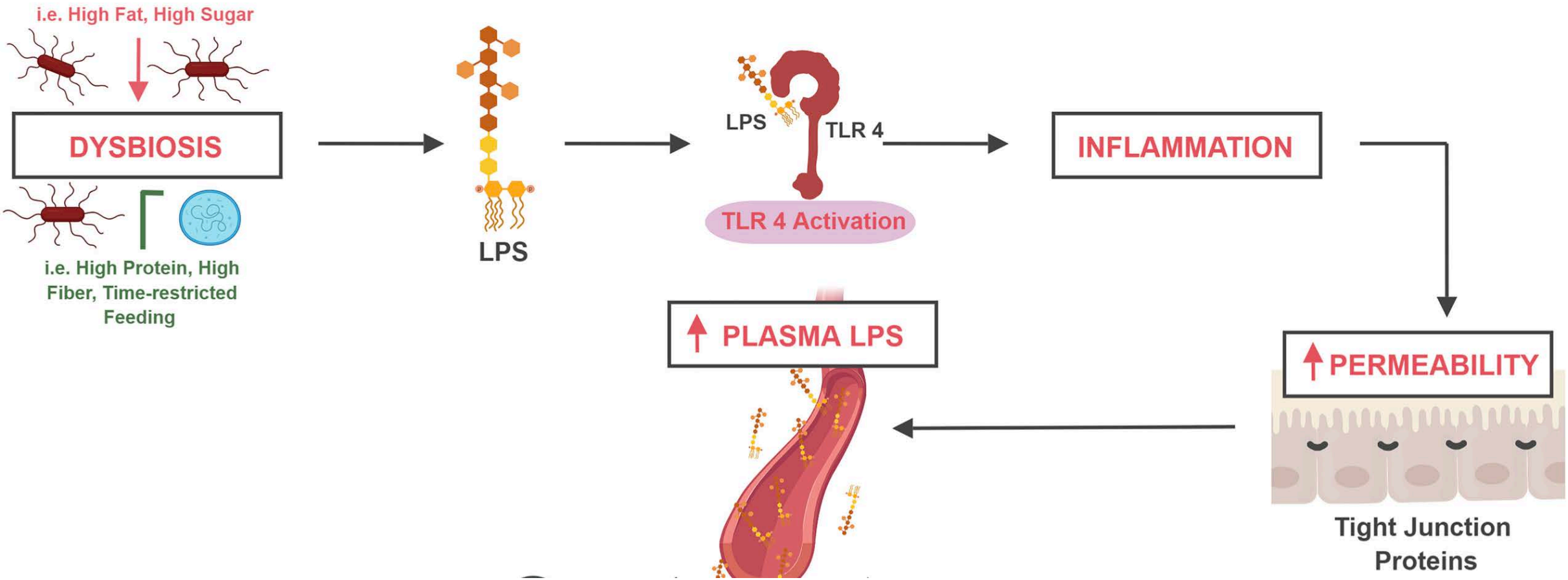



Dieta ricca in fibre determina:

↑ produzione di SCFAs

↑ produzione di PYY sazietà

↑ produzione di GLP-1 regola la secrezione insulinica, andando a migliorare il controllo glicemico


i.e. High Fat, High Sugar
DYSBIOSIS
i.e. High Protein, High Fiber, Time-restricted Feeding
LPS
LPS
TLR 4
TLR 4 Activation
INFLAMMATION
PERMEABILITY
Tight Junction Proteins
PLASMA LPS

KDA Ketogenic Diet ACADEMY

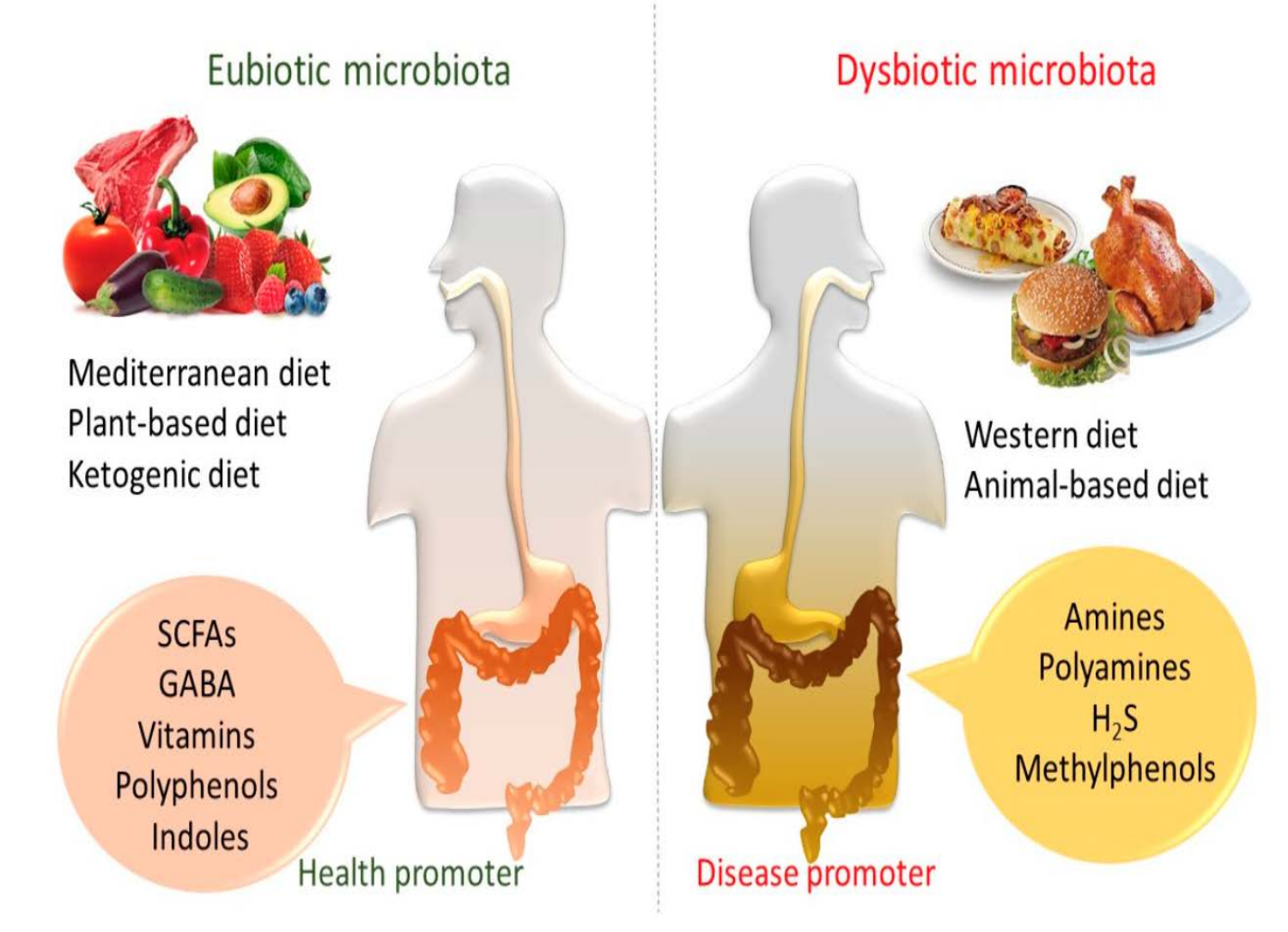
SINut Società Italiana di Nutraceutica

*microorganisms* MDPI

*Review*

# The Influence of Probiotics on the Firmicutes/Bacteroidetes Ratio in the Treatment of Obesity and Inflammatory Bowel disease

Spase Stojanov [1,2], Aleš Berlec [1,2] and Borut Štrukelj [1,2,*]



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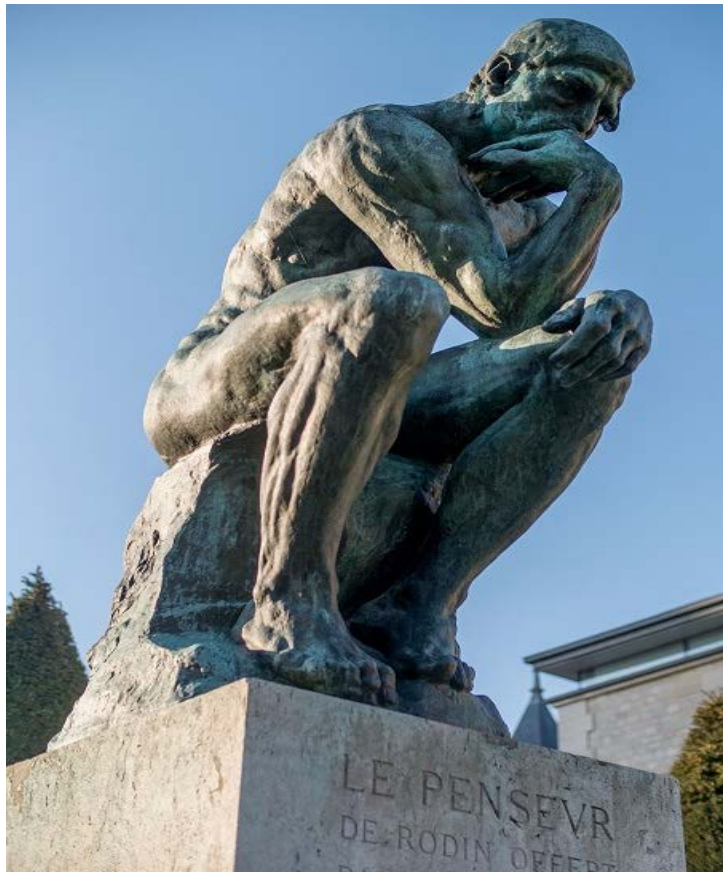
# Ketogenic Diet and Microbiota: Friends or Enemies?



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*Review*

# Ketogenic Diet and Microbiota: Friends or Enemies?

Antonio Paoli [1,2,*], Laura Mancin [3], Antonino Bianco [4], Ewan Thomas [4], João Felipe Mota [5] and Fabio Piccini [3]

- La composizione del microbiota è influenzata da molti fattori e la stabilità del microbiota viene raggiunta tra i due e i cinque anni di età.
- Il **rapporto Firmicutes / Bacteroidetes** è considerato significativo per la salute dell'intestino, il rapporto è **chiaramente collegato all'aumento dell'indice di massa corporea (BMI)**

**GRASSI**

La composizione del microbiota è influenzata da molti fattori e la composizione ottimale di una KD (ed in particolar modo di una VLCKD) considera sia grassi saturi che mono-polinsaturi, mentre la dieta occidentale è ricca di grassi saturi-trans e povera di grassi mono-polinsaturi.

Recente revisione sistematica: **diete ricche di acidi grassi saturi hanno portato a effetti negativi sul microbiota intestinale**. Mentre **le diete ricche di acidi grassi polinsaturi (con effetti opposti quando si confrontano i grassi omega 3 vs omega 6) non hanno modificato la ricchezza e la diversità**.

## PROTEINE

La **fonte e il tipo di proteine** devono essere considerati per dieta KD e VLCKD (fonte proteica è fondamentale per mantenere la massa magra).

**Come e quanto i tipi di proteine (vegetali vs animali) modificano il microbiota**? Anche se una dieta ricca di proteine in genere compromette la salute dell'intestino (diminuisce l'abbondanza e cambia la composizione), sul microbiota intestinale compaiono numerosi e disparati effetti.

Le proteine di origine vegetale, come le **proteine del fagiolo verde** (come parte di una dieta ricca di grassi), **hanno aumentato i Bacteroidetes e ridotto Firmicutes** e le **proteine dei piselli** aumentavano i ceppi di Bifidobacterium e Lactobacillus.

Durante un periodo di VLCKD, raccomandiamo l'uso di una **fonte di proteine vegetali** più benefiche in termini di salute del microbiota intestinale.

Research on protein and the gut microbiota has focused on transitioning obese animals from a HFD and HSD to a diet high in protein to investigate the potential antiobesity effects of a high-protein diet (HPD).

Stengel et al. found that DIO-rats that were switched from a HFD and HSD to a HPD reduced their daily food intake by 30% on *day 1* and maintained a 14% reduction throughout the remaining 2 wk of the study.

The same group of rats had decreased body weight, maintained lean body mass, and improved glucose control.

HPD consumption in male rats has been associated with an increase in *Bacteroides* and ***Akkermansia spp.*** **abundances**

microbial biotechnology
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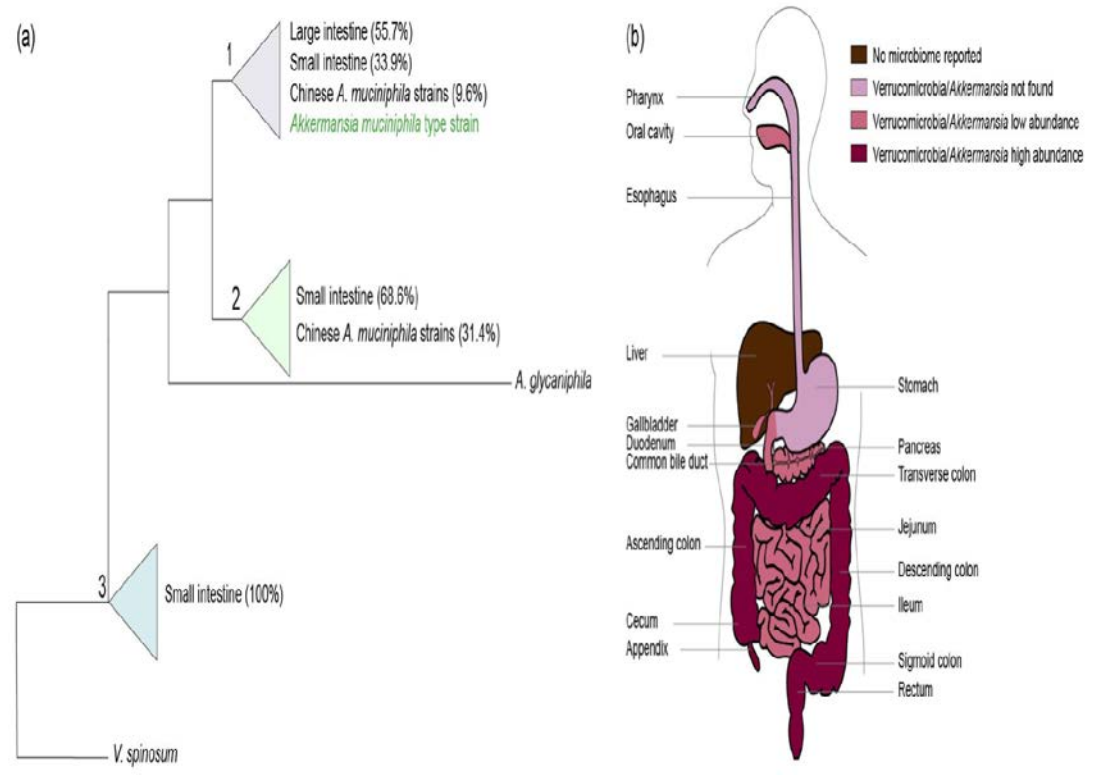
Minireview

**_Akkermansia muciniphila_ is a promising probiotic**




*microorganisms*
MDPI

*Review*

**_Akkermansia muciniphila_ in the Human Gastrointestinal Tract: When, Where, and How?**

Sharon Y. Geerlings [1], Ioannis Kostopoulos [1], Willem M. de Vos [1,2] and Clara Belzer [1,*]

*Akkermansia muciniphila* is a mucin-degrading bacterium of the phylum Verrucomicrobia.

The presence of *A. muciniphila* has been associated with healthy intestine and its abundance has been inversely correlated to several disease states.

Obese children were shown to have a significant reduction in *A. muciniphila*-like bacteria.
In a comprehensive study of infants in daycare, *A. muciniphila*-based sequences were found to be reduced in children that had received multiple antibiotic courses and were at risk for later life obesity.

***Akkermansia*** *muciniphila* is the sole intestinal representative of the *Verrucomicrobia* that is present, though at very low levels, in the human gut since early life.

*A. muciniphila* also is 3 to 5% of the total gut microbiome population in healthy adult humans based on an analysis of its distinctive 16SrRNA signature, although this amount differs by several factors

The presence of *A. muciniphila* **has been correlated with intestinal integrity, and its relative abundance and absolute numbers are known to increase rapidly with age and specifically after weaning**.

Mouse experiments confirmed the effect of *A. muciniphila* on intestinal barrier function and demonstrated that its administration protects against diet-induced obesity.

*Review*

# Recognizing the Benefits of Pre-/Probiotics in Metabolic Syndrome and Type 2 Diabetes Mellitus Considering the Influence of *Akkermansia muciniphila* as a Key Gut Bacterium

Raluca Anca Corb Aron [1], Areha Abid [2], Cosmin Mihai Vesa [1], Aurelia Cristina Nechifor [3], Tapan Behl [4], Timea Claudia Ghitea [5], Mihai Alexandru Munteanu [6], Ovidiu Fratila [6], Felicia Liana Andronie-Cioara [7], Mirela Marioara Toma [5] and Simona Bungau [5,*]

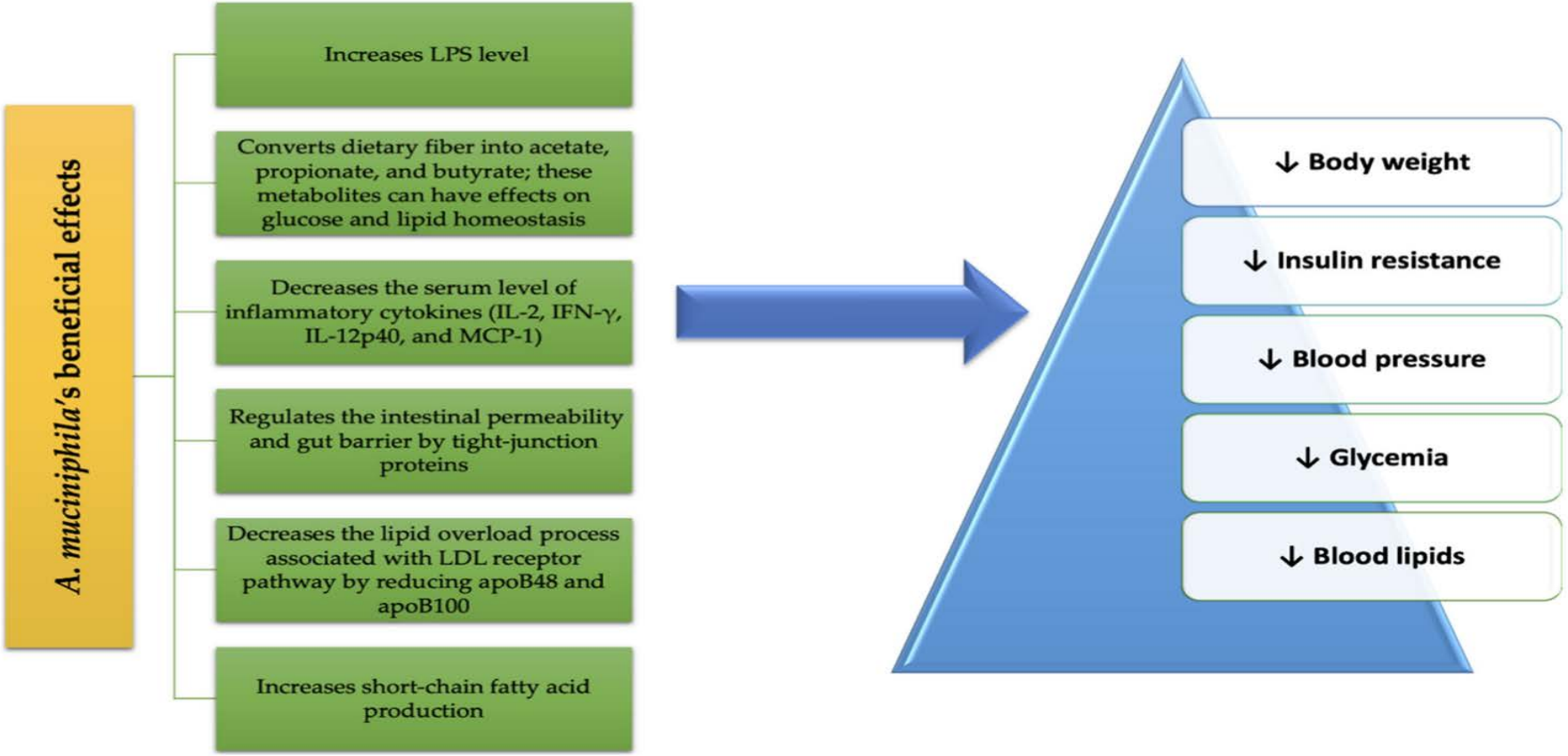


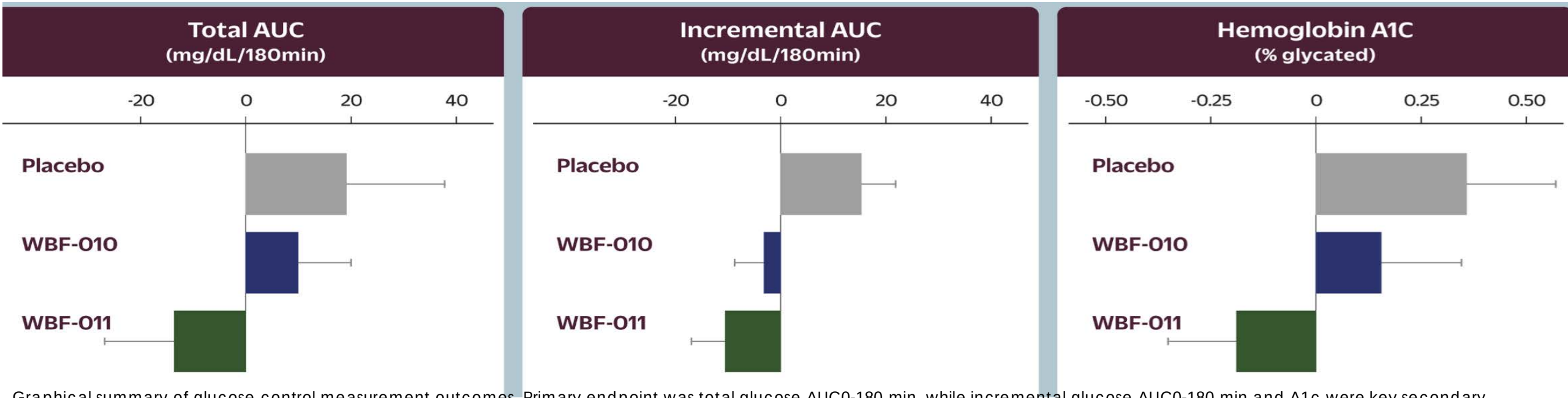

**Figure 2.** *A. muciniphila*'s benefits in MetS.

According to all data, it can be concluded that *A. muciniphila* influences the reaction of humans in terms of improving inflammation, insulin resistance, and glycemia on their diet of caloric constraint

# Improvements to postprandial glucose control in subjects with type 2 diabetes: a multicenter, double blind, randomized placebo-controlled trial of a novel probiotic formulation

Fanny Perraudeau, Paul McMurdie, James Bullard, Andrew Cheng, Colleen Cutcliffe, Achal Deo, John Eid, Jessica Gines, Mohan Iyer, Nicholas Justice, Wesley T Loo, Madeleine Nemchek, Marcus Schicklberger, Michael Souza, Brendon Stoneburner, Surabhi Tyagi, Orville Kolterman

| Ingredients | Placebo | WBF-010 | WBF-011 |
|---|---|---|---|
| Colloidal silicon dioxide | ● | ● | ● |
| Inulin | | ● | ● |
| *Clostridium beijerinckii* (CBEI) | | ● | ● |
| *Clostridium butyricum* (CBUT) | | ● | ● |
| *Bifidobacterium infantis* (BINF) | | ● | ● |
| *Akkermansia muciniphila* (AMUC) | | | ● |
| *Anaerobutyricum hallii* (EHAL) | | | ● |




Graphical summary of glucose control measurement outcomes. Primary endpoint was total glucose AUC0-180 min, while incremental glucose AUC0-180 min and A1c were key secondary measures. Additional detail is provided in table 2 and online supplementary figure S1. AUC, area under the curve.

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RESEARCH ARTICLE

Journal of Applied Toxicology WILEY

## Toxicological safety evaluation of pasteurized *Akkermansia muciniphila*

Céline Druart[1] | Hubert Plovier[1] | Matthias Van Hul[2] | Alizée Brient[3] | Kirt R. Phipps[4] | Willem M. de Vos[5,6] | Patrice D. Cani[2]

Gut microorganisms are vital for many aspects of human health, and the commensal bacterium *Akkermansia muciniphila* has repeatedly been identified as a key compo- nent of intestinal microbiota. Reductions in *A. muciniphila* abundance are associated with increased prevalence of metabolic disorders such as obesity and type 2 diabetes. **It was recently discovered that administration of *A. muciniphila* has beneficial effects and that these are not diminished, but rather enhanced after pasteurization**

No test item-related adverse effects were observed in the 90-day study. These results support that pas- teurized *A. muciniphila* is safe for use as a food ingredient

EFSA Journal

SCIENTIFIC OPINION

ADOPTED: 7 July 2021

doi: 10.2903/j.efsa.2021.6780

## Safety of pasteurised *Akkermansia muciniphila* as a novel food pursuant to Regulation (EU) 2015/2283

EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA),
Dominique Turck, Torsten Bohn, Jacqueline Castenmiller, Stefaan De Henauw, Karen Ildico Hirsch-Ernst, Alexandre Maciuk, Inge Mangelsdorf, Harry J McArdle, Androniki Naska, Carmen Pelaez, Kristina Pentieva, Alfonso Siani, Frank Thies, Sophia Tsabouri, Marco Vinceti, Francesco Cubadda, Thomas Frenzel, Marina Heinonen, Rosangela Marchelli, Monika Neuhäuser-Berthold, Morten Poulsen, Miguel Prieto Maradona, Josef Rudolf Schlatter, Henk van Loveren, Reinhard Ackerl and Helle Katrine Knutsen

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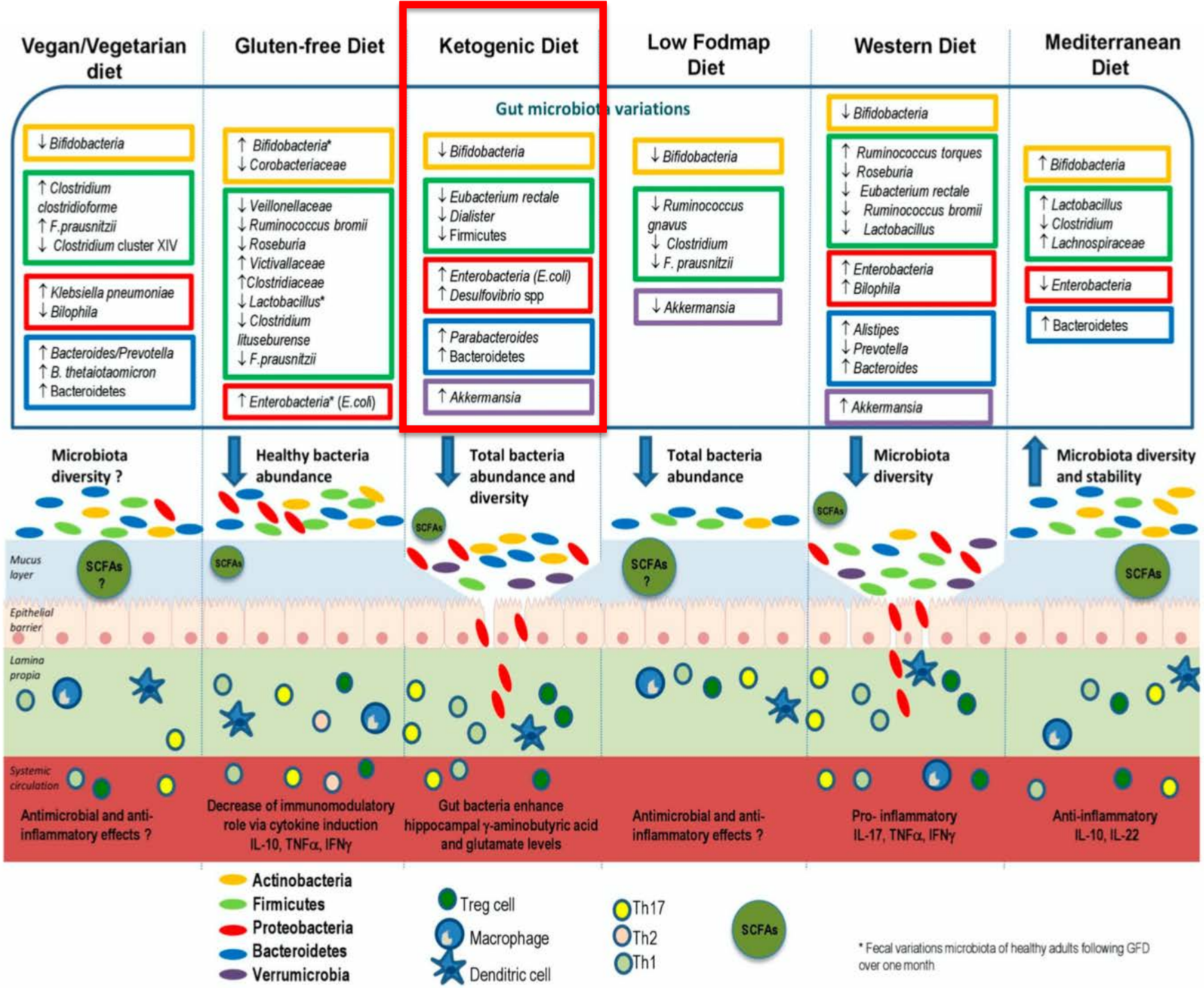

# FACCIAMO CHIAREZZA

Reviews in Endocrine and Metabolic Disorders (2020) 21:1–3
https://doi.org/10.1007/s11154-020-09546-9

# Confusion in the nomenclature of ketogenic diets blurs evidence

Pierpaolo Trimboli[1] · Marco Castellana[2] · Diego Bellido[3] · Felipe F. Casanueva[4]

Published online: 21 February 2020
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| Diet description | Abbreviation | Carbohydrates | Calories | Lipids |
|---|---|---|---|---|
| Very-low-calorie ketogenic diet | VLCKD | <30–50 g/day | <700–800 kcal/day | <30–40 g/day |
| Low-calorie ketogenic diet | LCKD | <30–50 g/day | >700–800 kcal/day and < TEE | >30–40 g/day |
| Isocaloric ketogenic diet | ICKD | <30–50 g/day | In line with TEE | 70–80% of daily calorie intake |

Legend: *TEE* total energy expenditure

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Journal of Endocrinological Investigation
https://doi.org/10.1007/s40618-019-01061-2

CONSENSUS STATEMENT

**Very-low-calorie ketogenic diet (VLCKD) in the management of metabolic diseases: systematic review and consensus statement from the Italian Society of Endocrinology (SIE)**

M. Caprio[1,2] · M. Infante[3] · E. Moriconi[1,4] · A. Armani[1] · A. Fabbri[3] · G. Mantovani[5] · S. Mariani[4] · C. Lubrano[4] · E. Poggiogalle[4] · S. Migliaccio[6] · L. M. Donini[4] · S. Basciani[4] · A. Cignarelli[7] · E. Conte[7] · G. Ceccarini[8] · F. Bogazzi[9] · L. Cimino[10] · R. A. Condorelli[10] · S. La Vignera[10] · A. E. Calogero[10] · A. Gambineri[11] · L. Vignozzi[12] · F. Prodam[13] · G. Aimaretti[13] · G. Linsalata[14] · S. Buralli[14] · F. Monzani[14] · A. Aversa[15] · R. Vettor[16] · F. Santini[8] · P. Vitti[9] · L. Gnessi[4] · U. Pagotto[11] · F. Giorgino[7] · A. Colao[17] · A. Lenzi[4] on behalf of the Cardiovascular Endocrinology Club of the Italian Society of Endocrinology

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| Strong recommendations | Strength of recommendations and quality of evidence according to GRADE system |
|---|---|
| Severe obesity | (1 ØØØO) |
| Management of severe obesity before bariatric surgery | (1 ØØØO) |
| Sarcopenic obesity | (1 ØØØO) |
| Obesity associated with type 2 diabetes (preserved beta cell function) | (1 ØØØO) |
| Obesity associated with hypertriglyceridemia | (1 ØØØO) |
| Obesity associated with hypertension | (1 ØØØO) |
| Pediatric obesity associated with epilepsy and/or with a high level of insulin resistance and/or comorbidities, not responsive to standardized diet | (1 ØØØO) |
| Weak recommendations | |
| Obesity associated with dysbiosis of the gut microbiota | (2 ØØØO) |
| Obesity associated with high levels of LDL-cholesterol and/or low levels of HDL-cholesterol | (2 ØØØO) |
| Obesity associated with non-alcoholic fatty liver disease (NAFLD) | (2 ØØØO) |
| Obesity associated with heart failure (NYHA I–II) | (2 ØOOO) |
| Obesity associated with atherosclerosis | (2 ØOOO) |
| Male obesity secondary hypogonadism | (2 ØØØO) |
| Obesity associated with polycystic ovary syndrome (PCOS) | (2 ØOOO) |
| Menopausal transition-related obesity | (2 ØOOO) |
| Neurodegenerative disorders associated with sarcopenic obesity | (2 ØOOO) |

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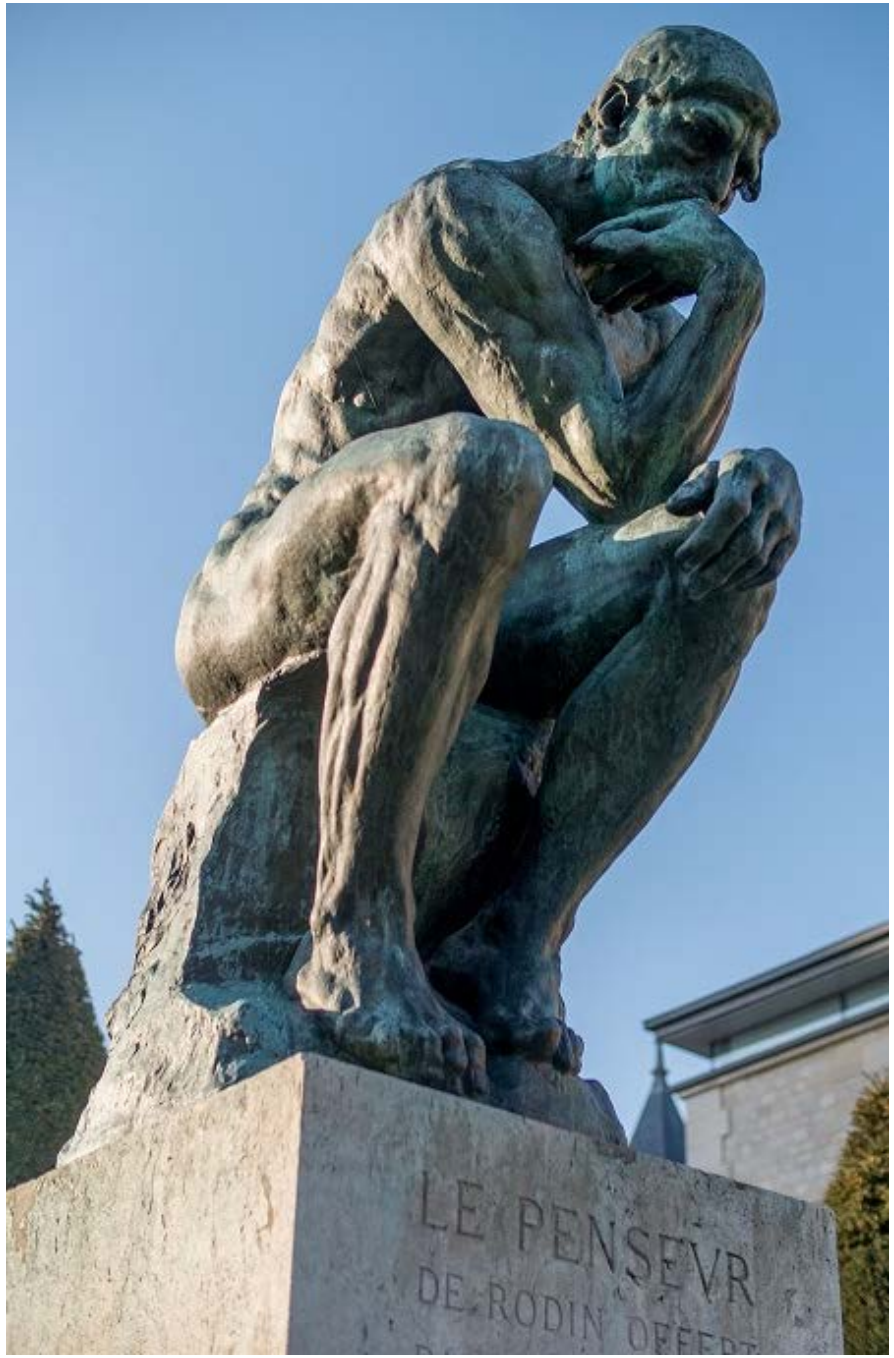
# QUAL E' LO STRETTO LINK TRA ALIMENTAZIONE, OBESITA' E MICROBIOTA?



# MICROBIOTA E VLCKD

## Very-Low-Calorie Ketogenic Diets With Whey, Vegetable, or Animal Protein in Patients With Obesity: A Randomized Pilot Study

Sabrina Basciani,[1] Elisabetta Camajani,[1,*] Savina Contini,[1,*] Agnese Persichetti,[2,*] Renata Risi,[1] Loris Bertoldi,[3] Lidia Strigari,[4] Giancarlo Prossomariti,[1] Mikiko Watanabe,[1] Stefania Mariani,[1] Carla Lubrano,[1] Alfredo Genco,[5] Giovanni Spera,[1] and Lucio Gnessi[1]

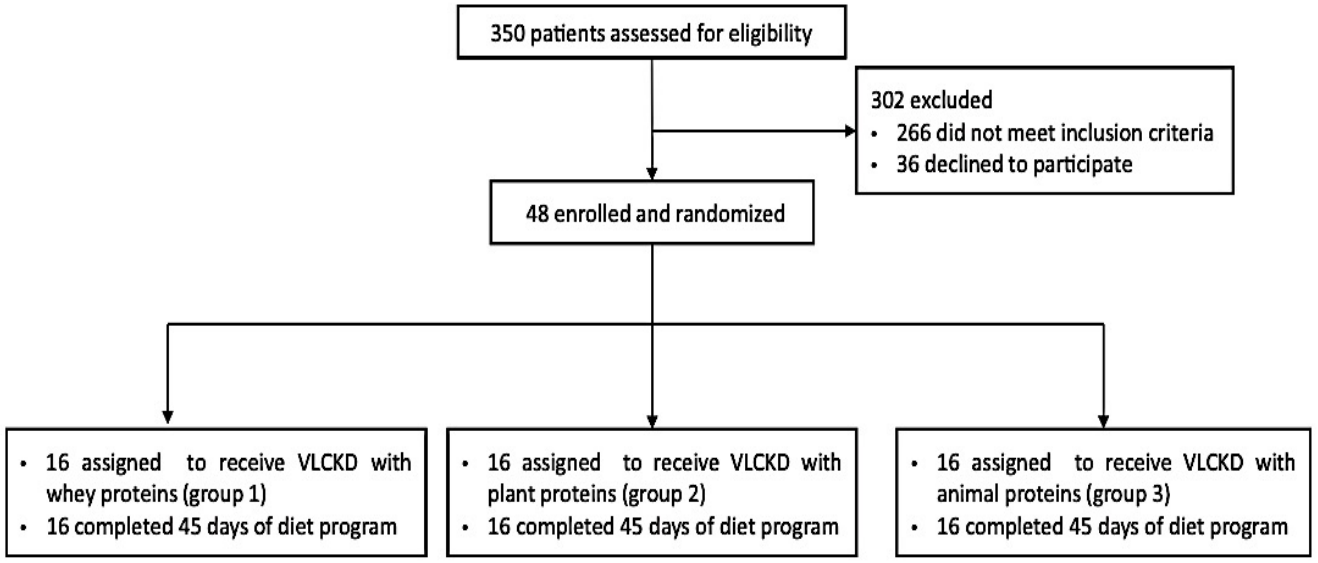
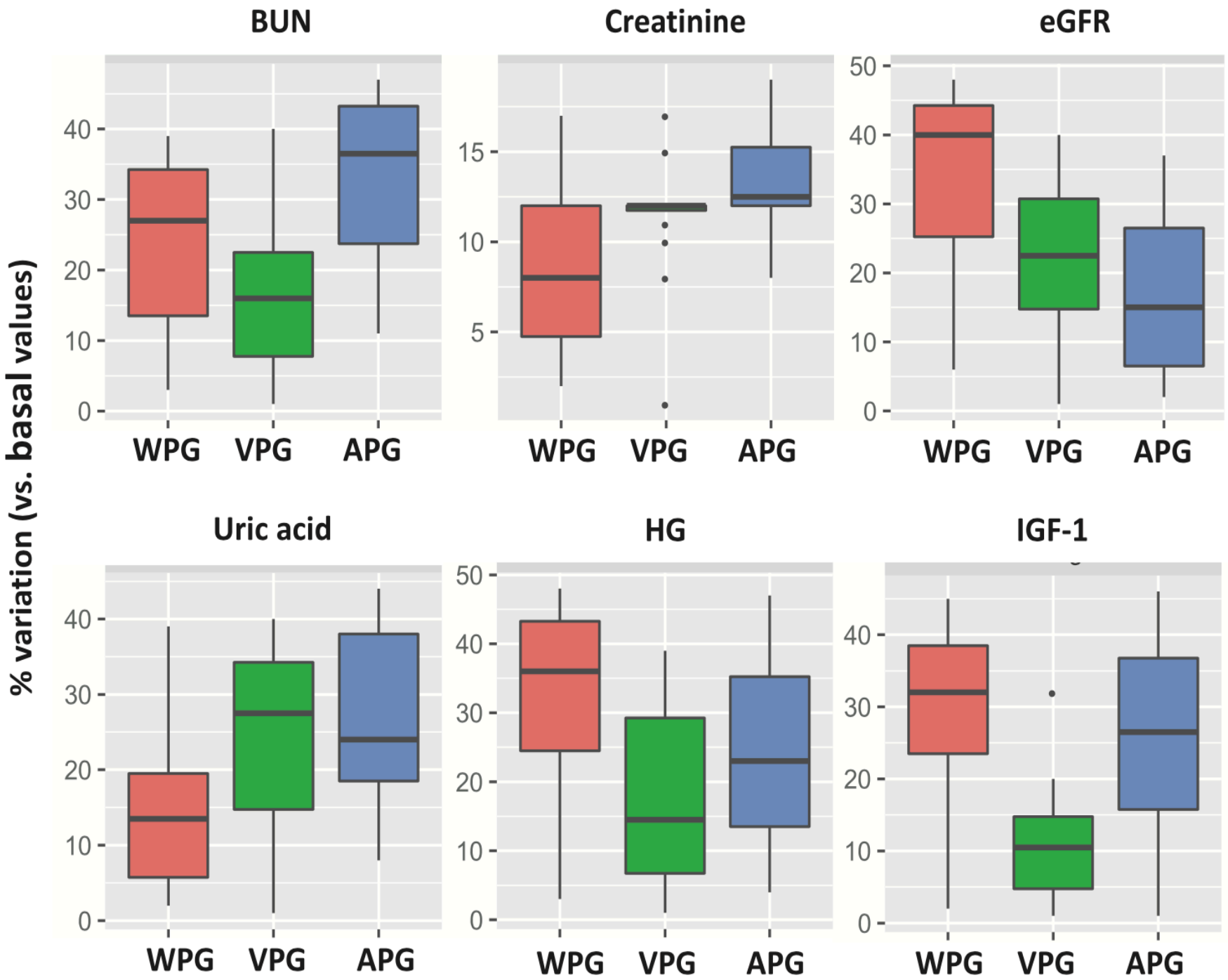


**Table 1. Participant characteristics at baseline (T0) and after 45 days (T45) of VLCKD consumption**

| | WPG | | | VPG | | | APG | | |
|---|---|---|---|---|---|---|---|---|---|
| | T0 | T45 | *P* | T0 | T45 | *P* | T0 | T45 | *P* |
| BW (kg) | 102.02 ± 12.04 | 94.05 ± 11.43 | **0.032** | 102.10 ± 12.36 | 94.08 ± 11.92 | **0.041** | 98.36 ± 14.49 | 91.72 ± 14.48 | 0.106 |
| BMI (kg/m$^2$) | 35.8 ± 5.0 | 32.6 ± 4.8 | **0.035** | 36.1 ± 4.3 | 32.9 ± 4.0 | **0.020** | 35.7 ± 3.7 | 32.8 ± 3.7 | **0.016** |
| WC (cm) | 110.0 ± 9.4 | 102.8 ± 8.4 | **0.014** | 108.2 ± 8.5 | 102.5 ± 7.6 | **0.031** | 105.3 ± 9.1 | 99.1 ± 10.2 | **0.040** |
| HC (cm) | 123.6 ± 12.1 | 117.9 ± 12.2 | 0.098 | 123.3 ± 9.3 | 117.9 ± 8.4 | **0.049** | 122.5 ± 10.6 | 116.1 ± 10.3 | **0.047** |
| TC (cm) | 63.6 ± 5.3 | 59.7 ± 5.2 | **0.022** | 64.1 ± 5.3 | 60.5 ± 5.9 | **0.043** | 65.4 ± 7.2 | 62.1 ± 6.6 | 0.091 |
| Arm circumference (cm) | 36.6 ± 3.9 | 34.6 ± 3.7 | 0.072 | 36.3 ± 3.7 | 34.5 ± 3.4 | 0.083 | 37.7 ± 3.0 | 35.6 ± 2.9 | **0.029** |
| Systolic BP (mmHg) | 132 ± 10 | 124 ± 13 | **0.032** | 131 ± 8 | 121 ± 10 | **0.005** | 129 ± 9 | 121 ± 16 | **0.036** |
| Diastolic BP (mmHg) | 78 ± 11 | 70 ± 9 | **0.020** | 78 ± 10 | 72 ± 10 | **0.030** | 78 ± 10 | 71 ± 9 | **0.014** |
| Fasting glycemia mg/dL | 108.1 ± 22.3 | 94.1 ± 11.4 | **0.017** | 106.5 ± 17.6 | 100.9 ± 17.6 | 0.193 | 99.7 ± 12.9 | 92.6 ± 9.2 | **0.042** |
| Fasting insulin (µIU/ml) | 25.0 ± 18.9 | 8.5 ± 4.1 | **0.001** | 19.4 ± 7.4 | 8.3 ± 4.7 | **0.000** | 17.7 ± 8.7 | 6.8 ± 4.1 | **0.000** |
| HOMA-IR (ng/ml) | 4.15 ± 1.34 | 2.1 ± 1.2 | **0.004** | 5.1 ± 2.0 | 2.1 ± 1.2 | **0.000** | 4.05 ± 1.72 | 1.6 ± 1.1 | **0.000** |
| IGF-1 (ng/ml) | 141.4 ± 15.91 | 167.46 ± 43.15 | **0.018** | 159.82 ± 19.25 | 116.52 ± 22.05 | **0.000** | 132.88 ± 26.92 | 148.86 ± 32.15 | 0.160 |
| Creatinine (mg/dl) | 0.90 ± 0.30 | 0.79 ± 0.22 | 0.12 | 0.78 ± 0.17 | 0.78 ± 0.15 | 0.465 | 0.80 ± 0.16 | 0.86 ± 0.19 | 0.163 |
| BUN (mg/dl) | 39.0 ± 12.5 | 38.5 ± 13.9 | 0.466 | 40.0 ± 13.1 | 37.4 ± 12.1 | 0.281 | 39.3 ± 6.8 | 48.0 ± 14.4 | **0.019** |
| eGFR (ml/min) | 131.9 ± 42.9 | 136.6 ± 56.1 | 0.395 | 146.4 ± 33.3 | 131.4 ± 26.8 | 0.091 | 134.8 ± 33.2 | 115.6 ± 30.2 | **0.049** |
| Proteins (g/L) | 74.3 ± 4.0 | 71.8 ± 2.9 | **0.028** | 75.0 ± 3.5 | 74.0 ± 4.1 | 0.237 | 74.3 ± 4.4 | 72.2 ± 3.5 | 0.070 |
| Albumin (g/L) | 44.13 ± 2.43 | 43.71 ± 2.90 | 0.328 | 44.55 ± 2.76 | 43.98 ± 2.69 | 0.283 | 44.68 ± 2.71 | 44.22 ± 1.91 | 0.293 |
| AST (U/L) | 23.8 ± 13.0 | 19.9 ± 5.8 | 0.146 | 25.3 ± 13.2 | 26.8 ± 14.0 | 0.385 | 19.8 ± 4.7 | 19.9 ± 3.7 | 0.450 |
| ALT (U/L) | 31.1 ± 15.4 | 24.0 ± 9.3 | 0.062 | 35.0 ± 24.0 | 35.5 ± 26.9 | 0.479 | 23.8 ± 7.0 | 21.6 ± 4.9 | 0.151 |
| HSI | 44.0 ± 5.1 | 41.6 ± 5.4 | 0.101 | 44.1 ± 5.4 | 40.9 ± 5.2 | 0.049 | 44.3 ± 4.4 | 42.1 ± 4.1 | 0.077 |
| Uric acid (mg/dl) | 5.4 ± 1.1 | 5.1 ± 1.4 | 0.257 | 5.2 ± 1.0 | 5.8 ± 1.1 | 0.072 | 4.9 ± 1.0 | 5.6 ± 0.8 | **0.021** |
| CRP (µg/L) | 4700 ± 6740 | 2662 ± 2414 | 0.132 | 7050 ± 5959 | 5913 ± 6435 | 0.307 | 5156 ± 4820 | 4087 ± 3383 | 0.237 |
| ESR (mm/h) | 26.8 ± 16.0 | 28.5 ± 15.8 | 0.379 | 28.0 ± 17.9 | 25.7 ± 17.1 | 0.357 | 28.8 ± 15.8 | 26.1 ± 12.1 | 0.292 |
| Total cholesterol (mg/dl) | 214.8 ± 31.5 | 166.2 ± 43.6 | **0.001** | 220.9 ± 51.6 | 170.7 ± 36.3 | **0.002** | 226.9 ± 32.7 | 191.2 ± 34.2 | **0.003** |
| LDL cholesterol (mg/dl) | 132.8 ± 30.8 | 100.8 ± 38.4 | **0.008** | 136.1 ± 41.3 | 97.5 ± 32.3 | **0.004** | 143.9 ± 25.8 | 118.5 ± 23.1 | **0.003** |
| Triglycerides (mg/dl) | 131.0 ± 44.9 | 94.6 ± 32.0 | **0.007** | 170.1 ± 126.9 | 117.6 ± 42.7 | 0.069 | 124.25 ± 58 | 82.25 ± 33.32 | **0.009** |
| HDL cholesterol (mg/dl) | 51.7 ± 12.3 | 46.1 ± 7.5 | 0.072 | 51.2 ± 12.8 | 49.0 ± 9.5 | 0.298 | 57.9 ± 23.7 | 56.2 ± 18.0 | 0.408 |
| Urine acetoacetic acid (mg/dL) | 1.8 ± 0.8 | 56.3 ± 31.3 | **0.000** | 1.8 ± 0.7 | 41.1 ± 15.4 | **0.000** | 1.6 ± 0.7 | 44.8 ± 15.3 | **0.000** |
| Total fat (kg) | 36.74 ± 10.83 | 31.92 ± 10.19 | 0.102 | 37.40 ± 7.77 | 32.00 ± 7.51 | 0.081 | 37.00 ± 8.23 | 32.85 ± 8.88 | 0.094 |
| Total lean (kg) | 62.95 ± 9.04 | 59.93 ± 7.66 | 0.158 | 62.32 ± 1.04 | 59.70 ± 10.02 | 0.246 | 57.24 ± 9.21 | 56.59 ± 12.18 | 0.434 |
| Total fat (%) | 35.71 ± 8.38 | 33.33 ± 8.33 | 0.213 | 36.69 ± 6.46 | 34.06 ± 6.82 | 0.144 | 37.75 ± 6.87 | 35.89 ± 8.04 | 0.247 |
| Total lean (%) | 62.01 ± 8.01 | 64.13 ± 7.88 | 0.438 | 60.96 ± 6.29 | 63.41 ± 6.59 | 0.072 | 58.57 ± 7.60 | 61.63 ± 7.99 | **0.026** |
| Trunk fat (kg) | 18.40 ± 5.54 | 15.43 ± 5.01 | **0.022** | 18.69 ± 3.36 | 15.96 ± 3.24 | **0.016** | 17.43 ± 3.27 | 15.46 ± 3.80 | 0.065 |
| HG (kg) | 32.47 ± 7.73 | 34.45 ± 7.34 | 0.23 | 30.13 ± 6.99 | 31.01 ± 6.92 | 0.36 | 32.64 ± 9.04 | 34.03 ± 9.25 | 0.33 |


BUN
Creatinine
eGFR
Uric acid
HG
IGF-1
% variation (vs. basal values)
WPG
VPG
APG

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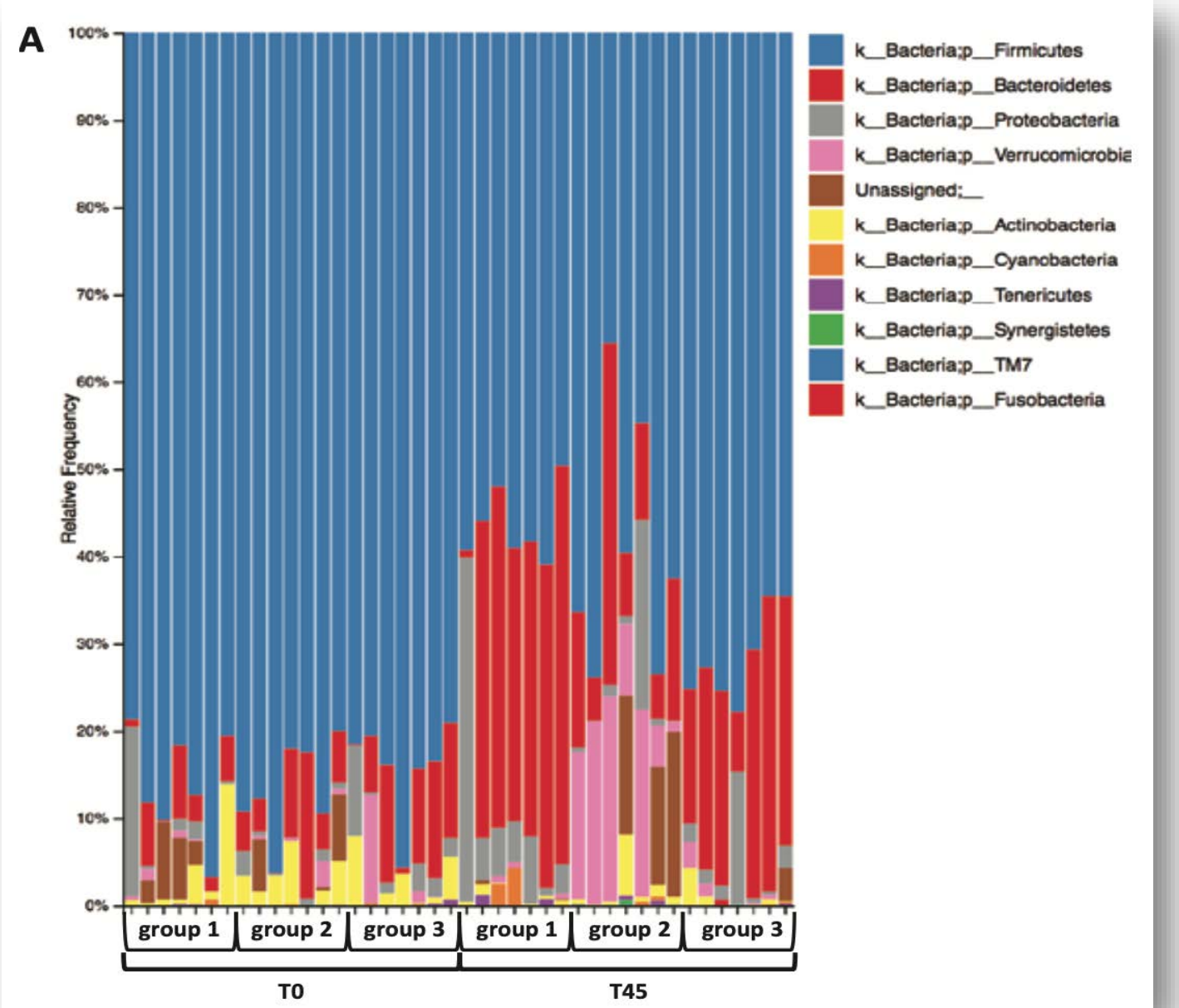


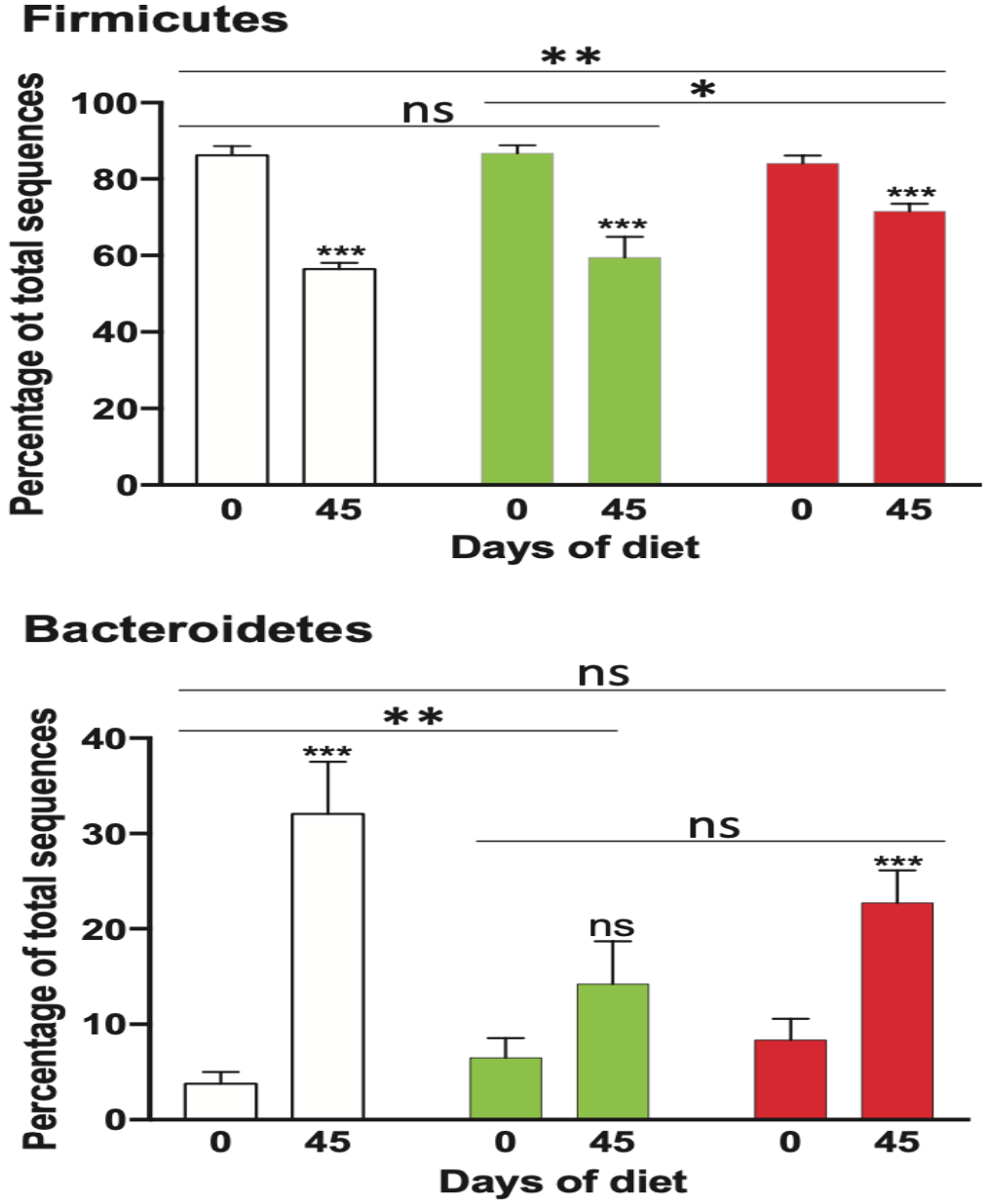


**Figure 4.** Effect of 45-day VLCKD dietary interventions with whey protein (white bars), vegetable protein (green bars), and animal protein (red bars) on the relative abundance of Firmicutes and Bacteroidetes. For each time point, values from all available samples were averaged (n = 7 per time point). Mean values ± standard deviations are plotted. $*P < 0.017$; $**P < 0.0023$; $***P < 0.001$.

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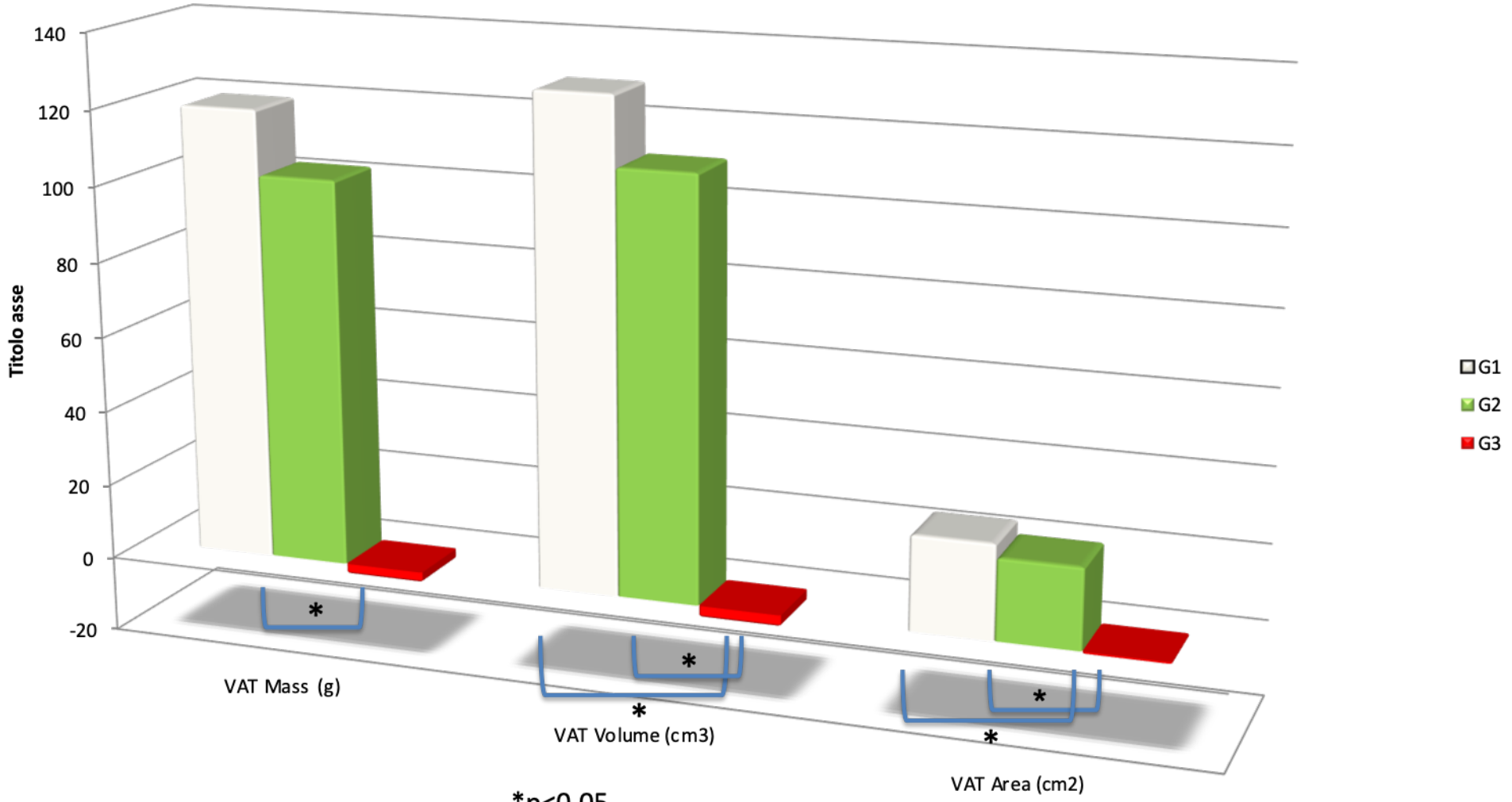
# Visceral Adipose Tissue (VAT) Delta T0-T45




*p<0.05

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PLOS | ONE

# Protein Quality and the Protein to Carbohydrate Ratio within a High Fat Diet Influences Energy Balance and the Gut Microbiota In C57BL/6J Mice

Liam McAllan[1,2], Peter Skuse[1,3], Paul D. Cotter[1,4], Paula O' Connor[1], John F. Cryan[4,5], R. Paul Ross[1], Gerald Fitzgerald[3], Helen M. Roche[6], Kanishka N. Nilaweera[1]*

Macronutrient quality and composition are important determinants of energy balance and the gut microbiota. Here, we investigated how changes to protein quality (casein versus whey protein isolate; WPI) and the protein to carbohydrate (P/C) ratio within a high fat diet (HFD) impacts on these parameters.

**Mice were fed a low fat diet (10% kJ) or a high fat diet (HFD; 45% kJ) for 21 weeks with either casein (20% kJ, HFD) or WPI at 20%, 30% or 40% kJ**

In comparison to casein, **WPI increased lean mass** and **caused a trend towards a reduction in fat mass**

analysis of faecal microbial populations revealed microbiota in the HFD-20% WPI group specifically **increased Lactobacillaceae/Lactobacillus and decreased Clostridiaceae/Clostridium**

Topi alimentati con una dieta ad alto contenuto di grassi, presentano feci ad alto contenuto di batteri della classe *Clostridiales*.

Una dieta a base di **proteine del siero di latte isolate**, determina una normalizzazione dell'*intake* energetico, aumenta la massa magra, riduce gli effetti negativi, quanto ad incremento della massa grassa, associati ad una dieta ad alto contenuto in grassi e **diminuisce significativamente i livelli di Clostridiaceae / Clostridium.**

**Table 5.** Gut microbiota composition as % of reads in mice fed a 45%kJ high fat diet (HFD) or HFD with 20%, 30% or 40% kJ whey protein isolate (WPI) for 21 weeks[1].

| | HFD | 20% WPI | 30% WPI | 40% WPI |
|---|---|---|---|---|
| **Phylum** | | | | |
| *Proteobacteria* | $0.36^{a}$ | $0.63^{b}$ | $0.34^{ab}$ | $0.32^{a}$ |
| *Actinobacteria* | $0.63^{a}$ | $1.82^{b}$ | $3.79^{b}$ | $0.36^{c}$ |
| *Deferribacteres* | $0.57^{a}$ | $1.61^{b}$ | $1.56^{ab}$ | $2.03^{b}$ |
| **Family** | | | | |
| *Desulfovibrionaceae* | $0.12^{a}$ | $0.31^{b}$ | $0.21^{ab}$ | $0.23^{ab}$ |
| *Rikenellaceae* | $6.71^{ab}$ | $7.54^{b}$ | $3.9^{a}$ | $6.4^{ab}$ |
| *Bacteroidaceae* | $0.44^{a}$ | $0.42^{a}$ | $0.16^{b}$ | $0.21^{b}$ |
| *Lactobacillaceae* | $0.21^{a}$ | $3.03^{b}$ | $4.6^{b}$ | $2.14^{b}$ |
| *Bifidobacteriaceae* | $0.43^{a}$ | $1.71^{b}$ | $3.66^{b}$ | $0.22^{c}$ |
| *Deferribacteraceae* | $0.57^{a}$ | $1.59^{b}$ | $1.32^{ab}$ | $2.03^{ab}$ |
| *Peptostreptococcaceae* | $0.62^{a}$ | $1.79^{a}$ | $1.54^{a}$ | $8.01^{b}$ |
| *Succinivibrionaceae* | $0.13^{a}$ | $0.15^{a}$ | $0^{b}$ | $0^{b}$ |
| *Clostridiaceae* | $1.31^{a}$ | $0^{b}$ | $0^{b}$ | $0^{b}$ |
| *Veillonellaceae* | $0.02^{a}$ | $0.12^{b}$ | $0^{a}$ | $0^{a}$ |
| **Genus** | | | | |
| *Anaerobiospirillum* | $0.13^{a}$ | $0.15^{a}$ | $0^{b}$ | $0^{b}$ |
| *Desulfovibrio* | $0.07^{a}$ | $0.22^{b}$ | $0.17^{ab}$ | $0.15^{ab}$ |
| *Alistipes* | $4.33^{ab}$ | $4.41^{a}$ | $2.24^{b}$ | $3.76^{ab}$ |
| *Rikenella* | $1.04^{ab}$ | $0.49^{b}$ | $0.68^{b}$ | $1.08^{b}$ |
| *Bacteroides* | $0.44^{a}$ | $0.4^{a}$ | $0.16^{b}$ | $0.21^{ab}$ |
| *Oscillibacter* | $0.24^{a}$ | $0.67^{ab}$ | $0.42^{ab}$ | $0.52^{b}$ |
| *Lactobacillus* | $0.2^{a}$ | $3.03^{b}$ | $4.6^{b}$ | $2.39^{b}$ |
| *Bifidobacterium* | $0.43^{a}$ | $1.71^{b}$ | $3.66^{b}$ | $0.22^{c}$ |
| *Mucispirillum* | $0.57^{a}$ | $1.61^{b}$ | $1.56^{ab}$ | $1.92^{ab}$ |
| *Coprococcus* | $0.11^{ab}$ | $0.23^{b}$ | $0.06^{a}$ | $0.06^{ab}$ |
| *Turicibacter* | $0.56^{a}$ | $0.35^{a}$ | $0.15^{ab}$ | $0^{b}$ |
| *Clostridium* | $1.3^{a}$ | $0^{b}$ | $0^{b}$ | $0^{b}$ |
| *Peptostreptococus* | $0.1^{a}$ | $0.14^{a}$ | $0.12^{a}$ | $0.78^{b}$ |

[1]Data are means ± SEM (n = 10). Statistically significant differences generated using the Kruskal-Wallis algorithm. In each row values without a common letter significantly differ, $P \leq 0.05$.

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Journal of Personalized Medicine

MDPI

*Review*

# Gallstone Disease, Obesity and the Firmicutes/Bacteroidetes Ratio as a Possible Biomarker of Gut Dysbiosis

Irina N. Grigor'eva

- Commensal *Clostridial* clusters XIVa and IV plays an important role in the host and gut homeostasis from the metabolic point of view through the production of short-chain fatty acids, normalizes intestinal permeability, involved the brain–gut axis regulation, in the immune system development.
- Many *Firmicutes'* abilities are related to the host's body weight: **obesity-associated gut microbiota is enriched in *Clostridium leptum***

# CLOSTRIDIUM/CLOSTRIDIACEAE

Obesity A Research Journal
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## Women With and Without Metabolic Disorder Differ in Their Gut Microbiota Composition

Eveliina Munukka[1], Petri Wiklund[1], Satu Pekkala[1], Eszter Völgyi[1], Leiting Xu[1], Shumei Cheng[1], Arja Lyytikäinen[1,2], Varpu Marjomäki[3], Markku Alen[4], Jussi Vaahtovuo[5], Sirkka Keinänen-Kiukaanniemi[6] and Sulin Cheng[1,7]

Correlazione positiva tra percentuale fecale di **Eubacterium rectale-Clostridium coccoides** e peso, BMI, massa grassa, **grasso viscerale**.

I batteri del gruppo **Eubacterium rectale-Clostridium coccoides possiedono attività enzimatica essenziale nella digestione di carboidrati** complessi altrimenti indigeribili, aumentano **quindi l'assorbimento di monosaccaridi, stimolando** ulteriormente la **lipogenesi e il deposito di trigliceridi negli adipociti.**

I metaboliti rilasciati dalla fermentazione di polisaccaridi complessi della dieta possono **aumentare l'assorbimento di glucosio**, **stimolare la lipogenesi**, modificare la composizione in acidi grassi del tessuto adiposo e del fegato, **alterare la permeabilità della barriera mucosa intestinale**, **alterare la risposta immunitaria**, contribuire ad uno stato di **infiammazione cronica sistemica e allo stato di insulinoresistenza** correlato all'obesità.

KDA Ketogenic Diet ACADEMY

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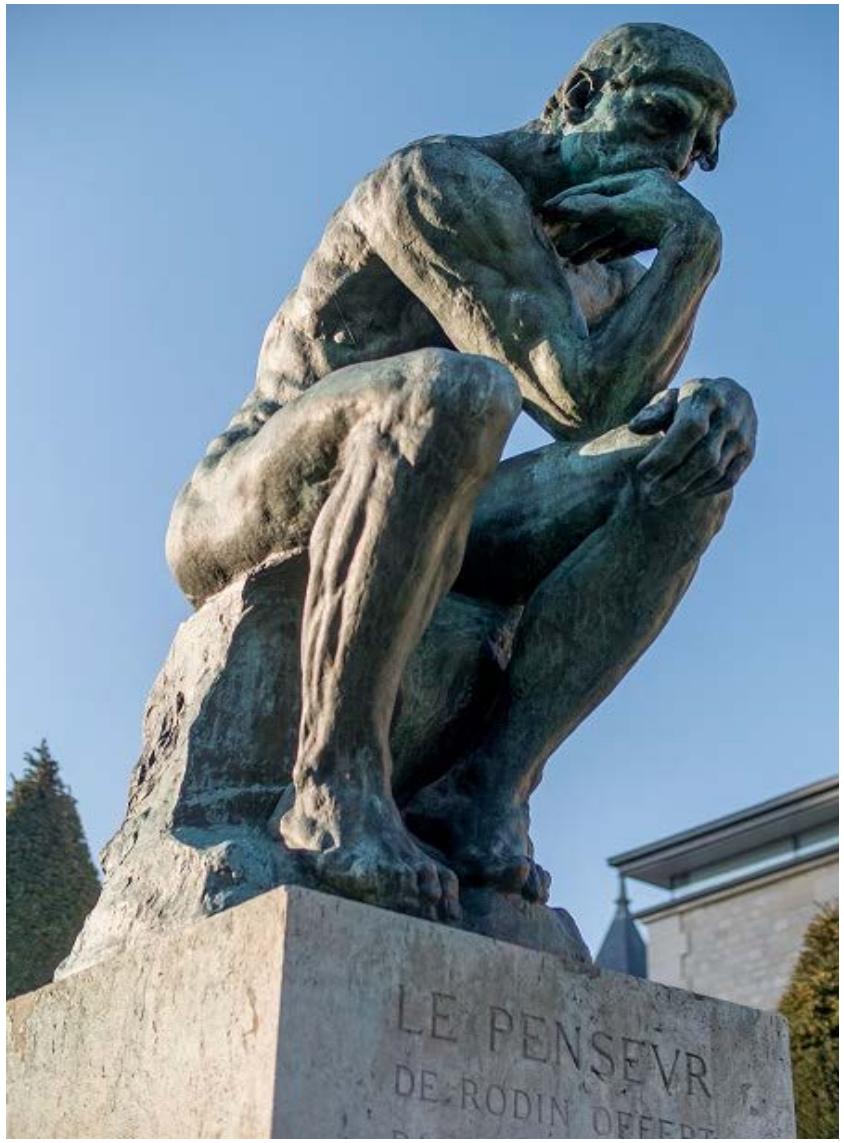
# LA TIPOLOGIA DI COTTURA O DI PROCESSO TECNOLOGICO DI UN ALIMENTO PUO' AVERE EFFETTI SUL MICROBIOTA?



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DOI: 10.1111/1541-4337.12593
COMPREHENSIVE REVIEWS IN FOOD SCIENCE AND FOOD SAFETY

# Dietary advanced glycation end-products: Perspectives linking food processing with health implications

Qiaozhi Zhang | Yanbo Wang | Linglin Fu

The consumption of highly processed foods has increased exponentially over the past decades.
Changes in processing technologies and diversity of raw materials have provided us unparalleled variety of food products, but also some known and unknown health-hazardous "contaminants."

Thermal treatments are commonly used procedures in the food industry to improve flavor, texture, preservation, and safety of food products, during which a series of nonenzymatic and biochemical reactions could occur.

**The Maillard reaction (MR) is the most predominant reaction that arose after heat treatments, where reducing sugars react with amino groups of proteins, peptides, or free amino acids to generate glycated products** (Nursten, 2005).

KDA Ketogenic Diet ACADEMY

*Review Article*

# Food Processing and Maillard Reaction Products: Effect on Human Health and Nutrition

Nahid Tamanna[1] and Niaz Mahmood[2]

The Maillard reaction has been named after the French physicist and chemist Louis Camille Maillard (1878–1936) who initially described it. It is often defined as nonenzymatic browning reaction. While foods are processed or cooked at high temperature, a chemical reaction occurs between amino acids and reducing sugars which generate different flavours and brown colour. So it is often used in food industry for giving food different taste, colour, and aroma

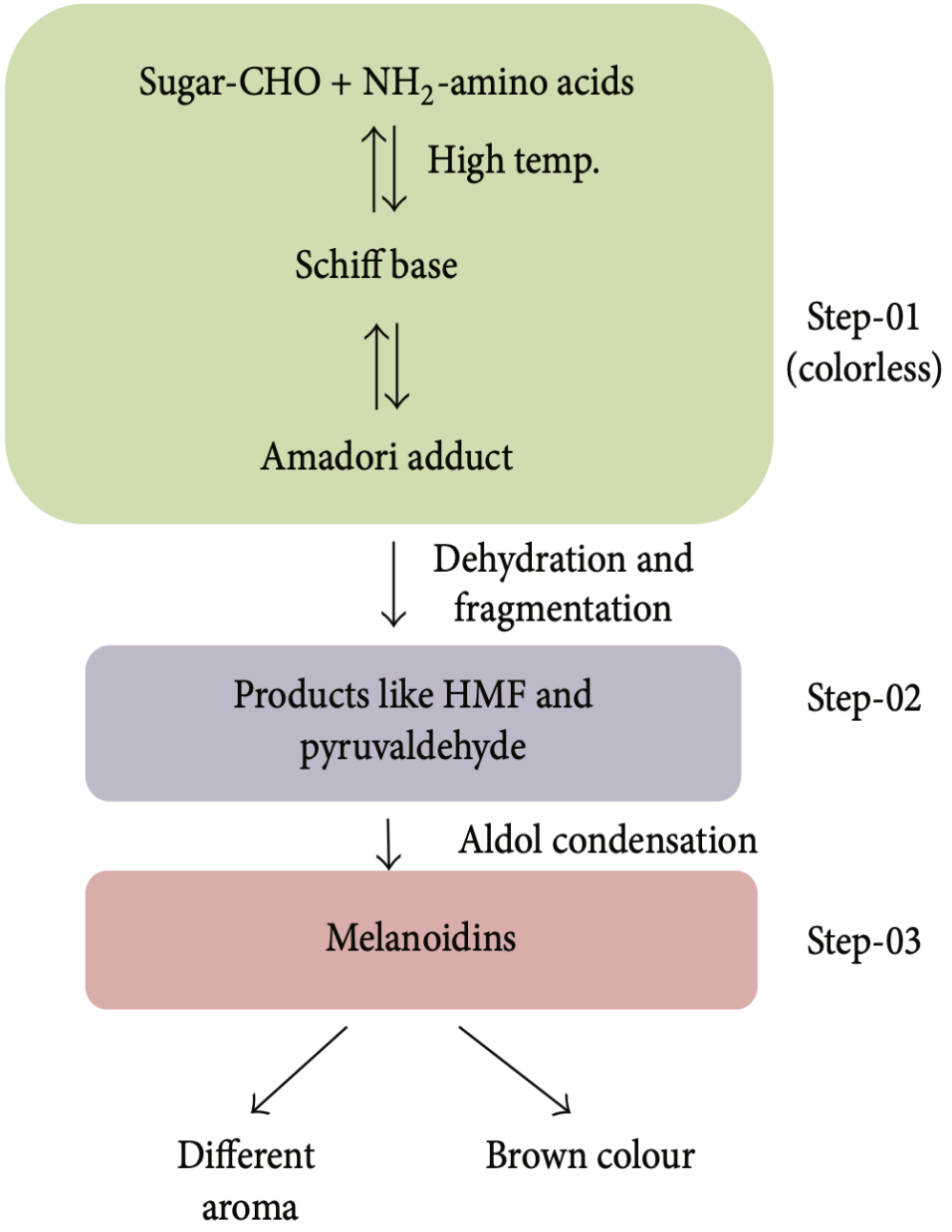
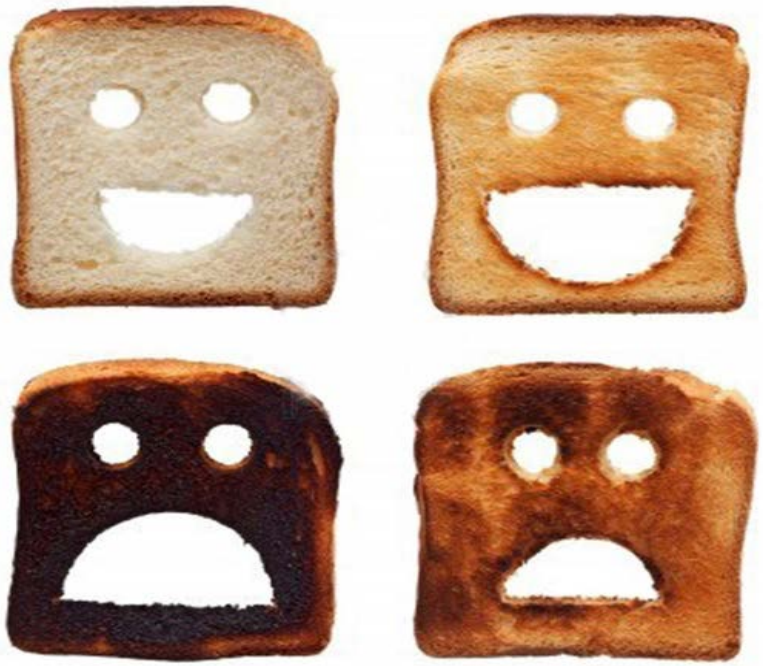


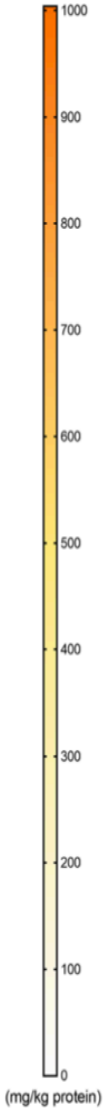

FIGURE 1: Schematic representation of "Maillard reaction" and flavour formation in food.

As the reaction proceeds, a large quantity of Maillard reaction products (MRPs) with different sizes and chemical structures can be formed, including those undesired carcinogens: **acrylamide, heterocyclic amines, and 5-hydroxymethylfurfural** (Abraham et al., 2011; Lee & Shibamoto, 2002; Zhang & Zhang, 2007).

Among them the **advanced glycation end-products (AGEs)** are a group of heterogeneous compounds derived from the “advanced” stage of MR, with some of them showing distinct photophysical properties, while some others exhibited no UV or fluorescence characteristics (Liang, Chen, Li, Li, & Yang, 2019; Nursten, 2005).



| Food categories | AGEs contents[1] | Analytical methods | References |
|---|---|---|---|
| **Dairy** | | | |
| Raw cow milk | 1.8 | LC–MS/MS (AH) | Delatour et al. (2009) |
| Pasteurized milk | 1.8 | | |
| Skimmed milk | 4.7 | | |
| UHT milk | 8.9 | | |
| Infant formula (regular) | 76 | | |
| Condensed milk | 205 | | |
| Cheddar cheese | 47.3 | UPLC–MS/MS (AH) | Hull, Woodside, Ames, and Cuskelly (2012) |
| Yoghurt (low-fat, fruit) | 89.8 | | |
| Whole egg (fried) | 56.3 | | |
| **Meat** | | | |
| Raw beef (minced) | 3.9 | UPLC-MS (AH) | Assar, Moloney, Lima, Magee, and Ames (2009) |
| Boiled beef (minced) | 27.3 | | |
| Fried beef (minced) | 61.1 | | |
| Fried chicken breast | 23.5 | | |
| Pork sausage (grilled) | 210.1 | UPLC–MS/MS (AH) | Hull et al. (2012) |
| Bacon rasher (fried) | 22.2 | | |
| Ham | 11.5 | | |
| Salmon (poached) [2] | 52.9 | ELISA (ED) | Gómez-Ojeda et al. (2018) |
| Salmon (grilled) [2] | 62.3 | | |
| Tuna (grilled) [2] | 86.9 | | |
| **Cereals and Breads** | | | |
| Kellogg's corn flakes | 439.7 | UPLC–MS/MS (AH) | Hull et al. (2012) |
| Weetabix | 212.7 | | |
| Spaghetti | 22.6 | | |
| Noodles (boiled) | 25.0 | | |
| White bread (crumb) [3] | 265.4 | LC–MS/MS (AH) | He, Zeng, Zheng, He, and Chen (2014) |
| White bread (crust) [3] | 737.1 | | |
| Wholemeal bread (crumb) [3] | 310.5 | | |
| Wholemeal bread (crust) [3] | 904.3 | | |
| Fried dough stick | 477.7 | | |
| Rice (boiled) [2] | 4.8 | LC–MS/MS (AH) | Scheijen et al. (2016) |
| Rice (fried) [2] | 8.1 | | |




| Food categories | AGEs contents[1] | Analytical methods | References |
|---|---|---|---|
| **Bakery** | | | |
| Muffin | 126.3 | UPLC–MS/MS (AH) | Hull et al. (2012) |
| Chocolate cake | 308.6 | | |
| Apple pie | 189.9 | | |
| **Beverage** | | | |
| Coffee | 84.1 | UPLC–MS/MS (AH) | Hull et al. (2012) |
| Green tea [3] | 47.9 | LC–MS/MS | Jiao et al. (2017) |
| Black tea [3] | 67.9 | | |
| Draft bear [2,3] | 44.6 | LC–MS/MS | Nomi et al. (2016) |
| **Fruits, vegetables and beans** | | | |
| Apple | 39.3 | UPLC–MS/MS (AH) | Hull et al. (2012) |
| Banana | 49.1 | | |
| Orange | 76.7 | | |
| Tomato | 10.2 | | |
| Potato chips (fried) [2] | 19.6 | LC–MS/MS (AH) | Scheijen et al. (2016) |
| Tofu (fried) [2] | 49.9 | | |
| Soy sauce[2] | 1.2 | | |
| **Sugars and snacks** | | | |
| Chew sweets | 195.8 | UPLC–MS/MS (AH) | Hull et al. (2012) |
| Chocolate | 502.1 | | |
| Popcorn (sweetened) | 86.5 | | |
| Cereal chewy bar | 436.8 | | |
| Ice cream (dairy) | 128.1 | | |
| Soda crackers [3] | 431.9 | LC–MS/MS (AH) | He et al. (2014) |
| Crisp biscuits [3] | 1003.8 | | |
| **Spreads, dressings and oils** | | | |
| Butter | 60.5 | UPLC–MS/MS (AH) | Hull et al. (2012) |
| Olive oil | 0 | | |
| Ketchup | 12.9 | | |
| Mustard dressing | 13.7 | | |
| **Combinations** | | | |
| Western diet [4] | ~650000 | NA | Lopez-Moreno et al. (2016) |
| Mediterranean diet [4] | ~400000 | NA | |

[1] Reported as CML content (mg/kg protein). [2] Results were transferred using the protein content of food of interest searched in the USDA FoodData Central.
[3] Results were presented as the mean value reported in the indicated reference.
[4] Reported as kU/4 w, thus not comparable with the other data tabulated.
Abbreviations: AH, acid hydrolysis; ED, enzymatic digestion; NA, not-available; UHT, ultrahigh-temperature.

**FIGURE 2** Contents of AGEs in selected factory-produced and home-made foodstuffs. Colors in the square represent AGEs levels referred to the scale bar. AH, acid hydrolysis; ED, enzymatic digestion; NA, not-available; UHT, ultrahigh-temperature

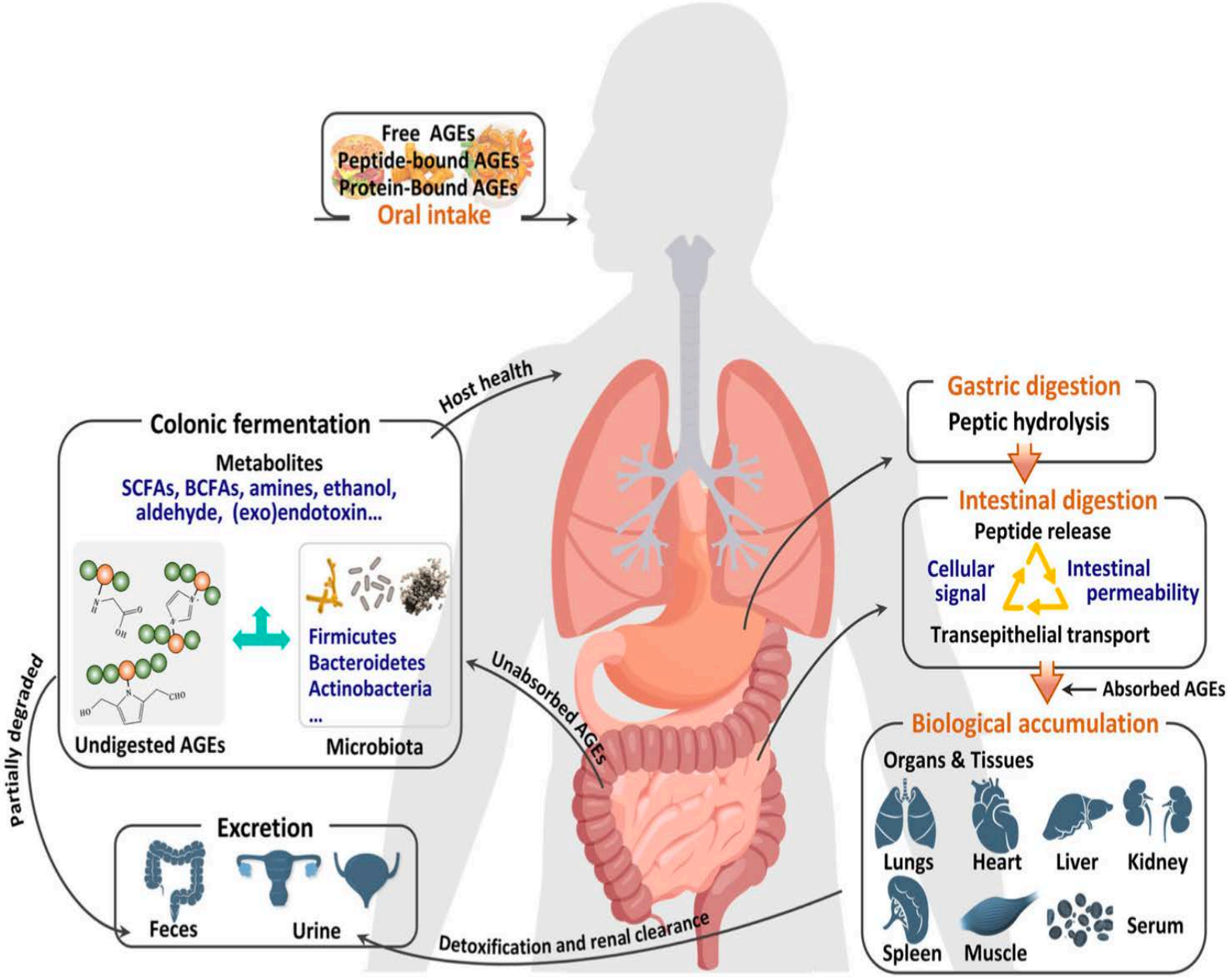



**FIGURE 3** Suggested pathways on the metabolic fates of dAGEs upon oral administration. SCFAs, short-chain fatty acids; BCFAs, branched-chain fatty acids

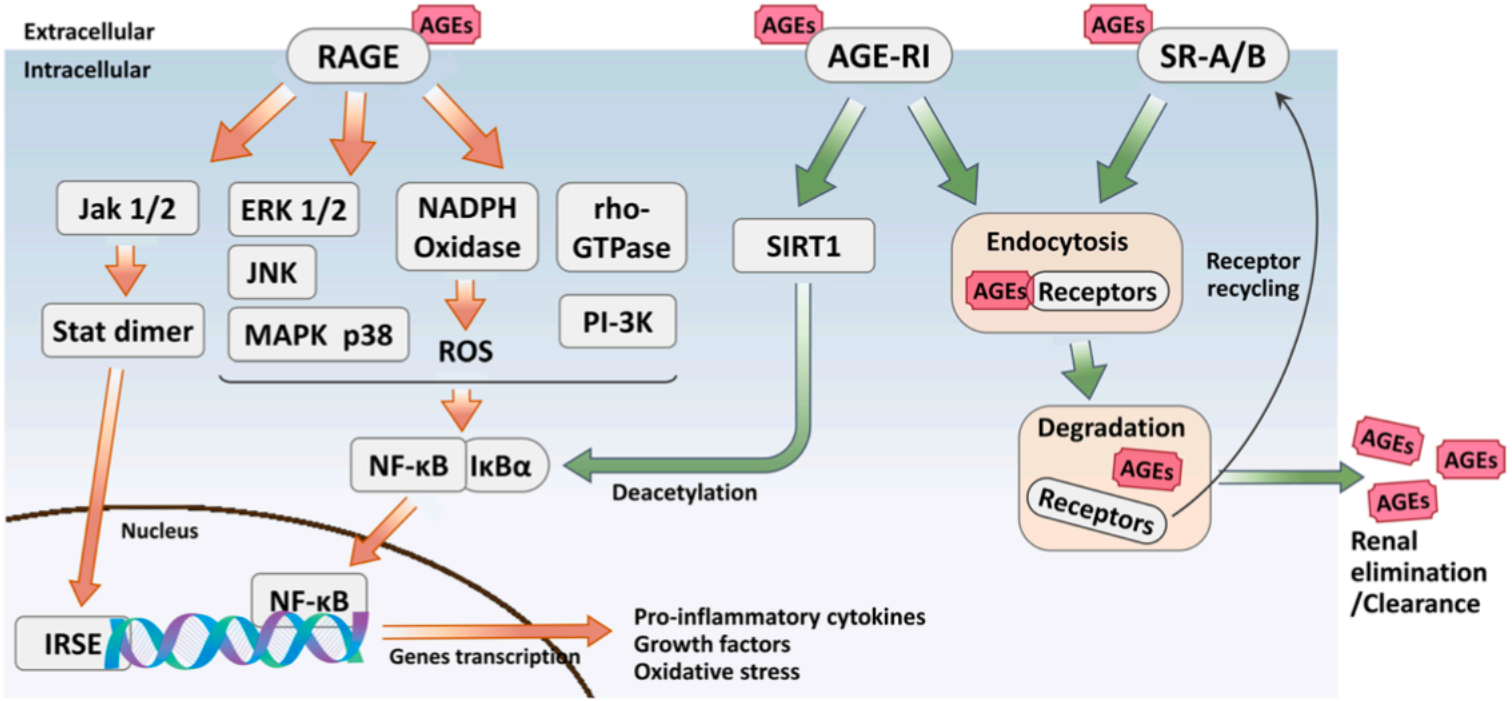



**FIGURE 4** The AGE-receptor system: downstream signaling pathways and detoxification of AGEs. The AGE-RAGE interaction activates a serious of downstream cell signals, including MAPK kinases, rho-GTPase, PI-3K, and JAK/STAT cascades; the AGE-RAGE interaction also promotes ROS generation via stimulating NADPH oxidase. The activated pathways further lead to transcription of genes associated with inflammation and oxidative stress. In the case of a high AGE burden, other receptors, namely AG-RI and SR receptors, bind with AGEs via receptor-mediated endocytosis, leading to intracellular uptake and degradation of excess AGEs. The AGE-RI also inhibits RAGE-mediated activation of NF-κB via upregulating SIRT1. Once the processed AGEs are transferred to the renal system, the receptors can be recycled and translocated back to the membranes (adapted from Ott et al., 2014, Poulsen et al., 2013, Sharma et al., 2015)

Understanding the interplay between MRPs and gut microbiota is essential to clarify the detrimental effects of dAGEs on host health. *In vivo* studies have implied that intake of AGEs strongly correlated with their fecal excretion (Delgado-Andrade et al., 2012).

Through incubation of glycated proteins with fecal samples from healthy individuals, the relative amounts of intestinal microbiota, primarily *Firmicutes* and *Bacteroidetesl*, was modulated at varying degrees (Helou et al., 2015; Xu et al., 2019; Yang et al., 2018). **In rodent models fed with heat-processed foods, an expansion in *Firmicutes* and a contraction in *Bacteroidetes* were observed** (Marungruang, Fåk, & Tareke, 2016)

At the genus level, a heat-processed diet rich in AGEs reduced the abundance of *Ruminococcaceae* and *Alloprevotella* (produce short-chain fatty acids, SCFAs), while increased the levels of *Desulfovibrio* in rats, leading to higher amounts of ammonia and branched- chain fatty acids (BCFAs) production (Qu et al., 2017).

In old mice fed with a similar high-AGE diet, the microbial *α*-diversity was reduced with the levels of *Helicobacter* expanded.

RESEARCH ARTICLE Open Access

# Gut microbial beta-glucuronidase and glycerol/diol dehydratase activity contribute to dietary heterocyclic amine biotransformation

Jianbo Zhang[1,3], Christophe Lacroix[1], Esther Wortmann[1], Hans-Joachim Ruscheweyh[2], Shinichi Sunagawa[2], Shana J. Sturla[1] and Clarissa Schwab[1*]

Consuming red and processed meat has been associated with an increased risk of colorectal cancer (CRC), **which is partly attributed to exposure to carcinogens such as heterocyclic amines (HCA) formed during cooking and preservation processes**. The interaction of gut microbes and HCA can result in altered bioactivities and it has been shown previously that human gut microbiota can transform mutagenic HCA to a glycerol conjugate with reduced mutagenic potential.

# Systematic Review of Beef Protein Effects on Gut Microbiota: Implications for Health

Kembra Albracht-Schulte, Tariful Islam, Paige Johnson, and Naima Moustaid-Moussa

*Department of Nutritional Sciences and Obesity Research Institute, Texas Tech University, Lubbock, TX, USA*

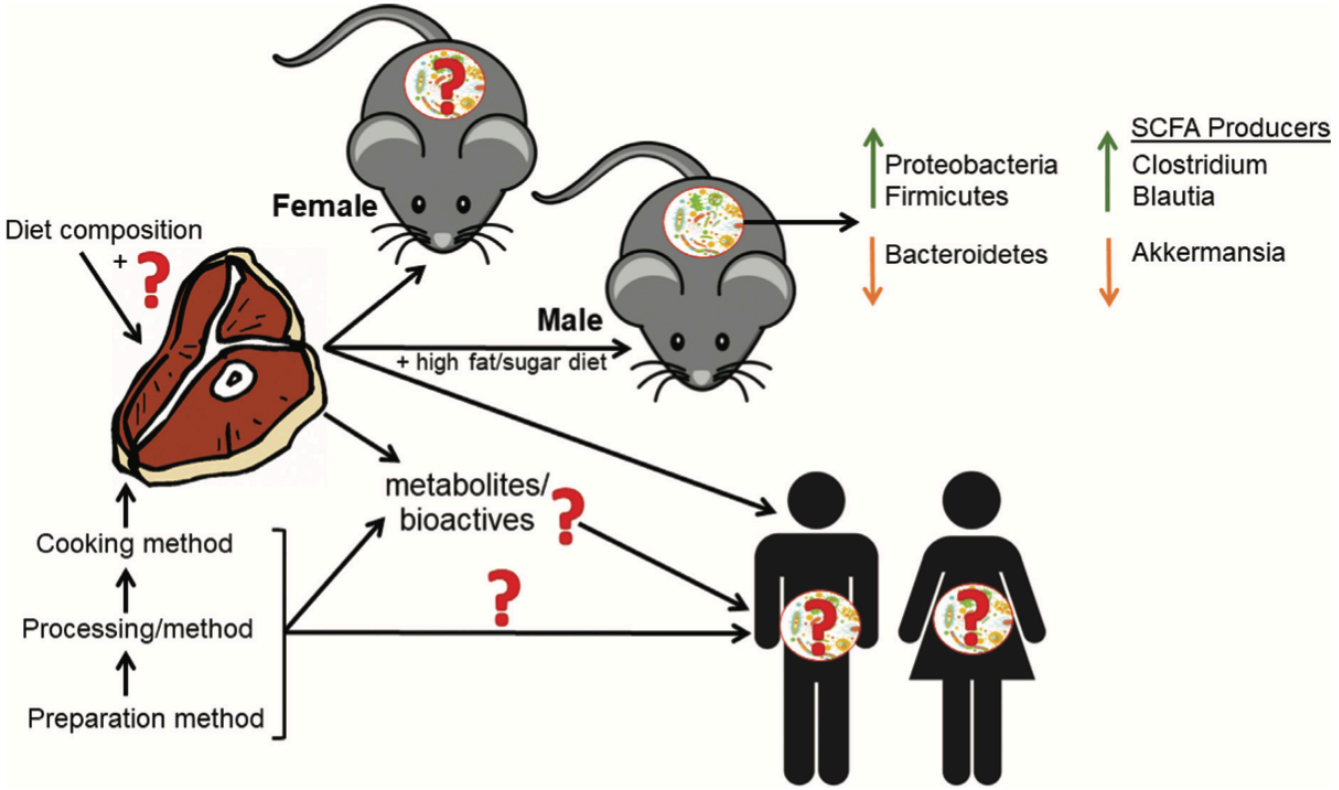



**FIGURE 2** Extensive gaps exist in the literature regarding beef, its related bioactive compounds, and effects on gut microbiota. Various preparations, processing and cooking methods, and temperatures are utilized in the examined literature, which likely impact the bioactivity of beef. Research subjects varied in age and models used from rodents to human subjects. The effects of beef on the male mice and rats were mostly consistent, indicating increased *Proteobacteria* and *Firmicutes* and decreased *Bacteroidetes*. Findings regarding effects on SCFA-producing bacterial genera were discrepant, with increases in *Clostridium* and *Blautia* and decreases in *Akkermansia*. Short-term (1–4-wk) beef intakes had little to no effect on microbial profiles in humans. Most studies with adverse findings (animal and human studies) examined the impact of red meat or excessive intakes of red meat in the context of a diet high in fat or sugar.

# Presenza degli idrocarburi policiclici aromatici negli alimenti

Beatrice Bocca (a), Riccardo Crebelli (b), Edoardo Menichini (c)

*(a) Laboratorio di Tossicologia Applicata*
*(b) Laboratorio di Tossicologia Comparata ed Ecotossicologia*
*(c) Laboratorio di Igiene Ambientale*

Una ricerca sull'effetto di diversi metodi di cottura (cottura in forno elettrico e a gas, cottura alla griglia su carbone, cottura alla griglia su carbone in un tegame che evita lo sgocciolamento) ha mostrato che la formazione di IPA può essere minimizzata con alcuni accorgimenti: evitare il contatto diretto dell'alimento con la fiamma, cucinare la carne a temperature più basse per periodi più lunghi, usare carne a basso contenuto di grasso (IPCS, 1998).

La concentrazione totale di sei IPA cancerogeni in salsiccia di carne d'agnello aumentava da 1,9 µg/kg, quando era grigliata su carbone in condizioni standard di *barbecue* (distanza tra la fiamma e la carne: 10 cm; temperatura della superficie della carne: 200-250°C), fino a 13,2 µg/kg quando era grigliata "fortemente" per un tempo prolungato (Mottier *et al.*, 2000).

# Food Chemicals Disrupt Human Gut Microbiota Activity And Impact Intestinal Homeostasis As Revealed By *In Vitro* Systems

Clémence Defois[1], Jérémy Ratel[2], Ghislain Garrait[1], Sylvain Denis[1], Olivier Le Goff[1], Jérémie Talvas[3,4], Pascale Mosoni[1], Erwan Engel[2] & Pierre Peyret[1]

I **rischi** associati all'**esposizione di tossine alimentari** potrebbero dipendere anche dal **microbiota intestinale:**

può modificare queste sostanze trasformandole in composti più o meno tossici
esercitare effetti protettivi sulle cellule intestinali e indurre una risposta infiammatoria.

- L'esposizione a sostanze tossiche come gli idrocarburi policiclici aromatici (**IPA**) e amine eterocicliche (**HCA**) derivanti dalla cottura degli alimenti sono associate a effetti tossici e sono classificate come potenziali agenti cancerogeni
- Ricerche condotte su modelli animali hanno concluso che queste sostanze possono alterare il microbiota intestinale.

**RISULTATI**

- in queste condizioni sperimentali **non viene indotta né necrosi né apoptosi**, anzi, il microbiota sembra limitare l'effetto necrotizzante di IPA
- le sostanze prodotte in seguito all'esposizione di IPA inducono un **aumento significativo della produzione di interleuchina-8** ↑ **infiammazione**
- l'esposizione a questi xenobiotici non induce la produzione di *Tumor Necrosis Factor-α* o interleuchina-10

# TAKE HOME MESSAGE

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- Il microbiota intestinale è soggetto ad alterazioni in base a vari «modificatori» tra cui l'alimentazione
- I soggetti obesi presentano un microbiota disbiotico
- La dieta chetogenica ha un impatto importante sul microbiota intestinale
- La VLCKD è raccomandata per un soggetto obeso per ripristinarne l'eubiosi (regolando finemente la qualità proteica e lipidica)
- Il trattamento termico tecnologico/industriale e casalingo degli alimenti può determinare la comparsa di IdrocarburiPolicicliciAromatici (IPA) o ammine eterocicliche che hanno un impatto sul microbiota intestinale

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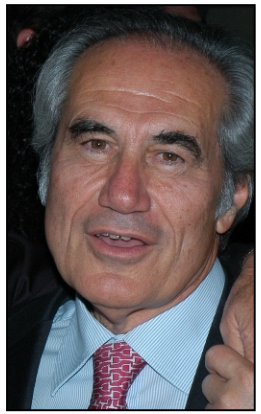

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