



DEPARTMENT OF BIOMEDICAL SCIENCES

Microbiome in health and disease

Advancing healthcare using the Research Infrastructure CeSAR
of UniCa: Nutrition during the first two years of life

Cagliari, 23rd and 24th November 2023



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Dr. Vanessa Palmas

UNIVERSITY OF CAGLIARI
DEPARTMENT OF BIOMEDICAL SCIENCES
MICROBIOLOGY AND VIROLOGY UNIT
MONSERRATO (CAGLIARI)

vanessa.palmas@unica.it
+39-07051096181



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Microbiome in Health and Disease

Definition

MICROBIOME

Ecosystem including all the microorganisms of a given environment, together with their genes and their environmental interactions.

MICROBIOTA

Set of microorganisms in a specific environment. In humans, an ecological community of commensal, symbiotic and pathogenic microorganisms that colonize the organism, including bacteria, archaea, viruses, fungi and other eukaryotic microorganisms (protozoa).



Microbiome in Health and Disease

Abundance of Bacterial Cells in Humans and Expressed Genes

Microbial cells



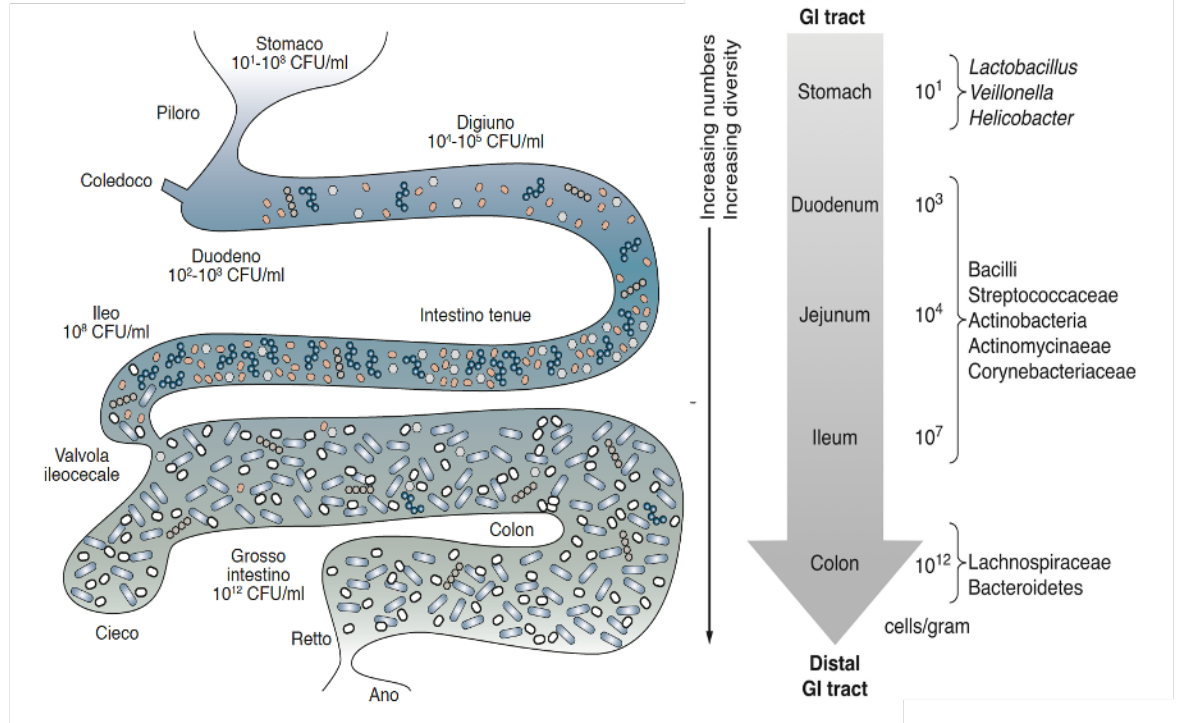
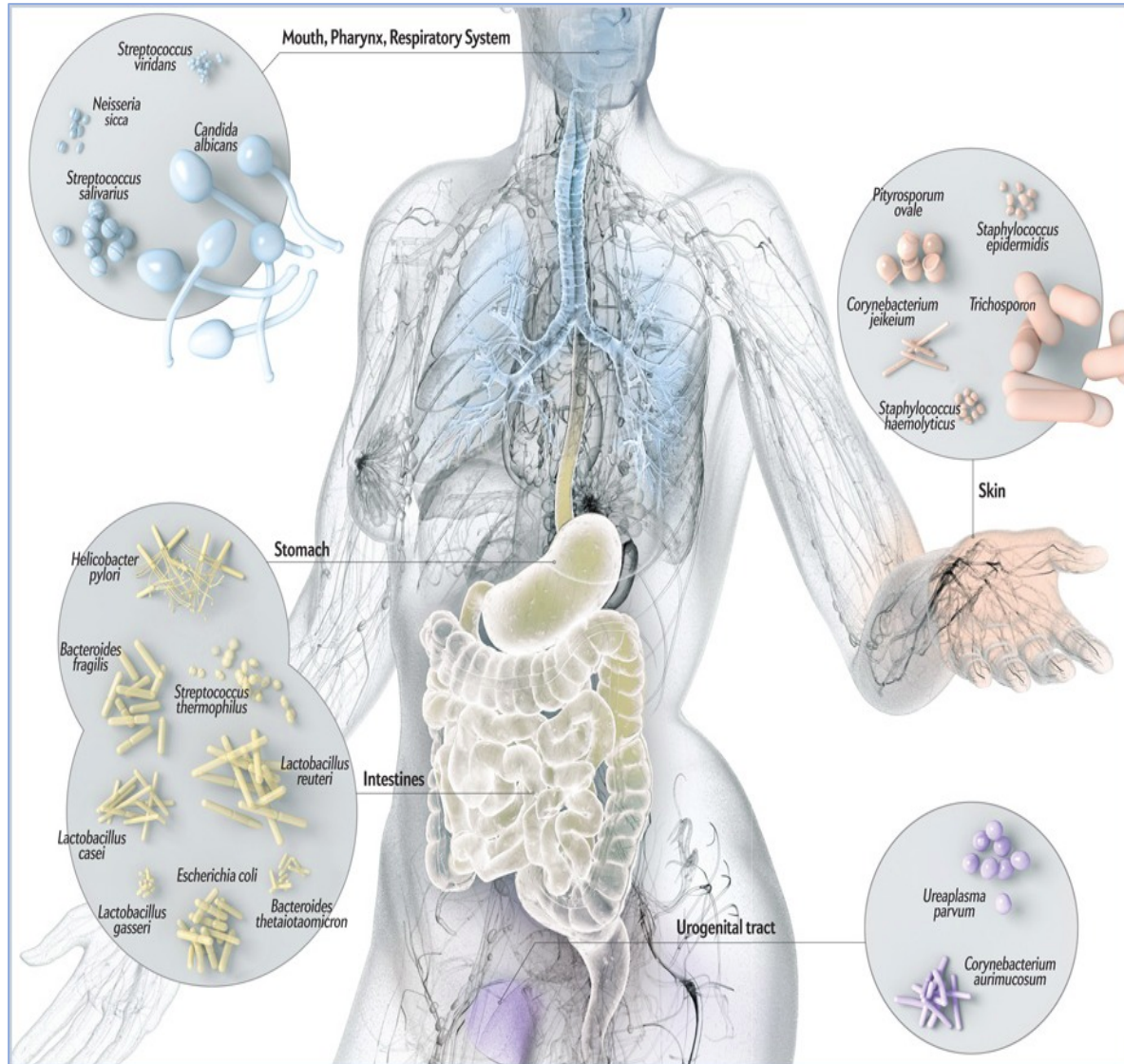
Human cells



HUMAN GENES
-23,000

Microbiome in Health and Disease

Intestinal Microbiota



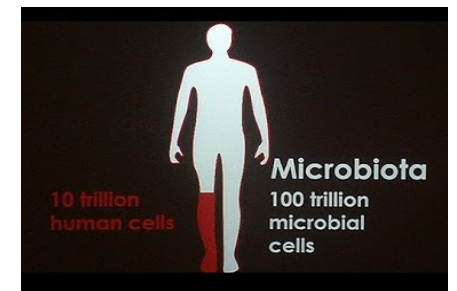
$10^{14} - 10^{15}$ microorganisms

500-1000/3000 species

Biomass ~ 1,5 kg

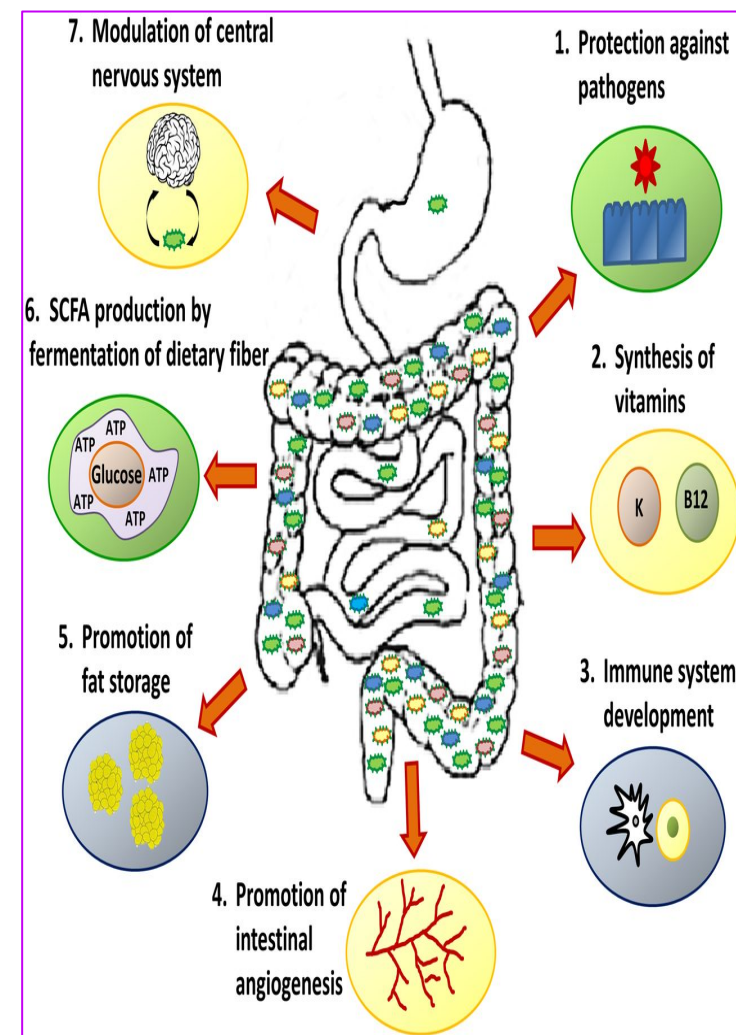
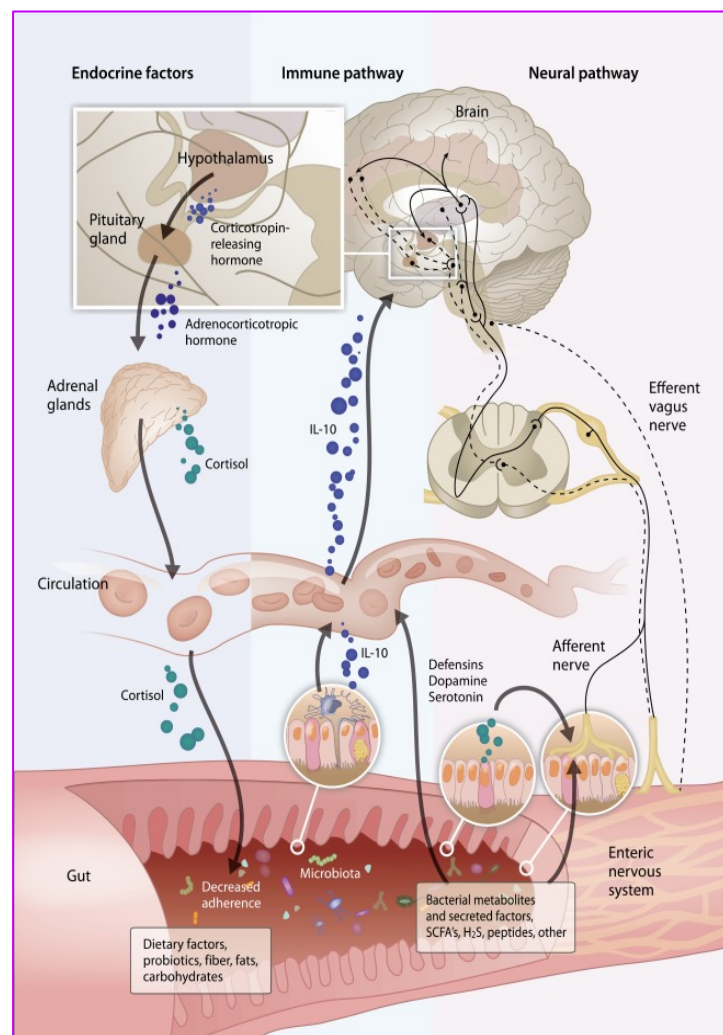
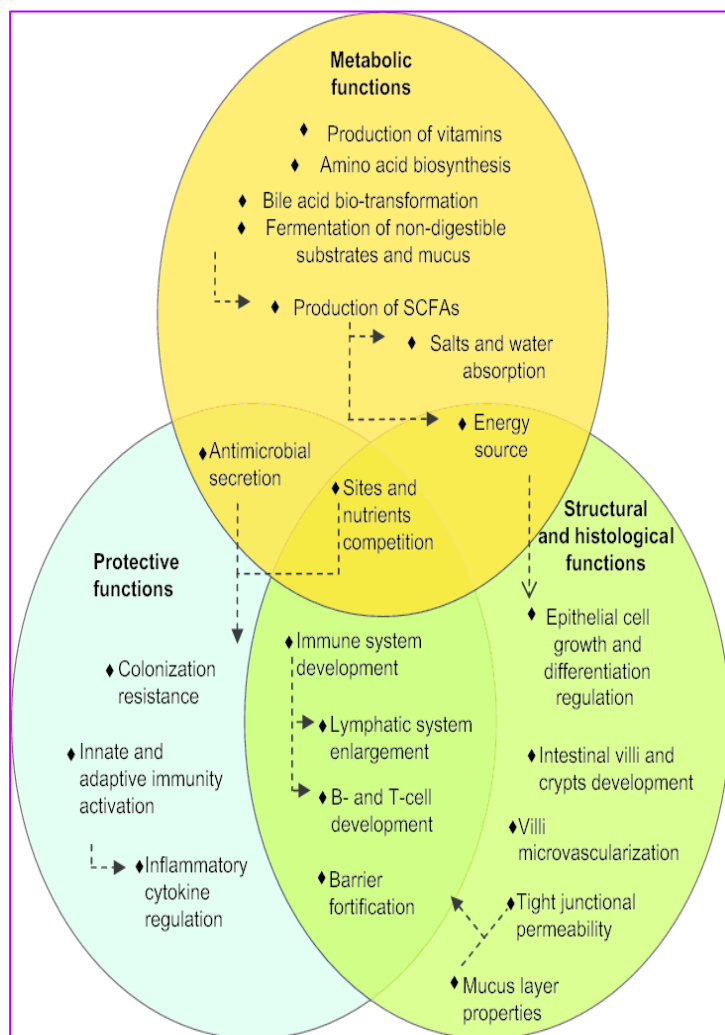
Genome – 150 times the human genome

(more than 5 million genes)



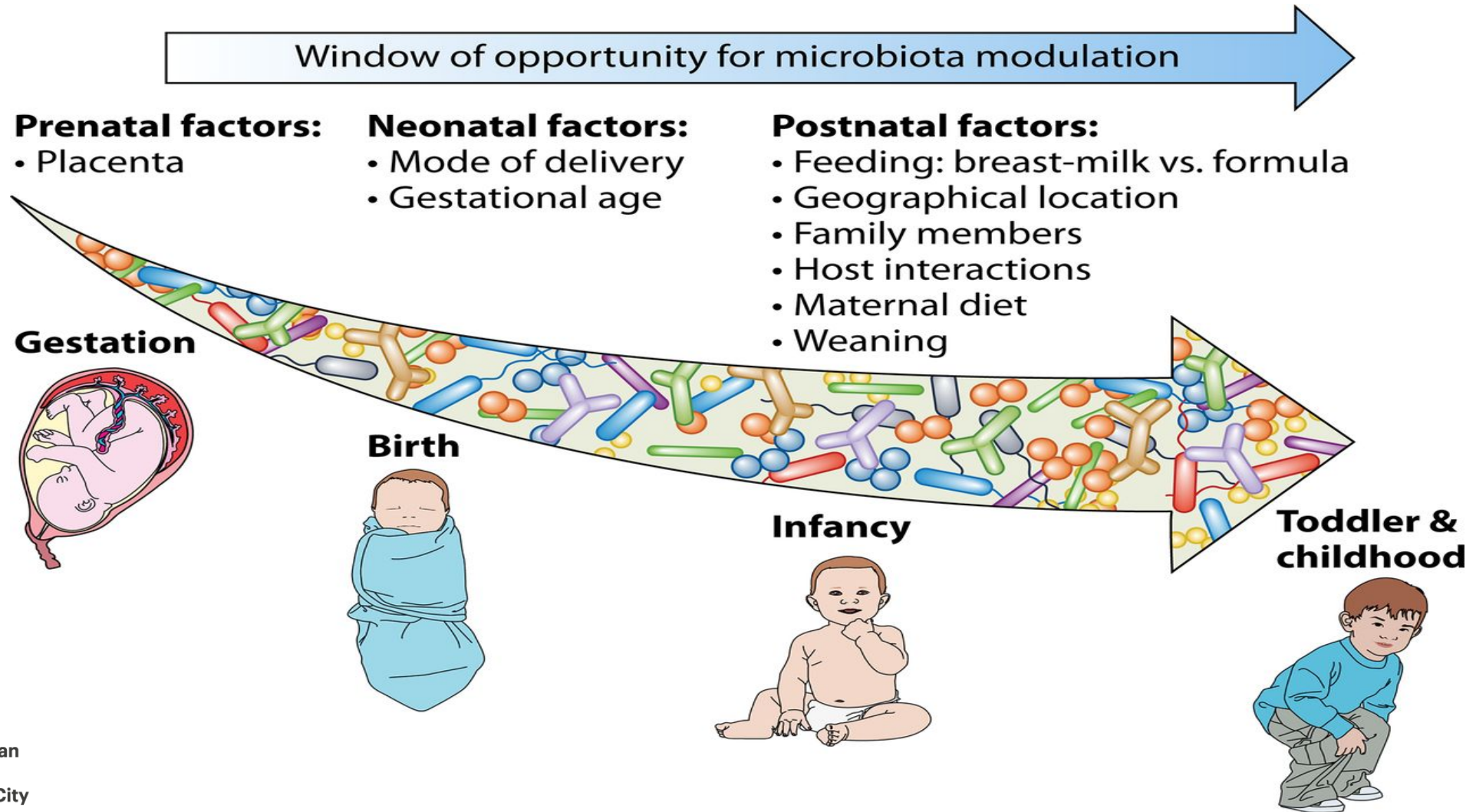
Microbiome in Health and Disease

Intestinal Microbiota Functions



Microbiome in Health and Disease

Changes over Lifecycle



Microbiome in Health and Disease

Changes over Lifecycle

Table 1. Microbiota variations within individuals.

		Gut Microbiota Abundance						Bacteria Diversity	Ref.	
		Actinobacteria	Bacteroidetes	Firmicutes	Proteobacteria	Fusobacteria	Verrucomicrobia	Euryarchaeota		
Anatomical part of gut tract	Small intestine			<i>Lactobacillus</i>	<i>Enterobacteriaceae</i> *					
	Colon		<i>Bacteroidaceae</i> * <i>Prevotellaceae</i> * <i>Rikenellaceae</i> *	<i>Lachnospiraceae</i> * <i>Ruminococcaceae</i> *					[14]	
Gestational age	Preterm birth (<37 weeks of gestation)	<i>Bifidobacterium</i> spp.↓ <i>Atopobium</i> spp.↓	<i>Bacteroides</i> *↓ (non-secretor mothers)	Firmicutes *↓ (non-secretor mothers) <i>Lactobacillus</i> ↑ <i>Ruminococcus</i> spp. <i>Lachnospiraceae</i> * <i>Peptostreptococcaceae</i> * <i>Clostridiaceae</i> *	<i>Enterobacteriaceae</i> *↑ <i>Enterococcus</i> spp.↑				↓	[15,16,19]
	Full-term birth	<i>Bifidobacterium</i> spp.↑	Bacteroidetes *↑	<i>Ruminococcus</i> spp. <i>Lachnospiraceae</i> * <i>Peptostreptococcaceae</i> * <i>Clostridiaceae</i> *	<i>Enterobacteriaceae</i> *				↑	[16,20]
Type of delivery	Vaginal delivery	<i>Bifidobacterium</i> spp.↑ <i>Bifidobacterium longum</i> ↑ <i>Bifidobacterium catenulatum</i> ↑	<i>Prevotella</i> ↑ <i>Bacteroides fragilis</i> ↑	<i>Lactobacillus</i> ↑ <i>Staphylococcus</i> ↑ <i>Streptococcus</i> ↑	<i>Escherichia</i> ↑	<i>Sneathia</i> ↑			↑	[22–26]
	C-section	<i>Corynebacterium</i> ↑ <i>Propionibacterium</i> ↑	<i>Bacteroides</i> *↓	<i>Staphylococcus</i> ↑	<i>Escherichia</i> ↓ <i>Shigella</i> ↓				↓	[21–23,27]
Methods of (milk) feedings	Breast milk	<i>Bifidobacterium</i> ↑↑		<i>Lactobacillus</i> ↑ <i>Staphylococcus</i> ↑	<i>Enterococcus</i> ↑				↑	[27,30–32,38]
	Artificial milk	<i>Bifidobacterium</i> ↑	<i>Bacteroides</i> ↑	<i>Clostridium</i> ↑ <i>Clostridium difficile</i> ↑ <i>Lactobacillus</i> ↑	<i>Escherichia</i> ↑				↓	[27,30–32]
	Introduction of solid food	<i>Bifidobacterium</i> ↑	Bacteroidetes *↑ <i>Bacteroides</i> ↑	Firmicutes *↑ <i>Lactobacilli</i> ↑ <i>Clostridium coccoides</i> ↑					↑	[36,37]

Microbiome in Health and Disease

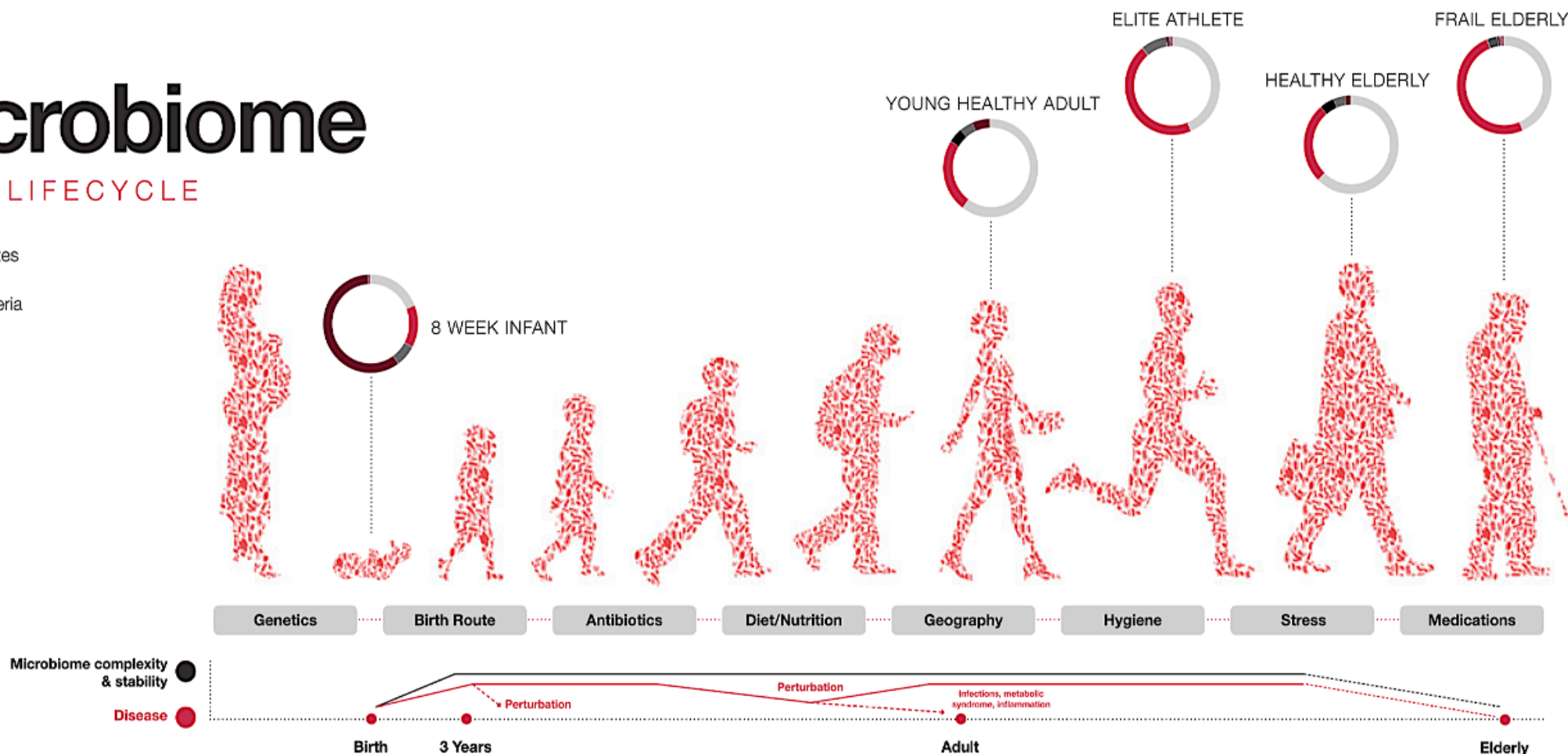
Changes over Lifecycle

Gut Microbiome

CHANGES OVER LIFECYCLE

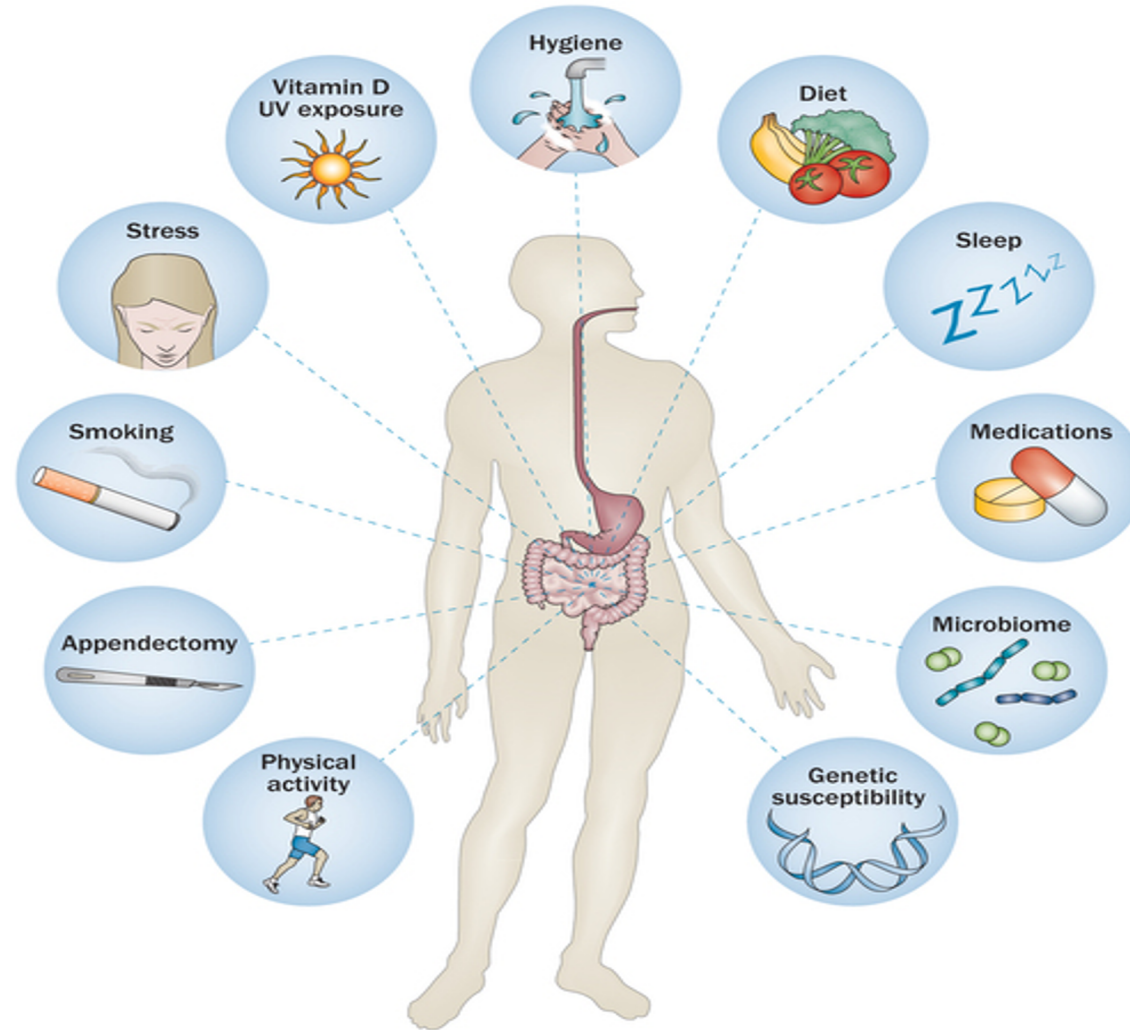
- Firmicutes
- Bacteroidetes
- Verrucomicrobia
- Proteobacteria
- Actinobacteria
- Other

Microbiota Composition



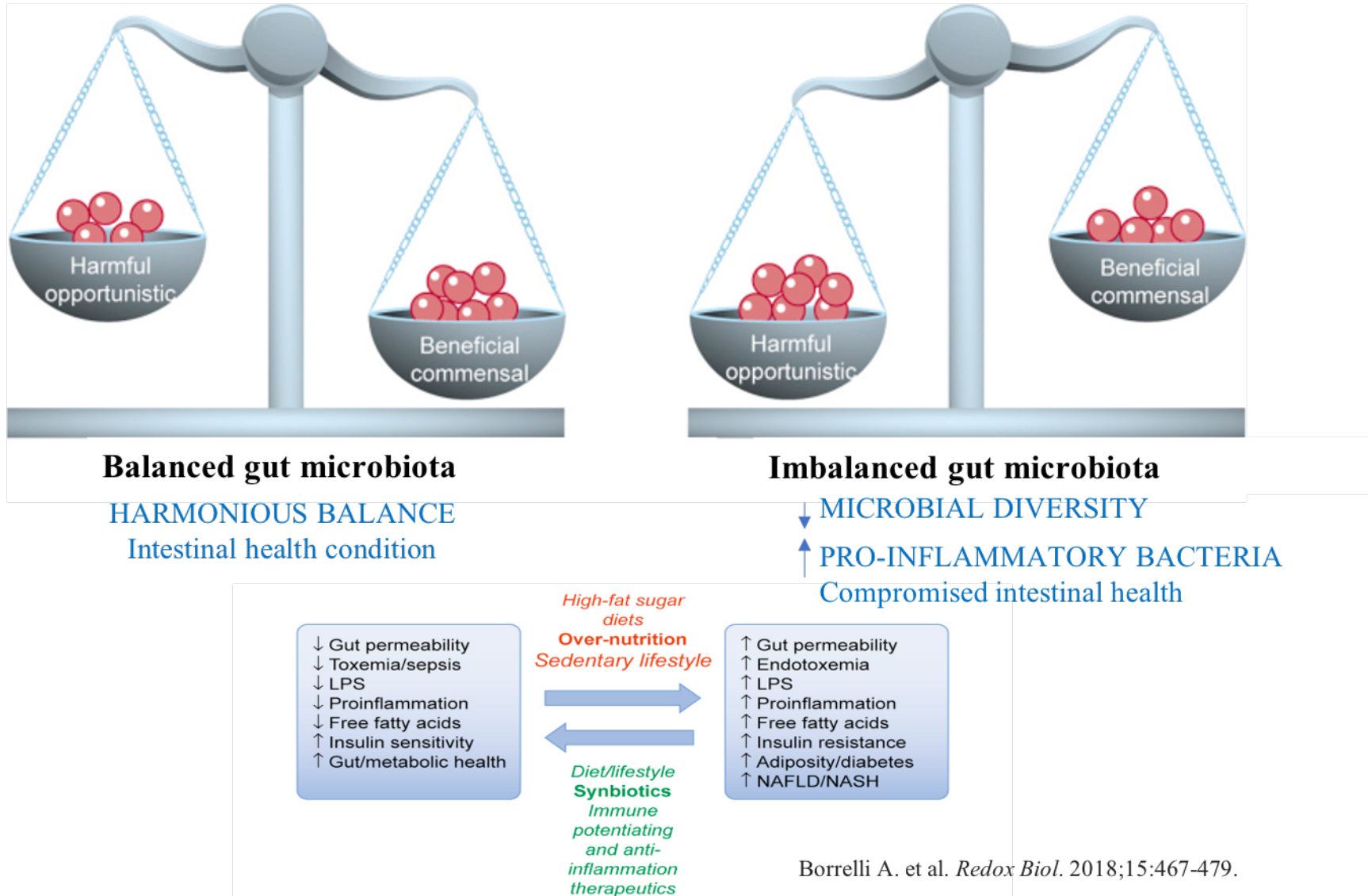
Microbiome in Health and Disease

Intestinal Microbiota Modulation



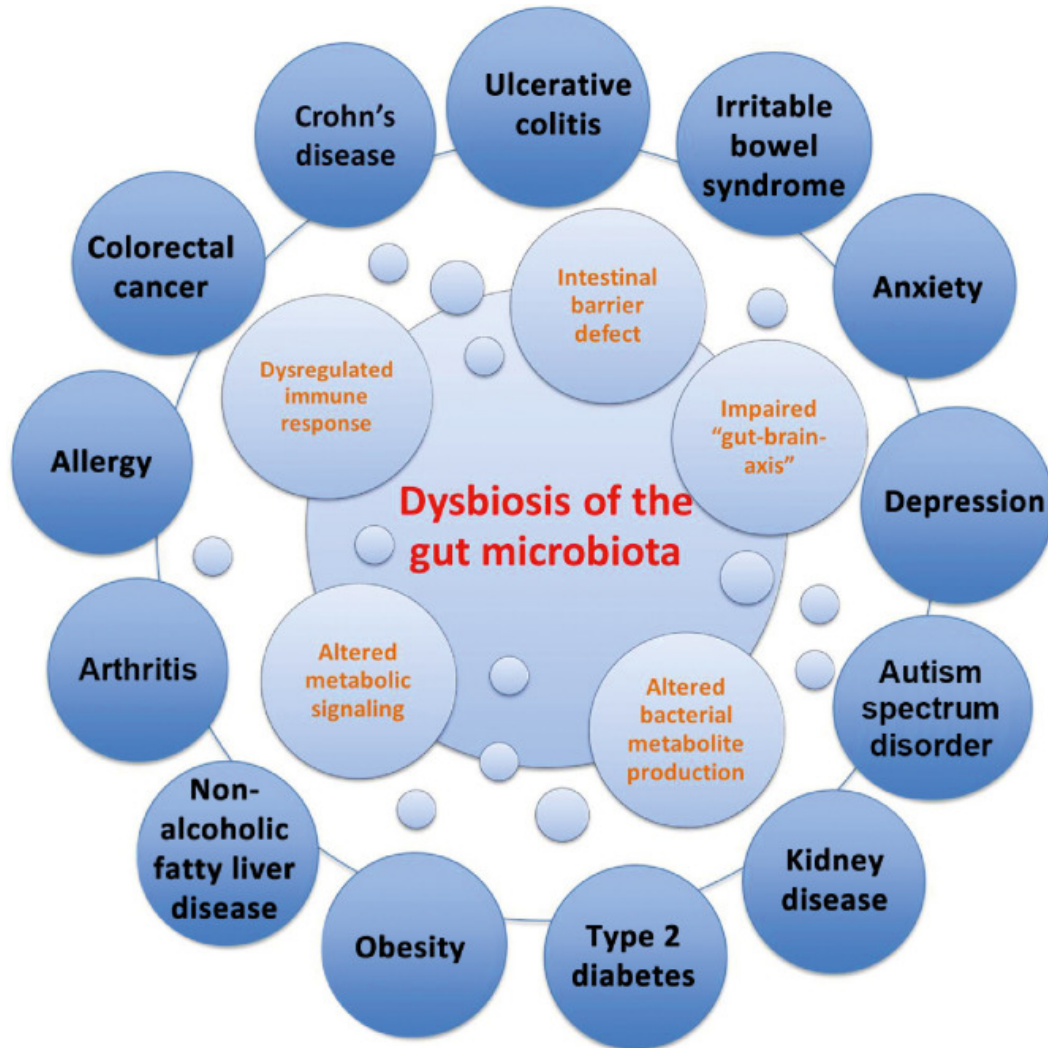
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Intestinal Eubiosis and Dysbiosis



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Association between Dysbiosis and Several Diseases



Diseases of the GUT

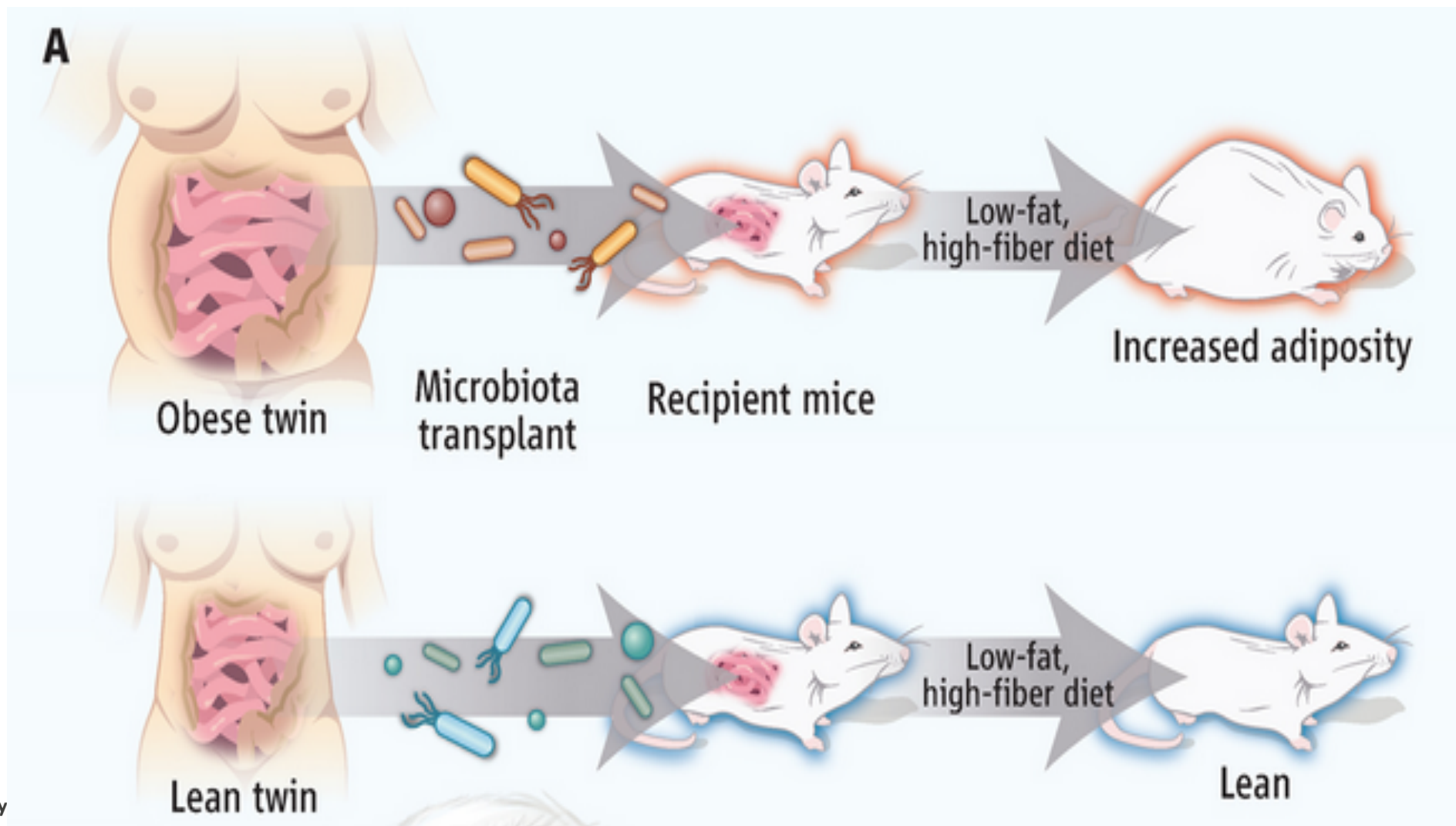
- ❖ Malabsorption syndrome
- ❖ Malignancies: Colorectal cancer
- ❖ Inflammatory Bowel Disease (IBD)
- ❖ Irritable Bowel Syndrome
- ❖ Diarrheal diseases

Non-mucosal diseases

- ❖ Obesity and metabolic syndrome
- ❖ Malignancies: liver cancer, breast cancer
- ❖ Complications of liver cirrhosis
- ❖ Allergic conditions
- ❖ Autoimmune disorders (T1DM, arthritis etc)
- ❖ Abnormalities of the gut-brain axis - Autism and other neurological disorders (Parkinson's disease)
- ❖ Obesity and other metabolic disorders
- ❖ Chronic fatigue syndrome
- ❖ Periodontal diseases
- ❖ ...

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Intrinsic and Transmissible Effects of Pathology-Associated GM

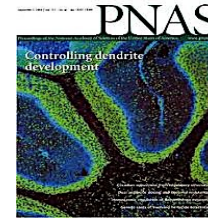


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Intestinal Microbiota and Diet

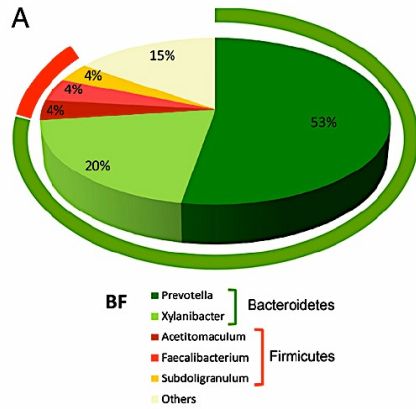
Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa

Carlotta De Filippo^a, Duccio Cavalieri^a, Monica Di Paola^b, Matteo Ramazzotti^c, Jean Baptiste Poullet^d, Sebastien Massart^d, Silvia Collini^b, Giuseppe Pieraccini^e, and Paolo Lionetti^{b,h,1}

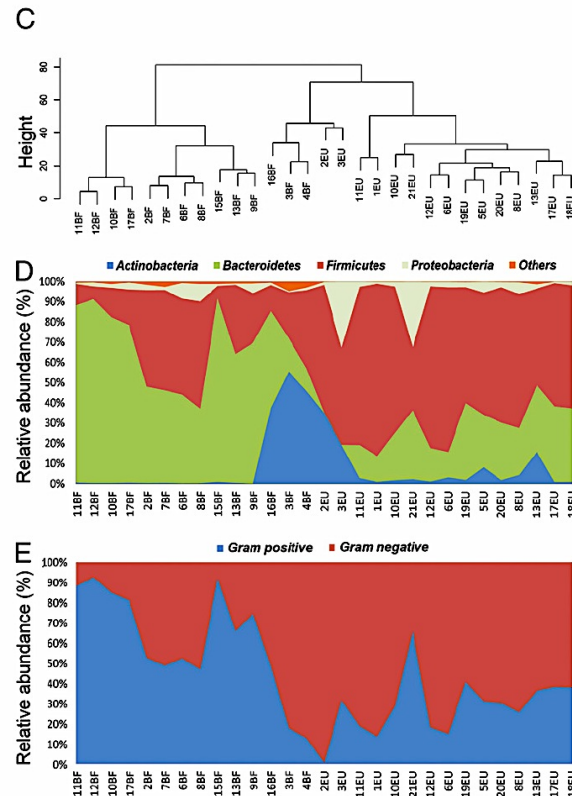
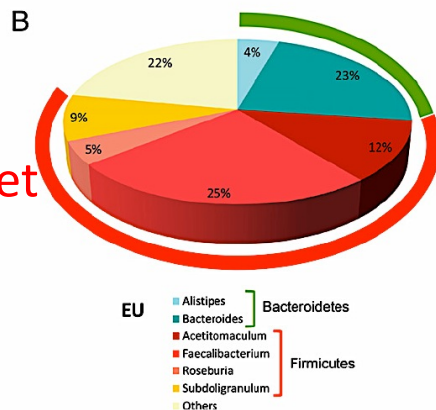


2010

African Rural diet



European Western diet

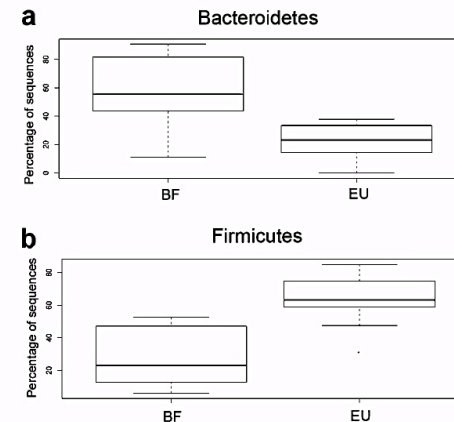


Rural Diet

- ↑ vegetable fibre
- ↑ Bacteroidetes
- ↑ Prevotella
- ↑ Xylanibacter
- ↑ SCFA
- ↓ Shigella and Escherichia

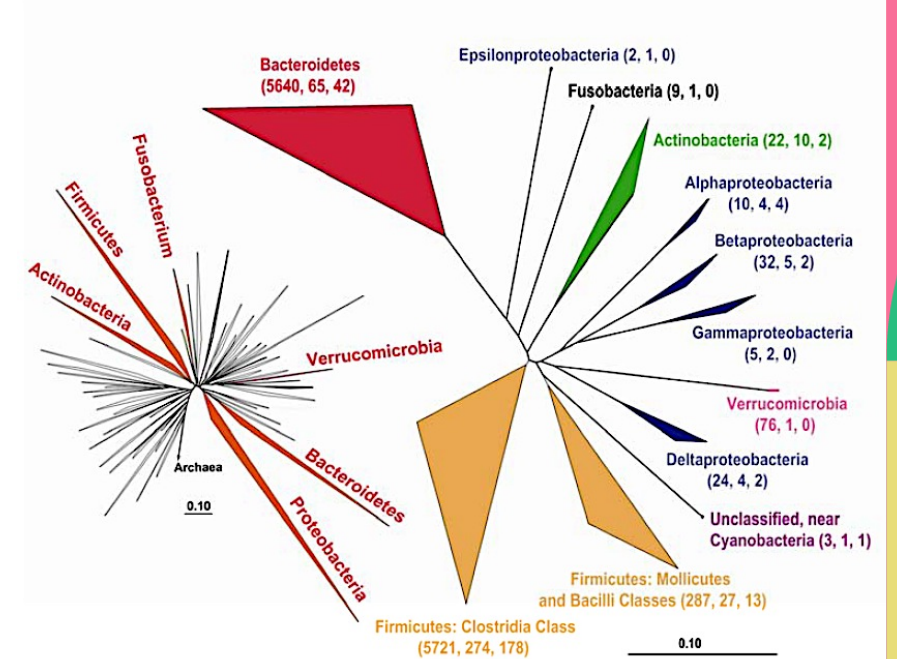
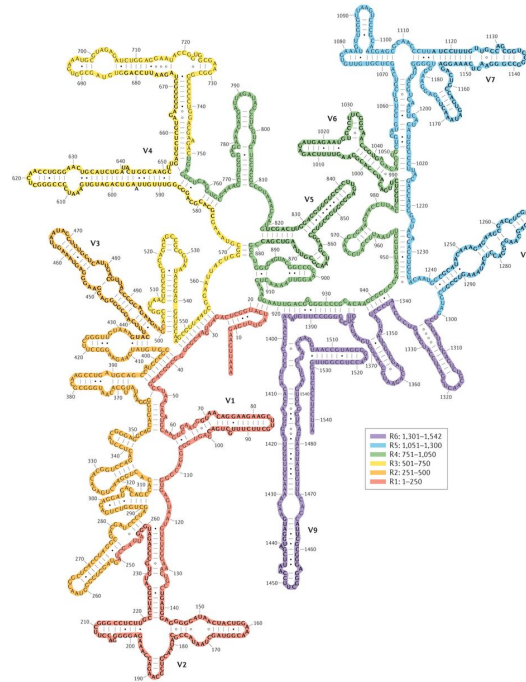
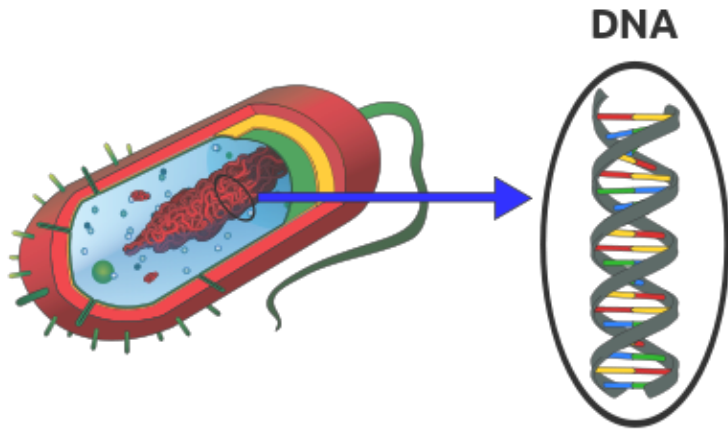
Western diet

- ↑ starch and protein
- ↑ Firmicutes
- ↑ Proteobacteria

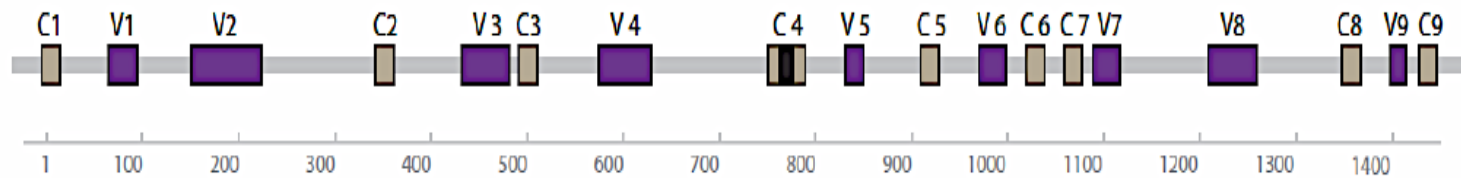


Microbiome in Health and Disease

Microbiota as a Potential Diagnostic and Therapeutic Target

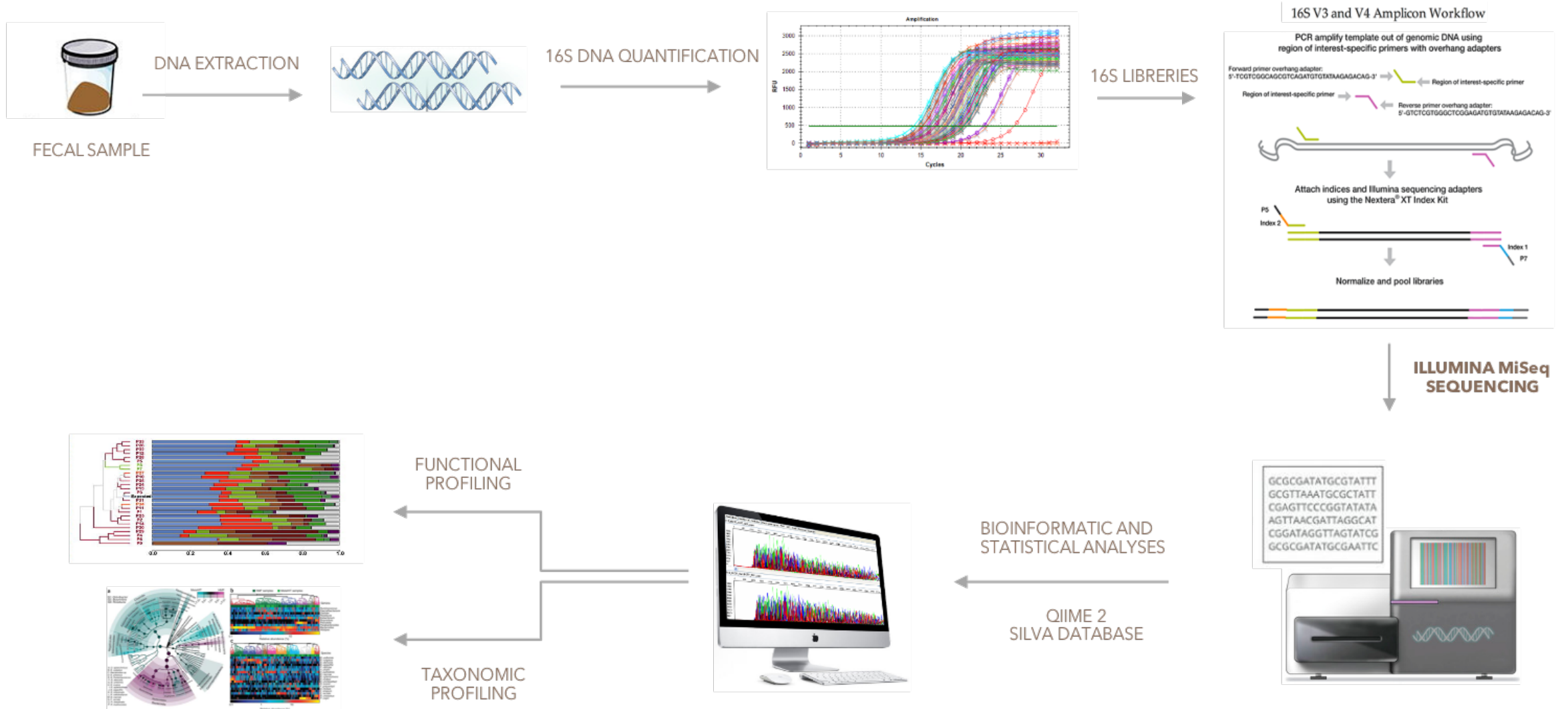


16S REGION



Microbiome in Health and Disease

Experimental Steps of Microbial Identification




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Gut microbiota markers associated with obesity and overweight in Italian adults


























[Vanessa Palmas](#), [Silvia Pisanu](#), [Veronica Madau](#), [Emanuela Casula](#), [Andrea Deledda](#), [Roberto Cusano](#), [Paolo Uva](#), [Sarah Vascellari](#), [Andrea Loviselli](#), [Aldo Manzin](#)  & [Fernanda Velluzzi](#)

[Scientific Reports](#) **11**, Article number: 5532 (2021) | [Cite this article](#)

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Open Access Article

Impact of a Moderately Hypocaloric Mediterranean Diet on the Gut Microbiota Composition of Italian Obese Patients

by  [Silvia Pisanu](#)^{1,†}   [Vanessa Palmas](#)^{1,†}   [Veronica Madau](#)¹   [Emanuela Casula](#)¹ ,  [Andrea Deledda](#)²   [Roberto Cusano](#)³   [Paolo Uva](#)³   [Sarah Vascellari](#)¹ ,  [Francesco Boi](#)²   [Andrea Loviselli](#)^{2,*}   [Aldo Manzin](#)^{1,†}   and  [Fernanda Velluzzi](#)^{2,‡} 

¹ Department of Biomedical Sciences, University of Cagliari, 09124 Cagliari, Italy

² Department of Medical Sciences and Public Health, University of Cagliari, 09124 Cagliari, Italy

³ CRS4, Science and Technology Park Polaris, Piscina Manna, Pula, 09010 Cagliari, Italy

* Author to whom correspondence should be addressed.

† These authors contributed equally to the work.

‡ These authors contributed equally to the work.

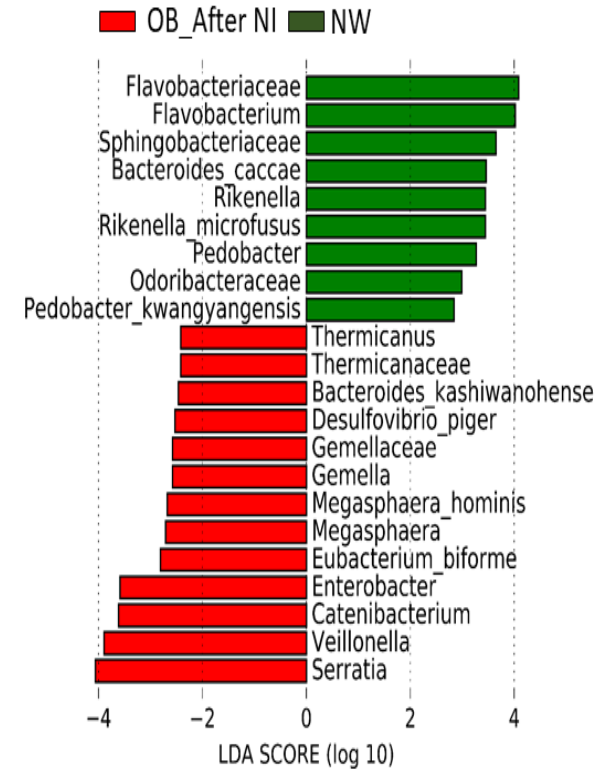
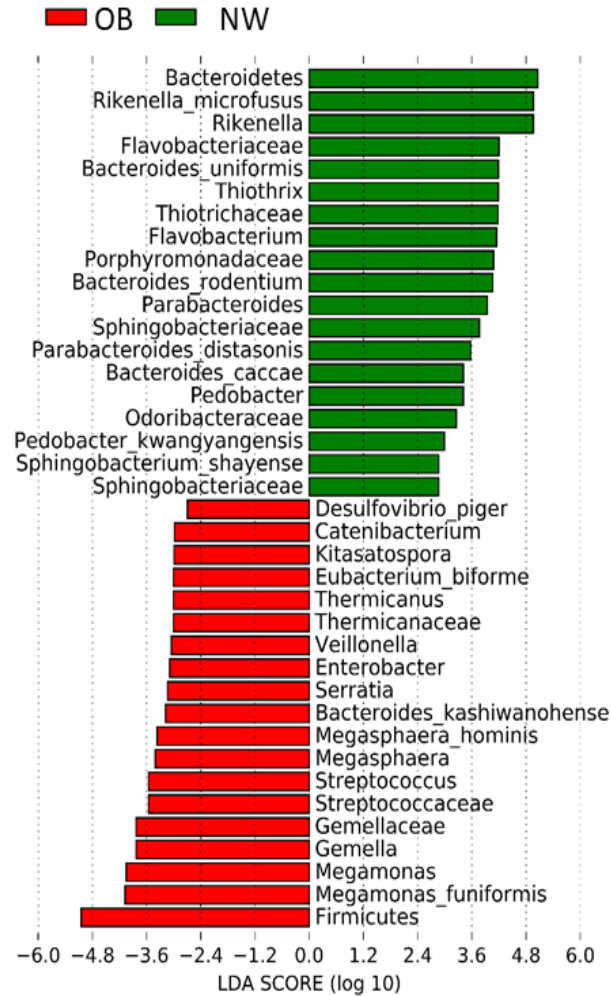
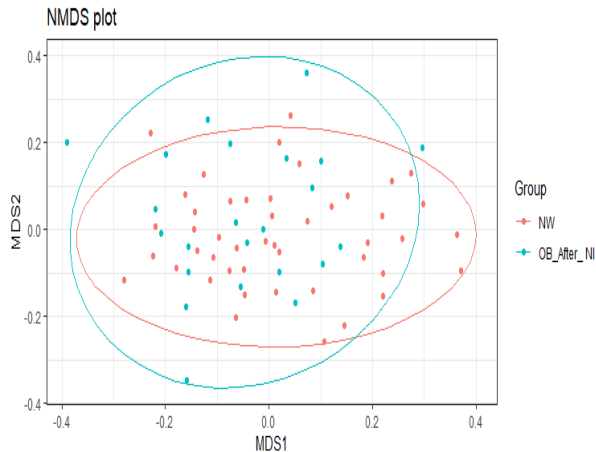
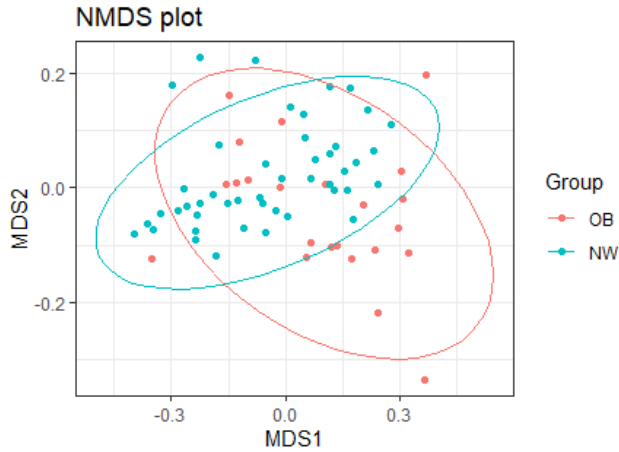
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(This article belongs to the Section **Clinical Nutrition**)

Microbiome in Health and Disease

Intestinal Microbiota Analysis



Microbiome in Health and Disease

Intestinal Microbiota Analysis

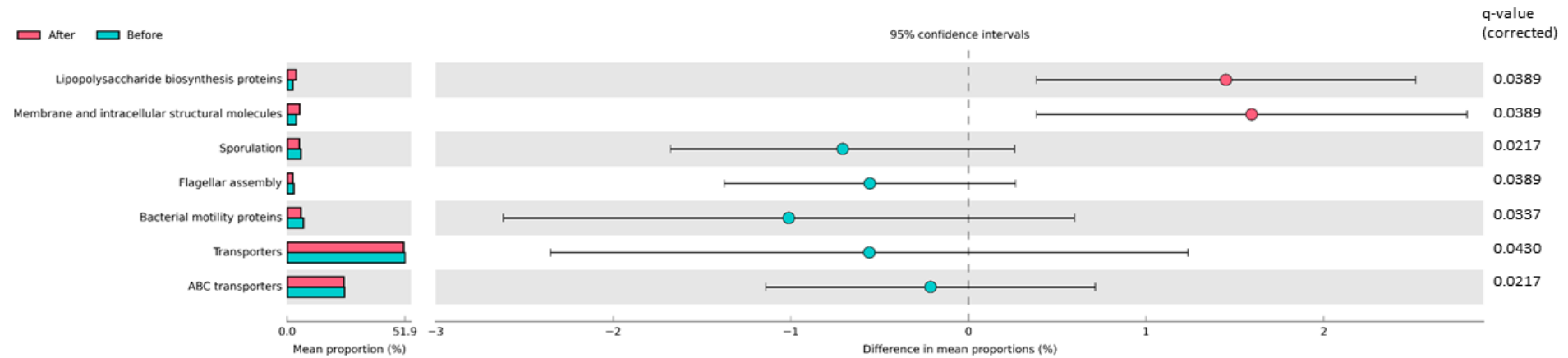
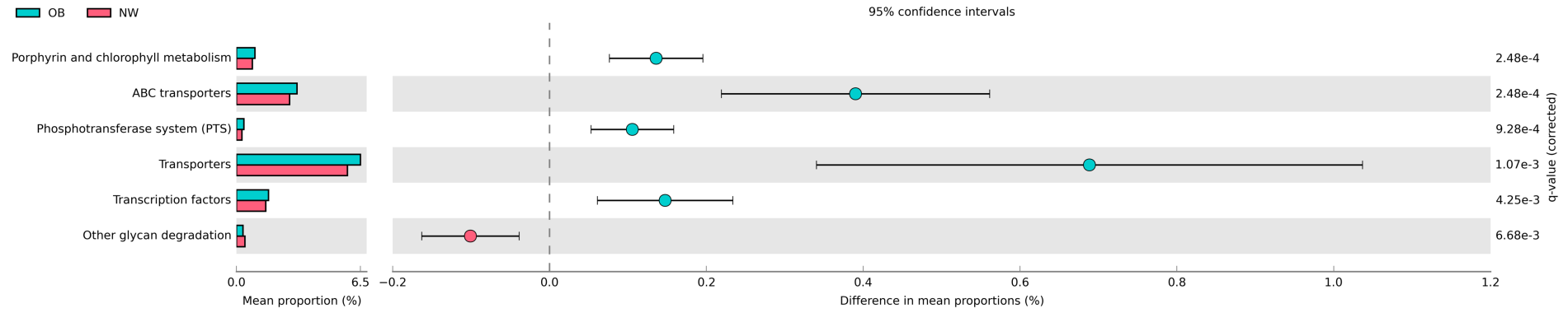
Table 4 Significant changes in bacterial relative abundance after the nutritional intervention in OB patients.

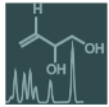
Phylum	Family	Genus	Species	MD	↑/↓	<i>p</i>	<i>q</i>	
Bacteroidetes	Bacteroidaceae	<i>Bacteroides</i>	<i>B. cellulosilyticus</i>	0.268	↑	0.006	0.039	
			<i>B. uniformis</i>	1.52	↑	0.005	0.036	
	Prevotellaceae	<i>Prevotella</i>	<i>P. stercorea</i>	0.109	↑	3,09E-05	0.001	
	Sphingobacteriaceae			0.185	↑	1,62E-04	0.003	
	Sphingobacteriaceae	<i>Sphingobacterium</i>		-0.067	↓	1,26E-03	0.011	
Firmicutes			<i>S. shayense</i>	0.062	↑	1,62E-04	0.003	
	Erysipelotrichaceae	<i>Catenibacterium</i>		0.706	↑	0.007	0.049	
	Lachnospiraceae	<i>Coprococcus</i>	<i>C. eutactus</i>	0.175	↑	0.001	0.005	
			<i>Pseudobutyrvibrio</i>	<i>P. xylanivorans</i>	-0.334	↓	5,23E-05	0.001
			<i>Roseburia</i>		-2.8	↓	0.004	0.026
	Selenomonadaceae	<i>Megamonas</i>		<i>Roseburia</i>	-0.361	↓	0.000	0.001
			<i>Megamonas</i>	<i>M. funiformis</i>	-0.039	↓	0.007	0.046
	Ruminococcaceae	<i>Ruminococcus</i>			-0.207	↓	0.005	0.038
					-3.75	↓	2.62E-04	0.003
					-0.203	↓	2.70E-05	0.001
					<i>R. albus</i>	-0.066	↓	0.003
			<i>R. callidus</i>	-0.039	↓	0.001	0.008	
	unclassified		<i>Sedimentibacter</i>	<i>S. hydroxybenzoicus</i>	0.041	↑	0.000	0.004
Tissierellia		<i>Streptococcus</i>	<i>S. vestibularis</i>	-0.096	↓	3,09E-05	0.001	
Veillonellaceae				-0.989	↓	2.95E-04	0.004	
Veillonellaceae	<i>Veillonella</i>			1.379	↑	3.73E-04	0.004	
			<i>V. montpellierensis</i>	0.136	↑	1.27E-04	0.001	
Proteobacteria				3.942	↑	2.70E-05	0.001	
	Sutterellaceae	<i>Sutterella</i>		-0.201	↓	0.001	0.012	

MD = Mean difference of bacterial relative abundance after the NI. Results were obtained by the Wilcoxon test for paired data performed on R software (v. 3.5.2). *q* = *p* adjusted for Benjamini and Hochberg's false discovery rate (FDR) correction test for multiple comparisons (FDR < 0.05). ↓ = significantly reduced after the NI, ↑ = significantly increased after the NI. Bold values denote statistical significance (*q* ≤ 0.05).

Microbiome in Health and Disease

Functional Microbiome Prediction





metabolites



Article

Dynamics of Gut Microbiota and Clinical Variables after Ketogenic and Mediterranean Diets in Drug-Naïve Patients with Type 2 Diabetes Mellitus and Obesity

Andrea Deledda ^{1,†}, Vanessa Palmas ^{2,†}, Vitor Heidrich ^{3,4}, Michele Fosci ⁵, Mauro Lombardo ⁶, Giulia Cambarau ¹, Alessio Lai ⁷, Marietta Melis ¹, Elisabetta Loi ¹, Andrea Loviselli ⁵, Aldo Manzin ^{2,‡} and Fernanda Velluzzi ^{1,*}

¹ Obesity Unit, Department of Medical Sciences and Public Health, University of Cagliari, 09124 Cagliari, Italy

² Department of Biomedical Sciences, University of Cagliari, 09042 Monserrato, Italy

³ Departamento de Bioquímica, Instituto de Química, Universidade de São Paulo, São Paulo 05508-900, Brazil

⁴ Centro de Oncologia Molecular, Hospital Sírio-Libanês, São Paulo 01308-050, Brazil

⁵ Endocrinology Unit, Department of Medical Sciences and Public Health, University of Cagliari, 09042 Monserrato, Italy

⁶ Department of Human Sciences and Promotion of the Quality of Life, San Raffaele Roma Open University, 00166 Rome, Italy

⁷ Diabetologia, P.O. Binaghi, ASSL Cagliari, 09126 Cagliari, Italy

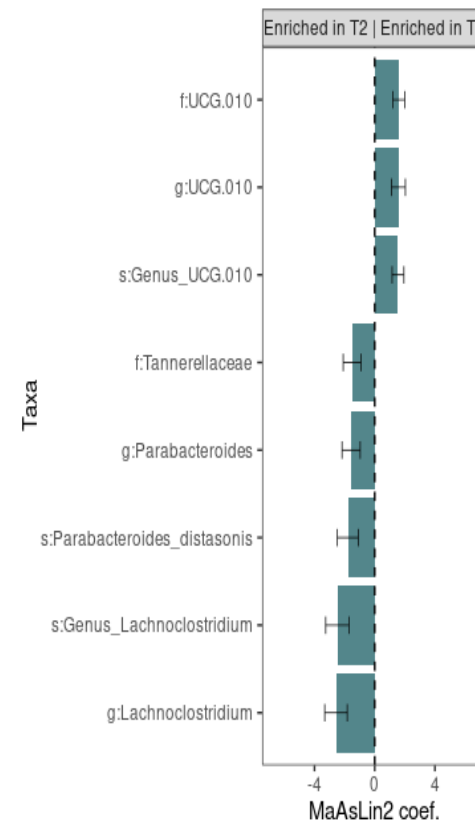
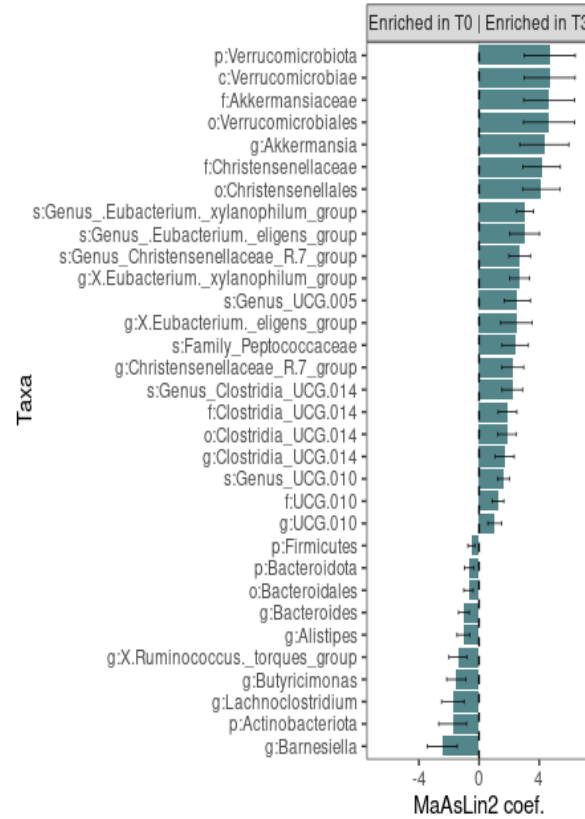
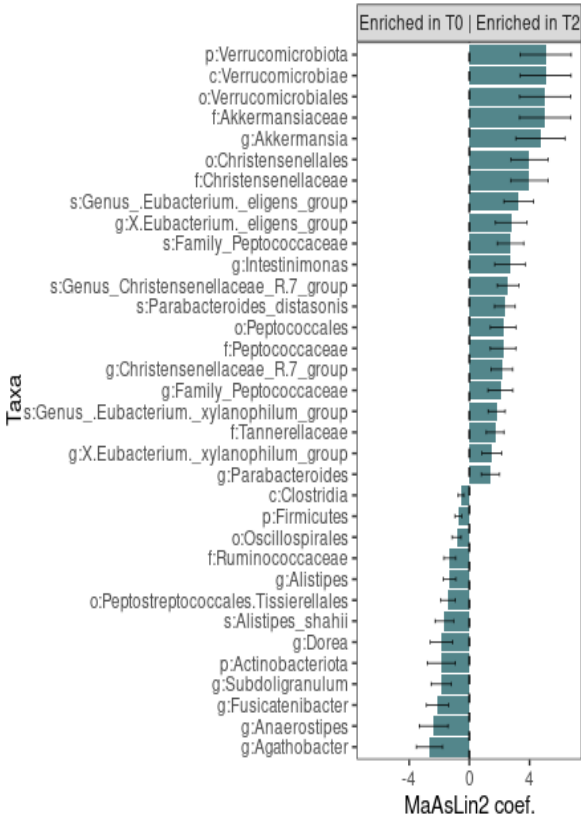
* Correspondence: fernandavelluzzi@gmail.com

† These authors contributed equally to the work.

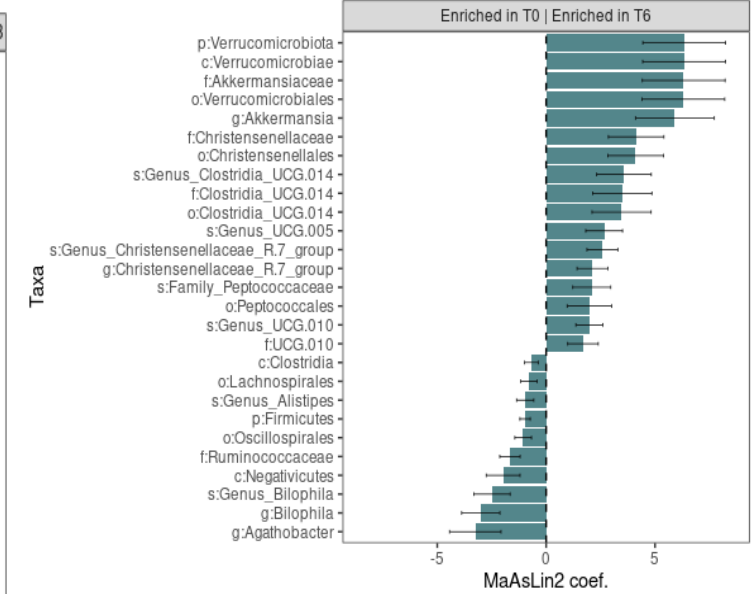
‡ These authors contributed equally to the work.

Intestinal Microbiota Analysis: Taxonomic Profile

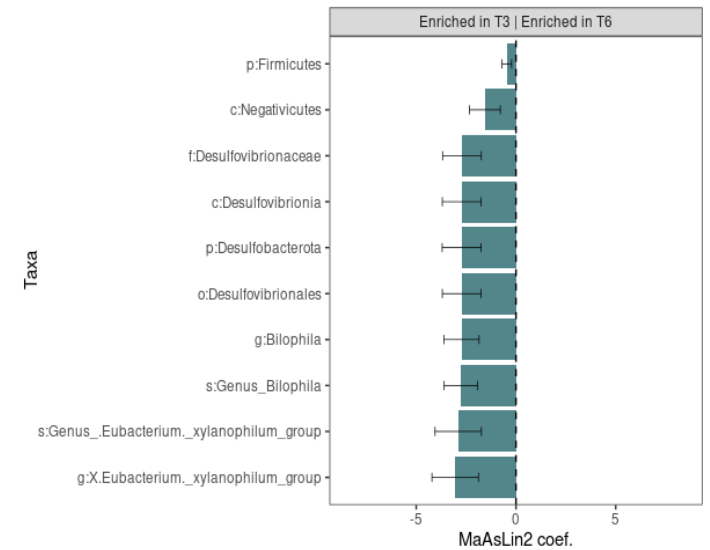
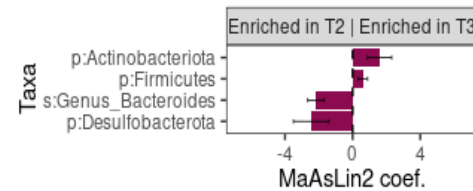
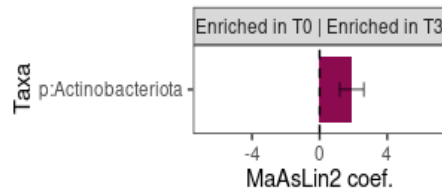
KETO



KETO

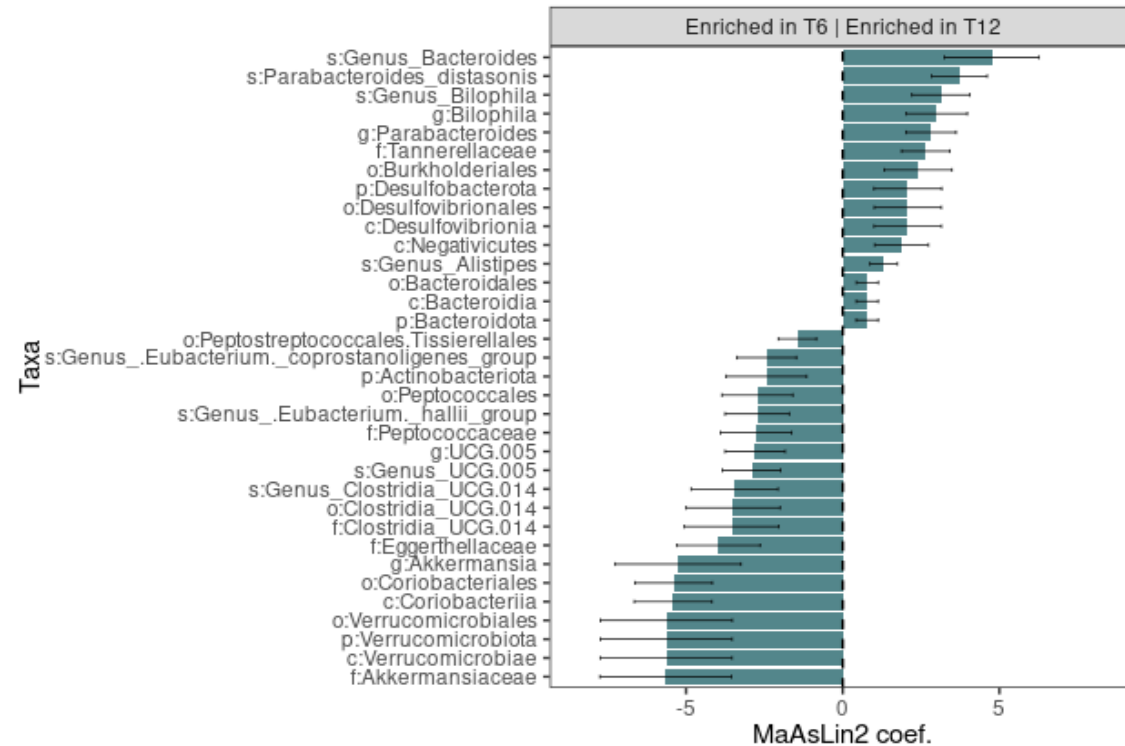
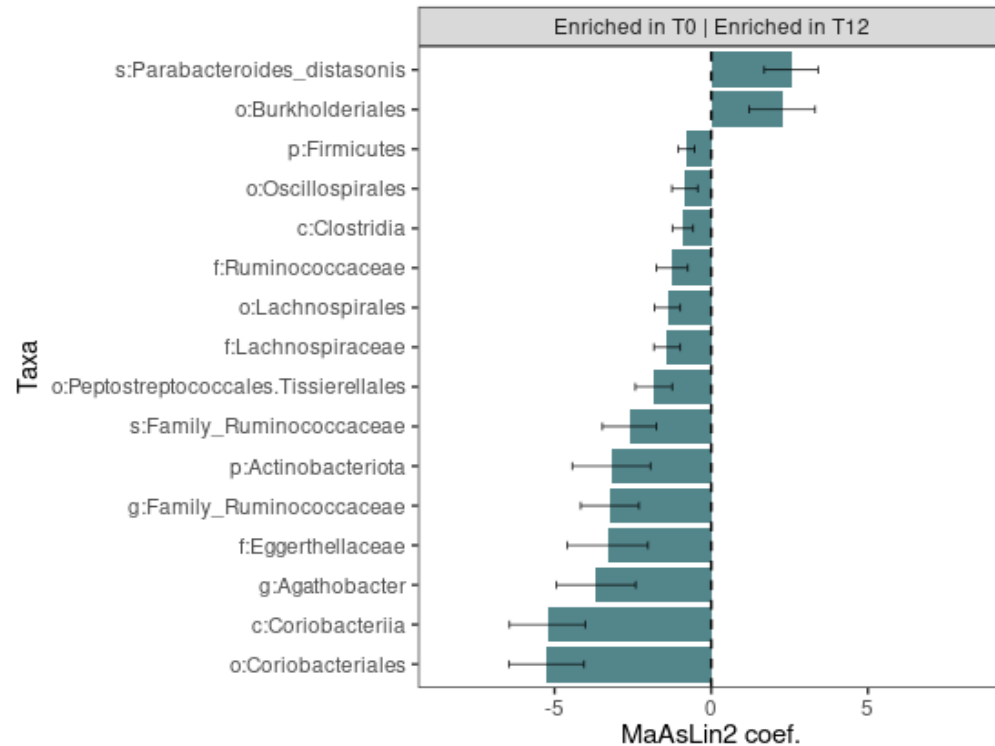


MEDI



Microbiome in Health and Disease

Intestinal Microbiota Analysis: Taxonomy Profiling



Open Access Article

Gut Microbiota Markers and Dietary Habits Associated with Extreme Longevity in Healthy Sardinian Centenarians

by  Vanessa Palmas¹ ,  Silvia Pisanu¹  ,  Veronica Madau¹ ,  Emanuela Casula¹ ,
 Andrea Deledda²  ,  Roberto Cusano³  ,  Paolo Uva⁴  ,  Andrea Loviselli² ,
 Fernanda Velluzzi^{2,†}   and  Aldo Manzin^{1,*†}  

¹ Department of Biomedical Sciences, Microbiology and Virology Unit, University of Cagliari, 09042 Monserrato, Italy

² Department of Medical Sciences and Public Health, University of Cagliari, 09124 Cagliari, Italy

³ Interdisciplinary Center for Advanced Studies, Research and Development in Sardinia (CRS4), Science and Technology Park Polaris, Piscina Manna, 09134 Pula, Italy

⁴ Clinical Bioinformatics Unit, IRCCS Istituto Giannina Gaslini, 16147 Genoa, Italy

* Author to whom correspondence should be addressed.

† These authors contributed equally to this work.

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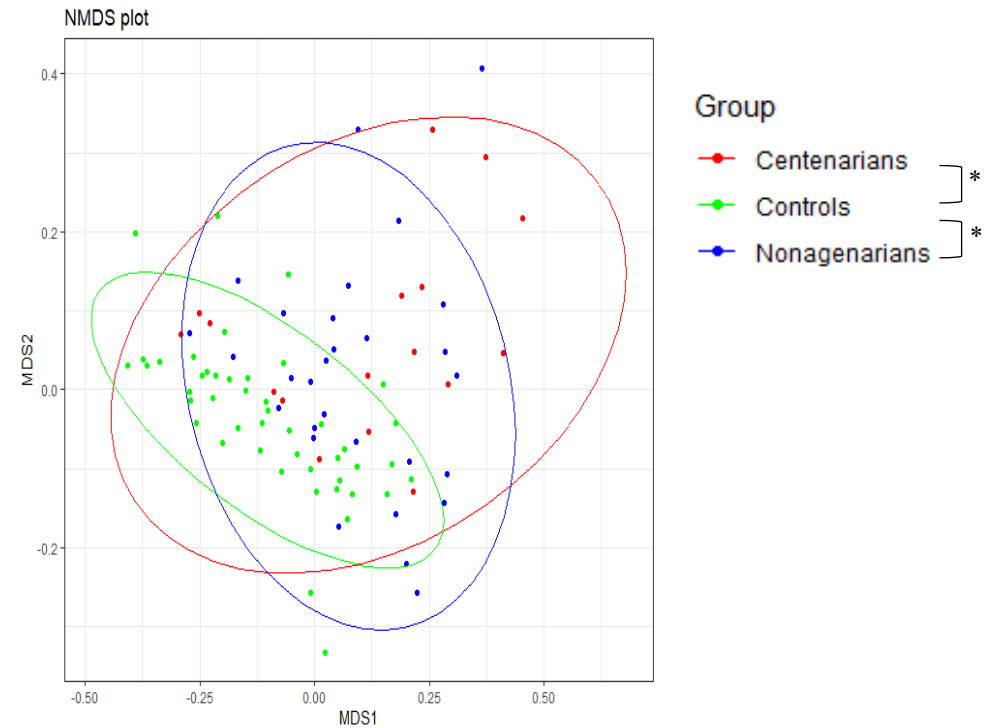
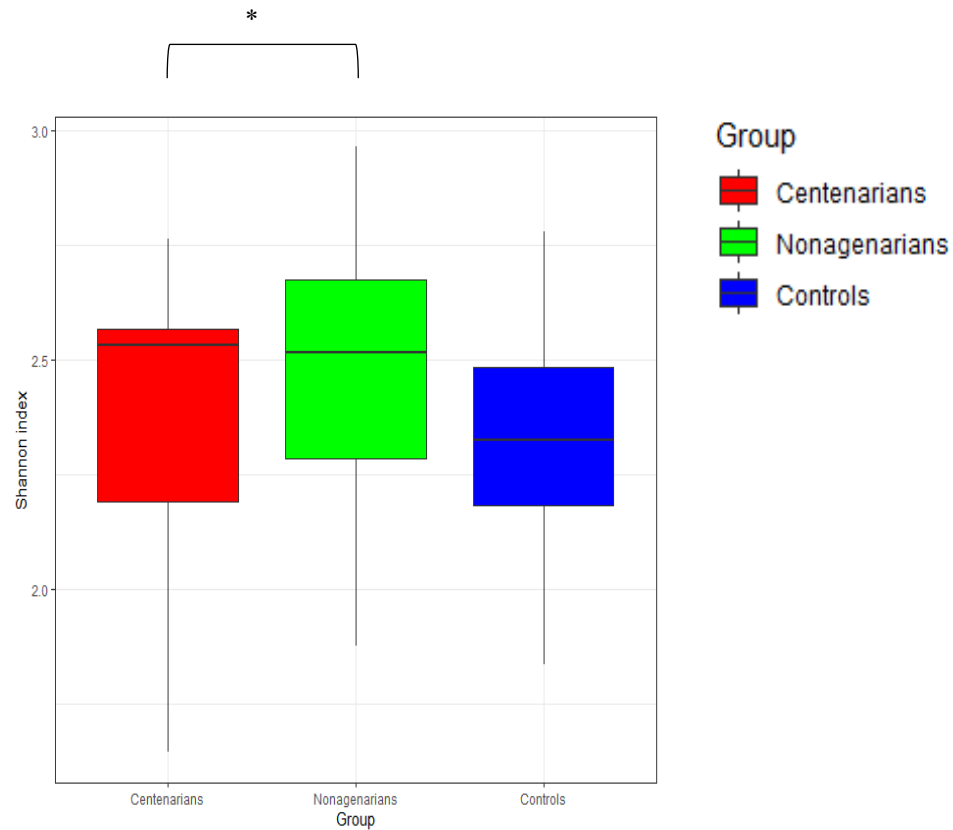
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Microbiome in Health and Disease

Intestinal Microbiota Analysis



CENTENARIANS

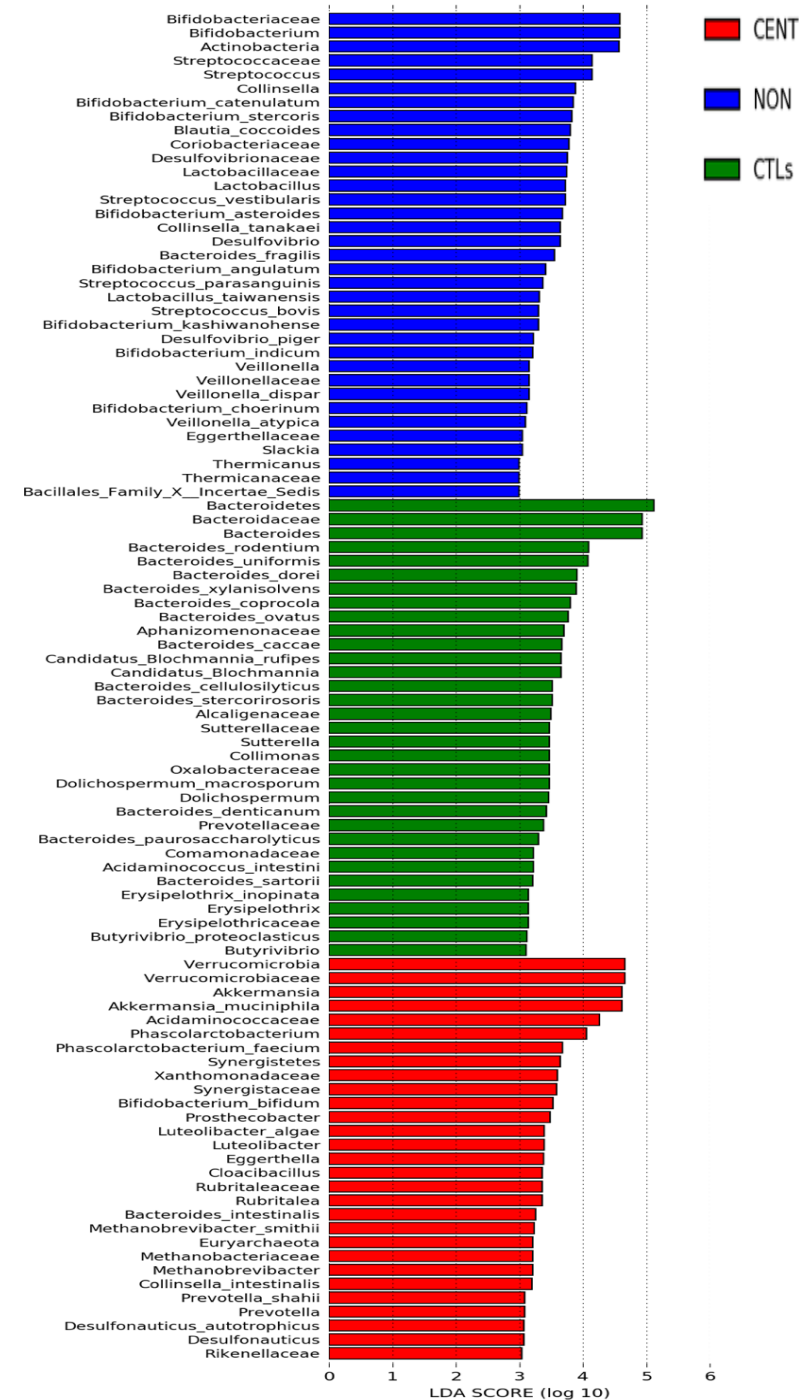
- Verrucomicrobia
- Verrucomicrobiaceae
- *Akkermansia*
- *A. muciniphila*
- *Bifidobacterium bifidum*
- *Bacteroides intestinalis*
- *Phascolarctobacterium*
- Methanobacteriaceae
- *Methanobrevibacter*
- *M. smithii*

NONAGENARIANS

- Actinobacteria
- Bifidobacteriaceae
- *Bifidobacterium*
- *Bifidobacterium* spp.
- Lactobacillaceae
- *Lactobacillus*
- *Lactobacillus* spp.
- Streptococcaceae
- *Streptococcus*
- *Streptococcus* spp.
- Veillonellaceae
- *Veillonella*
- *Veillonella* spp.
- Desulfovibrionaceae
- *Desulfovibrio*
- *Desulfovibrio piger*

CONTROLS

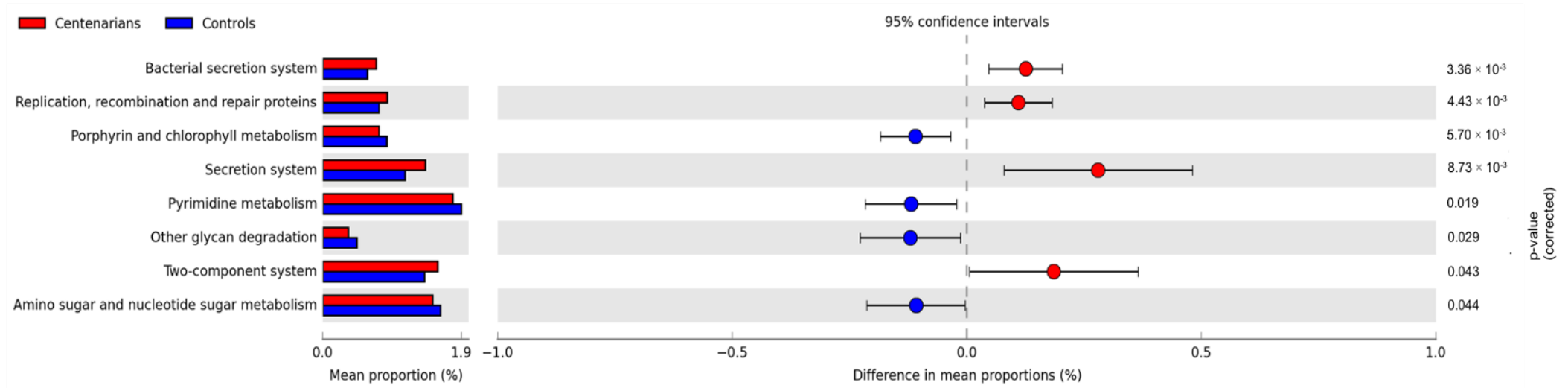
- Bacteroidetes
- Bacteroidaceae
- *Bacteroides*
- *Bacteroides* spp.



Microbiome in Health and Disease

Functional Metagenome Prediction Analysis

(B)



(C)

