Special diets to microbiota modulation

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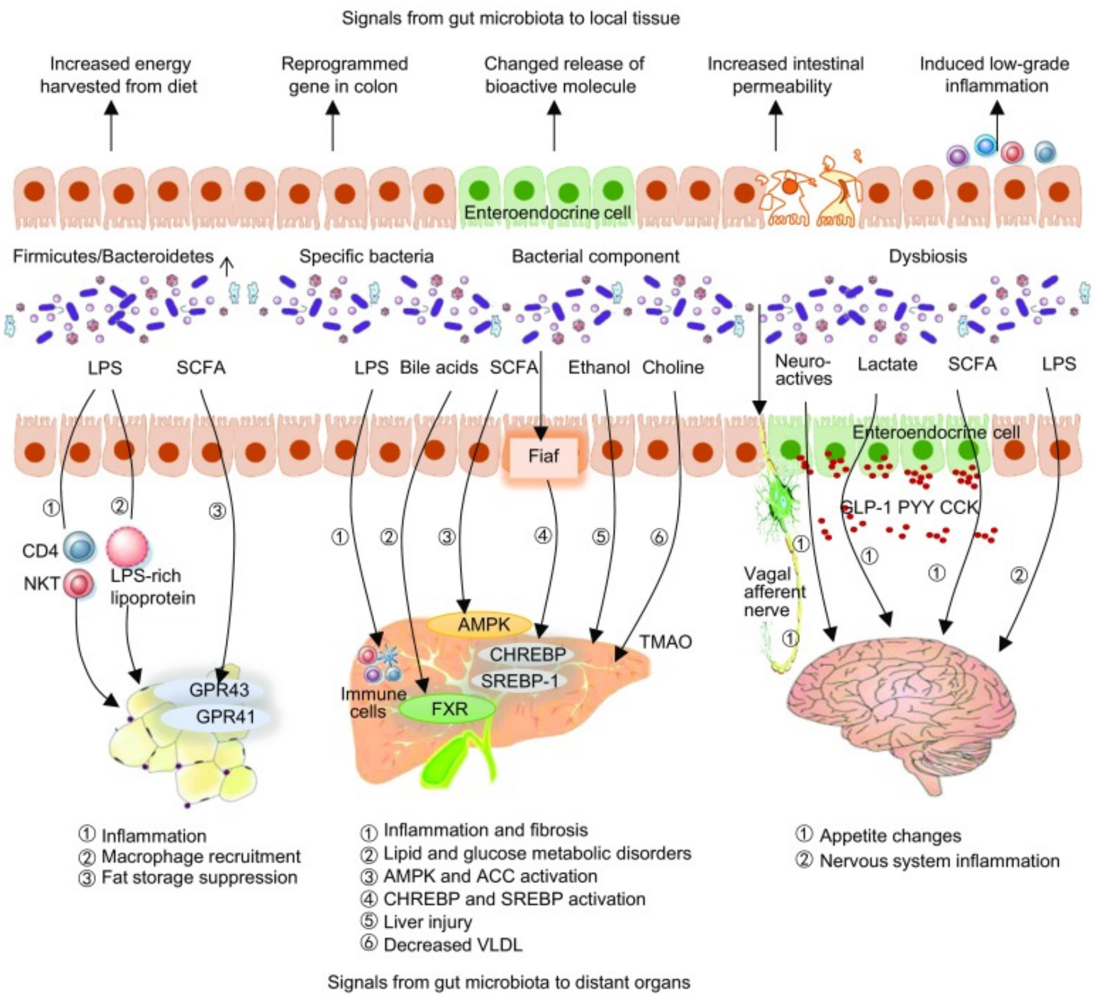
Impact of gut microbiota on local and distant organs contributes to obesity development and progression



Sun et al, Protein Cell. 2018 May; 9(5): 397–403.

Gut microbiome science in obesity translational research

Where are we now?

Where do we want to arrive?

Gut microbiome science in translational research

Where are we now?

Where do we want to arrive?

Microorganisms produce diseases

Gut microbiota is mostly commensal

Gut microbiota has a role in homeostasis

Gut microbiota has a role in non-communicable diseases

Gut microbiota can be modified

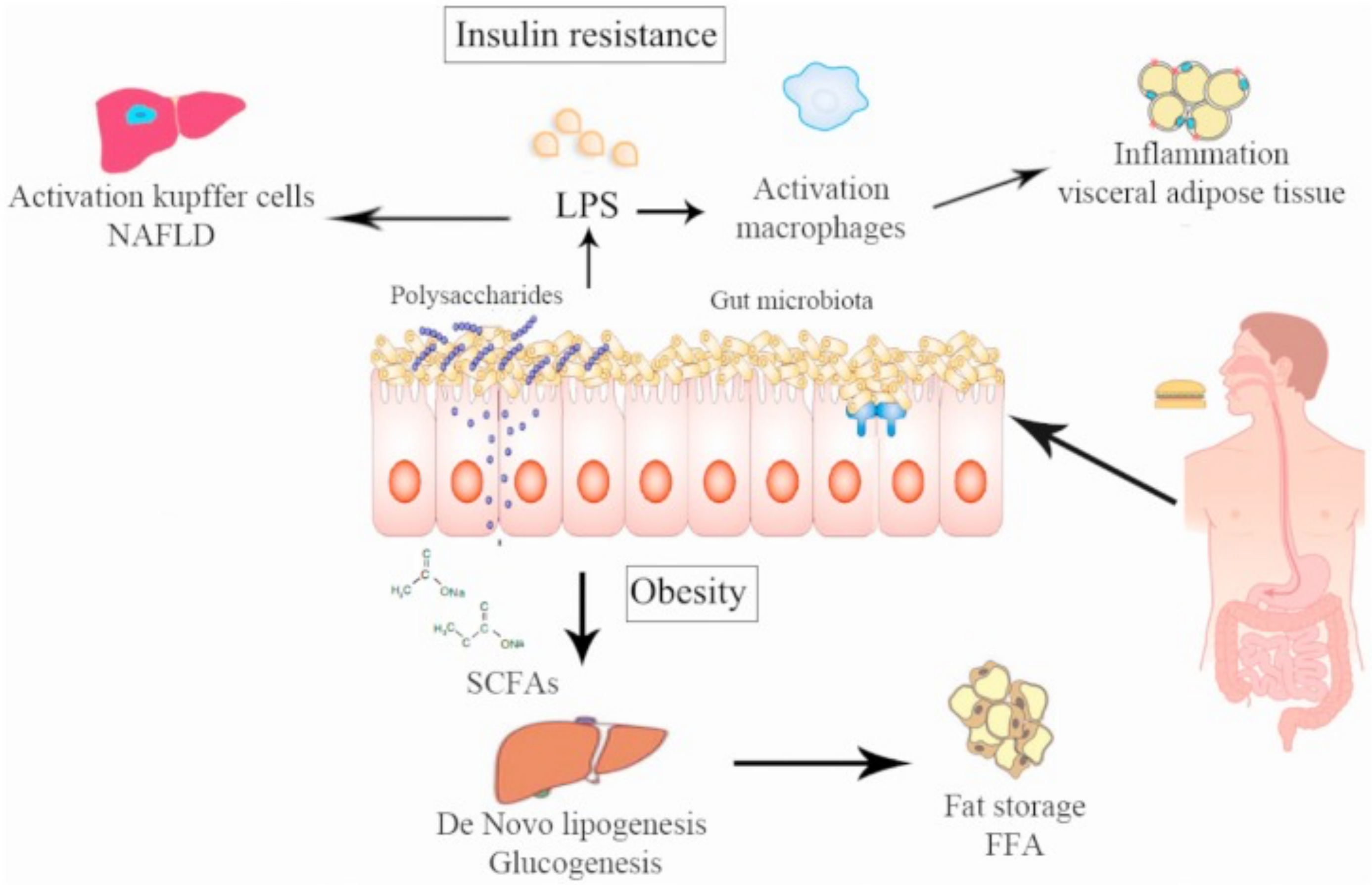
We are here

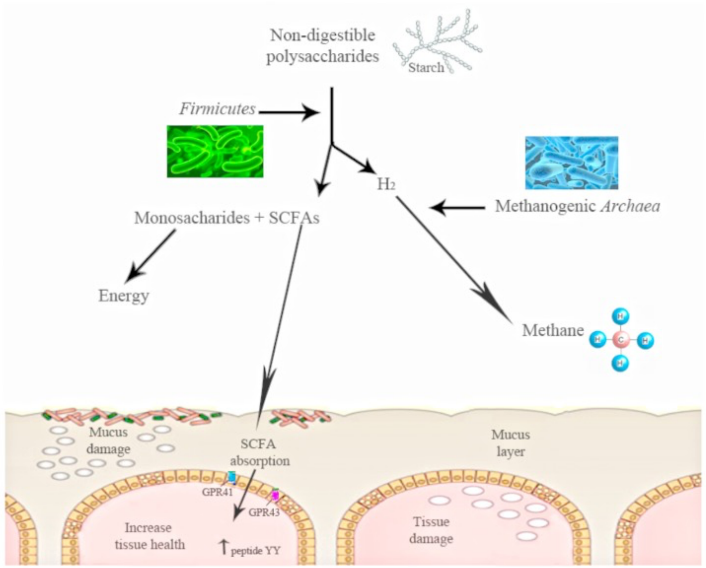
We want to arrive here

Gut microbiota-based therapeutics

Gut microbiota with a role in non-communicable diseases: metabolic diseases and obesity, in particular

Gut microbiota has a role in the development of insulin-resistance and obesity

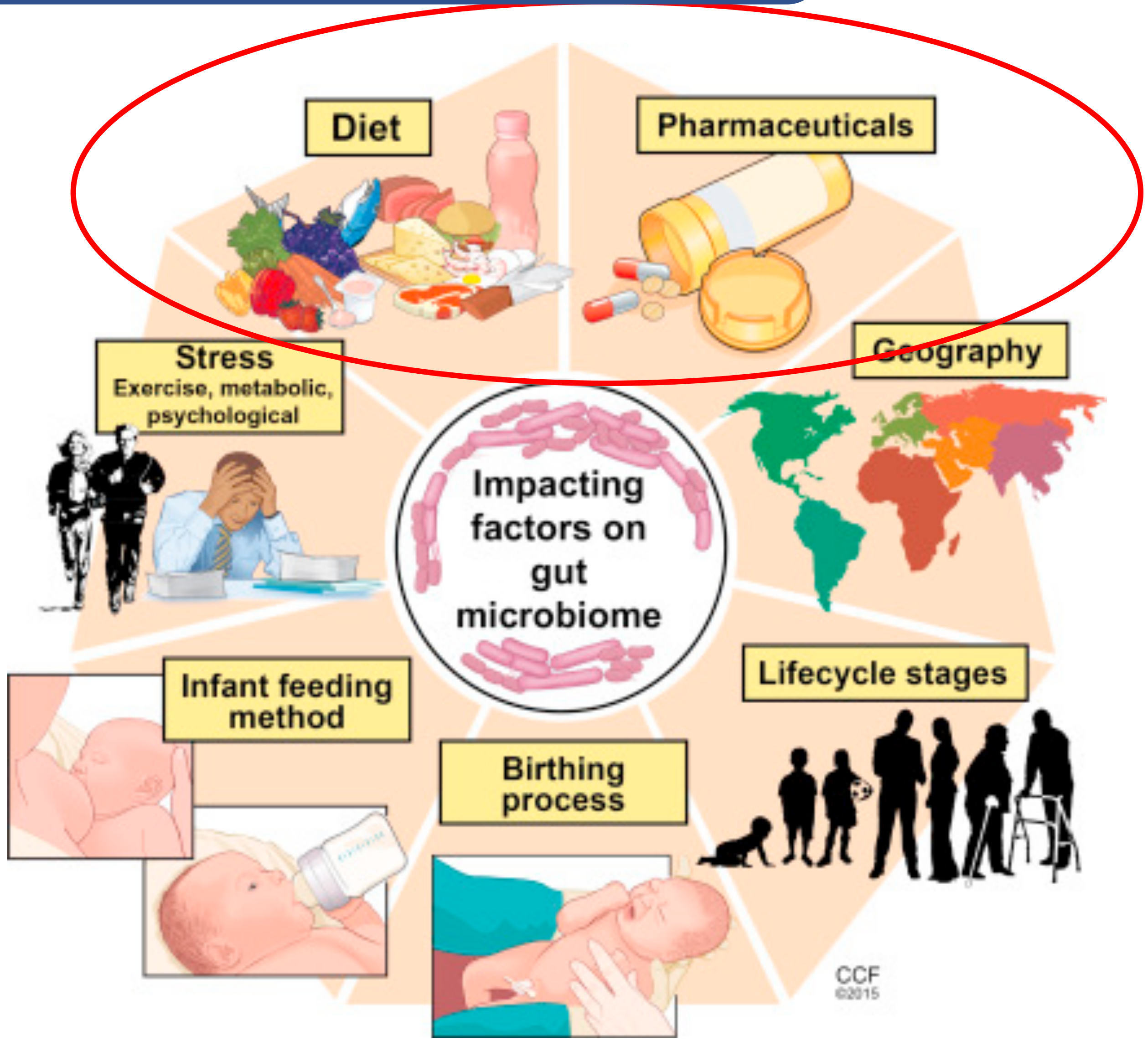




Moreno-Indias et al., 2014. Font Microbiol, 5:190. doi: 10.3389/fmicb.2014.00190.

Gut microbiota can be modified

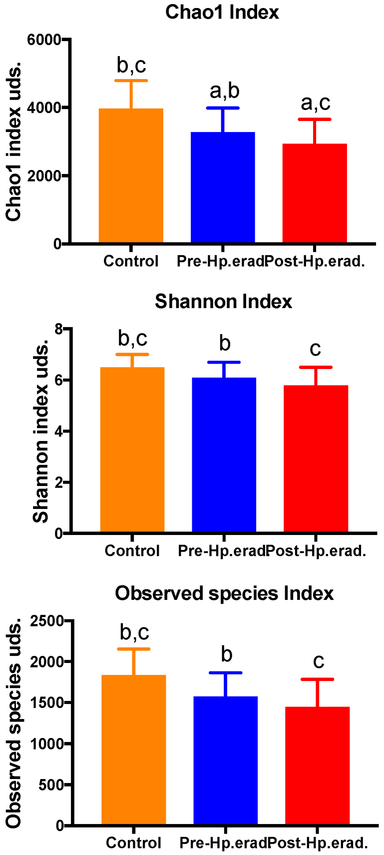
Gut microbiota can be modified



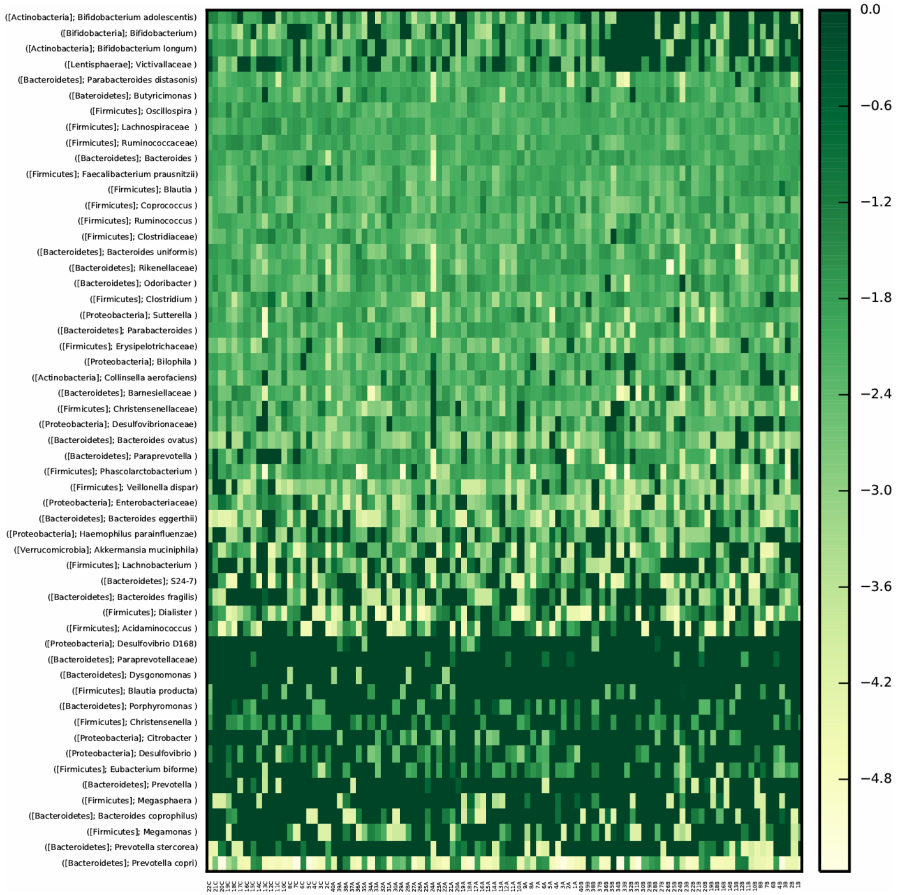
Gail et al. 2019. Adult Short Bowel Syndrome.

Helicobacter pilory eradication treatment alters gut microbiota profile and functionality

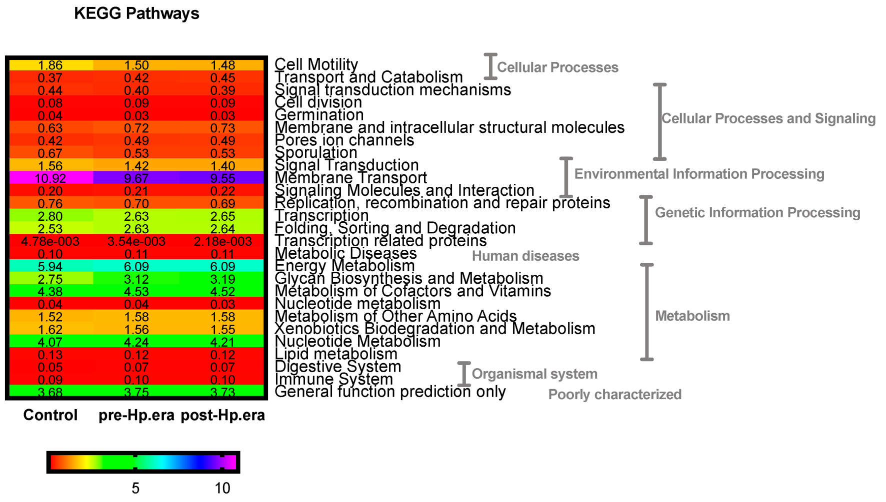
Diversity indexes



Microbiota profile



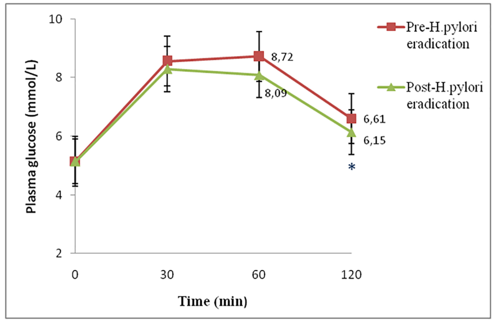
Gut microbiome metabolic pathways

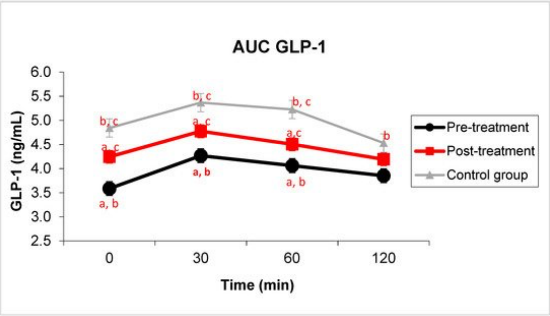


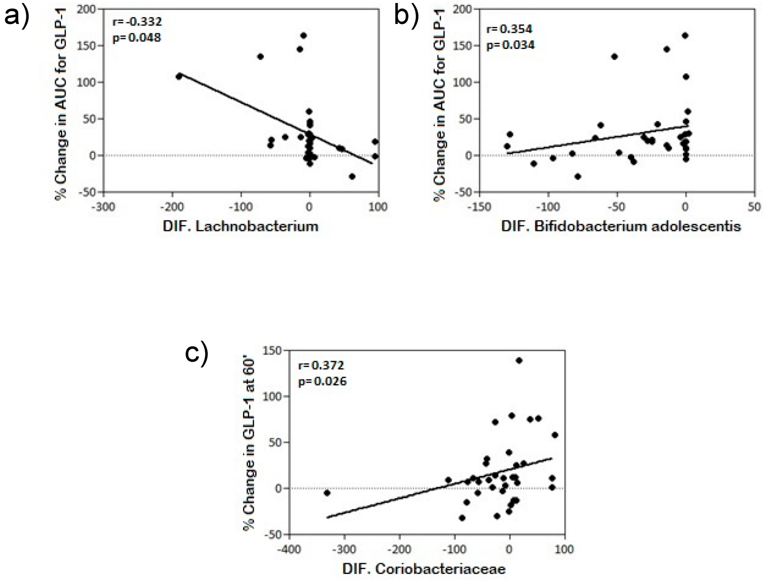
Martín-Núñez et al., 2019. PLoS One, 14(3):e0213548. doi: 10.1371/journal.pone.0213548.
Cornejo-Pareja et al 2019. J Clin Med, 8(4):451. doi: 10.3390/jcm8040451.
Martín-Nuñez et al 2020. Front Med (Lausanne), 7:417. doi: 10.3389/fmed.2020.00417.

Helicobacter pilory eradication treatment alters glucose and lipid metabolisms at least in part due to changes in gut microbiota

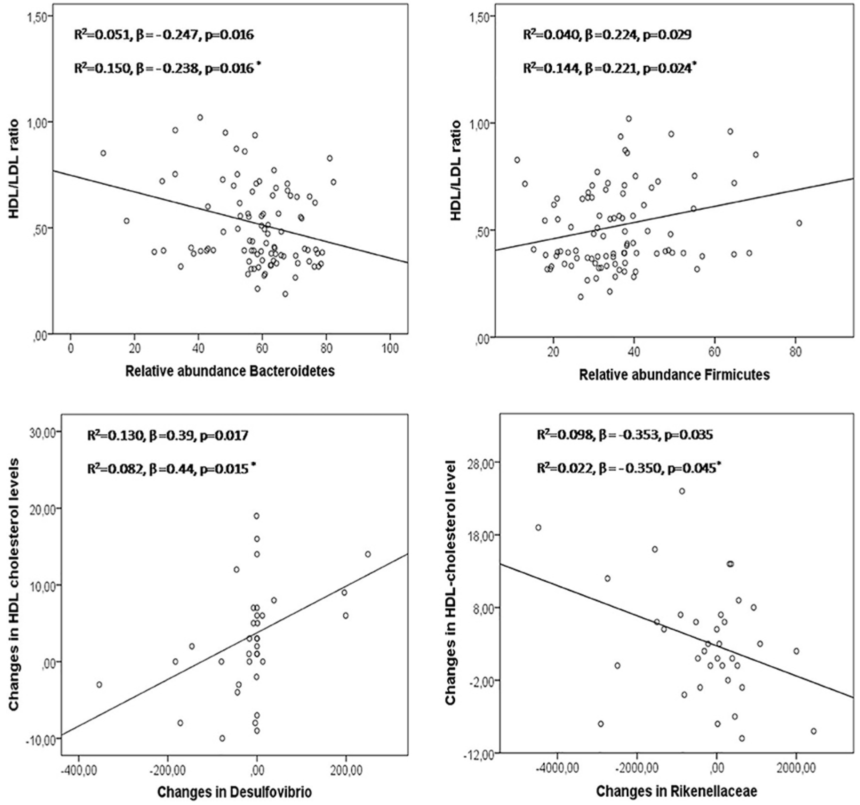
Glucose metabolism







HDL-Cholesterol



Martín-Núñez et al., 2019. PLoS One, 14(3):e0213548. doi: 10.1371/journal.pone.0213548.
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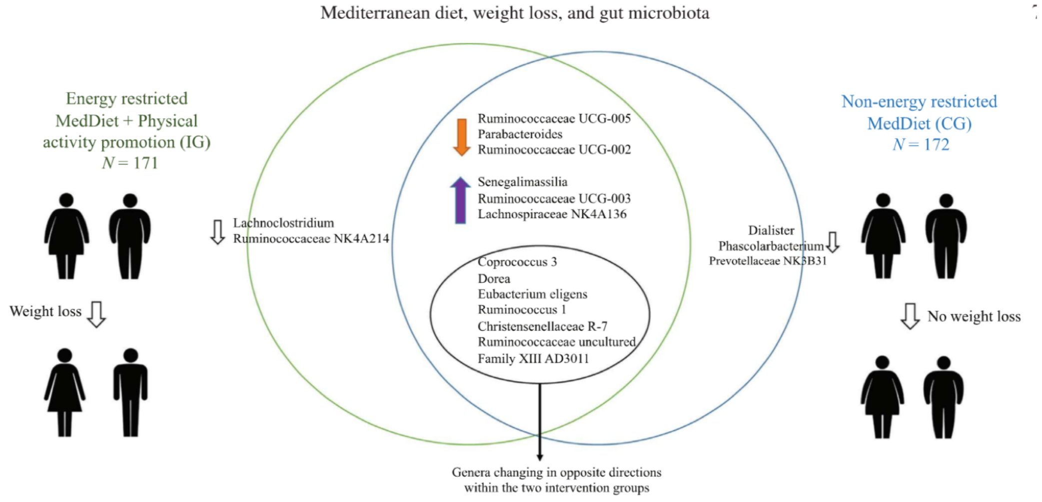
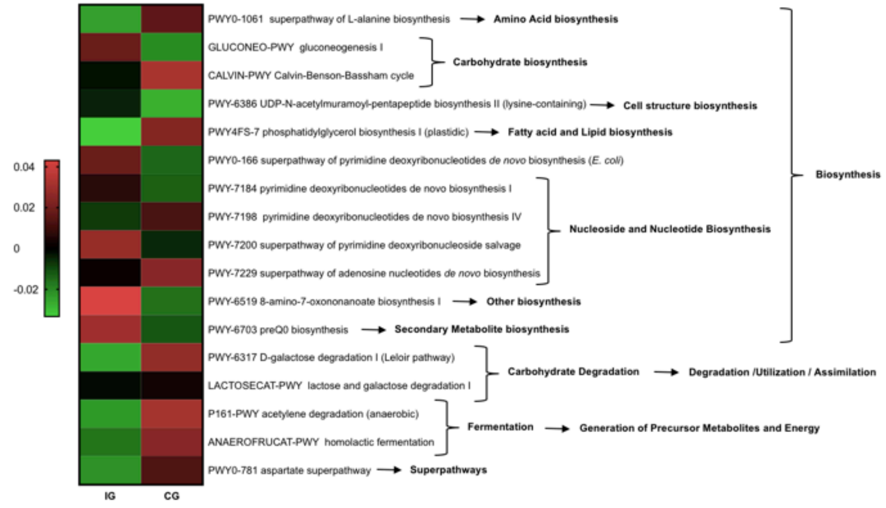
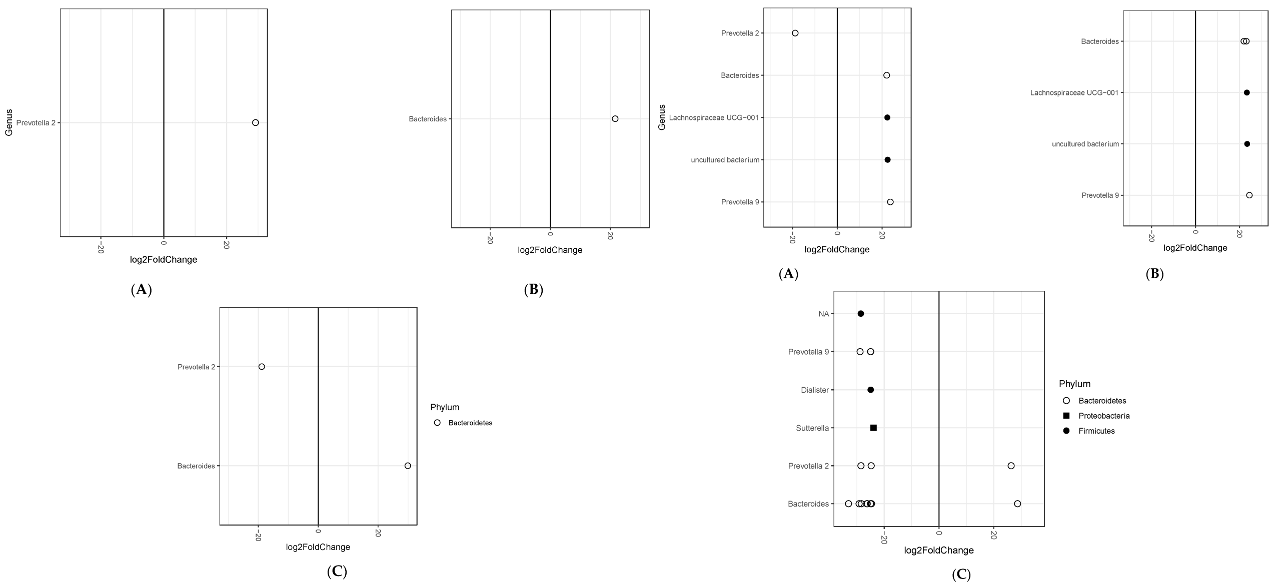
Martín-Nuñez et al 2020. Front Med (Lausanne), 7:417. doi: 10.3389/fmed.2020.00417.

A Mediterranean Diet is able to modulate gut microbiota specially throught the increase of SCFAs producers. A caloric restriction adds metabolic improvements that could be related to these gut microbiota changes.





Relationships with BMI changes



Muralidharan et al., 2021. Am J Clin Nutr, in press.
Atzeni et al., 2021. Microorganisms. 9(2):346. doi: 10.3390/microorganisms9020346

A very-low-calorie ketogenic diet produces important changes in gut microbiota. Moreover, the use of a symbiotic may help to lose more weight probably through the improvement of the inflammatory milieu

VLCKD

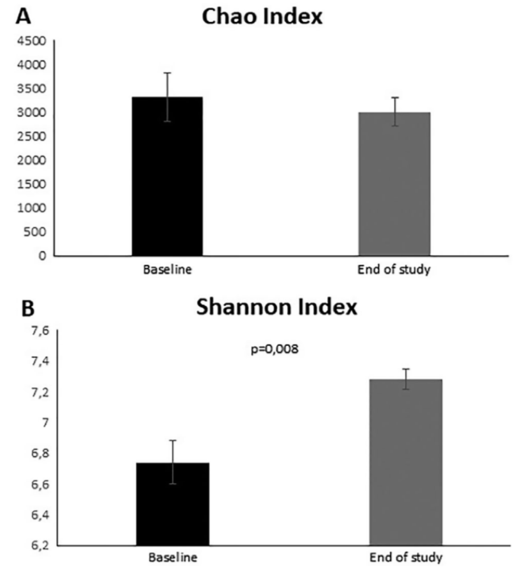


Table 3. Multiple linear regression models.

Dependent variable	R^2	Significant independent variables
Model 1		
Weight loss [%]	0.305	Placebo-synbiotic2 ($B = -0.626$; $p = 0.028$)
Model 2		
Glucose change [%]	0.239	Placebo-synbiotic2 ($B = 0.587$; $p = 0.016$)
LBP change [%]	0.239	Placebo-synbiotic2 ($B = -0.518$; $p = 0.040$)
CRP change [%]	0.216	Placebo-synbiotic2 ($B = -0.514$; $p = 0.041$)

Model 1: Independent variables—age, sex, treatment (dummy variable; reference category: control group), changes in glucose levels (%), changes in RCP levels (%), and changes in LBP levels (%); Model 2: Independent variables—age, sex, weight loss percentage, and treatment (dummy variable; reference category: control group).

	Synbiotic1-synbiotic2 group	Placebo-synbiotic2 group	Control group
Weight [kg]	−13.96 ± 3.00	−20.13 ± 9.49*	−14.10 ± 3.89
Waist circumference [cm]	−11.53 ± 4.03	−13.93 ± 4.52	−14.50 ± 4.53
BMI [kg m^{-2}]	−14.02 ± 2.97	−16.68 ± 4.09	−14.11 ± 3.92

The administration of synbiotics during VLCKD can improve weight loss through the amelioration of inflammation, which may be mediated by the gut microbiota

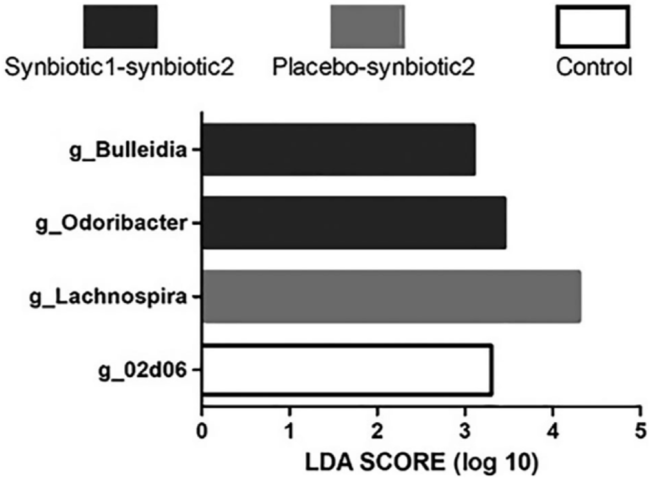
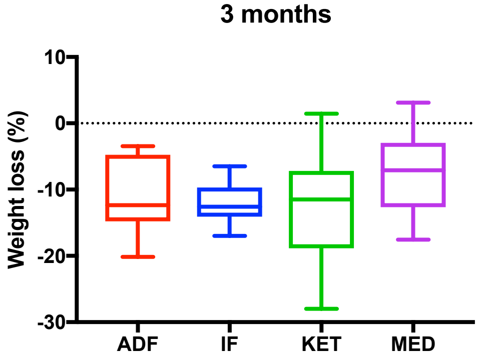


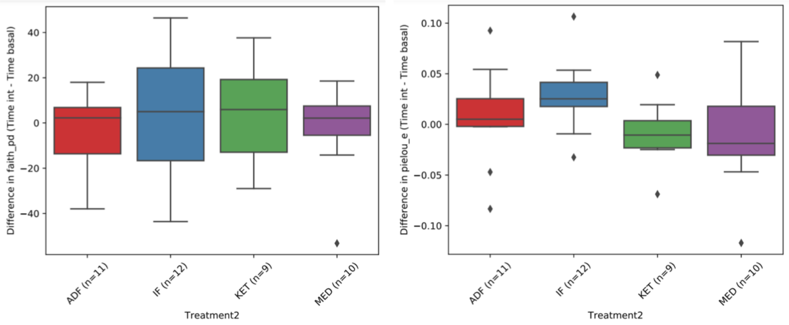
Figure 4. Histogram of the linear discriminant analysis (LDA) scores for differentially abundant bacterial groups in fecal samples between the three treatments. Black bars represent bacterial groups overabundant in the symbiotic1 group. Gray bars represent the bacterial group overabundant in the symbiotic2 group. White bars represent the bacterial group overabundant in the control group.

Gutiérrez-Repiso et al., 2019. Mol Nutr Food Res. 63(19):e1900167. doi: 10.1002/mnfr.201900167.

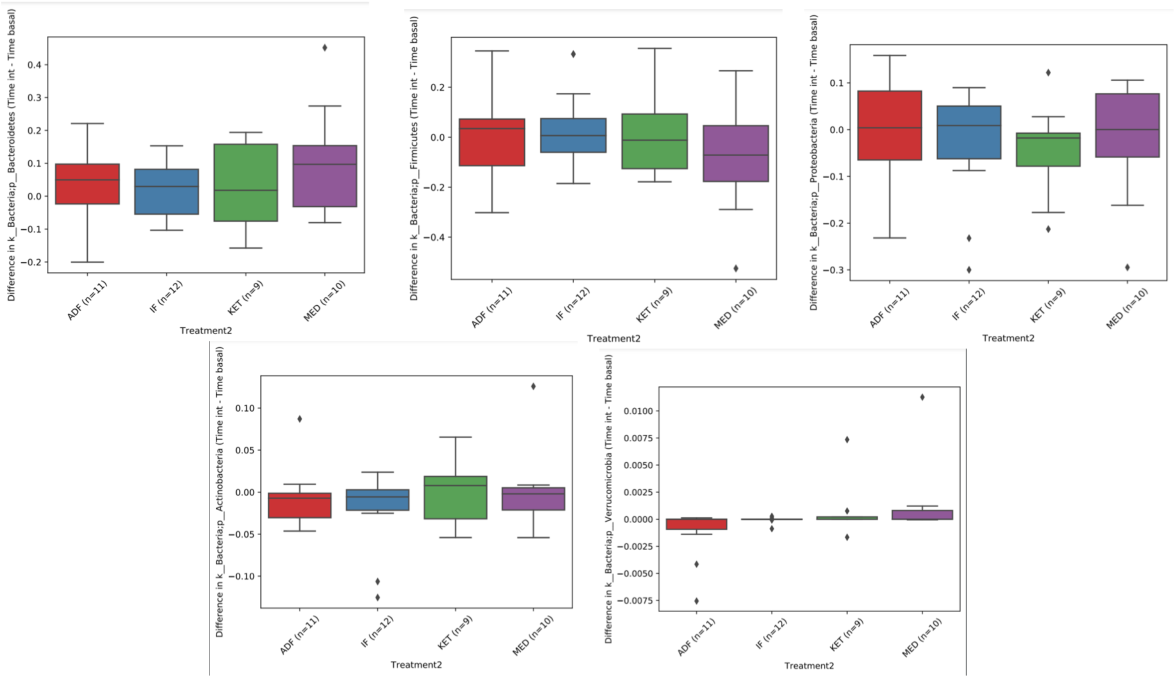
Caloric restriction and fasting promote different rearrangements of the gut microbiota population translated into different metabolic roles that may be involved in the metabolic changes of the host

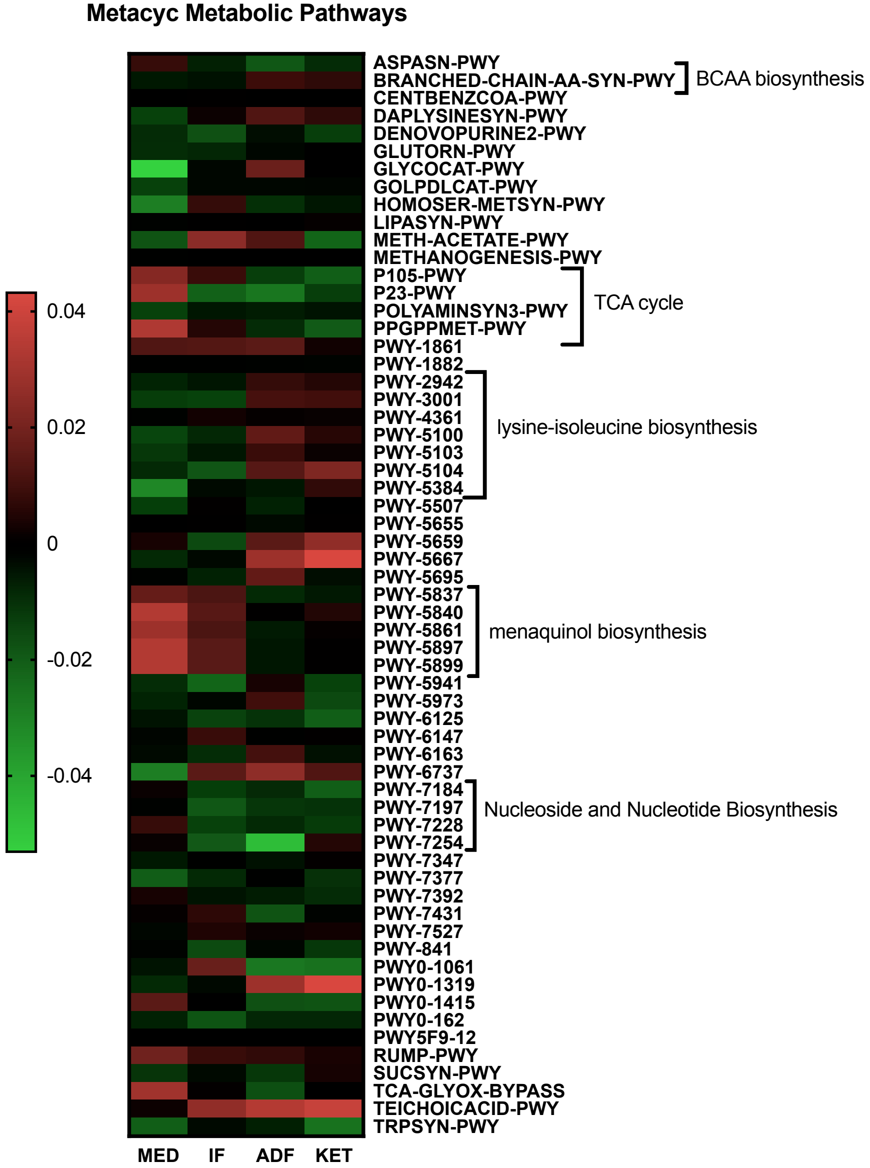


Diversity indexes



Phyla changes





Preliminary data, unpublished

Gut microbiota-based therapeutic for their use in metabolic diseases and obesity, in particular

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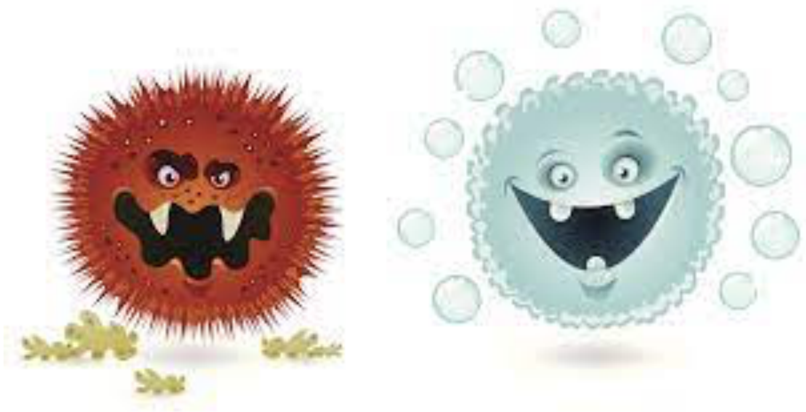
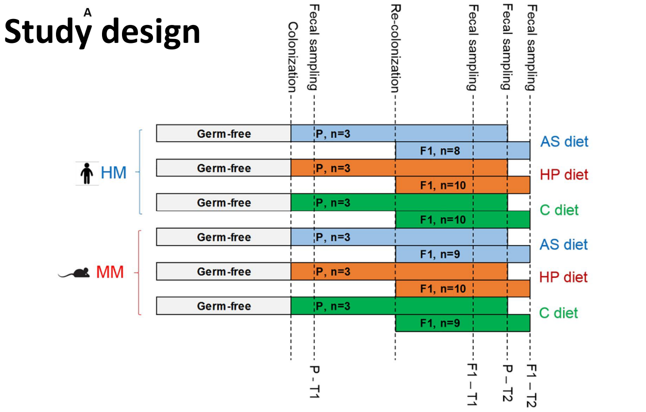


Gut microbiota is an adaptive component that allows host adaptation optimizing host physiology from daily life to lifespan scales and evolutionary history. Diet is a powerful modulator of its profile that can be used for the improvement of the host's physiology

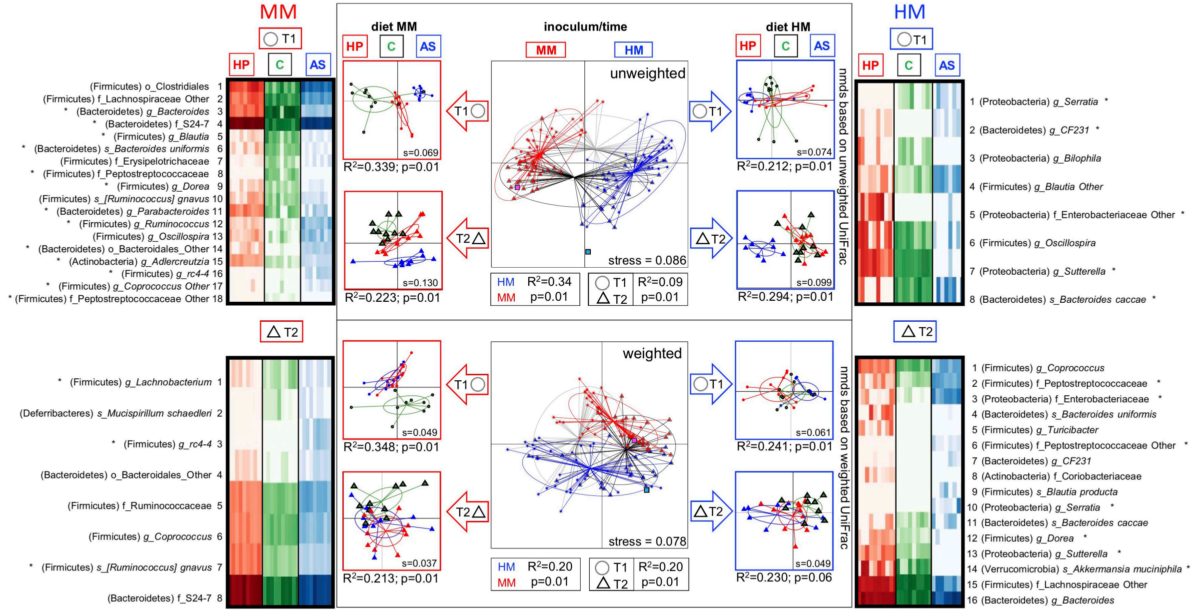
Study design



B

Macronutrient composition	AS diet (Animal Source)			HP diet (Human Profile)			C diet (Control)		
	Source	kcal%	gm%	Source	kcal%	gm%	Source	kcal%	gm%
Carbohydrates	Soy, corn, wheat	64	46.1	Soy, corn, wheat	55	48.3	Soy, corn, wheat	64	46.4
Proteins	Caseins, soy	24	19.2	Soy	20	19.1	Soy	24	19.2
Fats	Milk fat	12	4.3	Soybean oil	25	10.5	Soybean oil	12	4.3
Vitamins Minerals	Calcium carbonate, dicalcium phosphate, premixed vitamins, premixed minerals, trace elements								

The Animal Source Diet Resulted in the Most Distinct Microbiota Composition of Mice With Human and Mouse Microbiota



A diet with a humanized profile could support the establishment of a human microbiota in mice, which will, however, still elicit a lower colonization efficiency compared to mice inoculated with a mouse microbiota.

p = 0.000

	Human Microbiota						Mouse Microbiota					
Inoculum	100%						100%					
Diet	AS		HP		C		AS		HP		C	
Time[G]												
P - T1	42%	±16	50%	±23	37%	±11	68%	±7	37%	±5	37%	±4
P - T2	48%	±0	48%	±4	38%	±2	70%	±10	63%	±6	62%	±4
F1 - T1	30%	±6	37%	±12	33%	±3	65%	±3	55%	±6	53%	±7
F1 - T2	30%	±4	40%	±9	36%	±4	68%	±8	61%	±6	65%	±6

Human microbiota diet: p = 0.009; p = 0.053. Mouse microbiota diet: p = 0.000; p = 0.000. Time: p = 0.044 (Human); p = 0.013, p = 0.000, p = 0.001, p = 0.022 (Mouse). Scale: 100%, 70%, 60%, 50%, 40%, 30%.

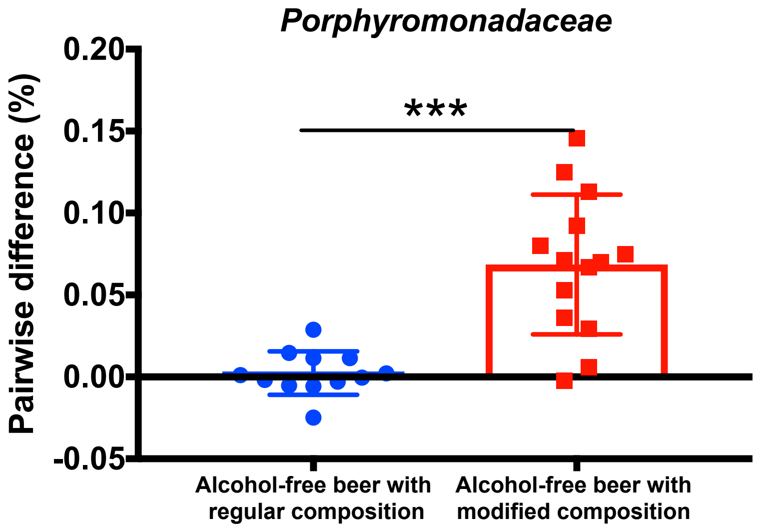
- Animal Source Diet Increased Regulatory T Cells in Mice With Human Microbiota.
- The Animal Source Diet Decreased the Number of Dendritic Cells in Mice With Mouse Microbiota.
- Mice With a Mouse Microbiota Have a Lower Expression of Some Pro-inflammatory Cytokine Genes.
- Mice With Human and Mouse Microbiota Differed in Gene Expression for Immune Cells, and the Human Profile Diet Increased the Expression of *Cd8a.*

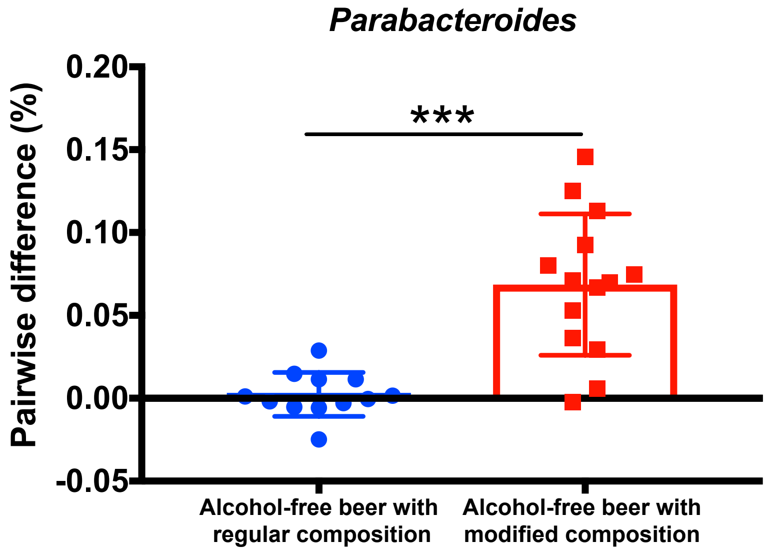
Moreno-Indias et al., 2020. Front Microbiol, 11:1336. doi: 10.3389/fmicb.2020.01336

Dietary fibre modulates specific gut microbiota members that may have beneficious metabolic functions for the host. The use of an alcohol-free beer with modified carbohydrates composition improves insulin-resistance in diabetic subjects with overweight or obesity through changes in gut microbiota.

Alcohol-free beer with modified carbohydrates composition:elimination of maltose and addiction of isomaltulose and resistant maltodextrin.

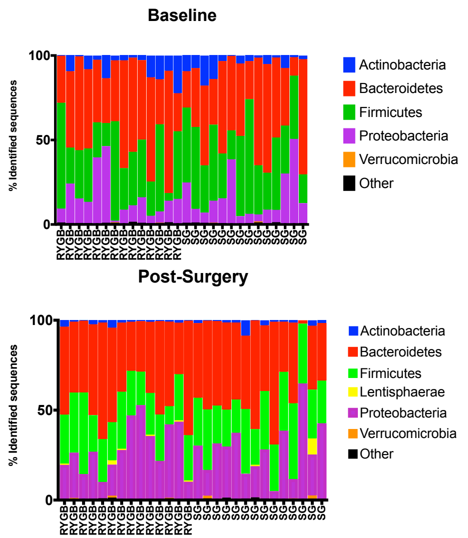
	Alcohol-free beer with regular composition			Alcohol-free beer with modified composition		
	$N = 14$			$N = 14$		
	Baseline	After intervention	*P*	Baseline	After intervention	*P*
Weight, kg	92.6 ± 13.7	89.6 ± 11.4	0.017	92.3 ± 12.1	89.8 ± 11.4	0.018
Body mass index, kg m^{-1} [b]	30.8 ± 3.48	29.9 ± 2.57	0.019	30.7 ± 2.66	29.9 ± 2.52	0.015
Waist circumference, cm	115 [104–121]	112 [103–113]	0.058	109 [97.5–113]	105 [96.6–113]	0.161
Fat mass, kg	28.82 ± 5.95	26.94 ± 4.95	0.042	27.9 ± 6.31	26.5 ± 5.64	0.214
Fat free mass, kg	62.0 ± 11.2	61.0 ± 11.2	0.589	63.3 ± 10.6	61.3 ± 10.4	0.457
Visceral fat, levels	14.2 ± 3.26	13.2 ± 2.76	0.027	13.4 ± 2.42	13.1 ± 2.92	0.355
Systolic blood pressure, mmHg	134± 13.3	132.43 ± 12.7	0.640	130 ± 12.2	130 ± 18.2	0.872
Diastolic blood pressure, mmHg	84.0 ± 8.34	81.9 ± 8.54	0.222	84.1 ± 9.74	81.1 ± 8.83	0.213
Total cholesterol, mg dL^{-1}	208 ± 25.4	204 ± 15.9	0.484	204 ± 20.9	206 ± 19.6	0.598
HDL cholesterol, mg dL^{-1}	54.3 ± 11.8	54.1 ± 8.87	0.931	54.6 ± 8.87	55.3 ± 11.9	0.605
Triglycerides, mg dL^{-1}	89.3 ± 23.5	92.0 ± 29.8	0.648	90.1 ± 26.4	79.6 ± 20.3	0.101
LDL cholesterol, mg dL^{-1}	136 ± 21.9	131 ± 14.4	0.336	132 ± 21.0	135 ± 18.7	0.249
Apolipoprotein B, mg dL^{-1}	101 ± 22.86	102 ± 11.3	0.221	102 ± 12.7	104 ± 14.8	0.473
Glucose, mg dL^{-1}	110 ± 13.3	107 ± 13.3	0.341	116 ± 20.0	111 ± 16.4	0.047
Insulin, μUI mL^{-1}	9.11 ± 4.61	8.69 ± 4.34	0.619	9.81 ± 4.10	8.52 ± 3.30	0.098
HOMA-IR	2.51 ± 1.49	2.27 ± 1.08	0.447	2.86 ± 1.48	2.36 ± 1.08	0.023
HbA1c, %	5.84 ± 0.61	5.75 ± 0.48	0.409	5.84 ± 0.49	5.77 ± 0.53	0.426
GGT, U L^{-1}	22.5 [18.8–35.8]	23.5 [18.8–30.0]	0.071	25.0 [17.8–34.3]	22.5 [16.0–31.8]	0.327
AST, U L^{-1}	29.5 [25.0–34.0]	24.0 [22.0–26.8]	0.005	24.0 [20.8–28.3]	25.0 [23.0–29.0]	0.779
ALT, U L^{-1}	28.5 [20.8–35.5]	23.5 [18.8–28.5]	0.013	23.5 [18.5–31.0]	25.0 [20.8–29.3]	0.681
CRP, mg dL^{-1}	0.16 [0.08–0.32]	0.17 [0.11–0.42]	0.177	0.15 [0.12–0.26]	0.19 [0.11–0.37]	0.959

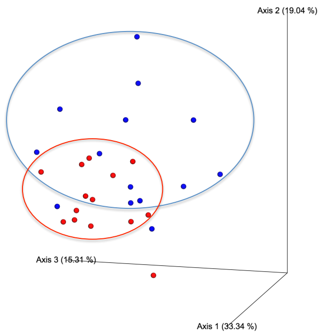


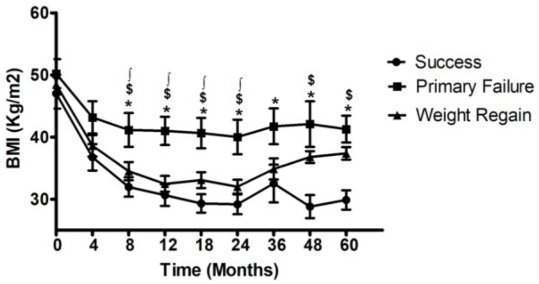


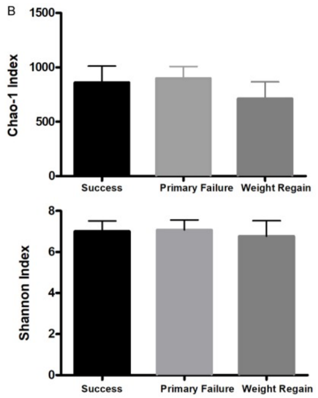
Mateo-Gallego et al., 2021. Food Funct. 12(8):3635-3646. doi: 10.1039/d0fo03160g.

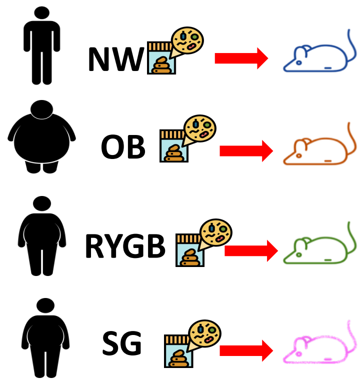
Bariatric surgery modified gut microbiota in a procedure-manner and may participate in the success of the operation. These changes are related to metabolic improvements that can be transferred by FMTs

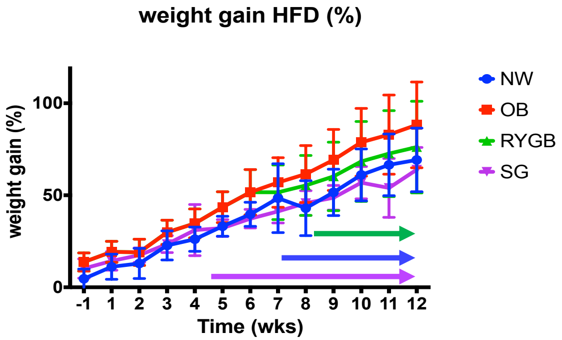


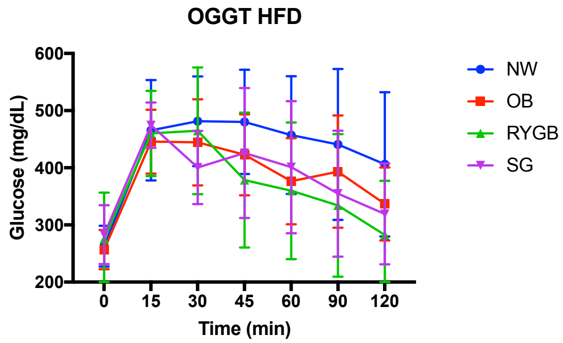












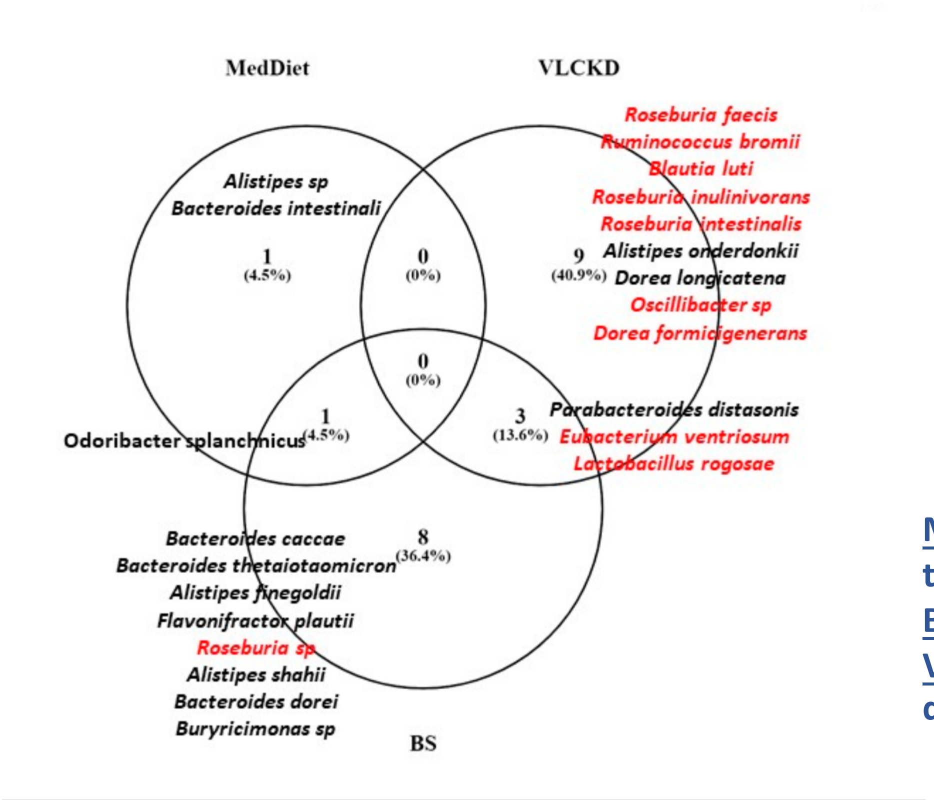
Sánchez-Alcoholado et al., 2019. Surg Obes Relat Dis. 15(11):1888-1895. doi: 10.1016/j.soard.2019.08.551

Gutiérrez-Repiso et al., 2019. Am J Transl Res., 11(2):942-952. PMCID: PMC6413284

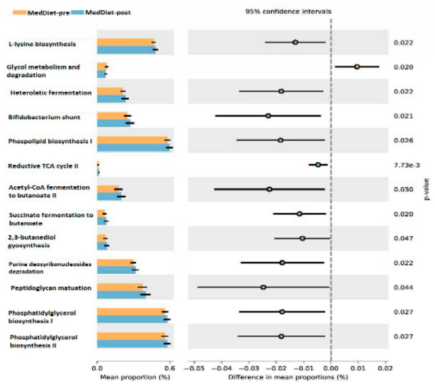
Aguilar-Lineros et al. 2021. ECO2021-ePoster Abstract discussion AD01.03

Weight loss has not a similar pattern of changes in gut microbiota, however each procedure is able to change gut microbiota functional pathways in a different manner

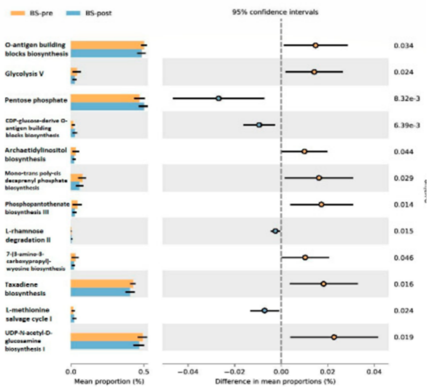
We could not identify a common taxon that had significantly changed within the three weight loss interventions



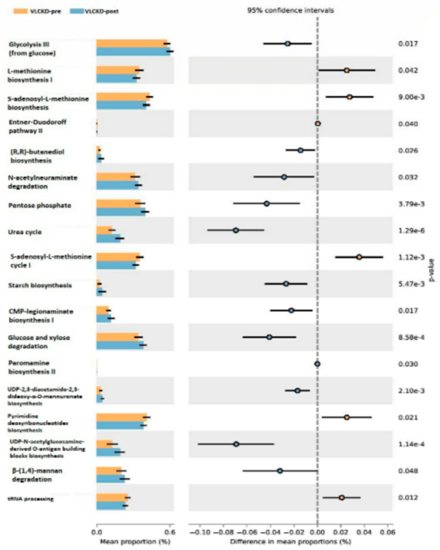
MedDiet



BS



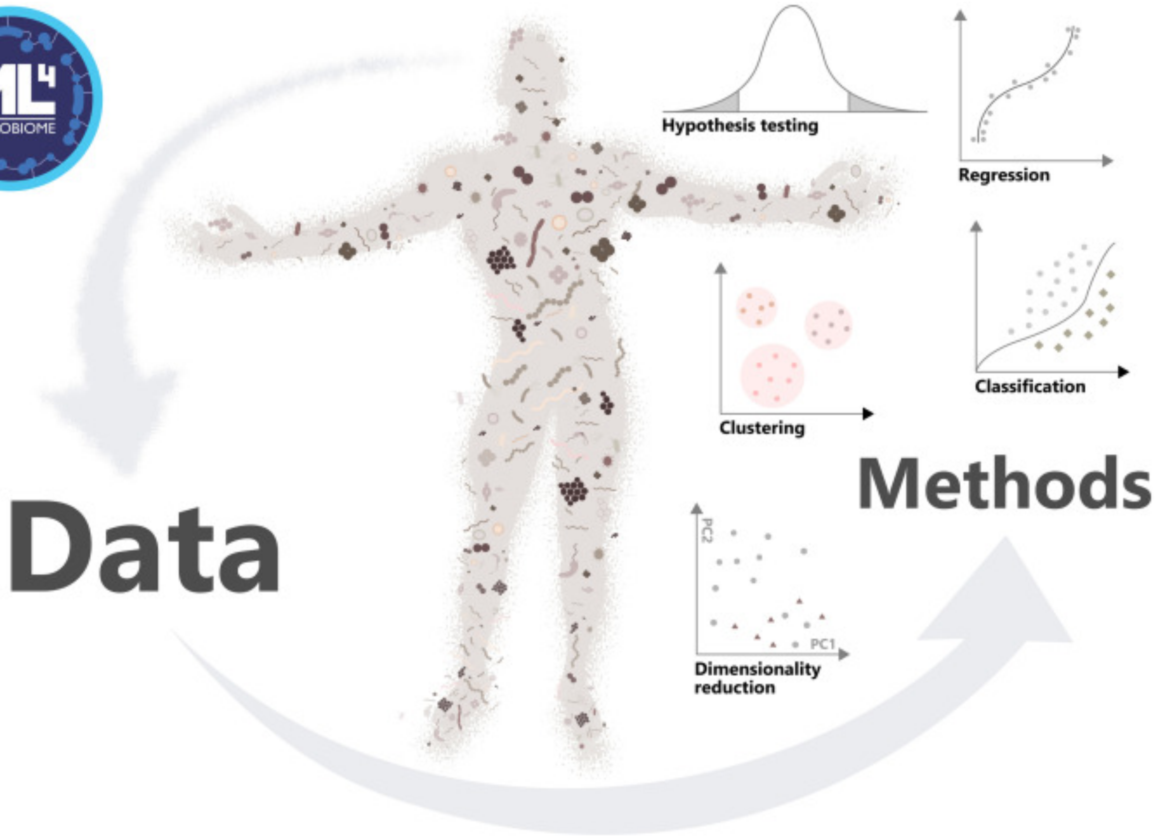
VLCKD



MedDiet: Enriched in several pathways related to fermentation to SCFAs.
BS: Decrease most of the biosynthesis pathways.
VLCKD: Biosynthesis and degradation/utilization/assimilation

Gutiérrez-Repiso et al., 2021. J Pers Med, 11(2):109. doi: 10.3390/jpm11020109.

Microbiome research will drive the change of the field in personalized medicine, but new approaches are needed to learn to see beyond apparent trends: Machine Learning techniques gather the necessary characteristics.



Please, visit: www.ml4microbiome.eu

Marcos-Zambrano et al., 2021. Front Microbiol. 12:634511. doi: 10.3389/fmicb.2021.634511
Moreno-Indias et al., 2021. Front Microbiol, 12:635781. doi: 10.3389/fmicb.2021.635781.

Take home messages

- Gut microbiota should be paid attention as any other organ.
- Gut microbiota is a group that interacts each other under ecological rules.
- Gut microbiota is multifaceting, displaying both beneficial and detrimental effects on the host.
- Gut microbiota can be modified. Dietary interventions and antibiotics produce generalized changes.
- Gut microbiota-based products are being developed: prebiotics, probiotics, symbiotics, dietary approaches, FMTs are the future. The more precision in the target, the better.

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THANK YOU!!
And if you have any question, please, ask or email me to Isabel.moreno@ibima.eu