Curso Nutrigenomica y Avanzado

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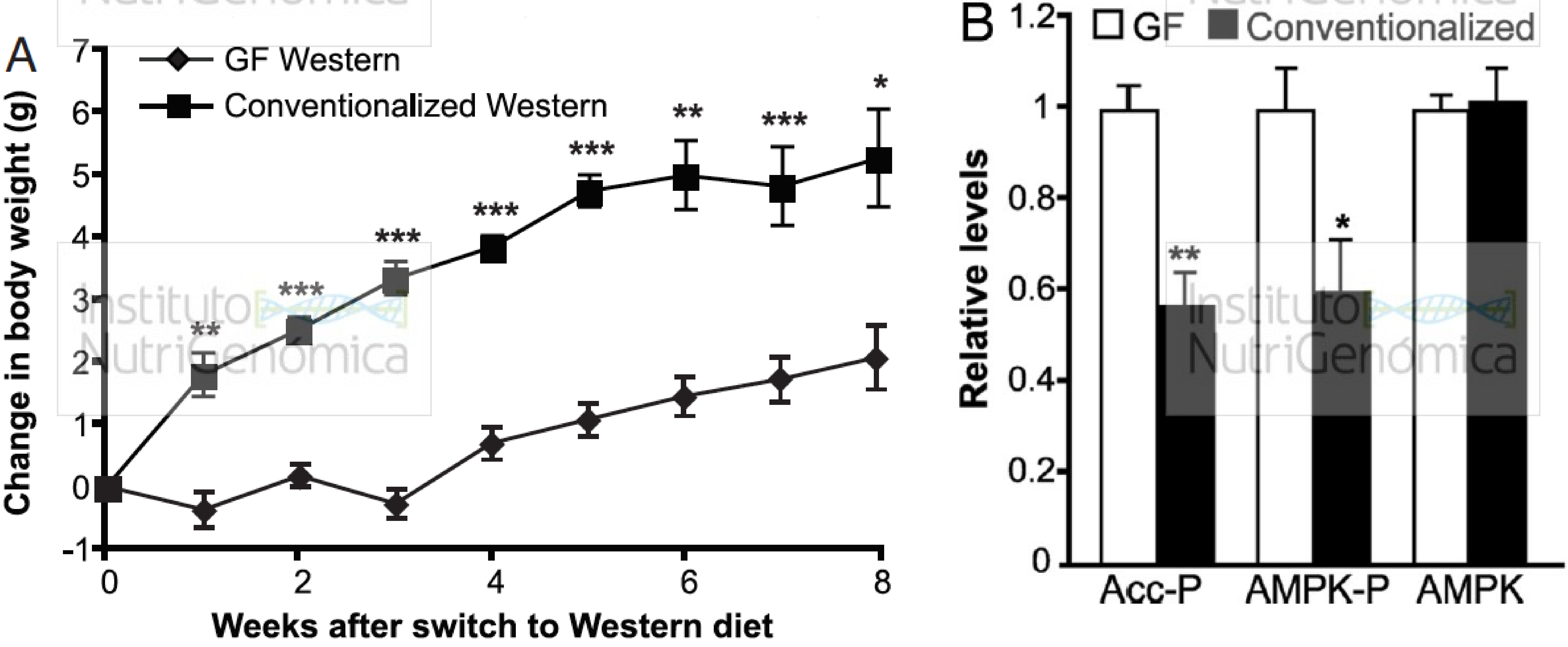
Microbiota y síndorme metabólico
- Obesidad e insulinorresistencia -

Índice

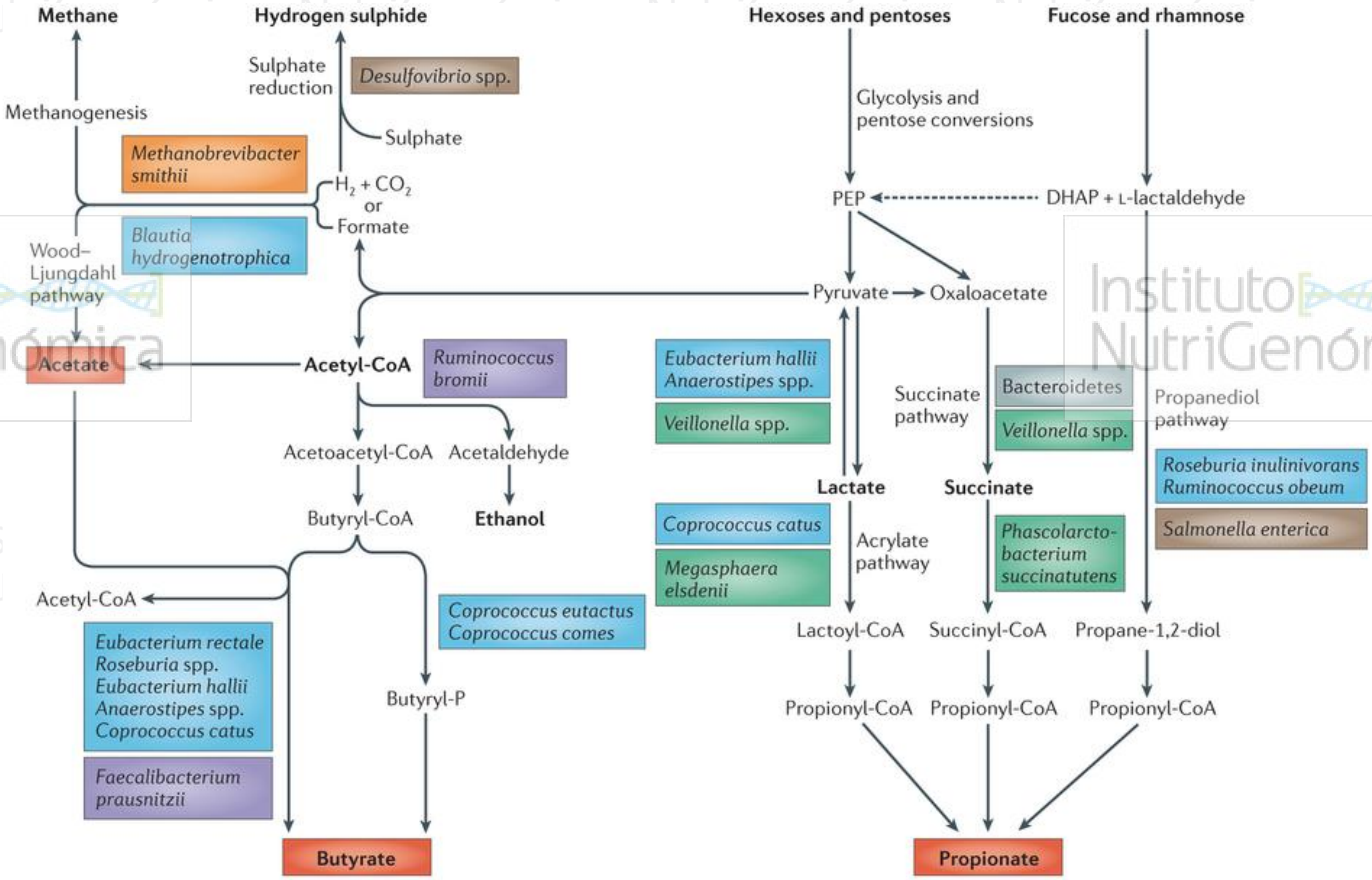
Mechanisms underlying the resistance to diet-induced obesity in germ-free mice

(Backhed et al, 2007)
PNAS 105:2117-2122



Fermentación colónica

Fracción indigerible + Flora bacteria = Gases (CO_2, H_2, metano)
+ Biomasa
+ Acidos grasos de cadena corta (acetico,propionico, butírico)
+ Acidos orgánicos (láctico, succínico y pirúvico)
+ Otros productos de fermentación (sustancias tóxicas, amoniaco, aminas, nitrosaminas), antioxidantes, etc.



Microbiota and SCFA in lean and overweight healthy subjects

(Schwiertz et al, 2009)
Obesity 18:190-195.

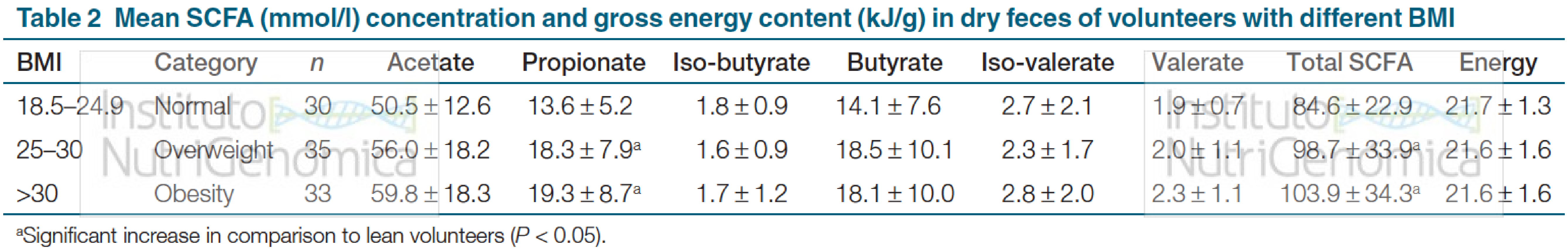


Table 2 Mean SCFA (mmol/l) concentration and gross energy content (kJ/g) in dry feces of volunteers with different BMI

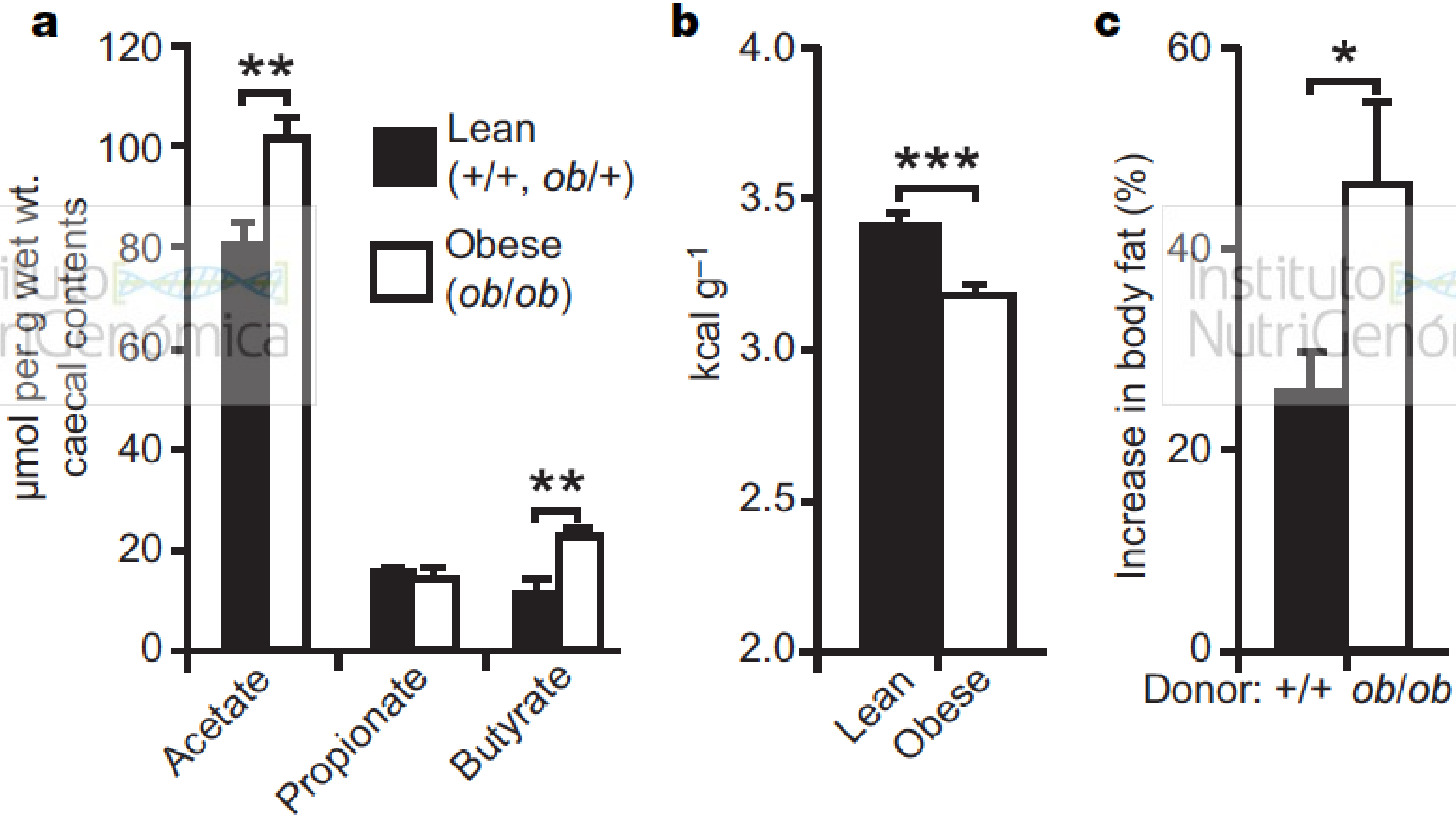
BMI	Category	*n*	Acetate	Propionate	Iso-butyrate	Butyrate	Iso-valerate	Valerate	Total SCFA	Energy
18.5–24.9	Normal	30	50.5 ± 12.6	13.6 ± 5.2	1.8 ± 0.9	14.1 ± 7.6	2.7 ± 2.1	1.9 ± 0.7	84.6 ± 22.9	21.7 ± 1.3
25–30	Overweight	35	56.0 ± 18.2	18.3 ± 7.9[a]	1.6 ± 0.9	18.5 ± 10.1	2.3 ± 1.7	2.0 ± 1.1	98.7 ± 33.9[a]	21.6 ± 1.6
>30	Obesity	33	59.8 ± 18.3	19.3 ± 8.7[a]	1.7 ± 1.2	18.1 ± 10.0	2.8 ± 2.0	2.3 ± 1.1	103.9 ± 34.3[a]	21.6 ± 1.6

[a] Significant increase in comparison to lean volunteers ($P < 0.05$).

An obesity-associated gut microbiome with increased capacity for energy harvest

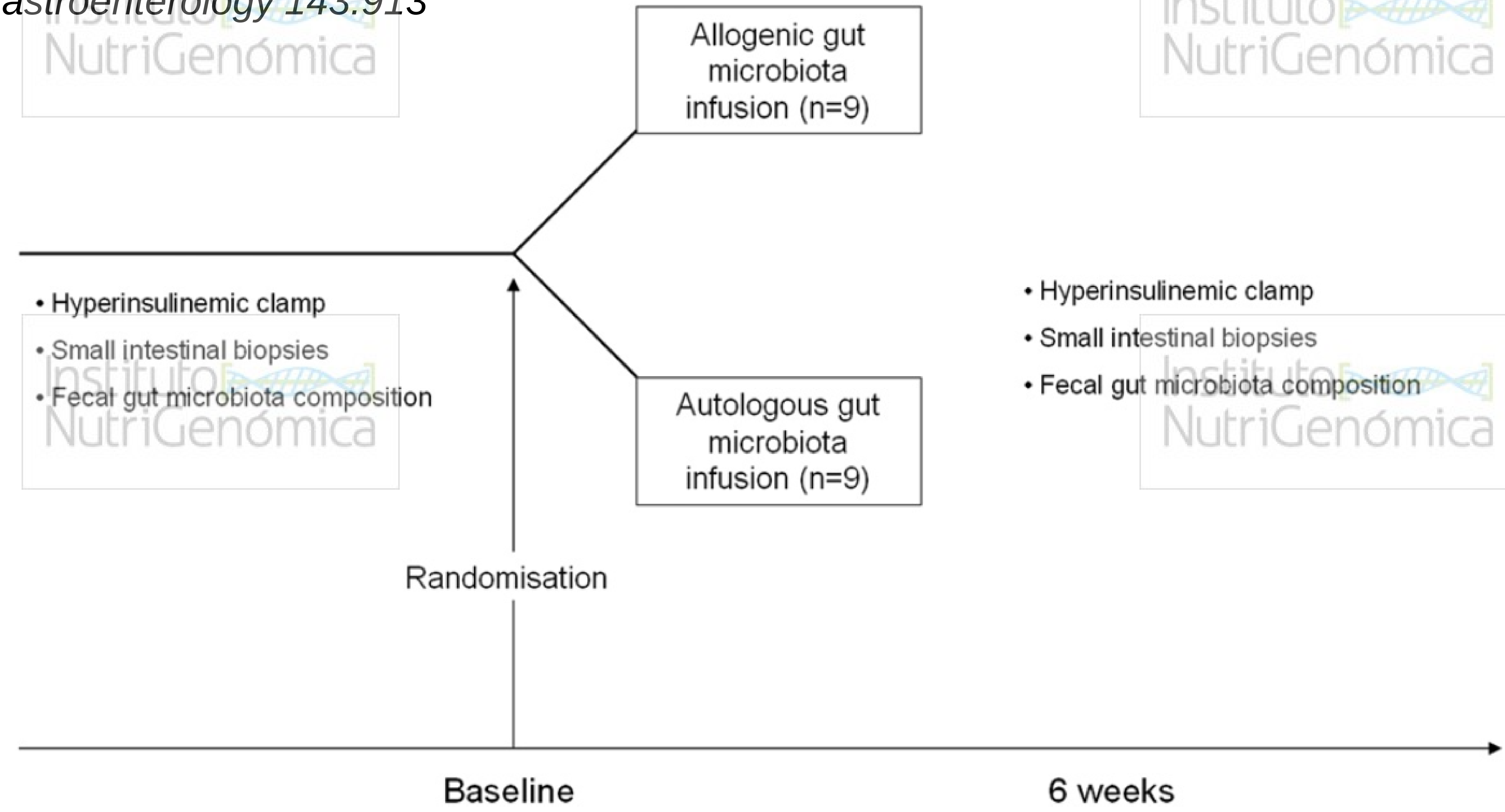
(Turnbaugh et al, 2006)

Nature 444:1027-1031



Transfer of intestinal microbiota from lean donors increases insulin sensitivity in individuals with metabolic syndrome

(Vrieze et al, 2012)
Gastroenterology 143:913



Allogenic gut microbiota infusion (n=9)

Autologous gut microbiota infusion (n=9)

- Hyperinsulinemic clamp
- Small intestinal biopsies
- Fecal gut microbiota composition

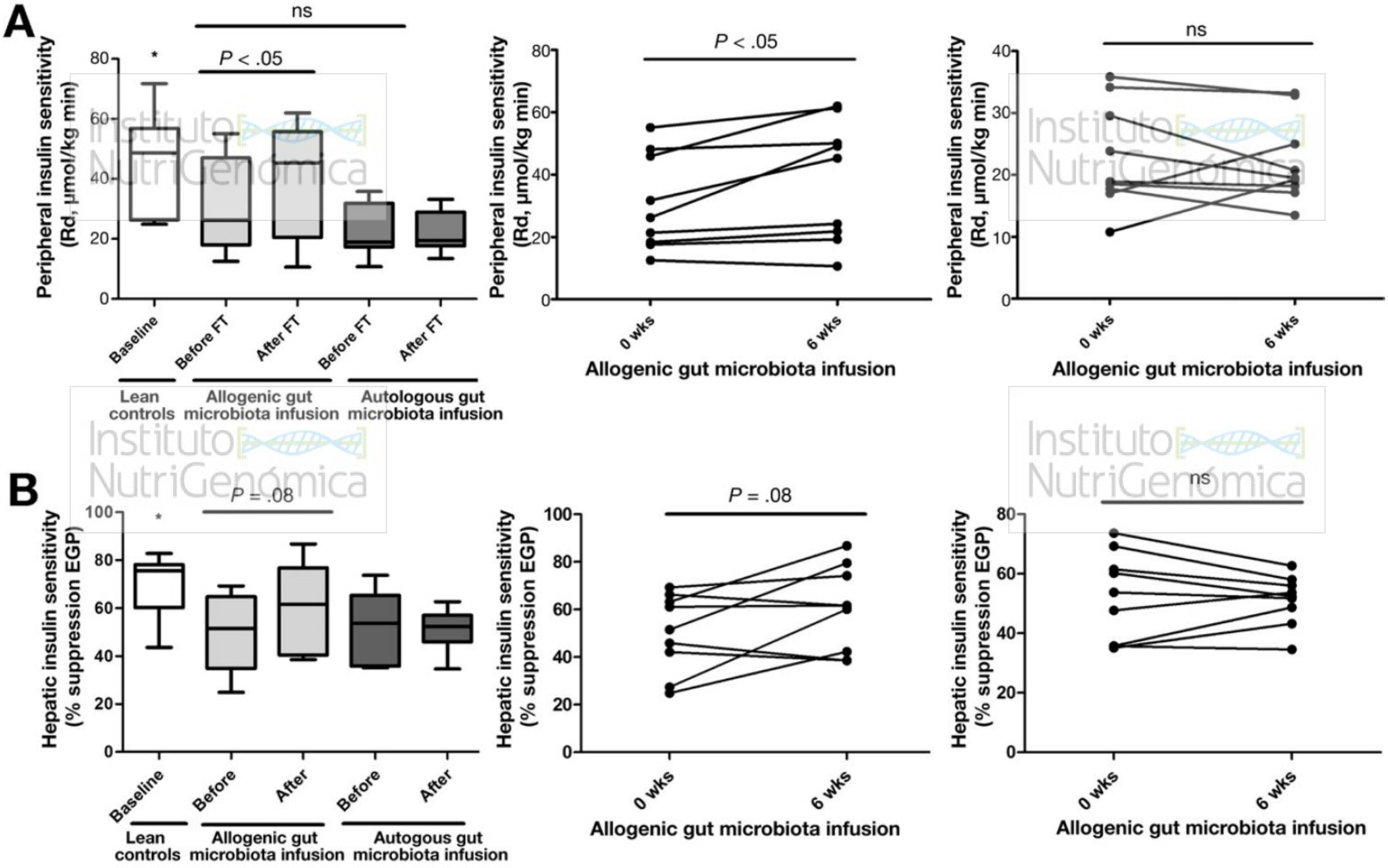
Randomisation

- Hyperinsulinemic clamp
- Small intestinal biopsies
- Fecal gut microbiota composition

Baseline

6 weeks

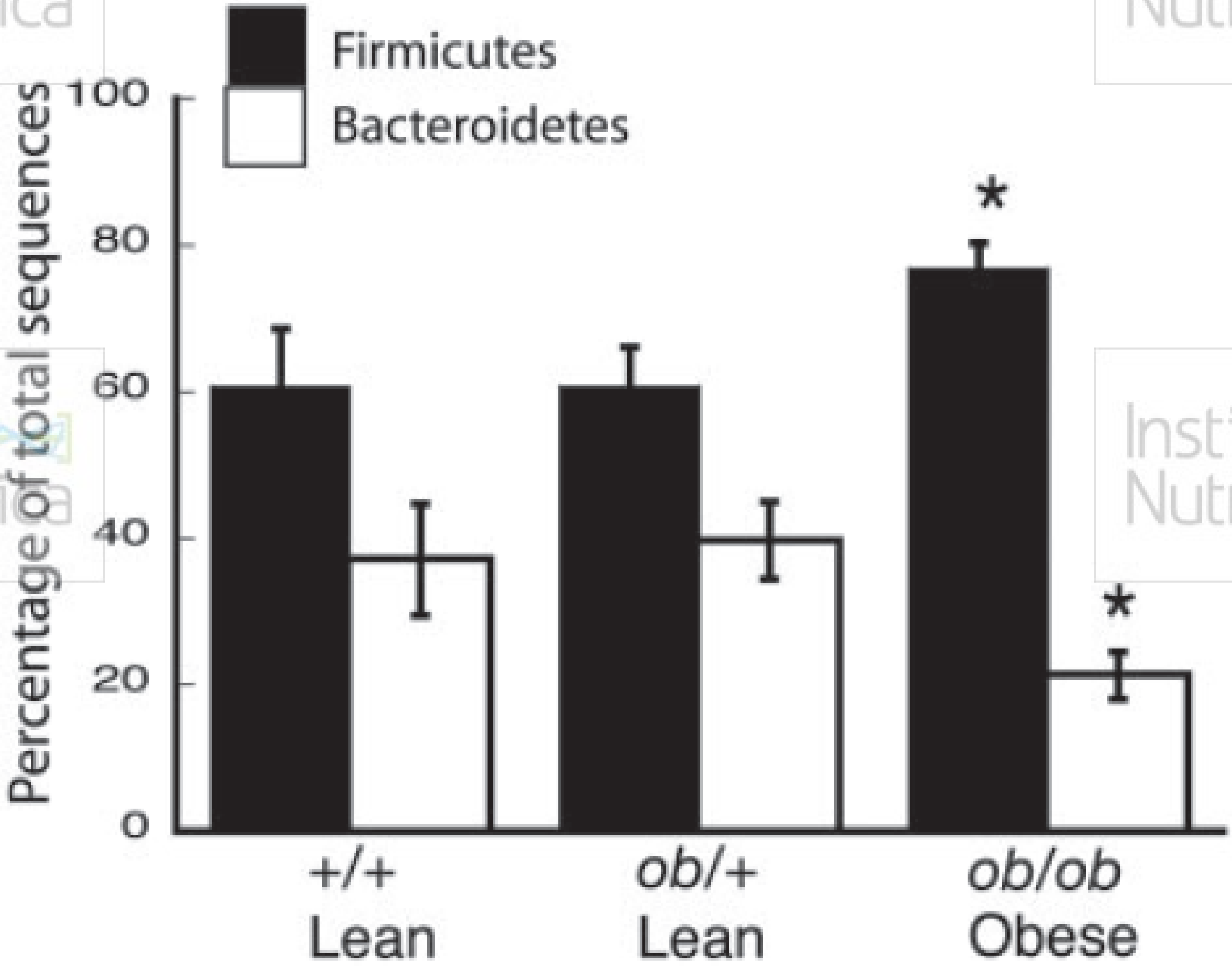
Supplementary Figure 1. Overview of study scheme.


A
ns
*
P < .05
Peripheral insulin sensitivity (Rd, µmol/kg min)
80
60
40
20
0
Baseline
Before FT
After FT
Before FT
After FT
Lean controls
Allogenic gut microbiota infusion
Autologous gut microbiota infusion
P < .05
0 wks
6 wks
Allogenic gut microbiota infusion
ns
40
30
20
10
0
0 wks
6 wks
Allogenic gut microbiota infusion
B
P = .08
*
Hepatic insulin sensitivity (% suppression EGP)
100
80
60
40
20
0
Baseline
Before
After
Before
After
Lean controls
Allogenic gut microbiota infusion
Autogous gut microbiota infusion
P = .08
0 wks
6 wks
Allogenic gut microbiota infusion
ns
0 wks
6 wks
Allogenic gut microbiota infusion

Obesity alters gut microbial ecology.

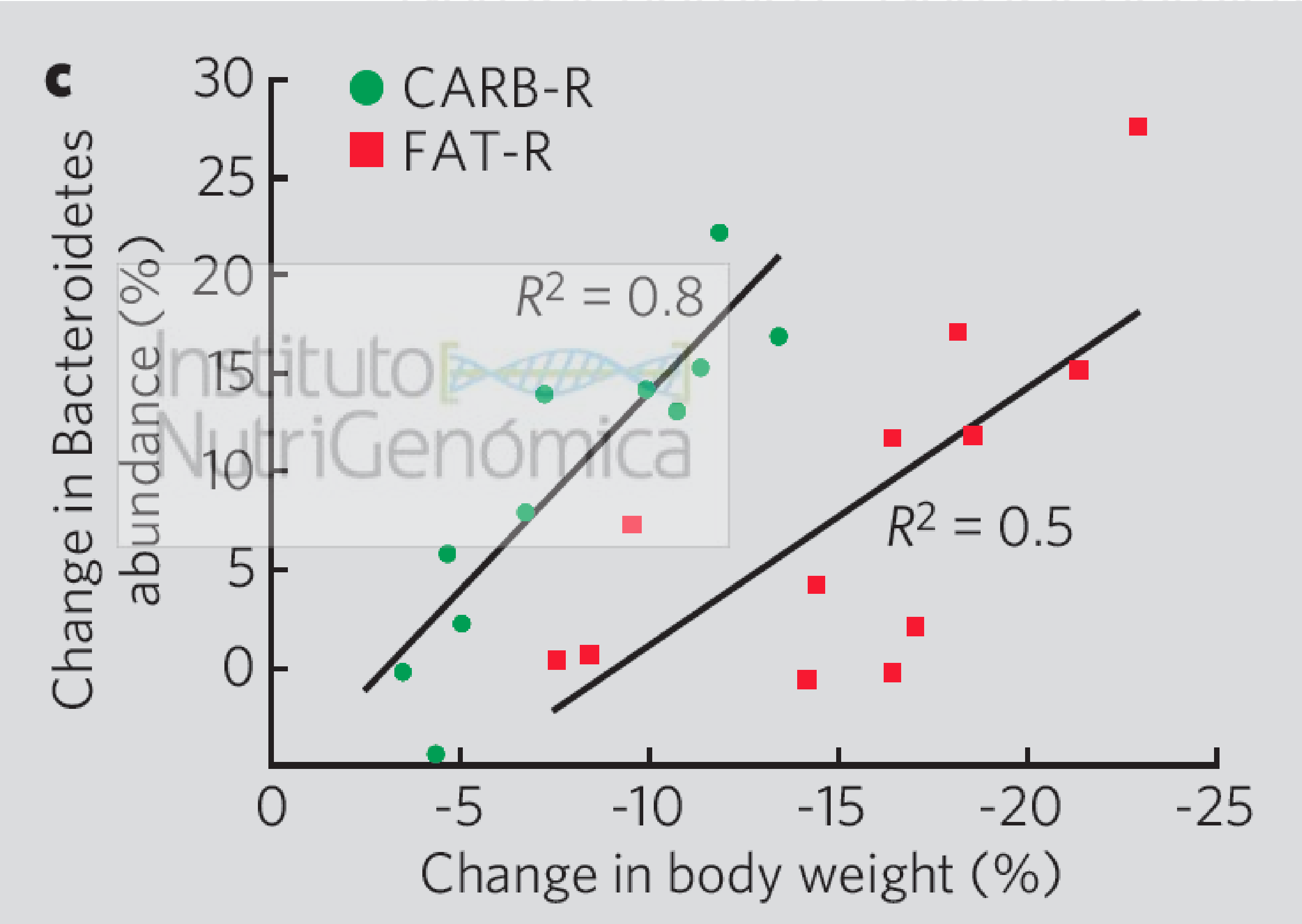
(Ley et al, 2005)

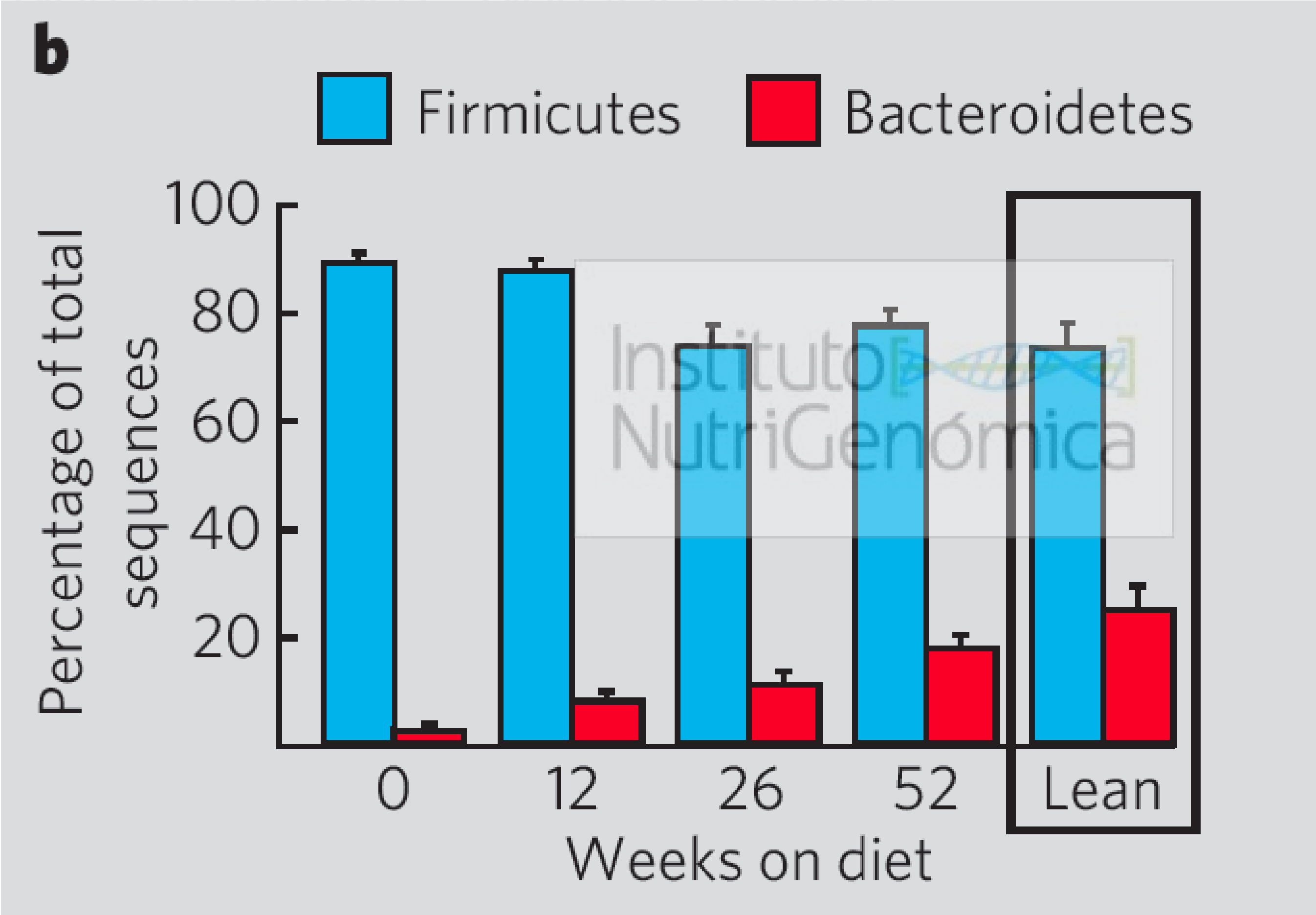
Proc Natl Acad Sci U S A. 102:11070-5.



Microbial ecology: Human gut microbes associated with obesity

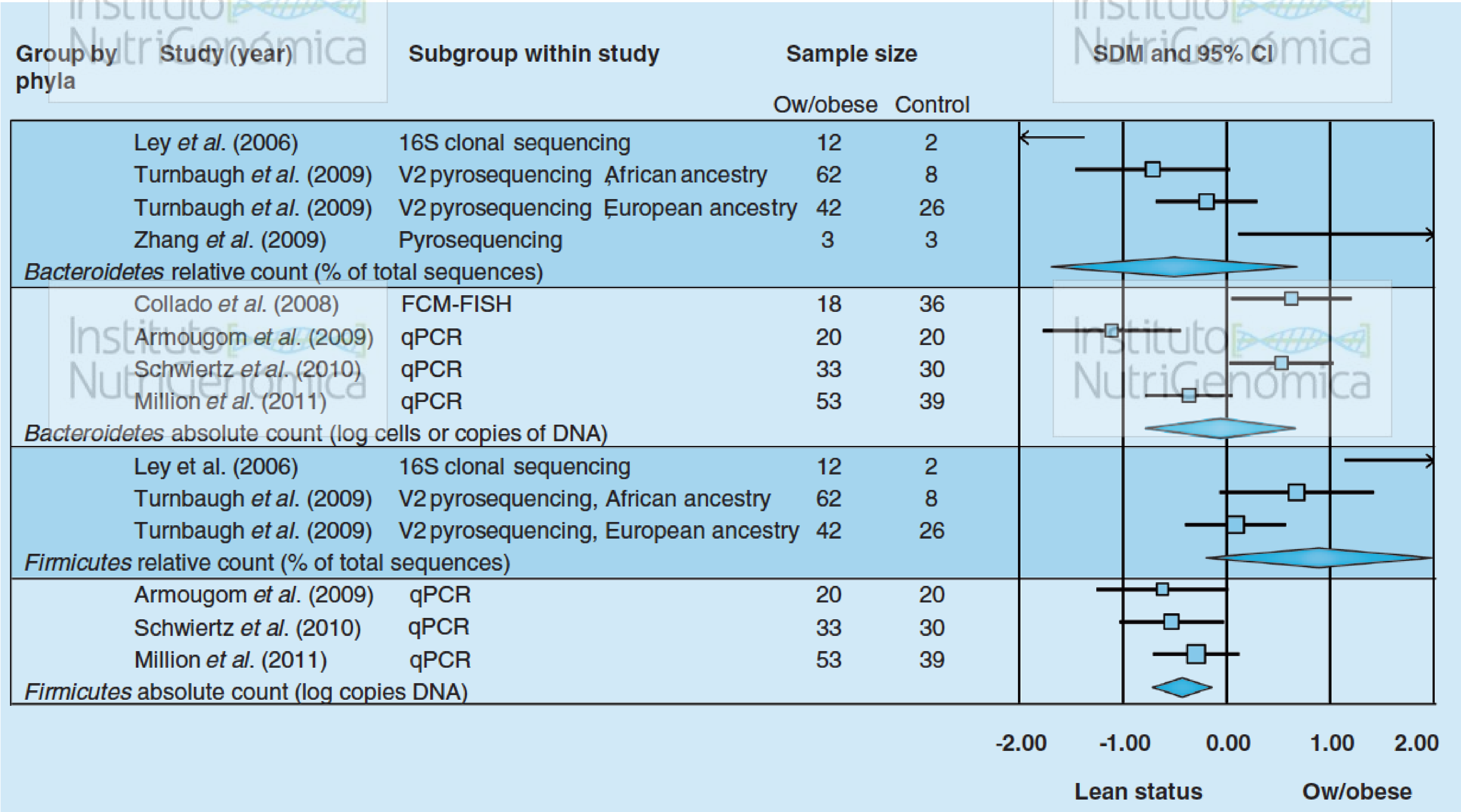
(Ley et al, 2006)
Nature 444:1022-1023





The relationship between gut microbiota and weight gain in humans

(Angelakis et al, 2012)
Fut Microbiol 7:91-109.



Group by phyla	Study (year)	Subgroup within study	Sample size Ow/obese	Sample size Control
	Ley *et al.* (2006)	16S clonal sequencing	12	2
	Turnbaugh *et al.* (2009)	V2 pyrosequencing African ancestry	62	8
	Turnbaugh *et al.* (2009)	V2 pyrosequencing European ancestry	42	26
	Zhang *et al.* (2009)	Pyrosequencing	3	3
Bacteroidetes relative count (% of total sequences)				
	Collado *et al.* (2008)	FCM-FISH	18	36
	Armougom *et al.* (2009)	qPCR	20	20
	Schwiertz *et al.* (2010)	qPCR	33	30
	Million *et al.* (2011)	qPCR	53	39
Bacteroidetes absolute count (log cells or copies of DNA)				
	Ley et al. (2006)	16S clonal sequencing	12	2
	Turnbaugh *et al.* (2009)	V2 pyrosequencing, African ancestry	62	8
	Turnbaugh *et al.* (2009)	V2 pyrosequencing, European ancestry	42	26
Firmicutes relative count (% of total sequences)				
	Armougom *et al.* (2009)	qPCR	20	20
	Schwiertz *et al.* (2010)	qPCR	33	30
	Million *et al.* (2011)	qPCR	53	39
Firmicutes absolute count (log copies DNA)				

The relationship between gut microbiota and weight gain in humans

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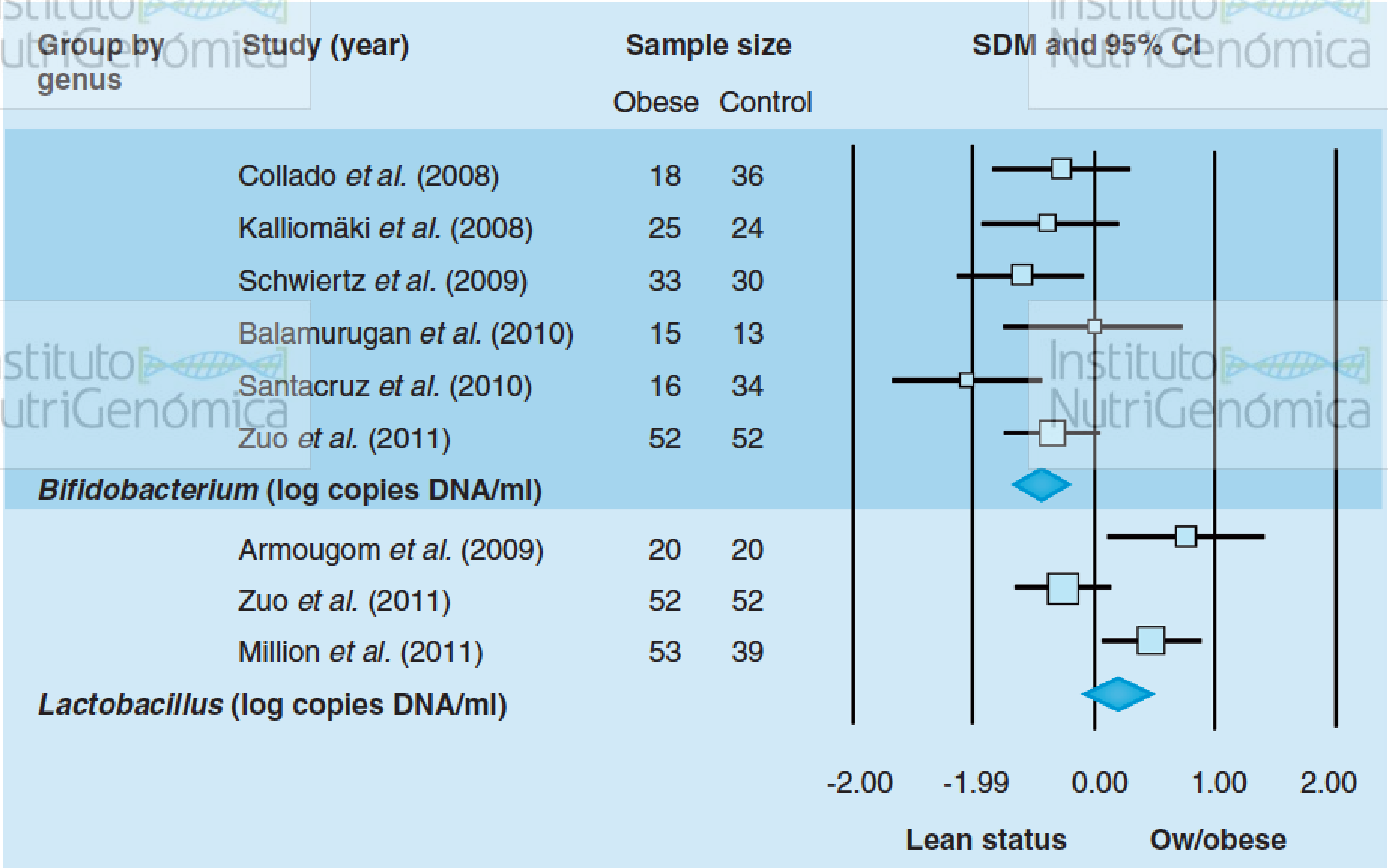
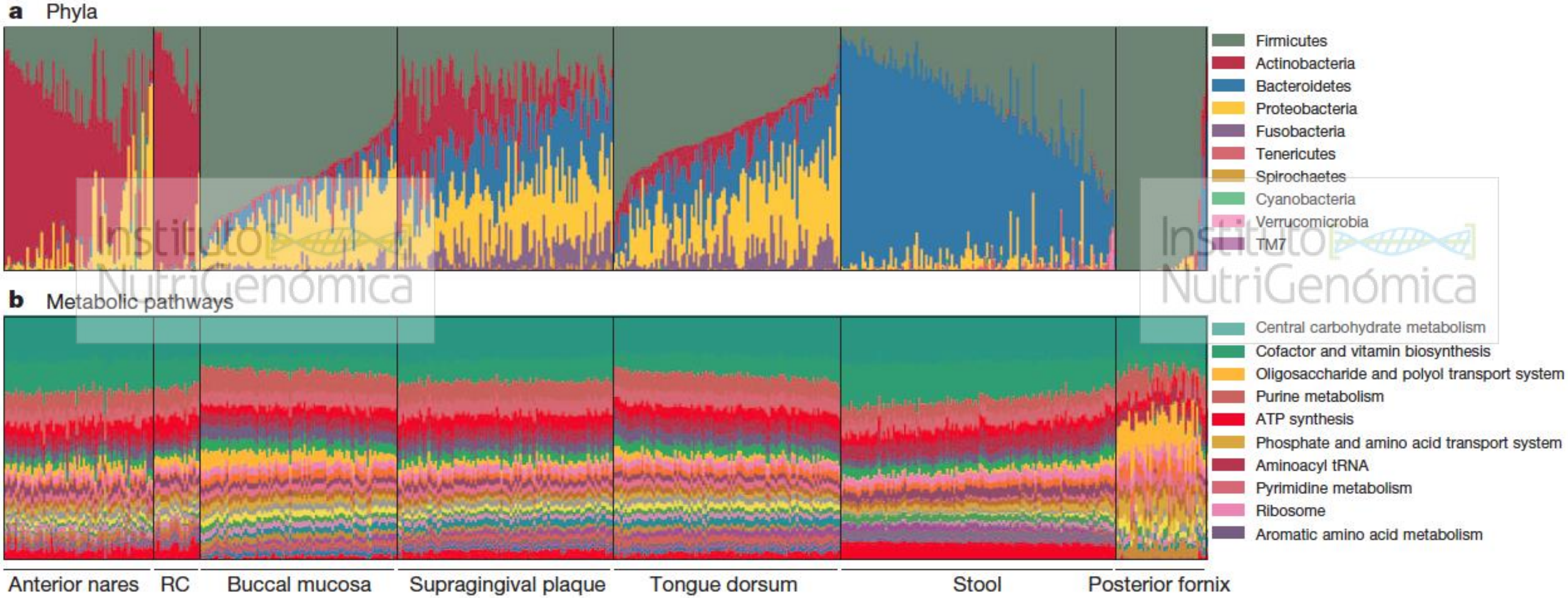


Group by genus	Study (year)	Sample size Obese	Sample size Control
	Collado *et al.* (2008)	18	36
	Kalliomäki *et al.* (2008)	25	24
	Schwiertz *et al.* (2009)	33	30
	Balamurugan *et al.* (2010)	15	13
	Santacruz *et al.* (2010)	16	34
	Zuo *et al.* (2011)	52	52
***Bifidobacterium* (log copies DNA/ml)**			
	Armougom *et al.* (2009)	20	20
	Zuo *et al.* (2011)	52	52
	Million *et al.* (2011)	53	39
***Lactobacillus* (log copies DNA/ml)**			

Structure, function and diversity of the healthy human microbiome

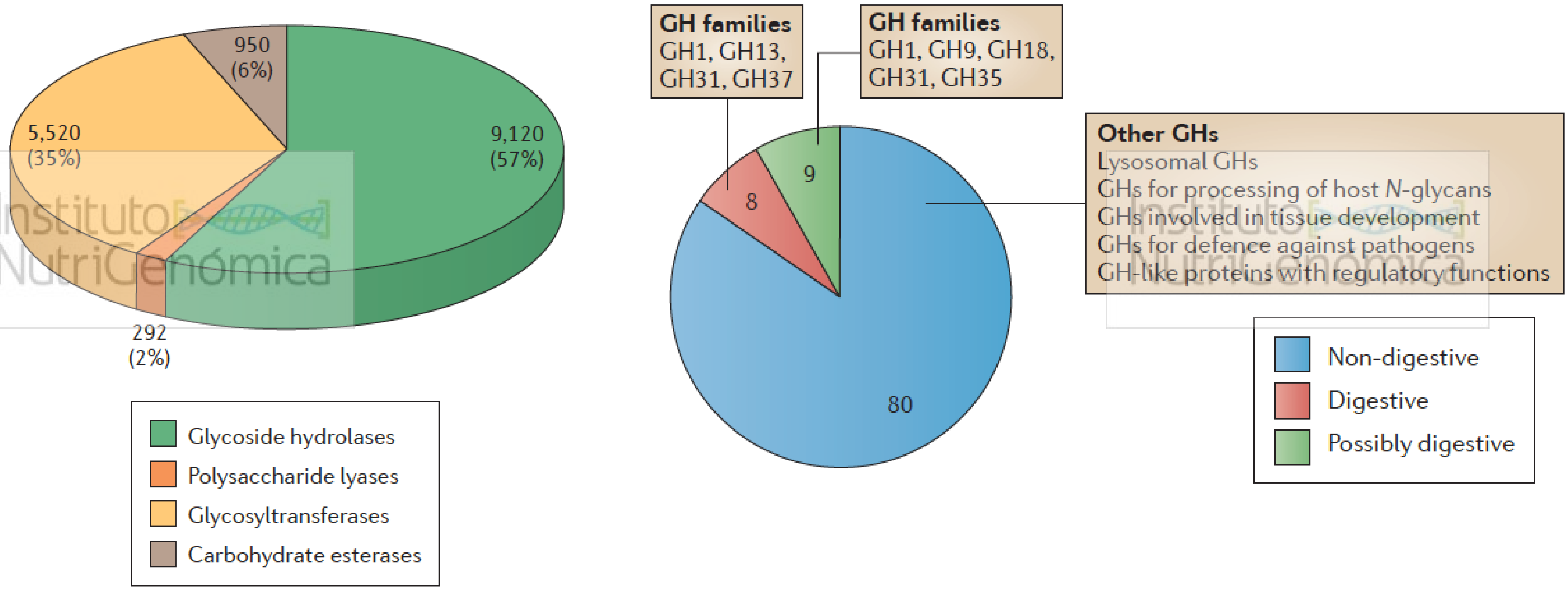
The human microbiome project consortium, 2012
Nature 486, 207-214.

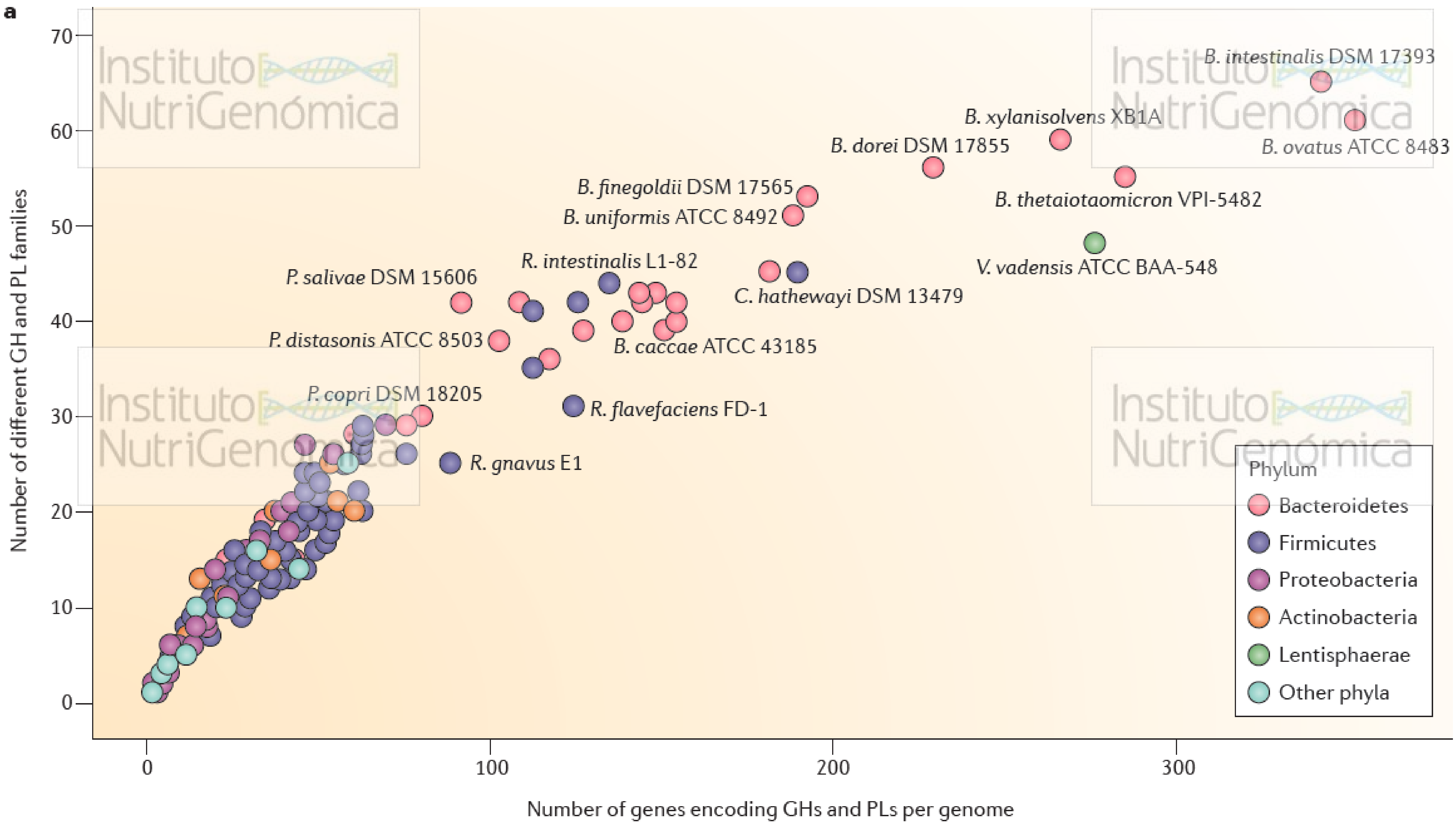


The abundance and variety of carbohydrate-active enzymes in the human gut microbiota

(El Kaoutari et al, 2013)

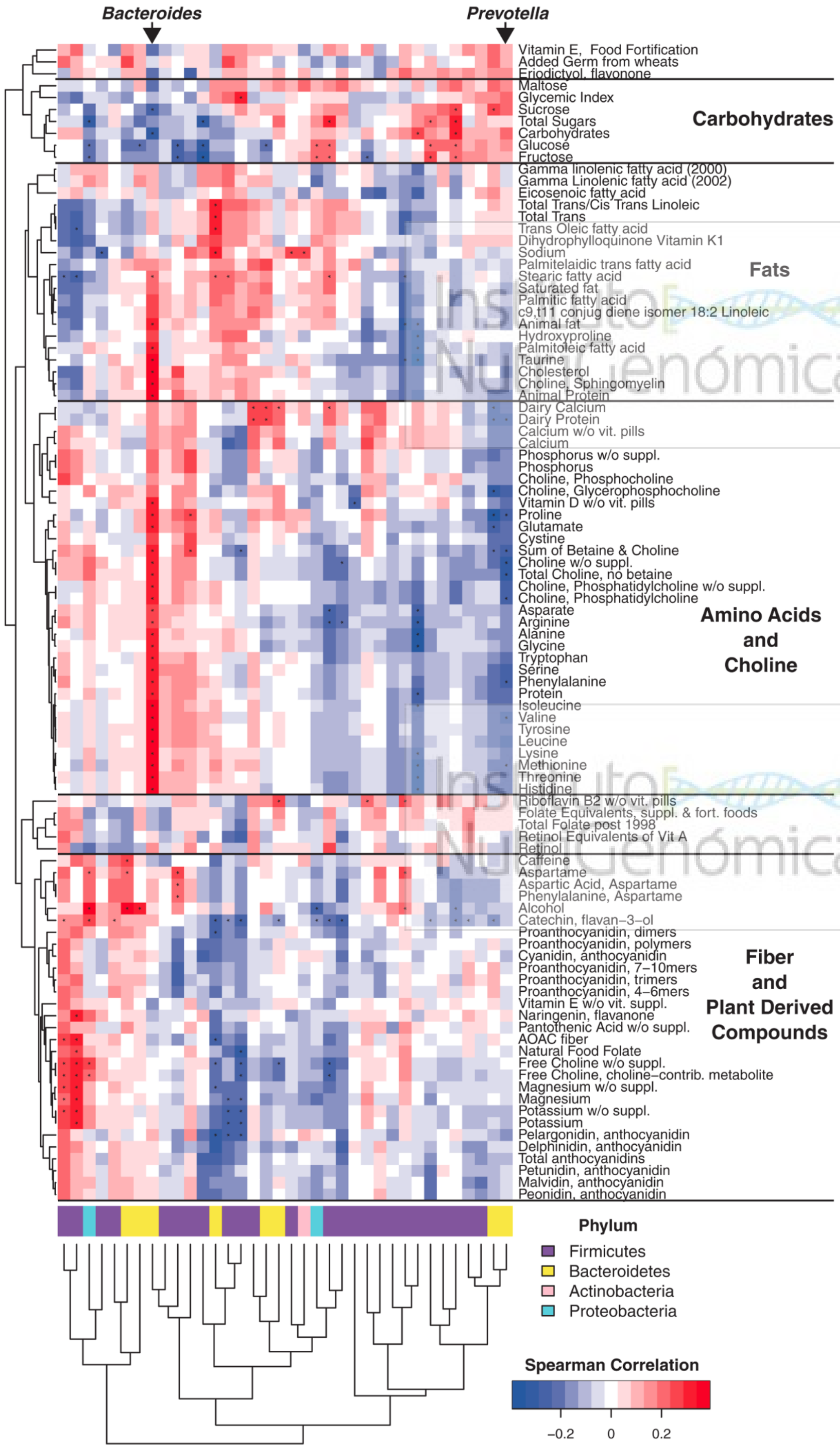
Nature reviews Microbiology 11:497




a
Number of different GH and PL families
70
60
50
40
30
20
10
0
0
100
200
300
Number of genes encoding GHs and PLs per genome
B. intestinalis DSM 17393
B. xylanisolvens XB1A
B. ovatus ATCC 8483
B. dorei DSM 17855
B. thetaiotaomicron VPI-5482
B. finegoldii DSM 17565
B. uniformis ATCC 8492
V. vadensis ATCC BAA-548
R. intestinalis L1-82
P. salivae DSM 15606
C. hathewayi DSM 13479
P. distasonis ATCC 8503
B. caccae ATCC 43185
P. copri DSM 18205
R. flavefaciens FD-1
R. gnavus E1
Phylum
Bacteroidetes
Firmicutes
Proteobacteria
Actinobacteria
Lentisphaerae
Other phyla

Linking long-term dietary patterns with gut microbial enterotypes

(Wu et al, 2011)
Science 334:105-8.



Microbiota y síndorme metabólico
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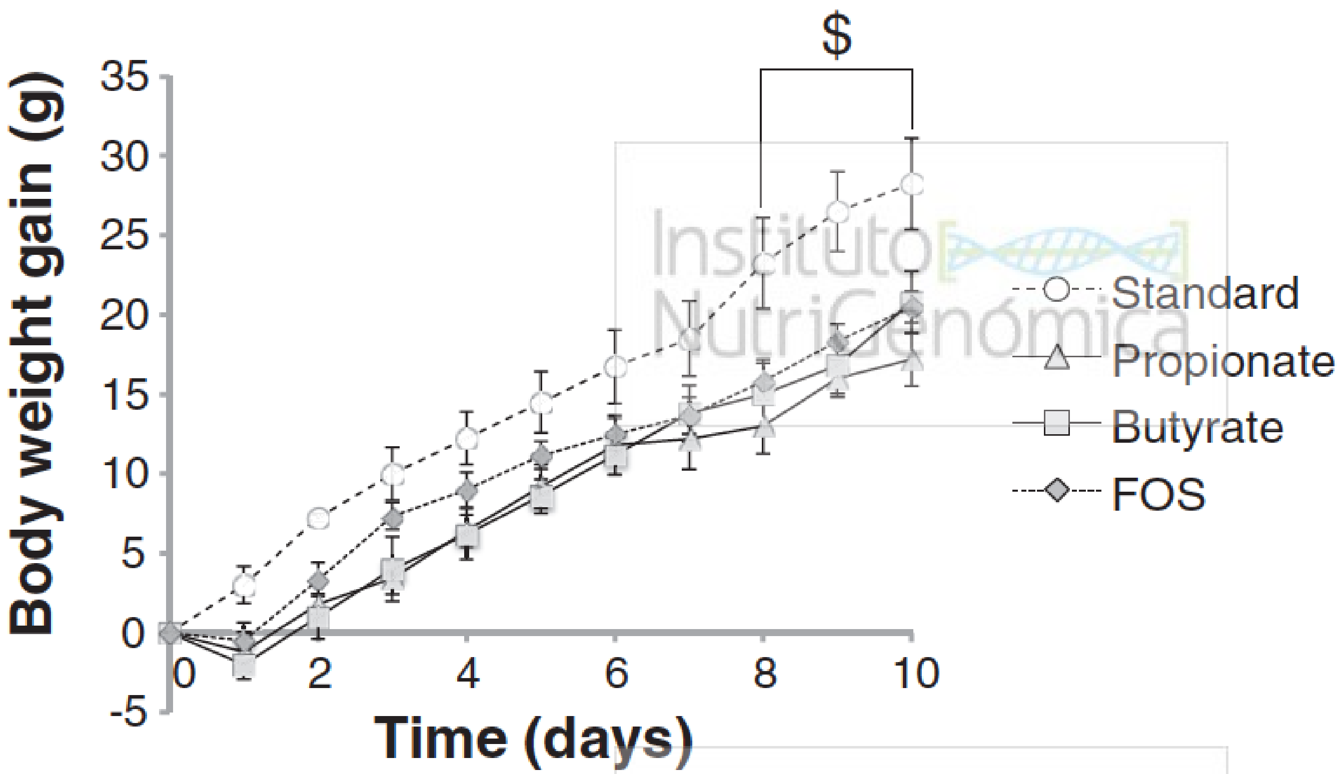
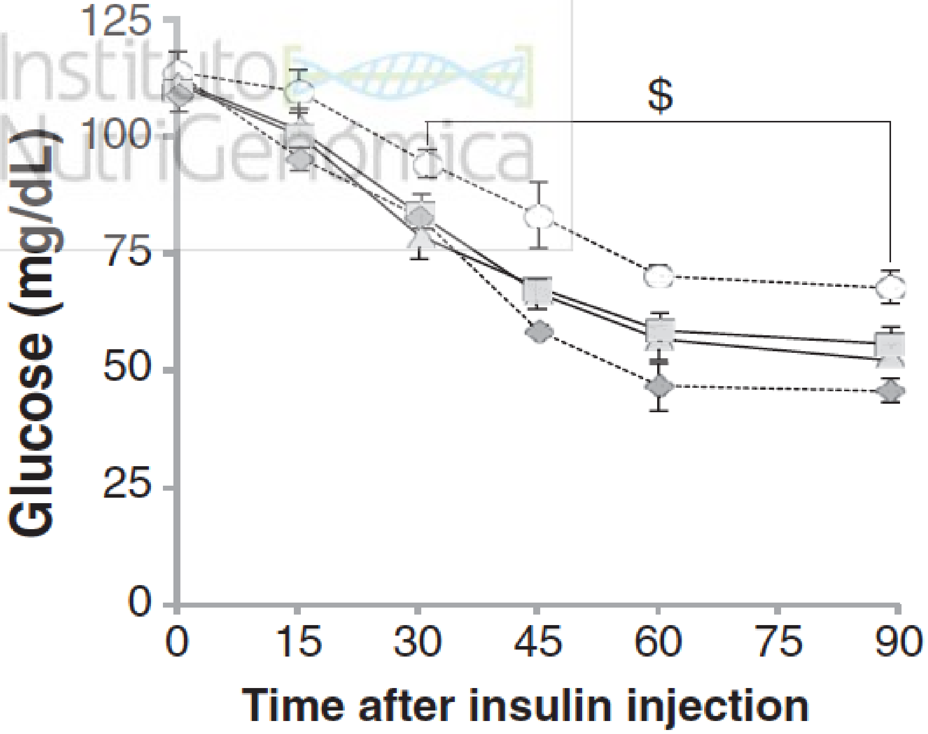
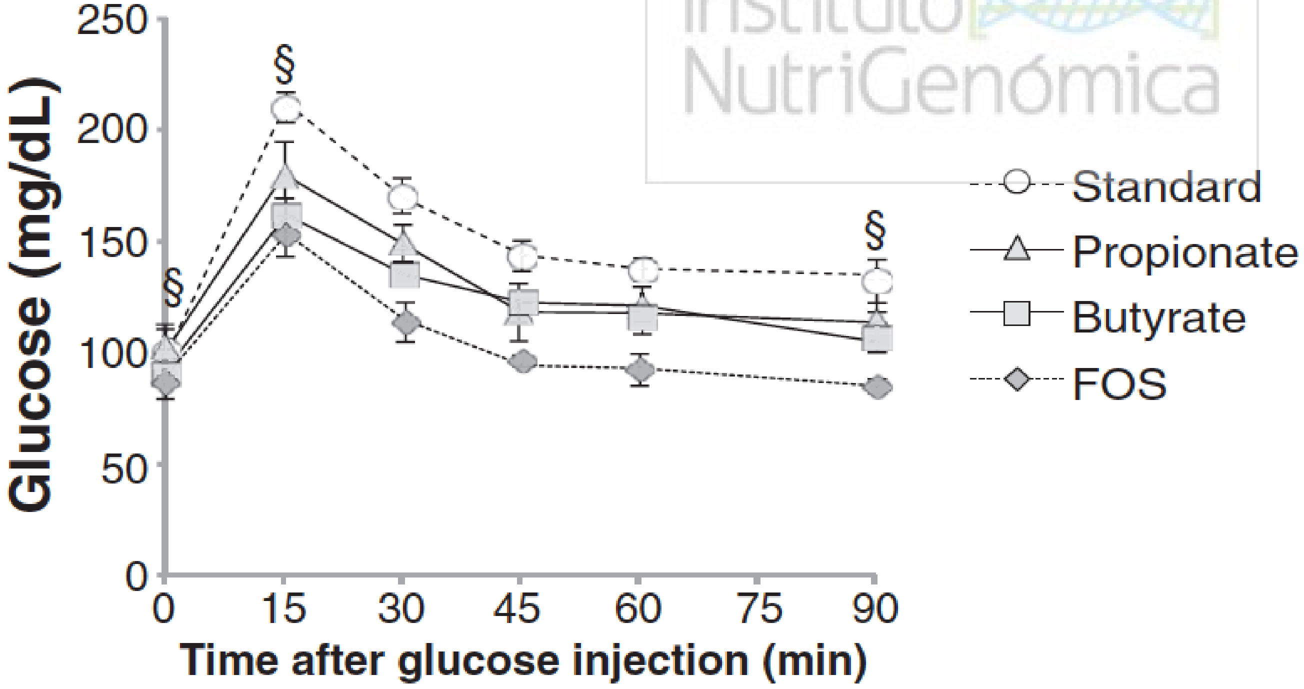
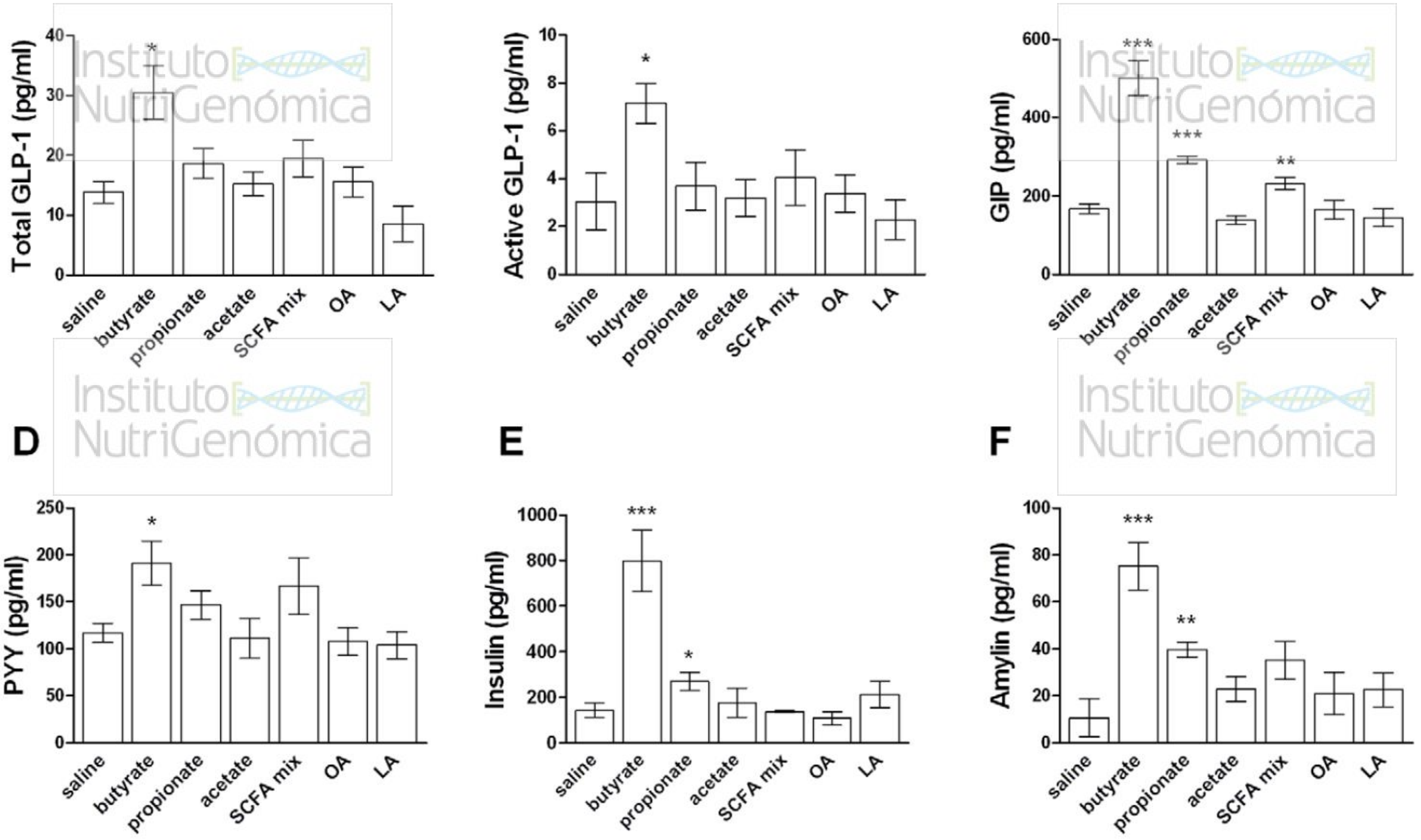
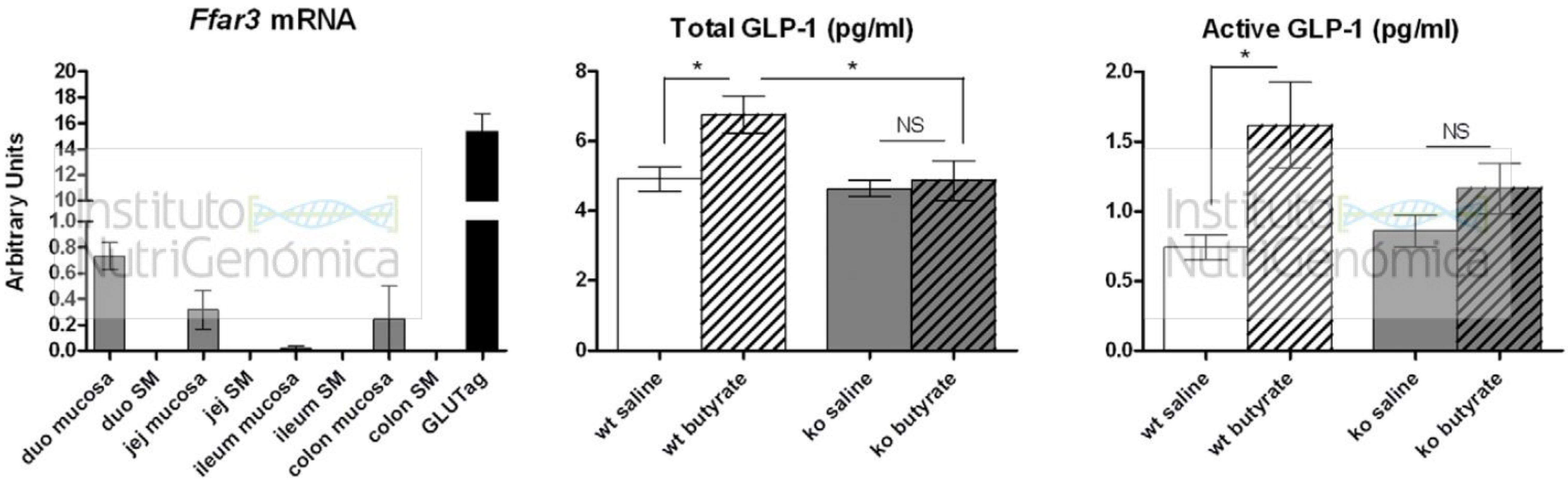
Efecto de ácidos grasos de cadena corta en parámetros de sensibilidad a la insulina

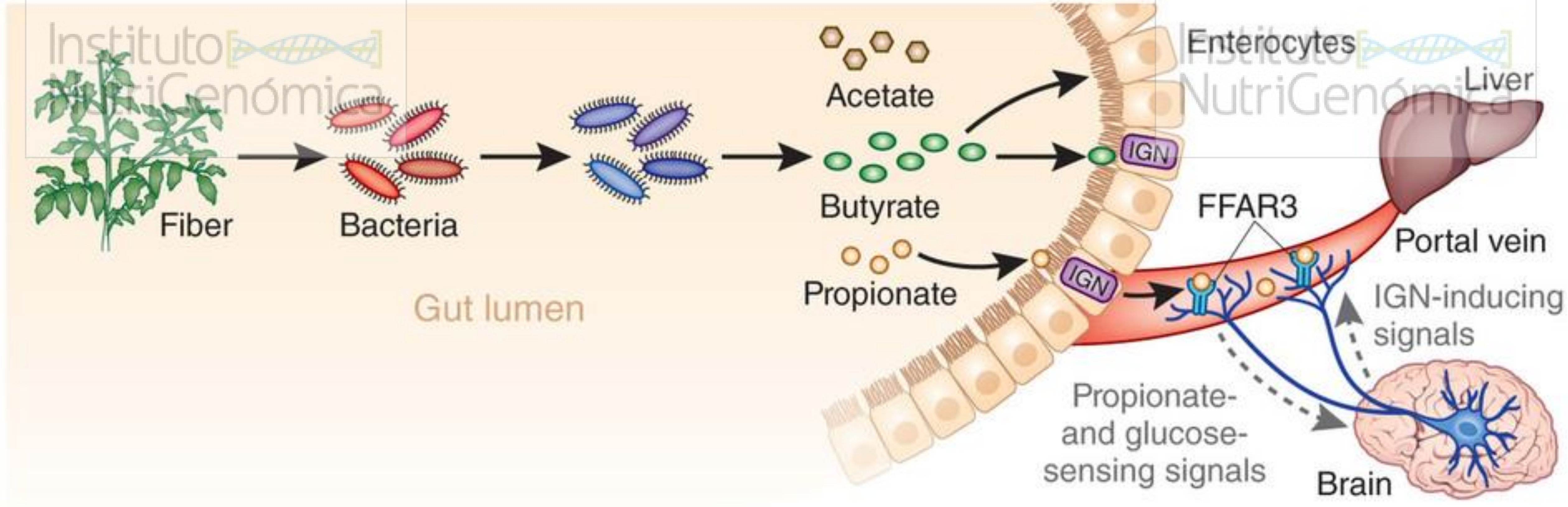







Total GLP-1 (pg/ml)
0
10
20
30
40
*
Active GLP-1 (pg/ml)
0
2
4
6
8
10
*
GIP (pg/ml)
0
200
400
600
***
***
**
saline
butyrate
propionate
acetate
SCFA mix
OA
LA
D
E
F
PYY (pg/ml)
0
50
100
150
200
250
*
Insulin (pg/ml)
0
200
400
600
800
1000
***
*
Amylin (pg/ml)
0
20
40
60
80
100
***
**

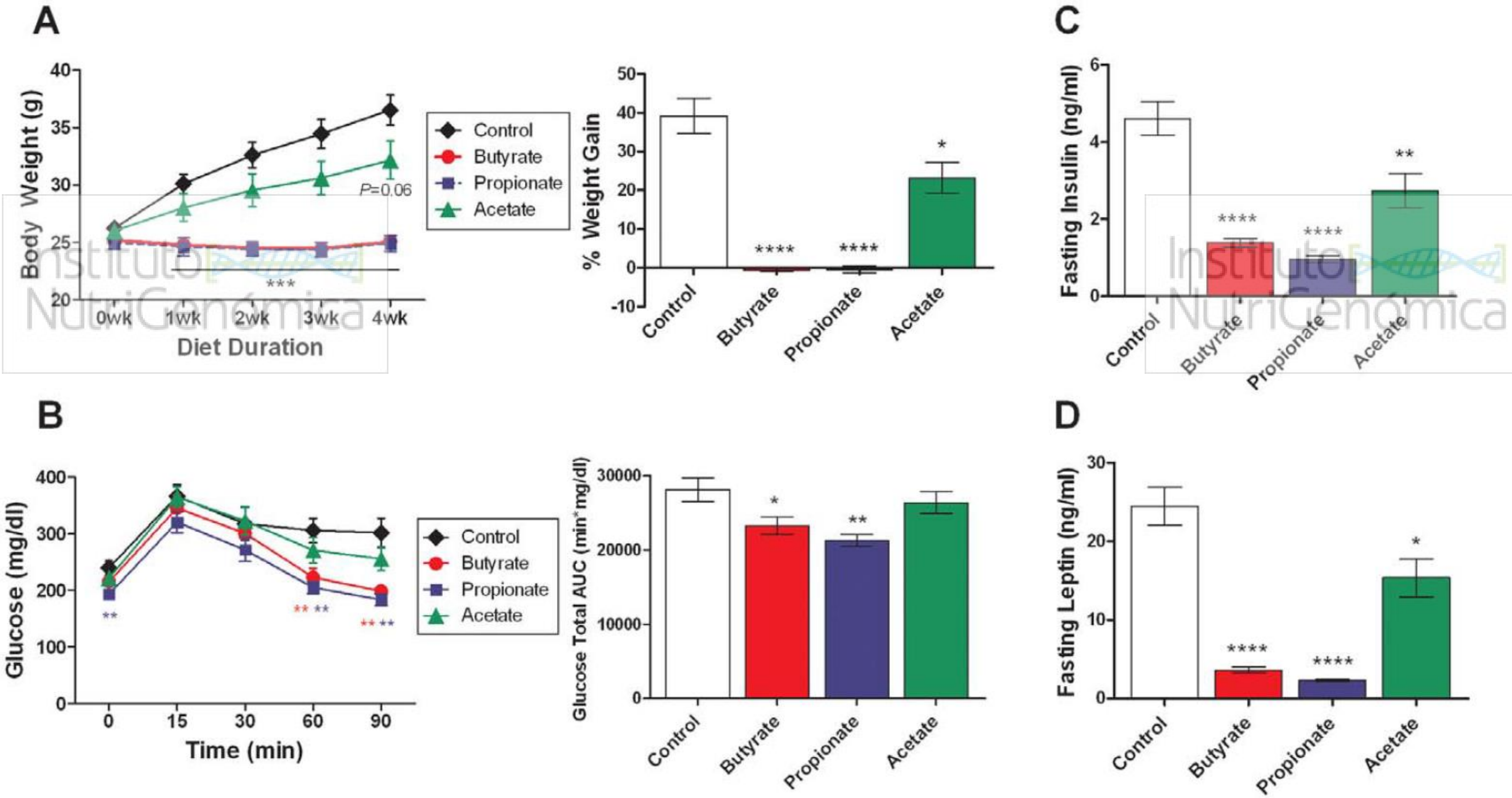

Ffar3 mRNA
Arbitrary Units
20
18
16
14
12
10
1.0
0.8
0.6
0.4
0.2
0.0
duo mucosa
duo SM
jej mucosa
jej SM
ileum mucosa
ileum SM
colon mucosa
colon SM
GLUTag
Total GLP-1 (pg/ml)
8
6
4
2
0
*
*
NS
wt saline
wt butyrate
ko saline
ko butyrate
Active GLP-1 (pg/ml)
2.0
1.5
1.0
0.5
0.0
*
NS
wt saline
wt butyrate
ko saline
ko butyrate


Acetate
Enterocytes
Liver
Butyrate
IGN
Fiber
Bacteria
FFAR3
Portal vein
Propionate
IGN
IGN-inducing signals
Gut lumen
Propionate- and glucose-sensing signals
Brain

Butyrate and Propionate Protect against Diet-Induced Obesity and Regulate Gut Hormones via Free Fatty Acid Receptor 3-Independent Mechanisms

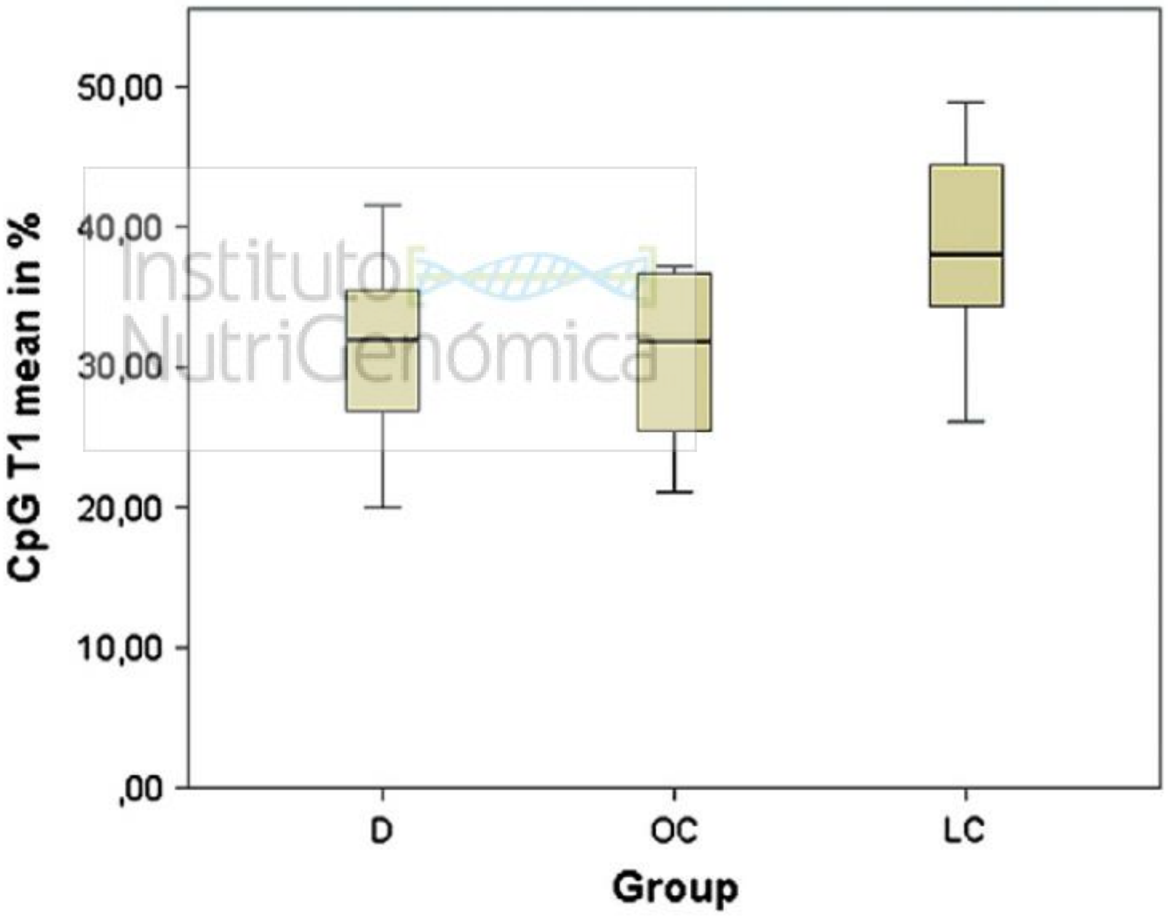
(Lin et al, 2012)

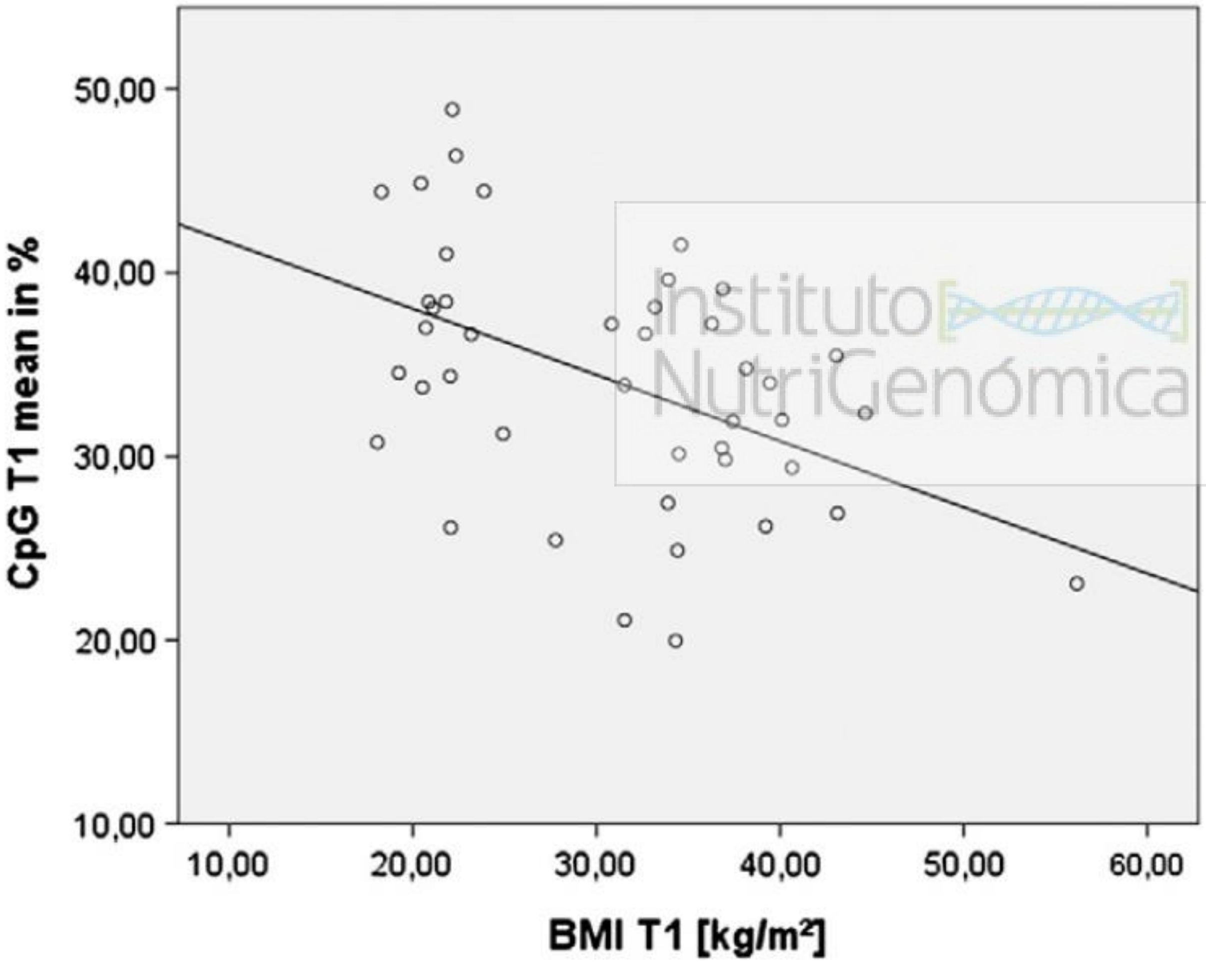
PLoS ONE 7:e35240

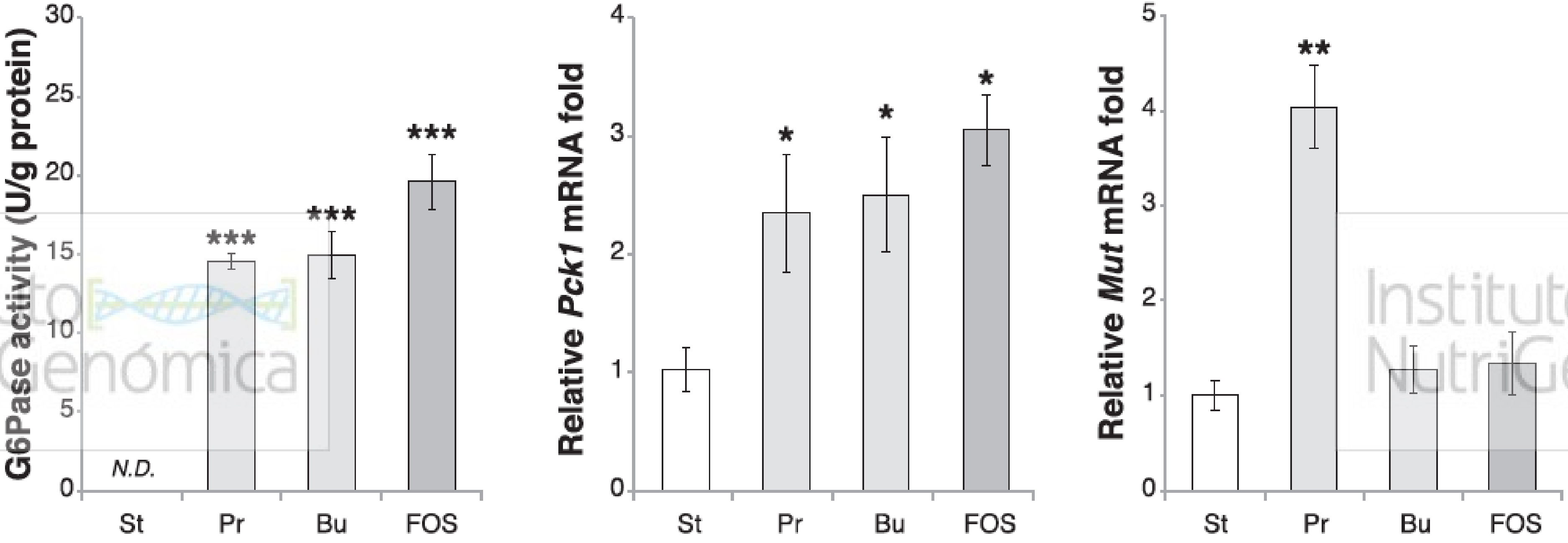


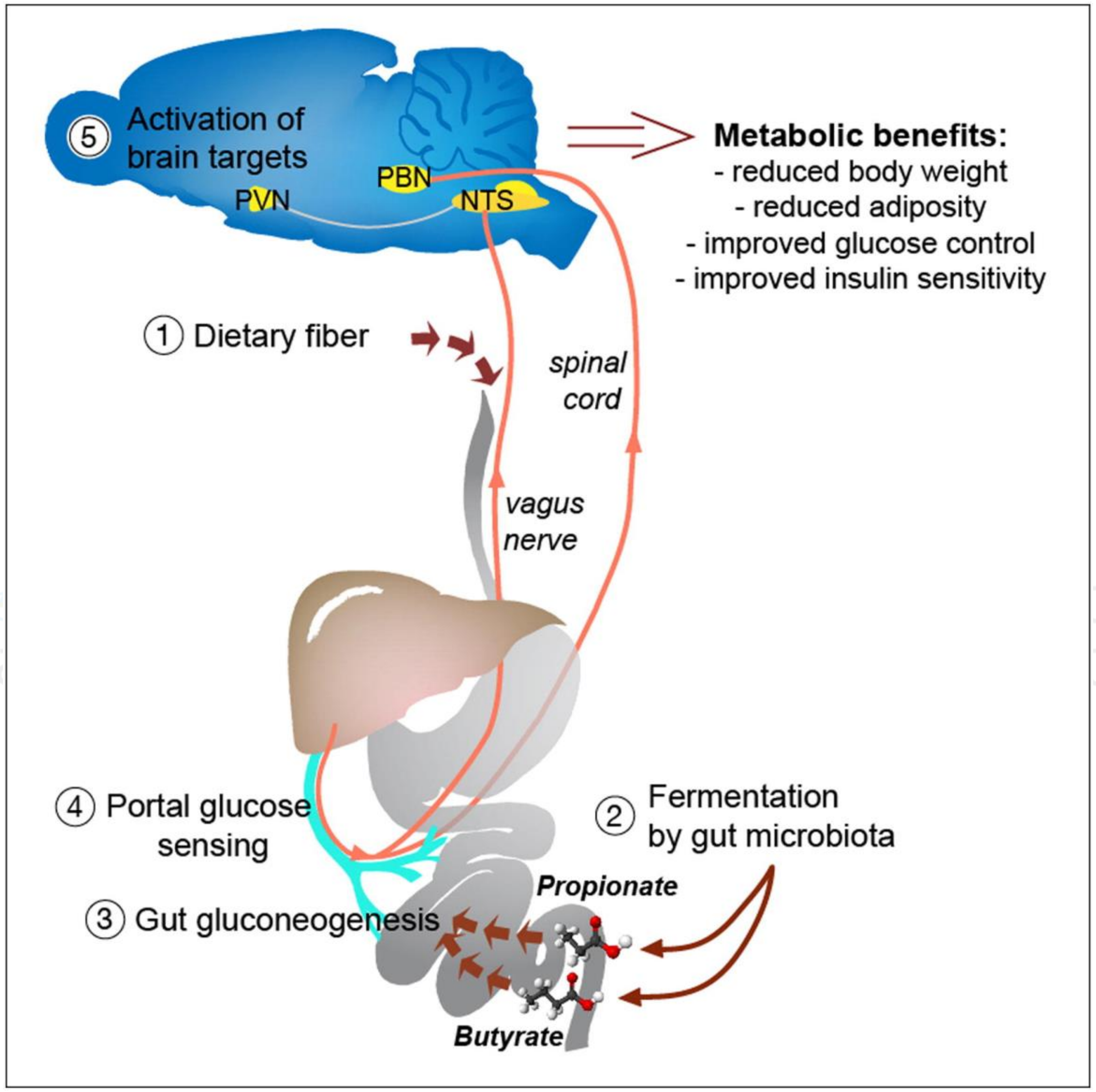
Effects of short chain fatty acid producing bacteria on epigenetic regulation of FFAR3 in type 2 diabetes and obesity

(Remely et al, 2014)
Gene 537:85-92









⑤ Activation of brain targets

PVN

PBN

NTS

Metabolic benefits:
- reduced body weight
- reduced adiposity
- improved glucose control
- improved insulin sensitivity

① Dietary fiber

spinal cord

vagus nerve

④ Portal glucose sensing

② Fermentation by gut microbiota

Propionate

③ Gut gluconeogenesis

Butyrate

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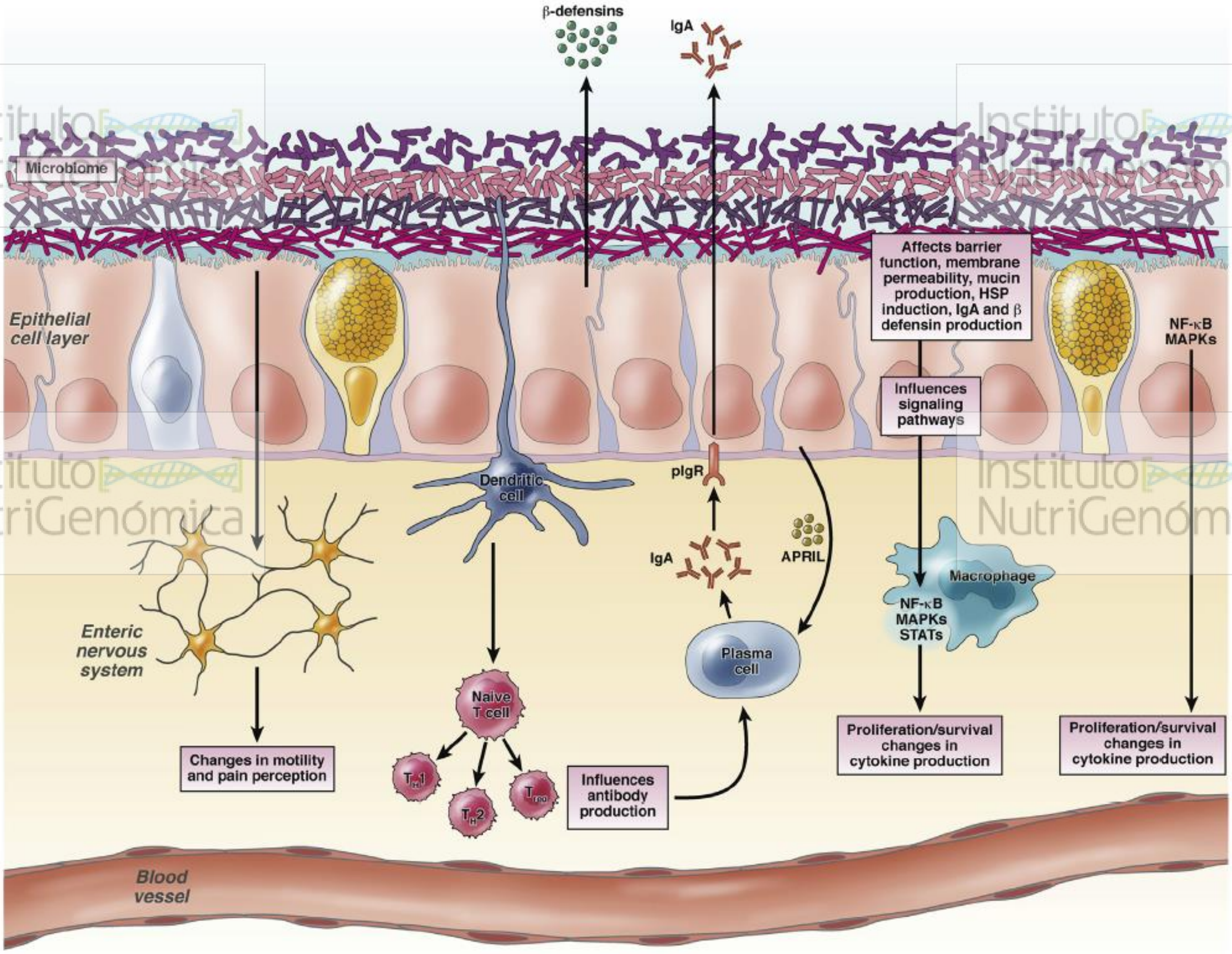
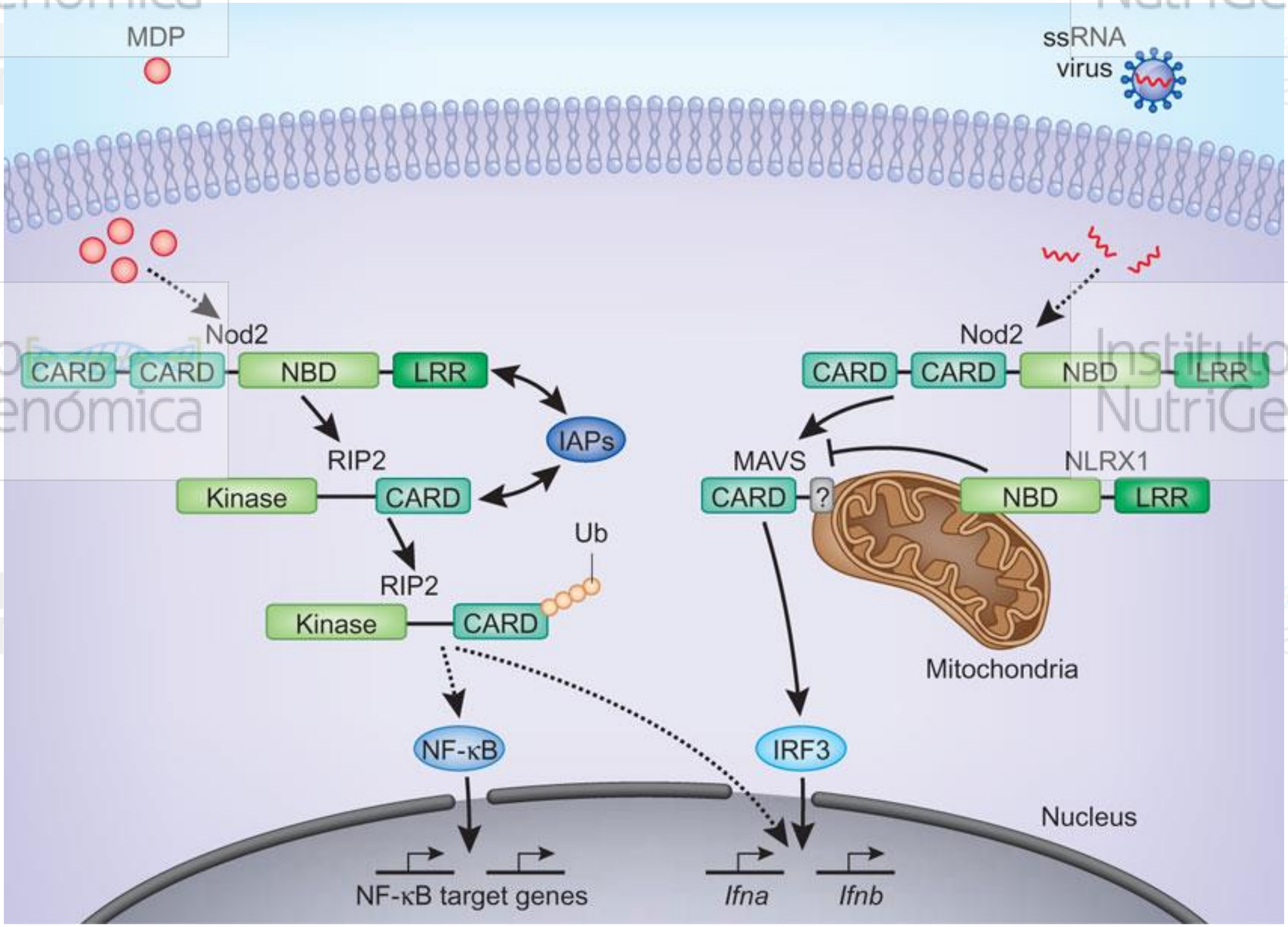
Entendiendo la simbiosis microbiota-huesped



Nod2 is essential for temporal development of intestinal microbial communities

(Rehman et al, 2011)
Gut 60:1354-1362



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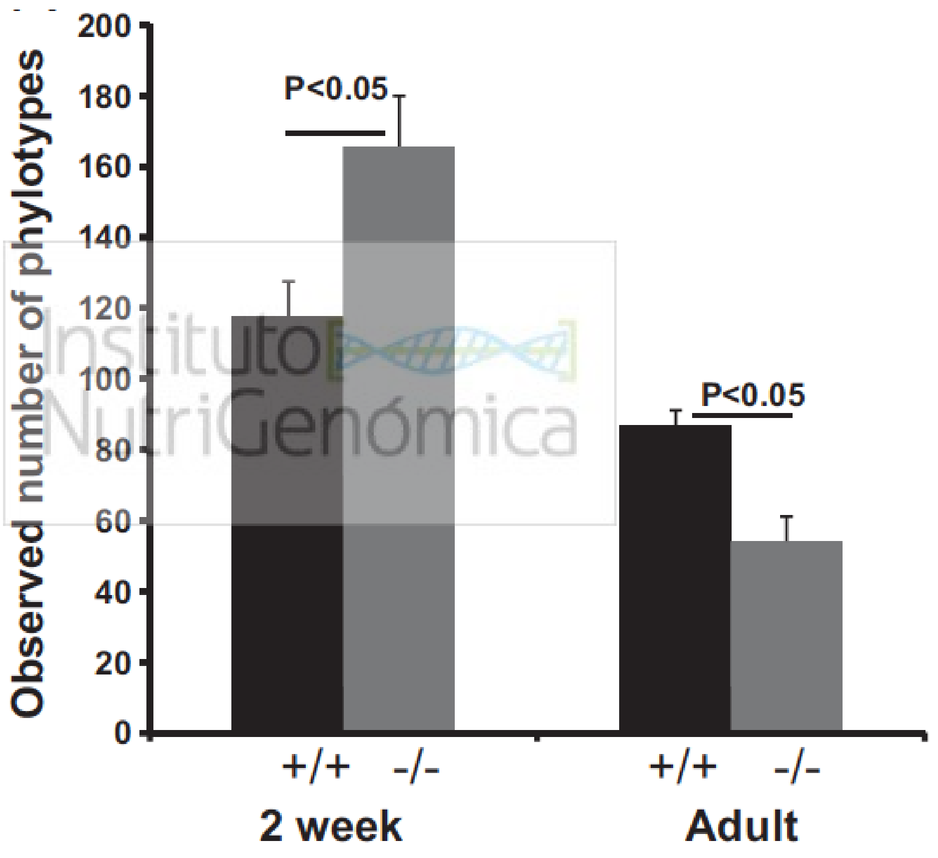

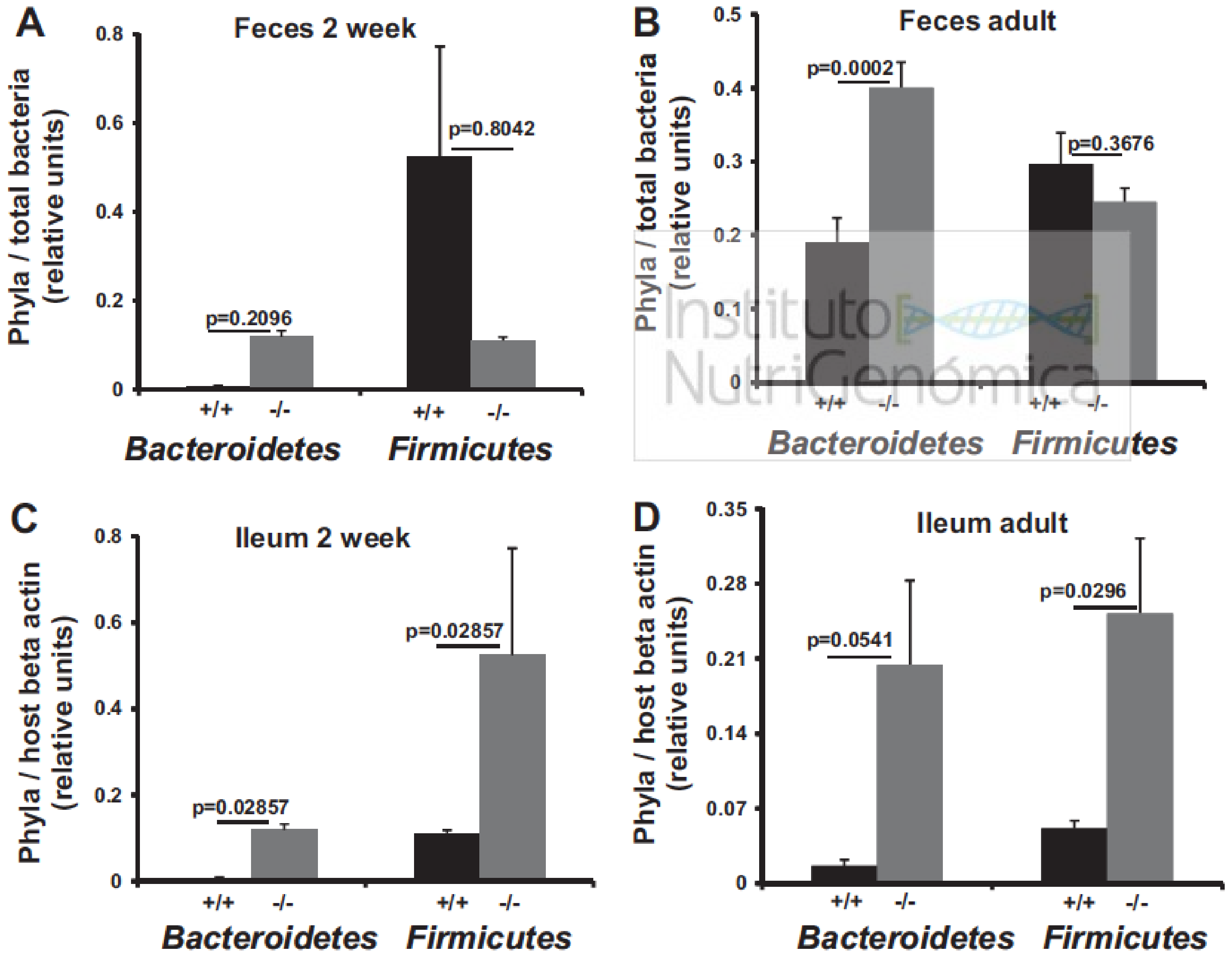

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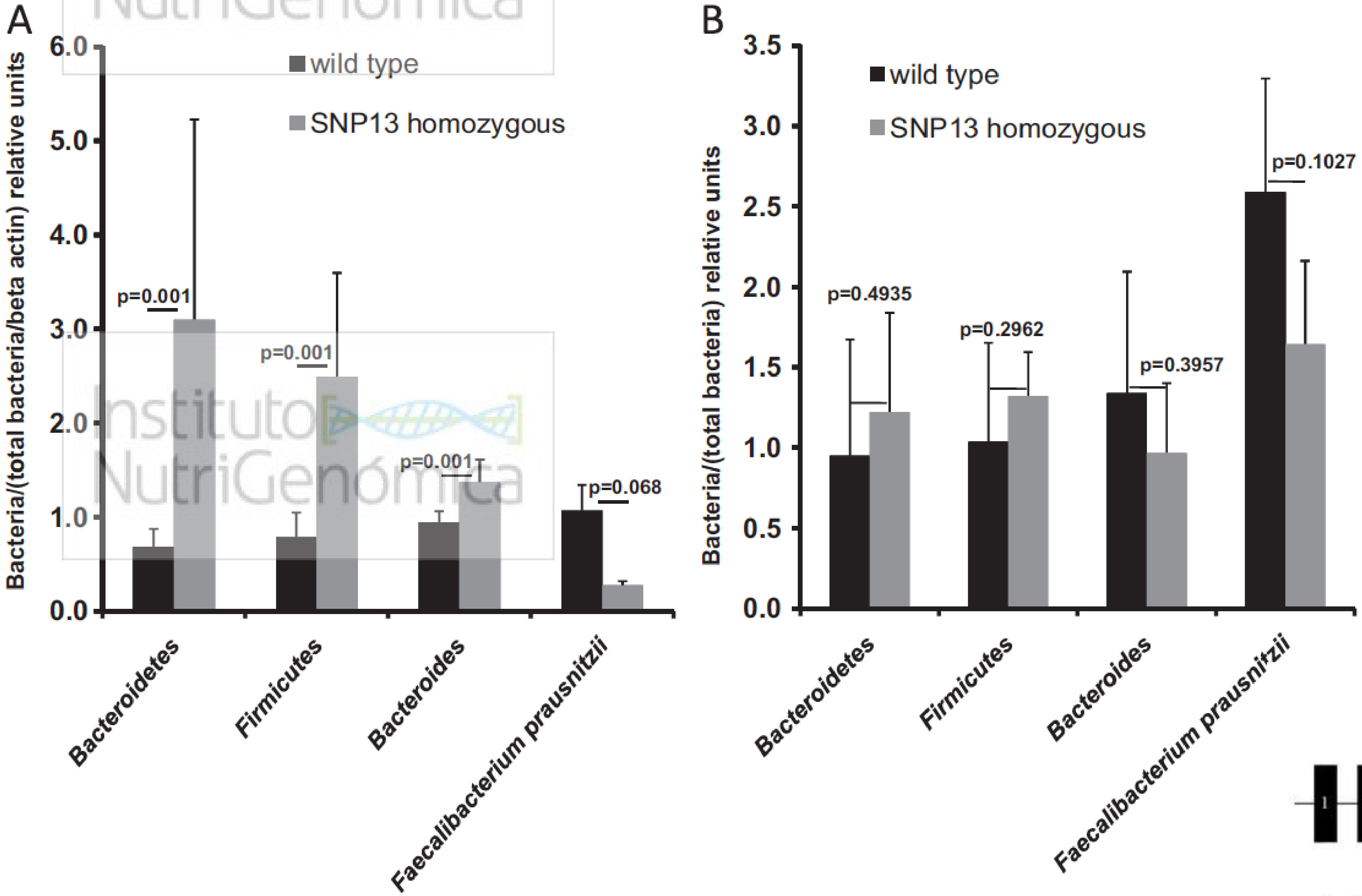
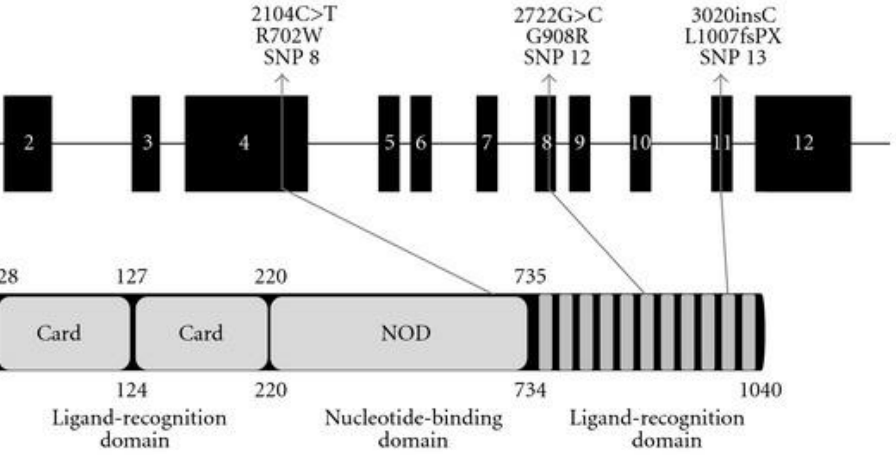
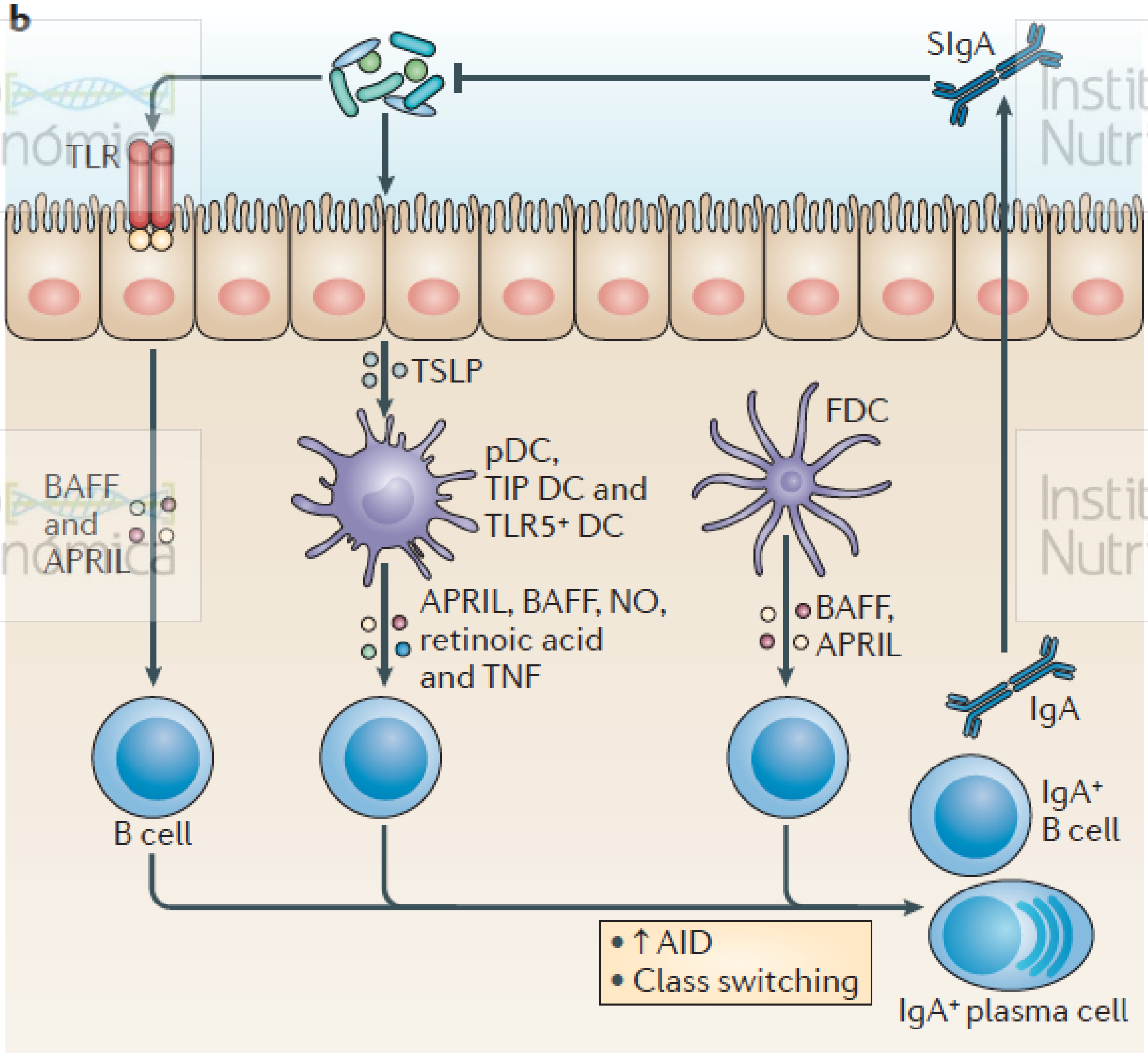
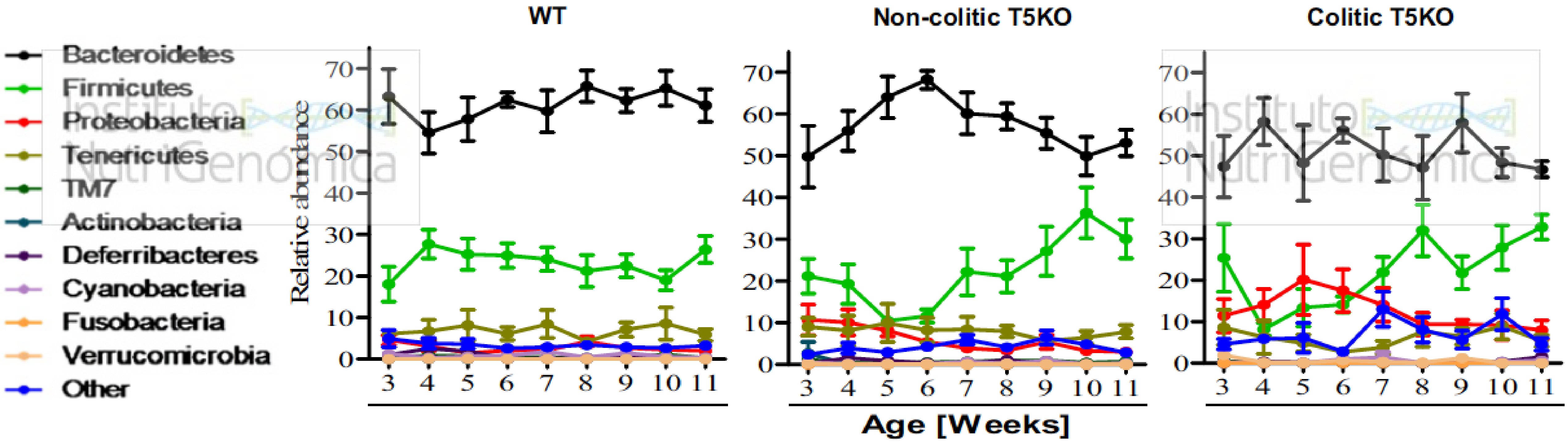





b
SIgA
TLR
TSLP
FDC
pDC,
TIP DC and
TLR5+ DC
BAFF
and
APRIL
APRIL, BAFF, NO,
retinoic acid
and TNF
BAFF,
APRIL
IgA
IgA+
B cell
B cell
• ↑ AID
• Class switching
IgA+ plasma cell

Transient inability to manage proteobacteria promotes chronic gut inflammation in TLR5-deficient mice.

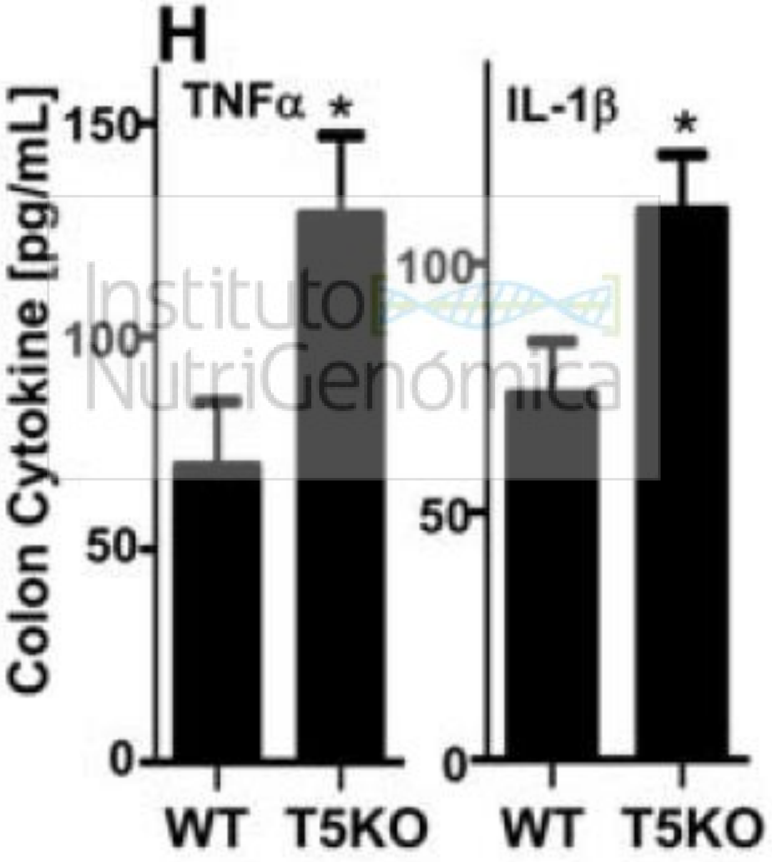
(Carvalho et al, 2012)
Cell Host Microbe 12:139-152

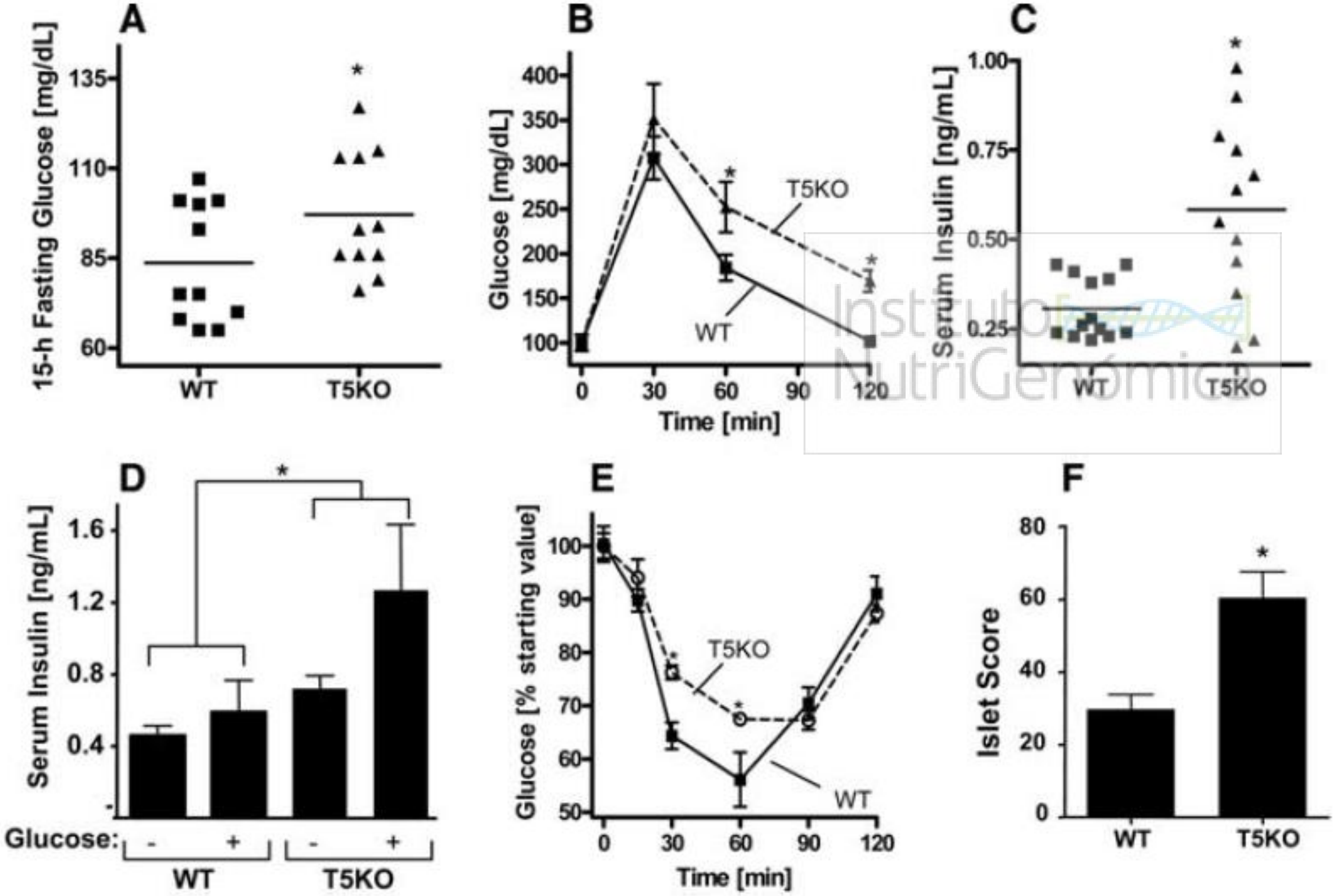


Metabolic syndrome and altered gut microbiota in mice lacking Toll-like Receptor 5

(Vijay-Kumar et al, 2010)

Science 328;228





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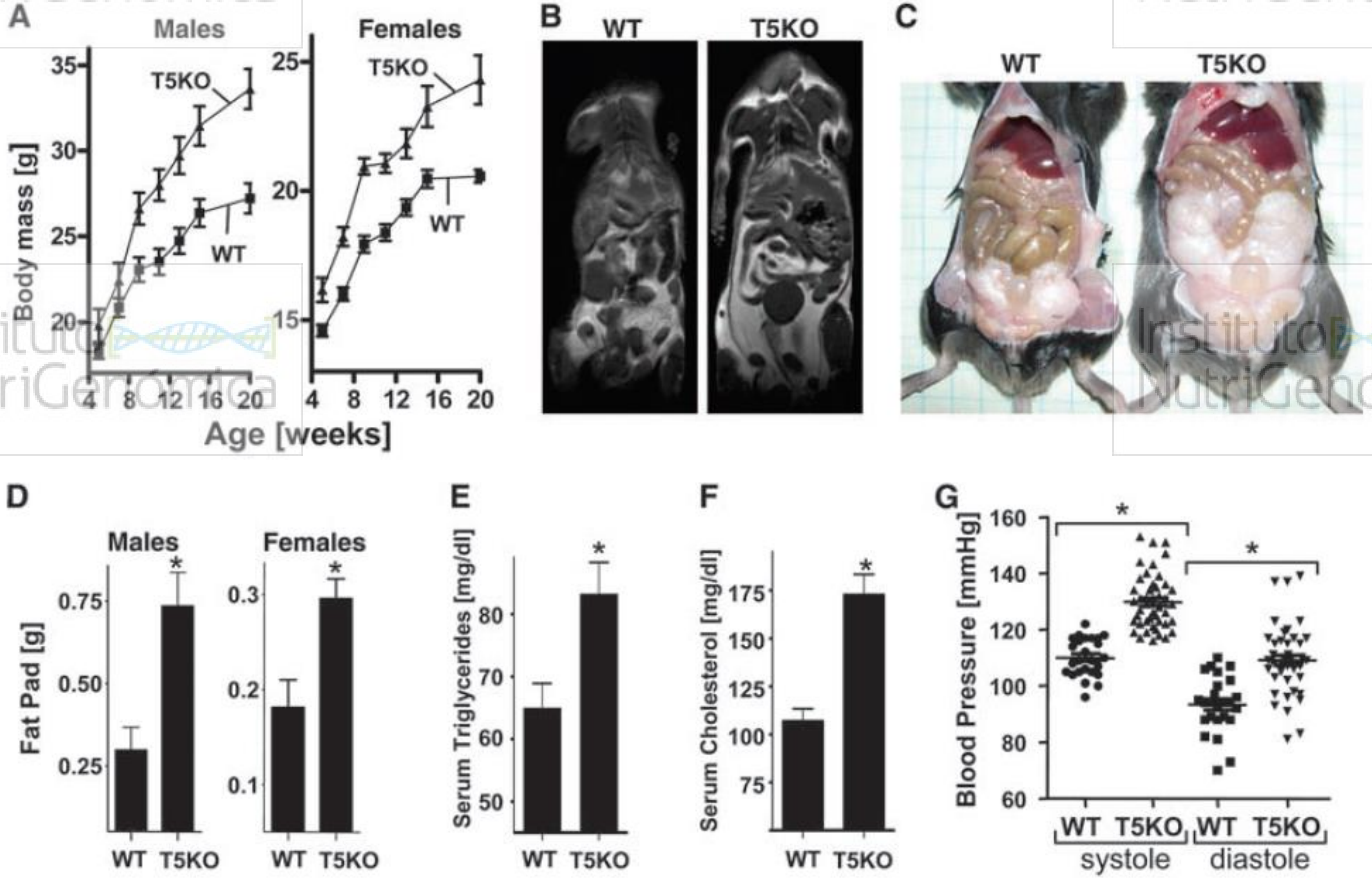
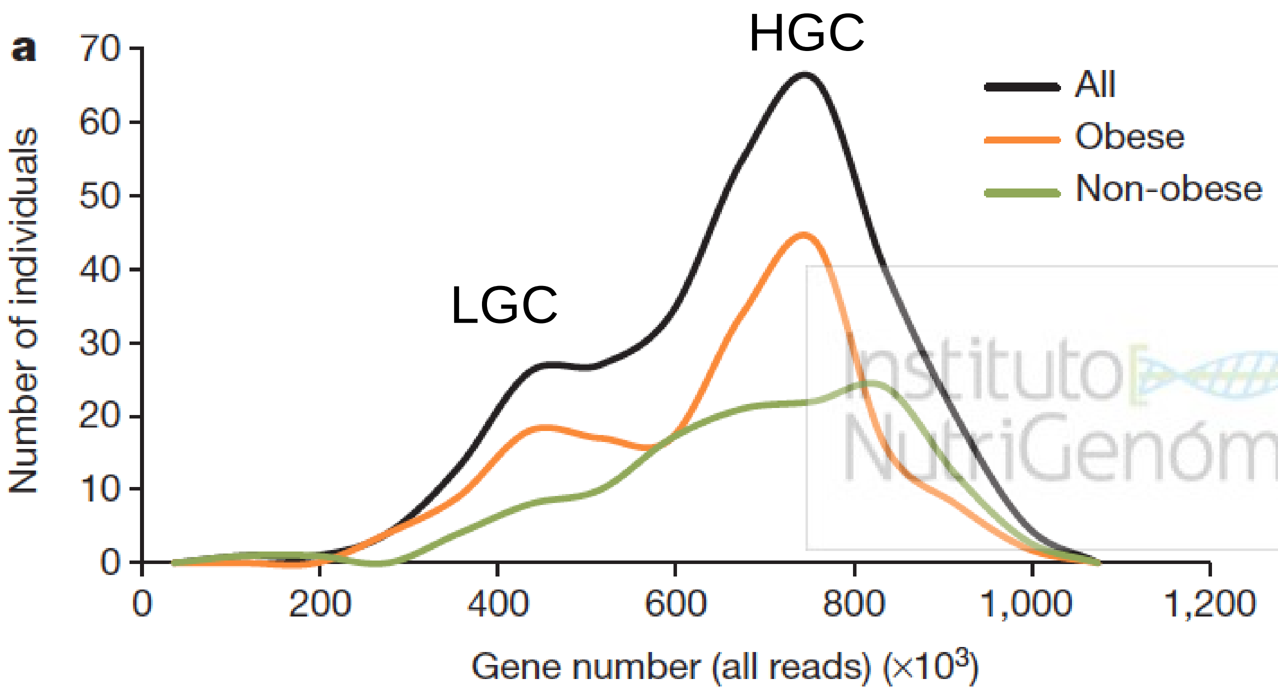
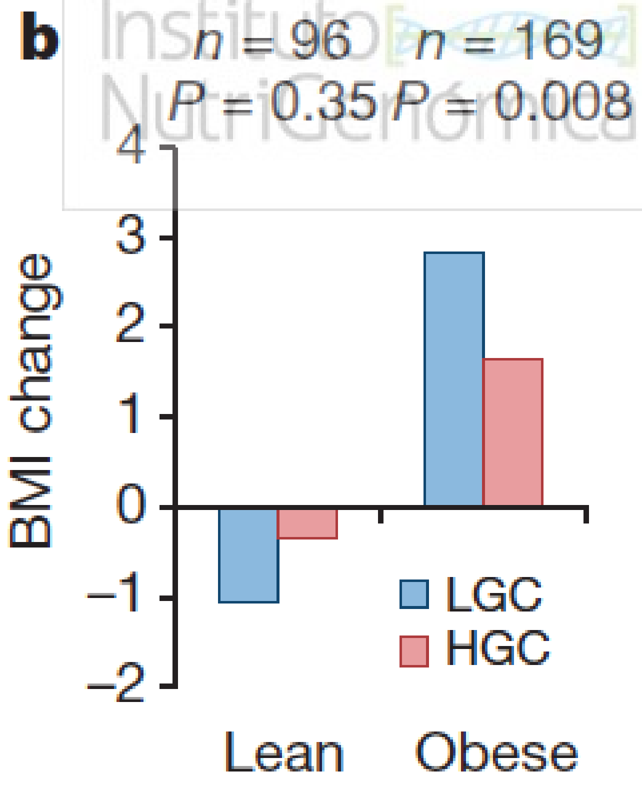
Science 328;228



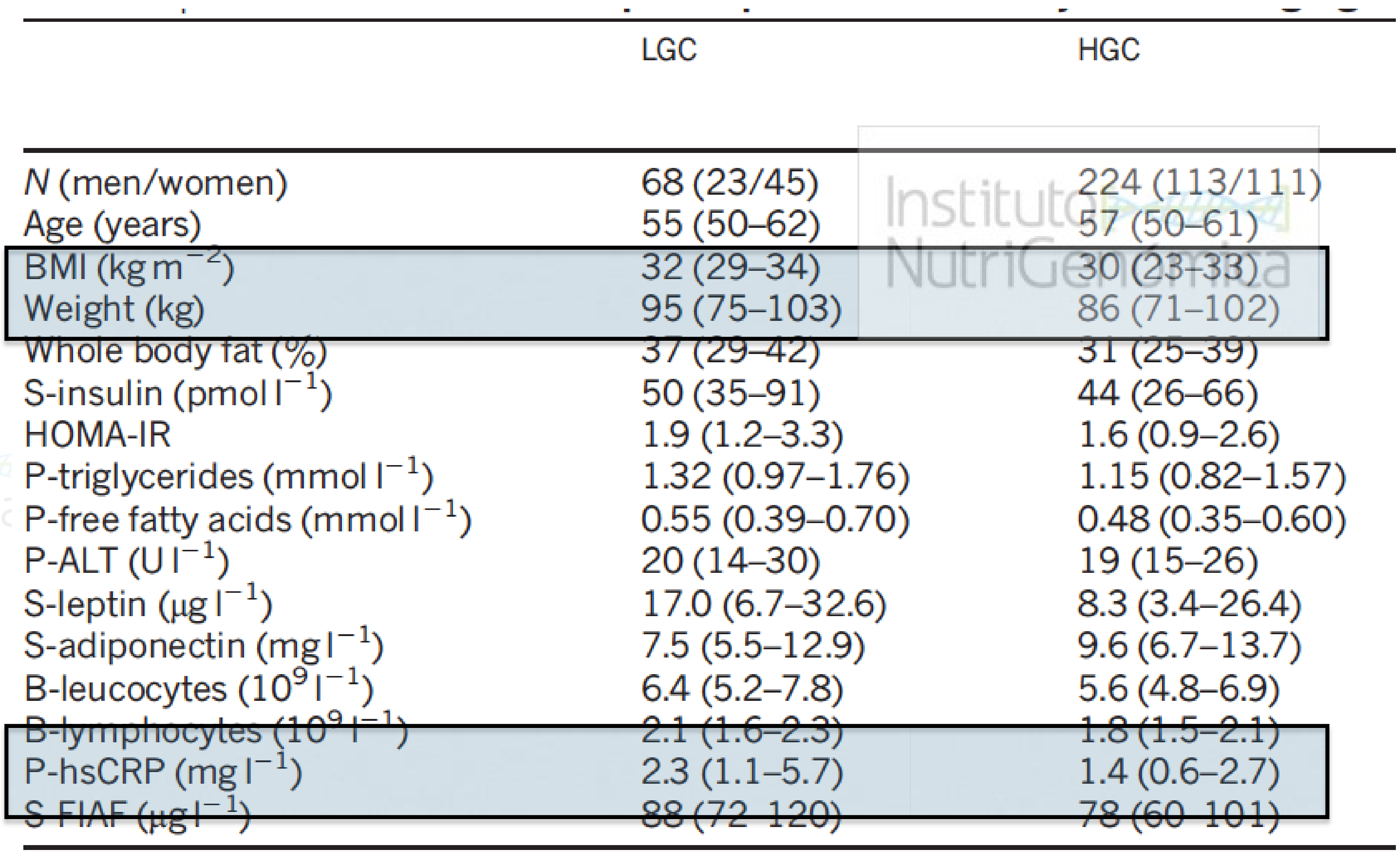
Richness of human gut microbiome correlates with metabolic markers

(Le Chatelier et al, 2013)
Nature 500:541.





9 años seguimiento



	LGC	HGC
N (men/women)	68 (23/45)	224 (113/111)
Age (years)	55 (50–62)	57 (50–61)
BMI (kg m^{-2})	32 (29–34)	30 (23–33)
Weight (kg)	95 (75–103)	86 (71–102)
Whole body fat (%)	37 (29–42)	31 (25–39)
S-insulin (pmol l^{-1})	50 (35–91)	44 (26–66)
HOMA-IR	1.9 (1.2–3.3)	1.6 (0.9–2.6)
P-triglycerides (mmol l^{-1})	1.32 (0.97–1.76)	1.15 (0.82–1.57)
P-free fatty acids (mmol l^{-1})	0.55 (0.39–0.70)	0.48 (0.35–0.60)
P-ALT (U l^{-1})	20 (14–30)	19 (15–26)
S-leptin (μg l^{-1})	17.0 (6.7–32.6)	8.3 (3.4–26.4)
S-adiponectin (mg l^{-1})	7.5 (5.5–12.9)	9.6 (6.7–13.7)
B-leucocytes (10^9 l^{-1})	6.4 (5.2–7.8)	5.6 (4.8–6.9)
B-lymphocytes (10^9 l^{-1})	2.1 (1.6–2.3)	1.8 (1.5–2.1)
P-hsCRP (mg l^{-1})	2.3 (1.1–5.7)	1.4 (0.6–2.7)
S-FIAF (μg l^{-1})	88 (72–120)	78 (60–101)

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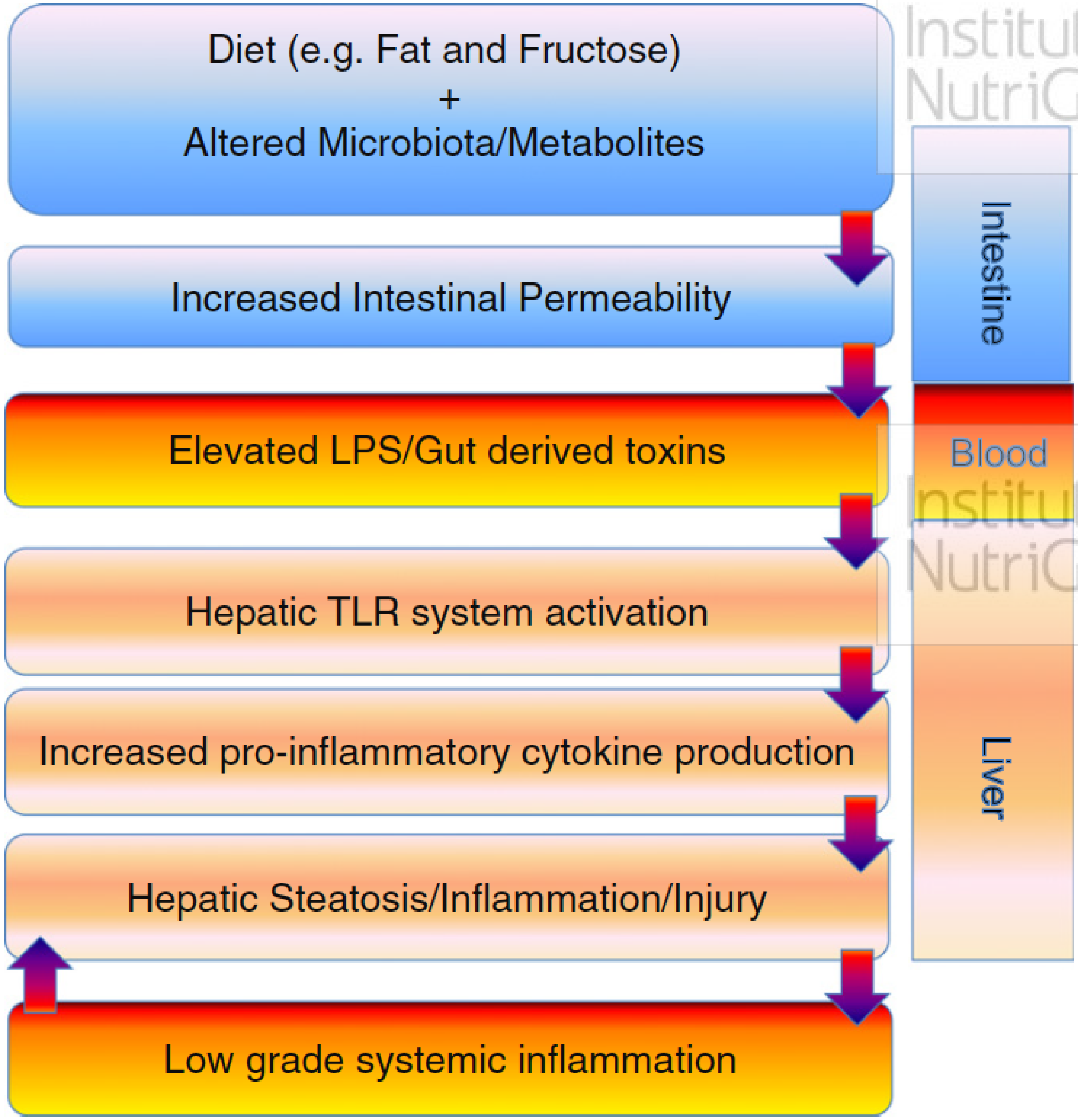
Índice

Eje intestino-hígado y esteatohepatitis no alcohólica



Diet (e.g. Fat and Fructose)
+
Altered Microbiota/Metabolites

Increased Intestinal Permeability

Elevated LPS/Gut derived toxins

Hepatic TLR system activation

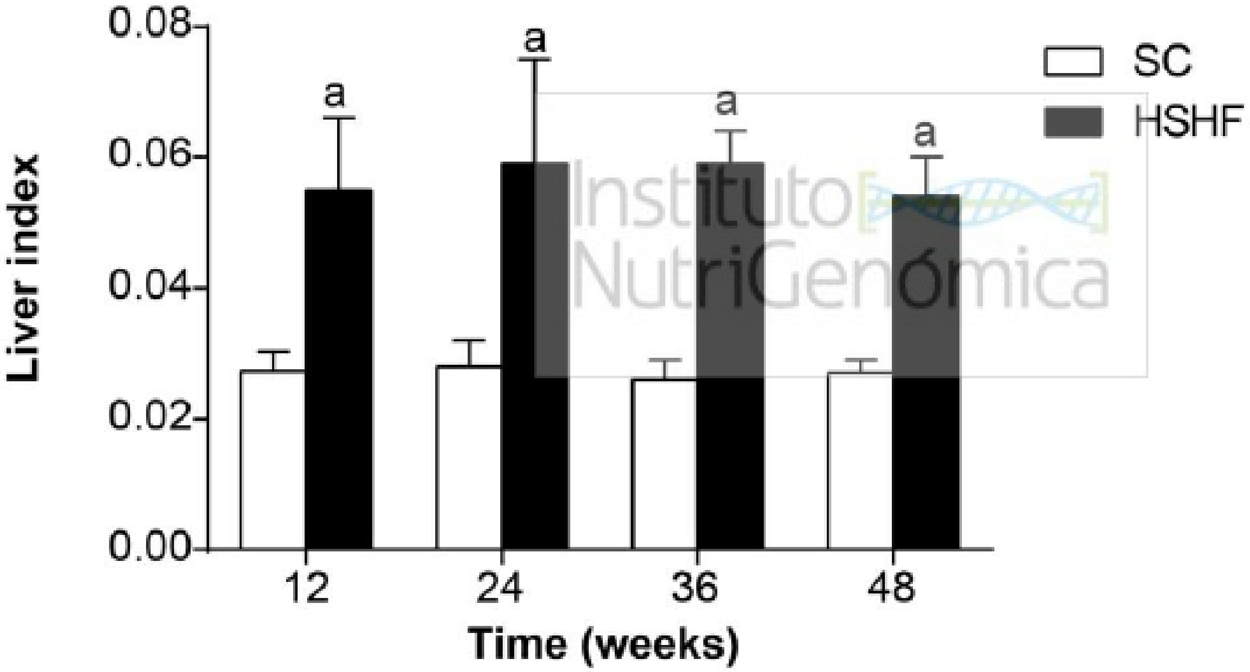
Increased pro-inflammatory cytokine production

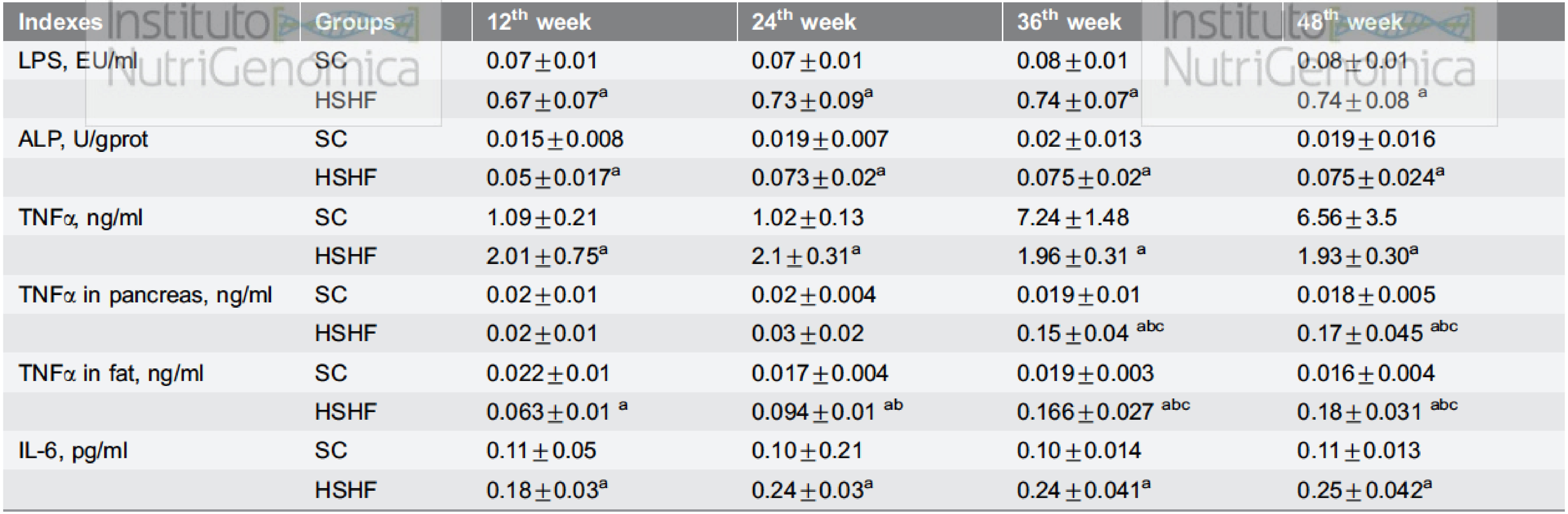
Hepatic Steatosis/Inflammation/Injury

Low grade systemic inflammation

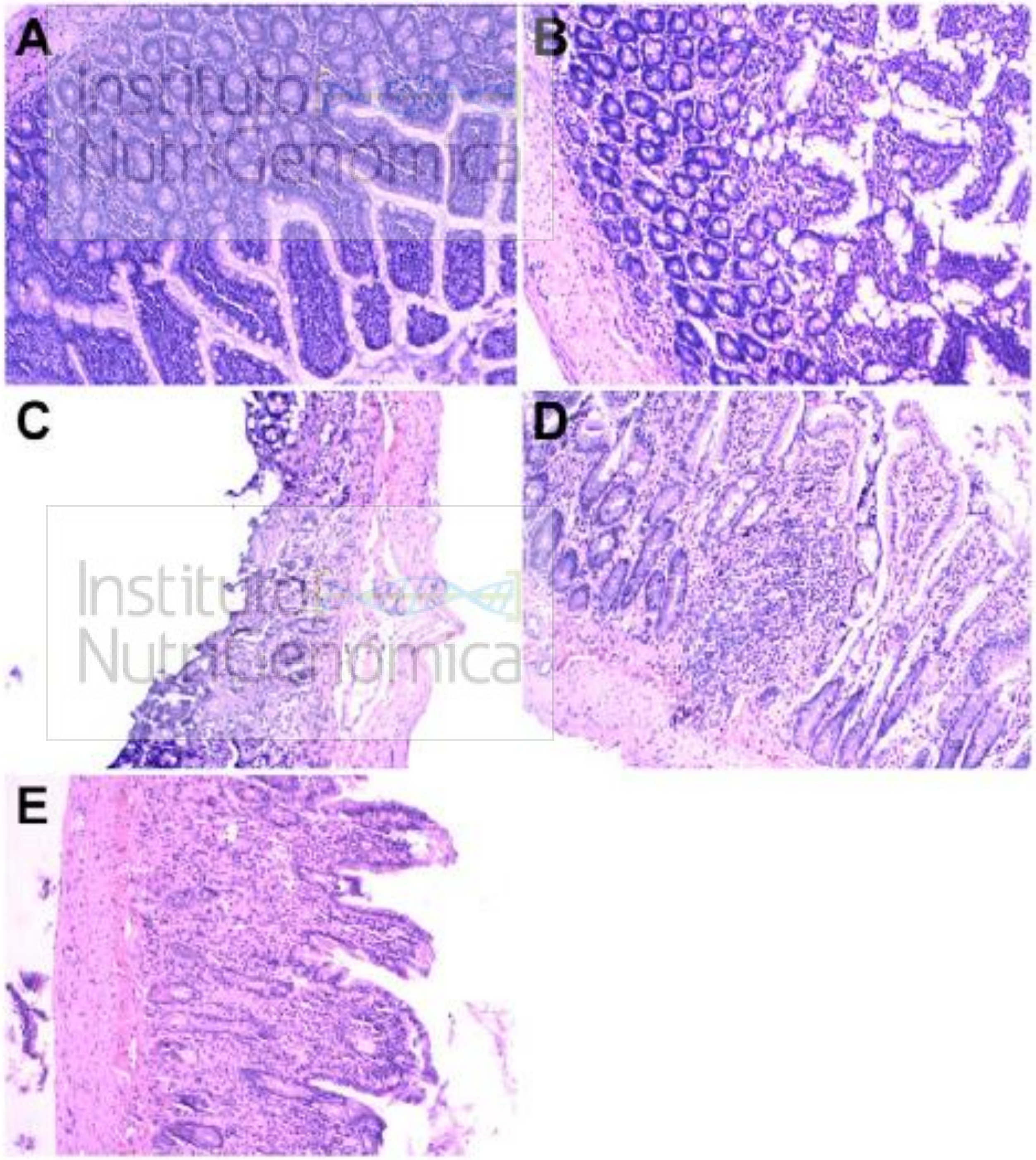
A model of metabolic syndrome and related diseases with intestinal endotoxemia in rats fed a high fat and high sucrose diet.

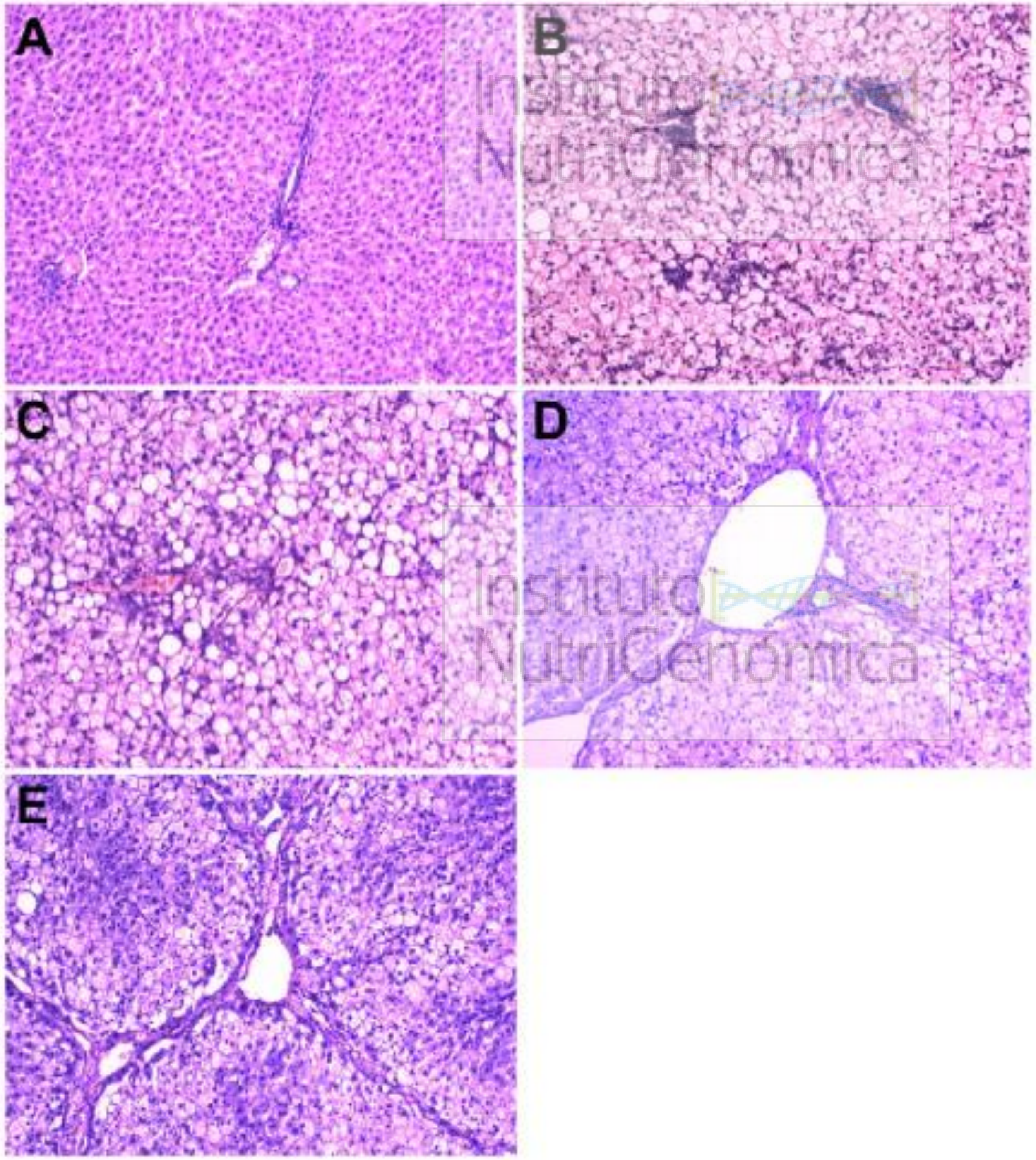
(Zhou et al, 2014)
PLoS One, 9:e115148





Indexes	Groups	12th week	24th week	36th week	48th week
LPS, EU/ml	SC	0.07±0.01	0.07±0.01	0.08±0.01	0.08±0.01
	HSHF	0.67±0.07^{a}	0.73±0.09^{a}	0.74±0.07^{a}	0.74±0.08 ^{a}
ALP, U/gprot	SC	0.015±0.008	0.019±0.007	0.02±0.013	0.019±0.016
	HSHF	0.05±0.017^{a}	0.073±0.02^{a}	0.075±0.02^{a}	0.075±0.024^{a}
TNFα, ng/ml	SC	1.09±0.21	1.02±0.13	7.24±1.48	6.56±3.5
	HSHF	2.01±0.75^{a}	2.1±0.31^{a}	1.96±0.31 ^{a}	1.93±0.30^{a}
TNFα in pancreas, ng/ml	SC	0.02±0.01	0.02±0.004	0.019±0.01	0.018±0.005
	HSHF	0.02±0.01	0.03±0.02	0.15±0.04 ^{abc}	0.17±0.045 ^{abc}
TNFα in fat, ng/ml	SC	0.022±0.01	0.017±0.004	0.019±0.003	0.016±0.004
	HSHF	0.063±0.01 ^{a}	0.094±0.01 ^{ab}	0.166±0.027 ^{abc}	0.18±0.031 ^{abc}
IL-6, pg/ml	SC	0.11±0.05	0.10±0.21	0.10±0.014	0.11±0.013
	HSHF	0.18±0.03^{a}	0.24±0.03^{a}	0.24±0.041^{a}	0.25±0.042^{a}


A
B
C
D
E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B
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D
E

Microbiota y síndorme metabólico
- Obesidad e insulinorresistencia -

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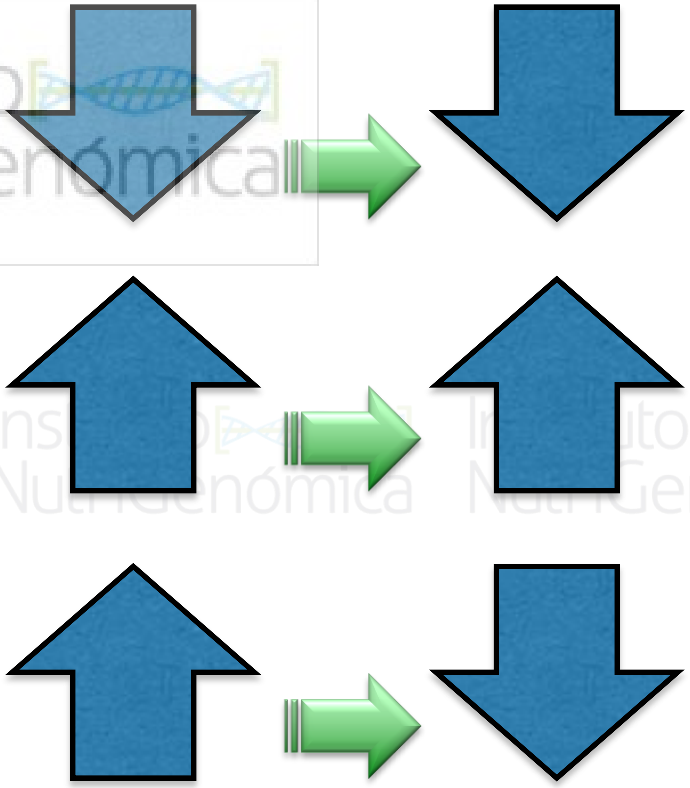
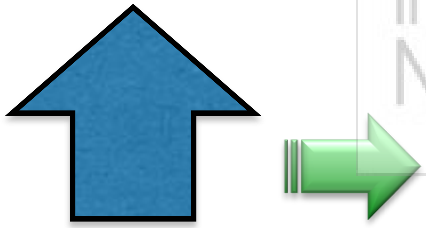
Limitaciones de la información actual

Estudios observacionales

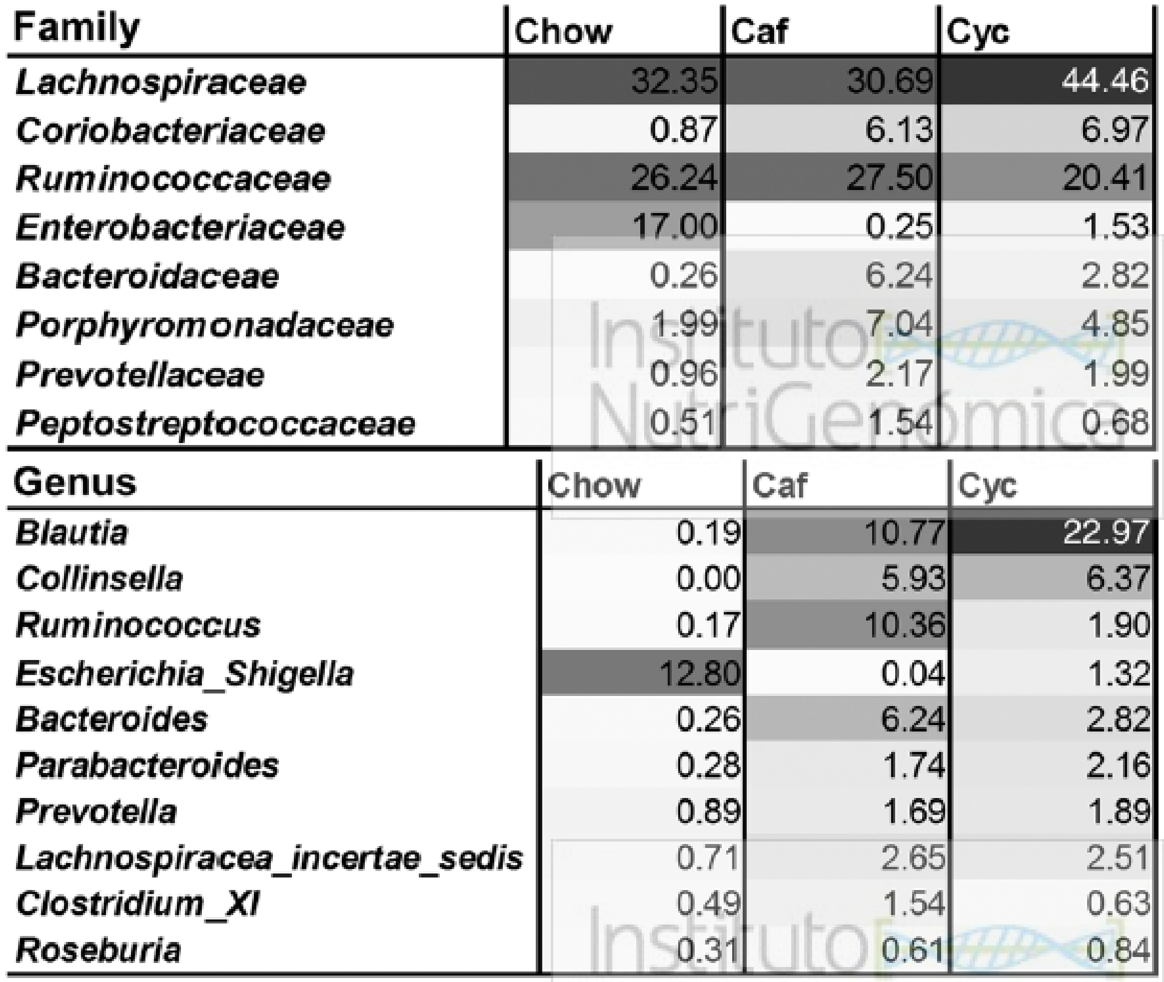
Estudio intervención





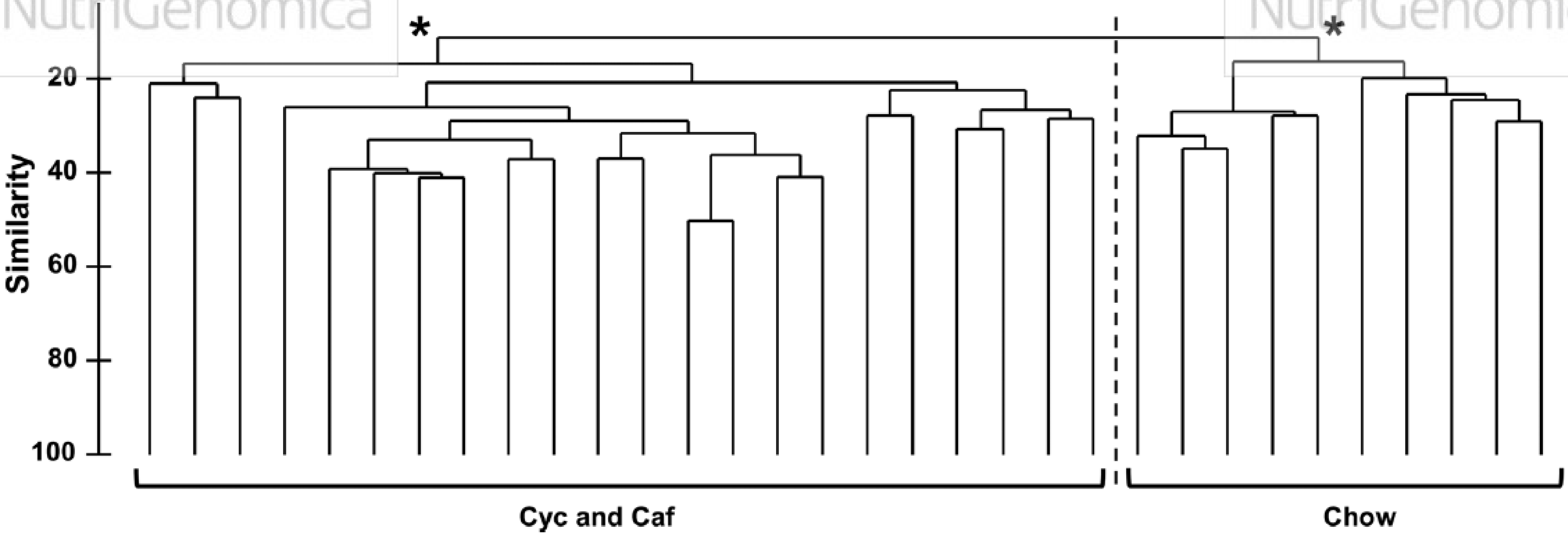
Alternating or continous exposure to cafeteria diet leads to similar shifts in gut microbiota compared to chow diet

(Kaakoush et al, 2016)
Mol Nutr Food Res



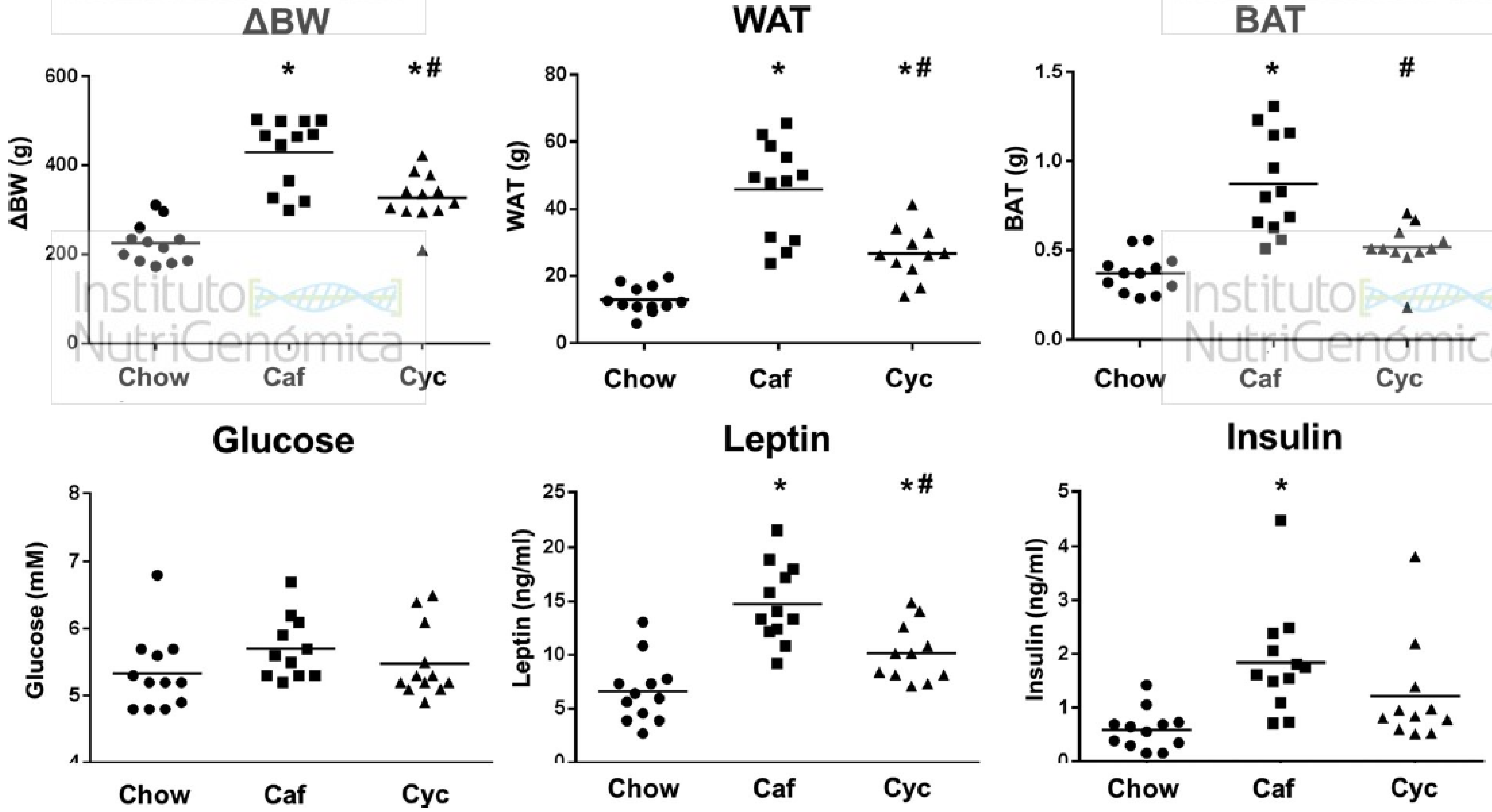
Family	Chow	Caf	Cyc
Lachnospiraceae	32.35	30.69	44.46
Coriobacteriaceae	0.87	6.13	6.97
Ruminococcaceae	26.24	27.50	20.41
Enterobacteriaceae	17.00	0.25	1.53
Bacteroidaceae	0.26	6.24	2.82
Porphyromonadaceae	1.99	7.04	4.85
Prevotellaceae	0.96	2.17	1.99
Peptostreptococcaceae	0.51	1.54	0.68

Genus	Chow	Caf	Cyc
Blautia	0.19	10.77	22.97
Collinsella	0.00	5.93	6.37
Ruminococcus	0.17	10.36	1.90
Escherichia_Shigella	12.80	0.04	1.32
Bacteroides	0.26	6.24	2.82
Parabacteroides	0.28	1.74	2.16
Prevotella	0.89	1.69	1.89
Lachnospiracea_incertae_sedis	0.71	2.65	2.51
Clostridium_XI	0.49	1.54	0.63
Roseburia	0.31	0.61	0.84



Alternating or continous exposure to cafeteria diet leads to similar shifts in gut microbiota compared to chow diet

(Kaakoush et al, 2016)
Mol Nutr Food Res



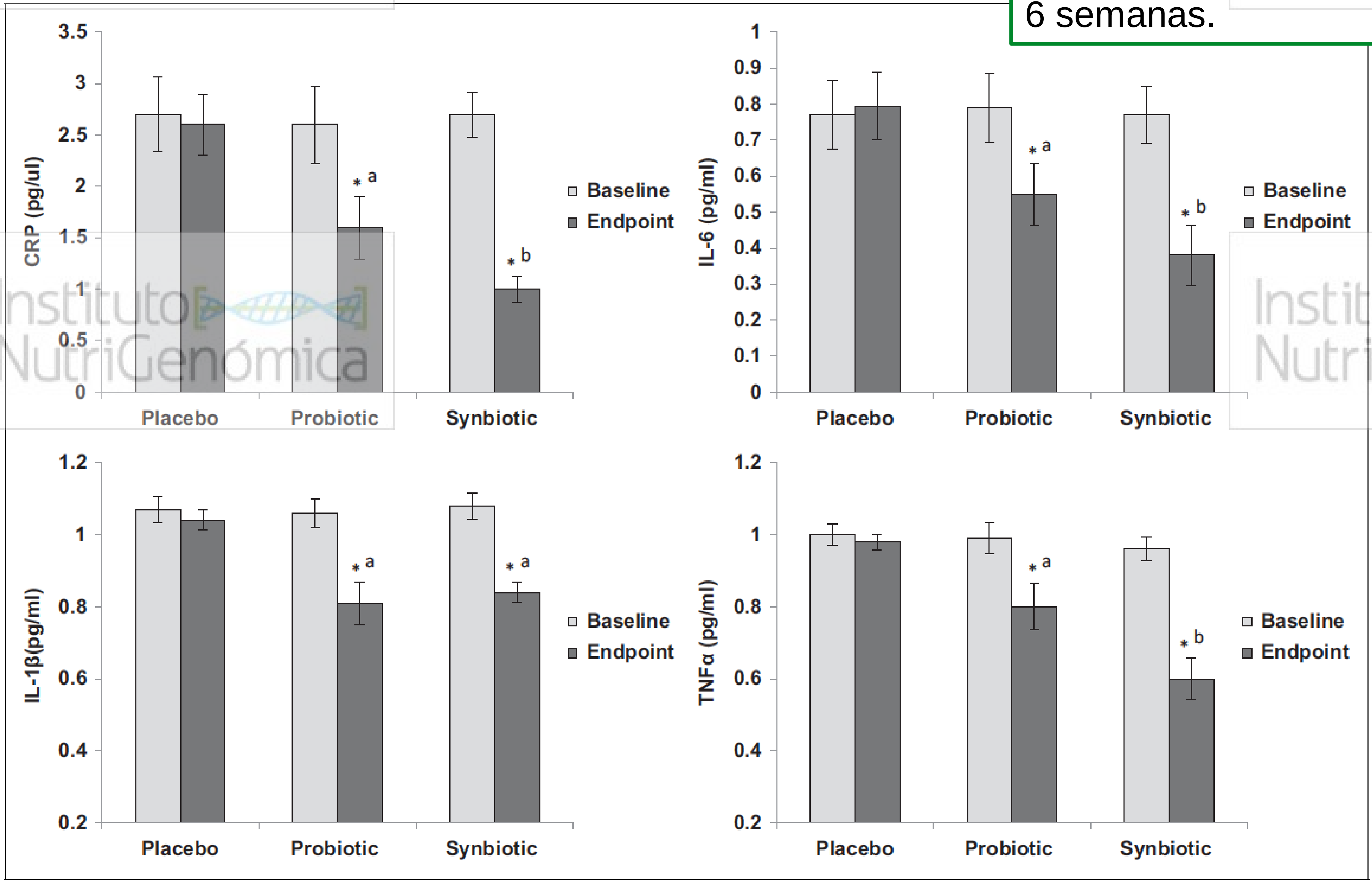
Microbiota y síndorme metabólico
- Obesidad e insulinorresistencia -

Índice

Effect of Probiotic Lactobacillus salivarius UBL S22 and Prebiotic Fructo-oligosaccharide on Serum Lipids, Inflammatory Markers, Insulin Sensitivity, and Gut Bacteria in Healthy Young Volunteers: A Randomized Controlled Single-Blind Pilot Study

(Rajkumar et al, 2015)
J Cardiovasc Pharmacol Ther 20:289-98

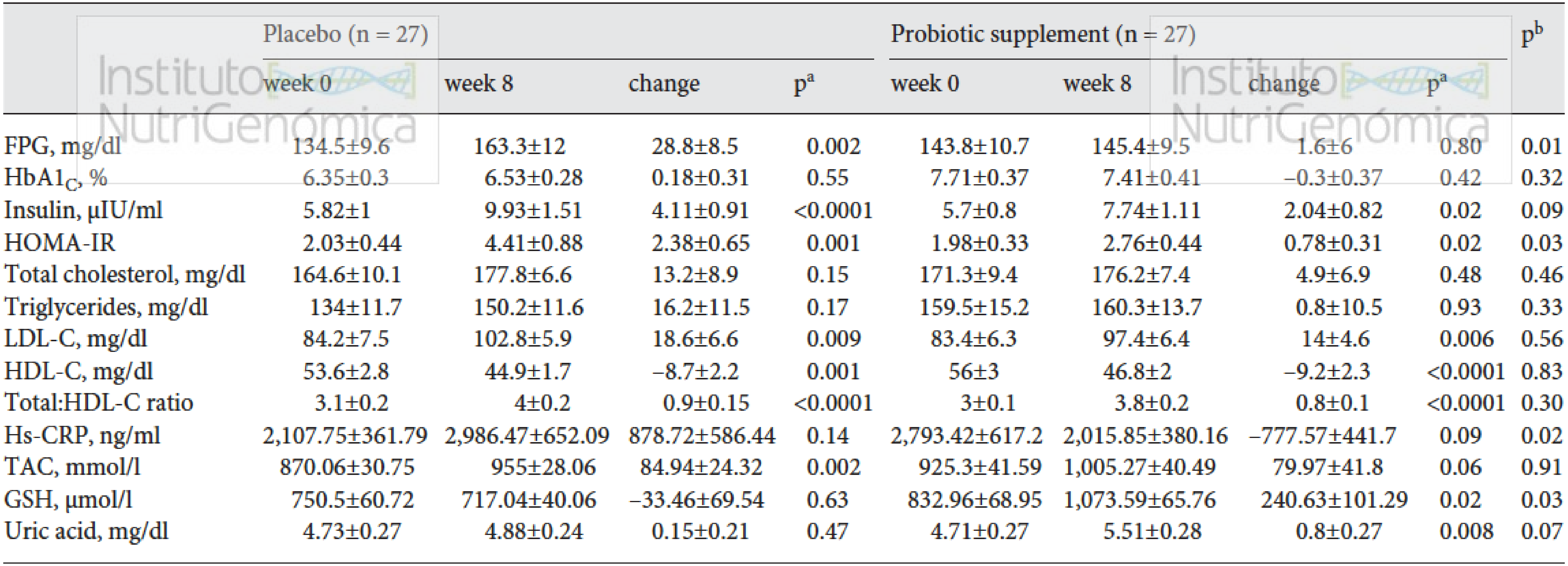
(Placebo) gelatina,
(Probiotic) $2x10^9$ CFUs L .salivarius
(Synbiotic) L salivarius y FOS (10 g/d)
6 semanas.



Effect of multispecies probiotic supplements on metabolic profiles, hs-CRP, and oxidative stress in patients with type 2 diabetes

(Asemi et al, 2013)
Ann Nutr Metab 63:1-9

- Lactobacillus acidophilus (2 × 10(9) CFU),
- L. casei (7 × 10(9) CFU),
- L. rhamnosus (1.5 × 10(9) CFU),
- L. bulgaricus (2 × 10(8) CFU),
- Bifidobacterium breve (2 × 10(10) CFU),
- B. longum (7 × 10(9) CFU),
- Streptococcus thermophilus (1.5 × 10(9) CFU)



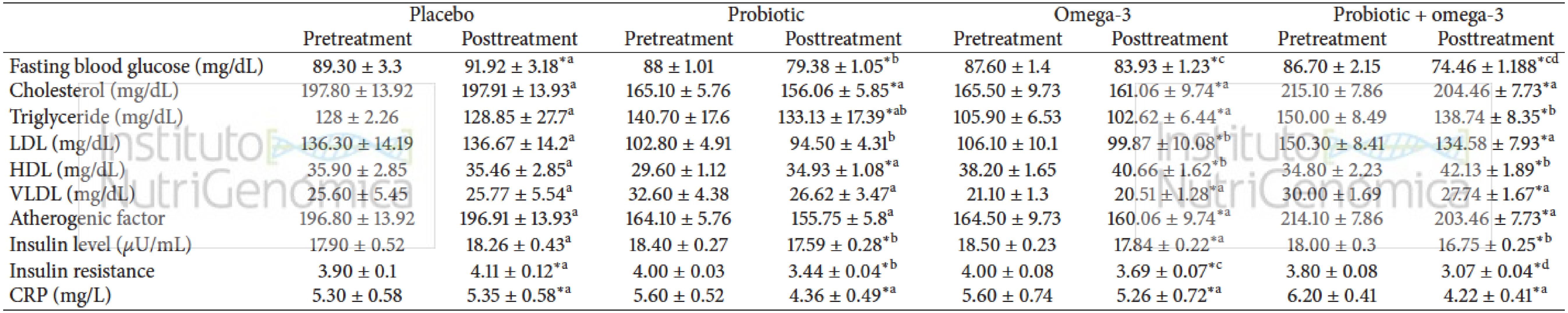
	Placebo (n = 27)				Probiotic supplement (n = 27)				p^b
	week 0	week 8	change	p^a	week 0	week 8	change	p^a	
FPG, mg/dl	134.5±9.6	163.3±12	28.8±8.5	0.002	143.8±10.7	145.4±9.5	1.6±6	0.80	0.01
$HbA1_C$, %	6.35±0.3	6.53±0.28	0.18±0.31	0.55	7.71±0.37	7.41±0.41	–0.3±0.37	0.42	0.32
Insulin, µIU/ml	5.82±1	9.93±1.51	4.11±0.91	<0.0001	5.7±0.8	7.74±1.11	2.04±0.82	0.02	0.09
HOMA-IR	2.03±0.44	4.41±0.88	2.38±0.65	0.001	1.98±0.33	2.76±0.44	0.78±0.31	0.02	0.03
Total cholesterol, mg/dl	164.6±10.1	177.8±6.6	13.2±8.9	0.15	171.3±9.4	176.2±7.4	4.9±6.9	0.48	0.46
Triglycerides, mg/dl	134±11.7	150.2±11.6	16.2±11.5	0.17	159.5±15.2	160.3±13.7	0.8±10.5	0.93	0.33
LDL-C, mg/dl	84.2±7.5	102.8±5.9	18.6±6.6	0.009	83.4±6.3	97.4±6.4	14±4.6	0.006	0.56
HDL-C, mg/dl	53.6±2.8	44.9±1.7	–8.7±2.2	0.001	56±3	46.8±2	–9.2±2.3	<0.0001	0.83
Total:HDL-C ratio	3.1±0.2	4±0.2	0.9±0.15	<0.0001	3±0.1	3.8±0.2	0.8±0.1	<0.0001	0.30
Hs-CRP, ng/ml	2,107.75±361.79	2,986.47±652.09	878.72±586.44	0.14	2,793.42±617.2	2,015.85±380.16	–777.57±441.7	0.09	0.02
TAC, mmol/l	870.06±30.75	955±28.06	84.94±24.32	0.002	925.3±41.59	1,005.27±40.49	79.97±41.8	0.06	0.91
GSH, µmol/l	750.5±60.72	717.04±40.06	–33.46±69.54	0.63	832.96±68.95	1,073.59±65.76	240.63±101.29	0.02	0.03
Uric acid, mg/dl	4.73±0.27	4.88±0.24	0.15±0.21	0.47	4.71±0.27	5.51±0.28	0.8±0.27	0.008	0.07

Effect of Probiotic (VSL#3) and Omega-3 on Lipid Profile, Insulin Sensitivity, Inflammatory Markers, and Gut Colonization in Overweight Adults: A Randomized, Controlled Trial

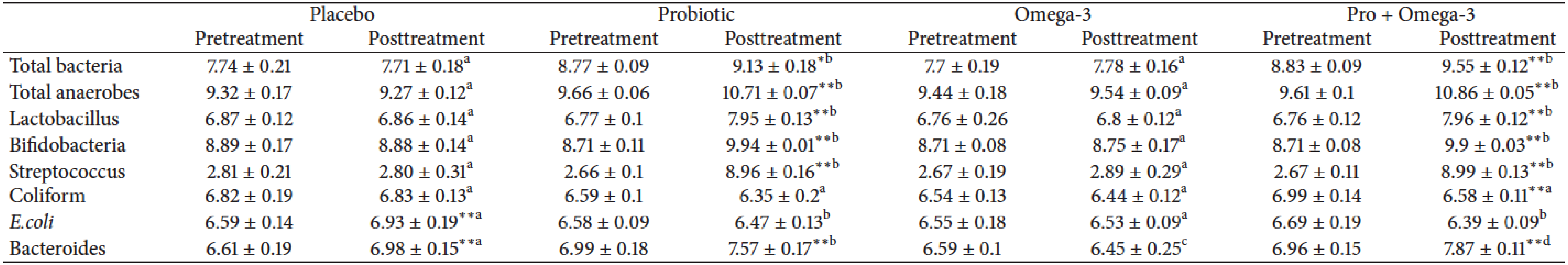
(Rajkumar et al, 2014)

Mediators of Inflammation, 2014:348959

VSL#3 (manufactured in India by Sun Pharmaceutical Ind. Ltd.) is a freeze-dried pharmaceutical probiotic preparation containing 112.5 × 109 CFU/capsule of three strains of bifidobacteria (*Bifidobacterium longum*, *Bifidobacterium infantis*, *and Bifidobacterium breve*), four strains of lactobacilli (*Lactobacillus acidophilus*, *Lactobacillus paracasei*, Lactobacillus *delbrueckii* subsp. *bulgaricus*, and *Lactobacillus plantarum*), and one strain of *Streptococcus salivarius* subsp. *thermophilus*



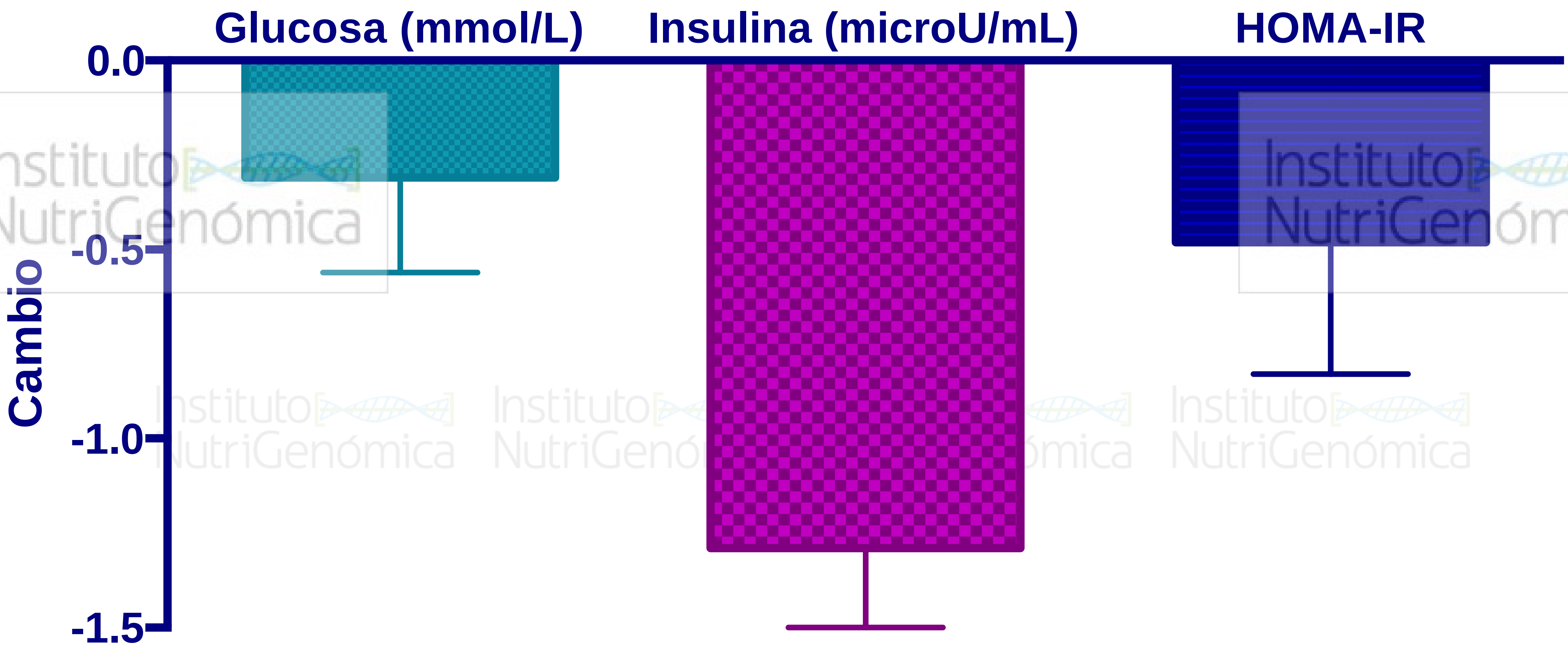
	Placebo		Probiotic		Omega-3		Probiotic + omega-3	
	Pretreatment	Posttreatment	Pretreatment	Posttreatment	Pretreatment	Posttreatment	Pretreatment	Posttreatment
Fasting blood glucose (mg/dL)	89.30 ± 3.3	$91.92 \pm 3.18^{*a}$	88 ± 1.01	$79.38 \pm 1.05^{*b}$	87.60 ± 1.4	$83.93 \pm 1.23^{*c}$	86.70 ± 2.15	$74.46 \pm 1.188^{*cd}$
Cholesterol (mg/dL)	197.80 ± 13.92	197.91 ± 13.93^{a}	165.10 ± 5.76	$156.06 \pm 5.85^{*a}$	165.50 ± 9.73	$161.06 \pm 9.74^{*a}$	215.10 ± 7.86	$204.46 \pm 7.73^{*a}$
Triglyceride (mg/dL)	128 ± 2.26	128.85 ± 27.7^{a}	140.70 ± 17.6	$133.13 \pm 17.39^{*ab}$	105.90 ± 6.53	$102.62 \pm 6.44^{*a}$	150.00 ± 8.49	$138.74 \pm 8.35^{*b}$
LDL (mg/dL)	136.30 ± 14.19	136.67 ± 14.2^{a}	102.80 ± 4.91	94.50 ± 4.31^{b}	106.10 ± 10.1	$99.87 \pm 10.08^{*b}$	150.30 ± 8.41	$134.58 \pm 7.93^{*a}$
HDL (mg/dL)	35.90 ± 2.85	35.46 ± 2.85^{a}	29.60 ± 1.12	$34.93 \pm 1.08^{*a}$	38.20 ± 1.65	$40.66 \pm 1.62^{*b}$	34.80 ± 2.23	$42.13 \pm 1.89^{*b}$
VLDL (mg/dL)	25.60 ± 5.45	25.77 ± 5.54^{a}	32.60 ± 4.38	26.62 ± 3.47^{a}	21.10 ± 1.3	$20.51 \pm 1.28^{*a}$	30.00 ± 1.69	$27.74 \pm 1.67^{*a}$
Atherogenic factor	196.80 ± 13.92	196.91 ± 13.93^{a}	164.10 ± 5.76	155.75 ± 5.8^{a}	164.50 ± 9.73	$160.06 \pm 9.74^{*a}$	214.10 ± 7.86	$203.46 \pm 7.73^{*a}$
Insulin level (μU/mL)	17.90 ± 0.52	18.26 ± 0.43^{a}	18.40 ± 0.27	$17.59 \pm 0.28^{*b}$	18.50 ± 0.23	$17.84 \pm 0.22^{*a}$	18.00 ± 0.3	$16.75 \pm 0.25^{*b}$
Insulin resistance	3.90 ± 0.1	$4.11 \pm 0.12^{*a}$	4.00 ± 0.03	$3.44 \pm 0.04^{*b}$	4.00 ± 0.08	$3.69 \pm 0.07^{*c}$	3.80 ± 0.08	$3.07 \pm 0.04^{*d}$
CRP (mg/L)	5.30 ± 0.58	$5.35 \pm 0.58^{*a}$	5.60 ± 0.52	$4.36 \pm 0.49^{*a}$	5.60 ± 0.74	$5.26 \pm 0.72^{*a}$	6.20 ± 0.41	$4.22 \pm 0.41^{*a}$



	Placebo		Probiotic		Omega-3		Pro + Omega-3	
	Pretreatment	Posttreatment	Pretreatment	Posttreatment	Pretreatment	Posttreatment	Pretreatment	Posttreatment
Total bacteria	7.74 ± 0.21	7.71 ± 0.18^{a}	8.77 ± 0.09	$9.13 \pm 0.18^{*b}$	7.7 ± 0.19	7.78 ± 0.16^{a}	8.83 ± 0.09	$9.55 \pm 0.12^{**b}$
Total anaerobes	9.32 ± 0.17	9.27 ± 0.12^{a}	9.66 ± 0.06	$10.71 \pm 0.07^{**b}$	9.44 ± 0.18	9.54 ± 0.09^{a}	9.61 ± 0.1	$10.86 \pm 0.05^{**b}$
Lactobacillus	6.87 ± 0.12	6.86 ± 0.14^{a}	6.77 ± 0.1	$7.95 \pm 0.13^{**b}$	6.76 ± 0.26	6.8 ± 0.12^{a}	6.76 ± 0.12	$7.96 \pm 0.12^{**b}$
Bifidobacteria	8.89 ± 0.17	8.88 ± 0.14^{a}	8.71 ± 0.11	$9.94 \pm 0.01^{**b}$	8.71 ± 0.08	8.75 ± 0.17^{a}	8.71 ± 0.08	$9.9 \pm 0.03^{**b}$
Streptococcus	2.81 ± 0.21	2.80 ± 0.31^{a}	2.66 ± 0.1	$8.96 \pm 0.16^{**b}$	2.67 ± 0.19	2.89 ± 0.29^{a}	2.67 ± 0.11	$8.99 \pm 0.13^{**b}$
Coliform	6.82 ± 0.19	6.83 ± 0.13^{a}	6.59 ± 0.1	6.35 ± 0.2^{a}	6.54 ± 0.13	6.44 ± 0.12^{a}	6.99 ± 0.14	$6.58 \pm 0.11^{**a}$
E.coli	6.59 ± 0.14	$6.93 \pm 0.19^{**a}$	6.58 ± 0.09	6.47 ± 0.13^{b}	6.55 ± 0.18	6.53 ± 0.09^{a}	6.69 ± 0.19	6.39 ± 0.09^{b}
Bacteroides	6.61 ± 0.19	$6.98 \pm 0.15^{**a}$	6.99 ± 0.18	$7.57 \pm 0.17^{**b}$	6.59 ± 0.1	6.45 ± 0.25^{c}	6.96 ± 0.15	$7.87 \pm 0.11^{**d}$

Effect of probiotics on glycemic control: a systematic review and meta-analysis of randomized, controlled trials.

(Ruan et al, 2015)
PlosOne 10:e0132121



Probiotic intervention has strain-specific anti-inflammatory effects in healthy adults

(Kekkonen et al, 2008)
World J Gastroenterol. 14:2029-36

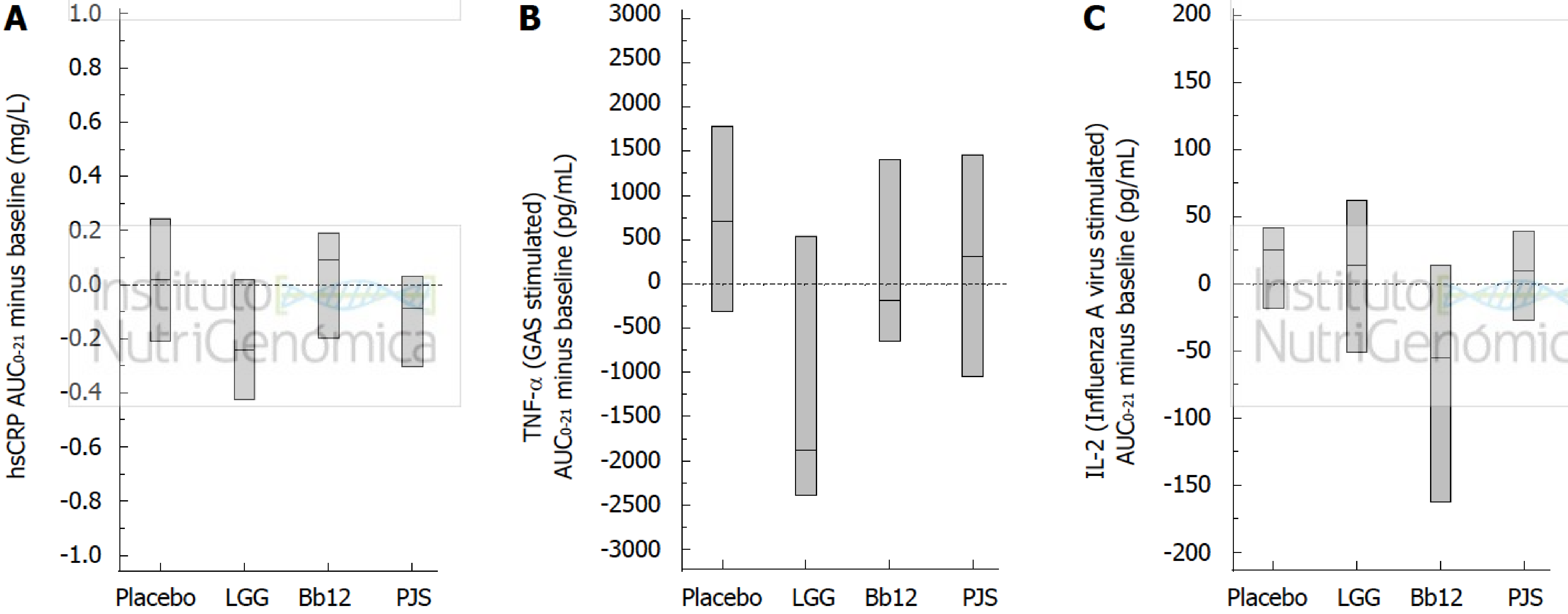
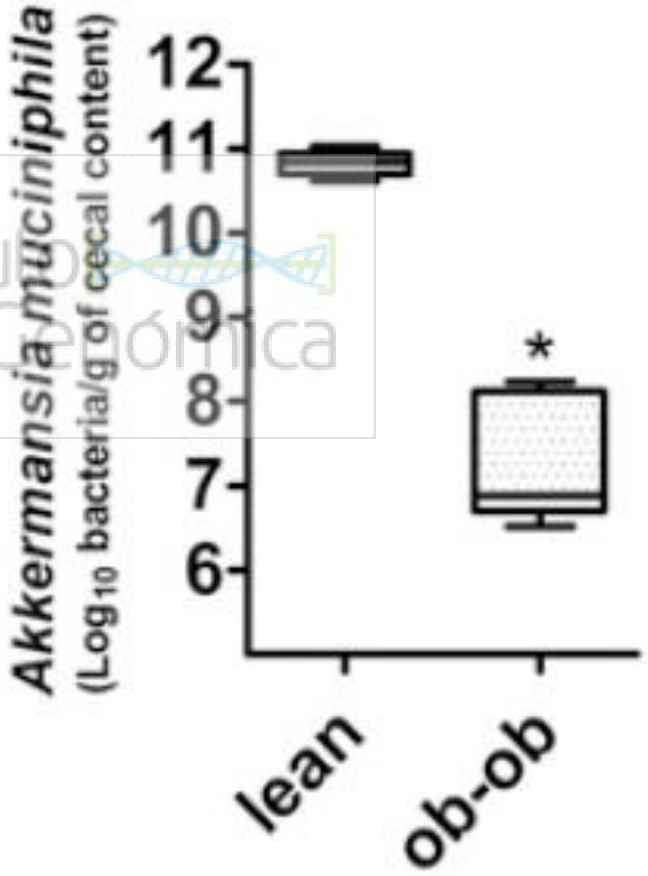
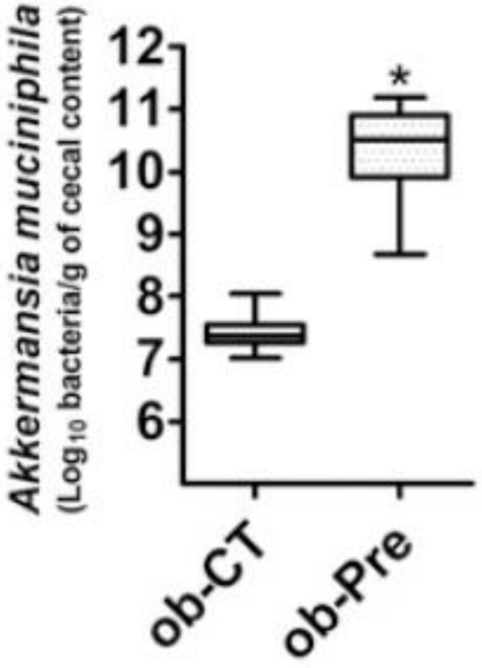


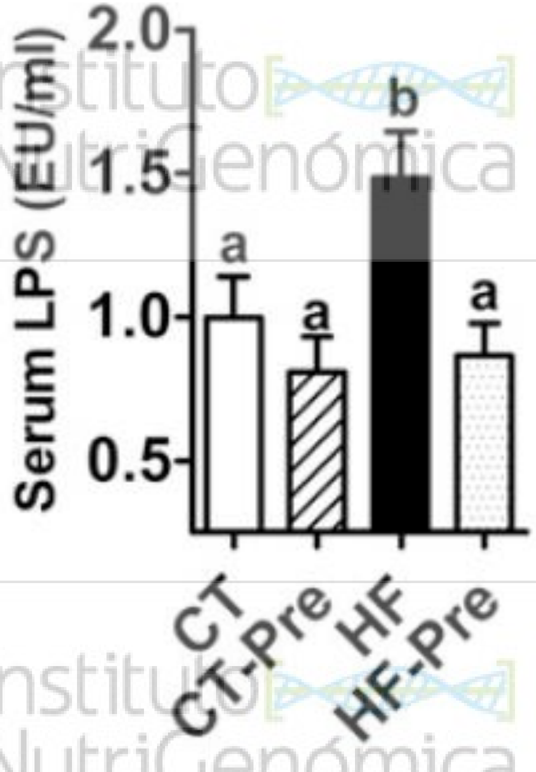
Figure 1 The median AUC$_{0\text{-}21}$ (minus baseline) with IQR for serum highly sensitive CRP (hsCRP) levels (**A**), for *Streptococcus pyogenes* (GAS) -stimulated TNF-α production from peripheral blood mononuclear cells (**B**) and for Influenza A virus-stimulated IL-2 production from peripheral blood mononuclear cells (**C**) during the 3-wk intervention period in healthy adults (*n* = 62). LGG: *Lactobacillus rhamnosus* GG; Bb12: *Bifidobacterium animalis* ssp. lactis Bb12; PJS: *Propionibacterium freudenreichii* ssp. *shermanii* JS.

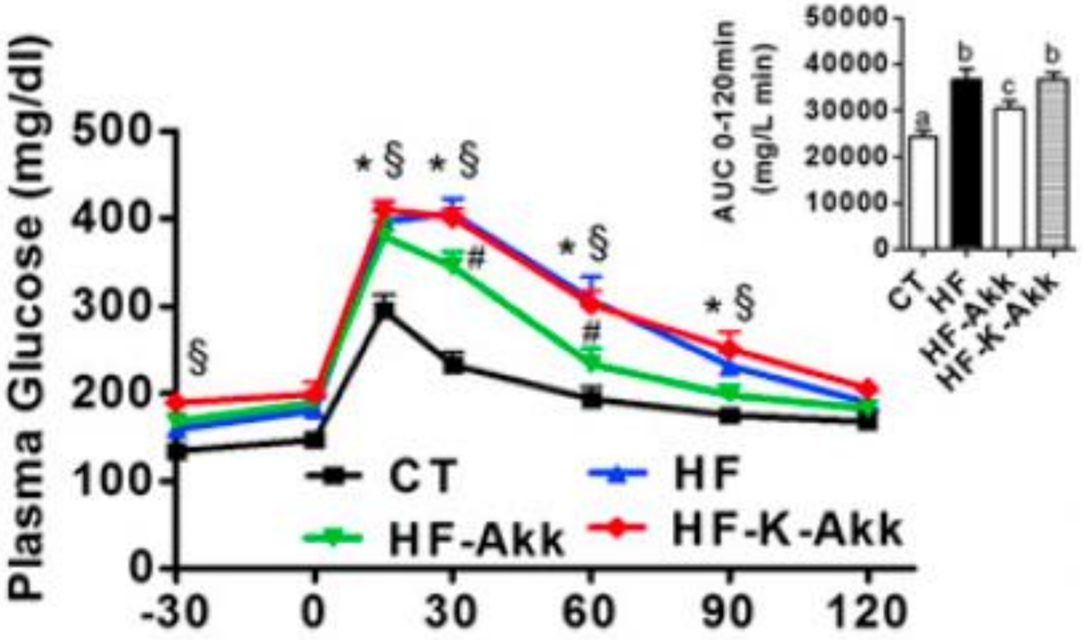
Cross-talk between *Akkermansia muciniphila* and intestinal epithelium controls diet-induced obesity

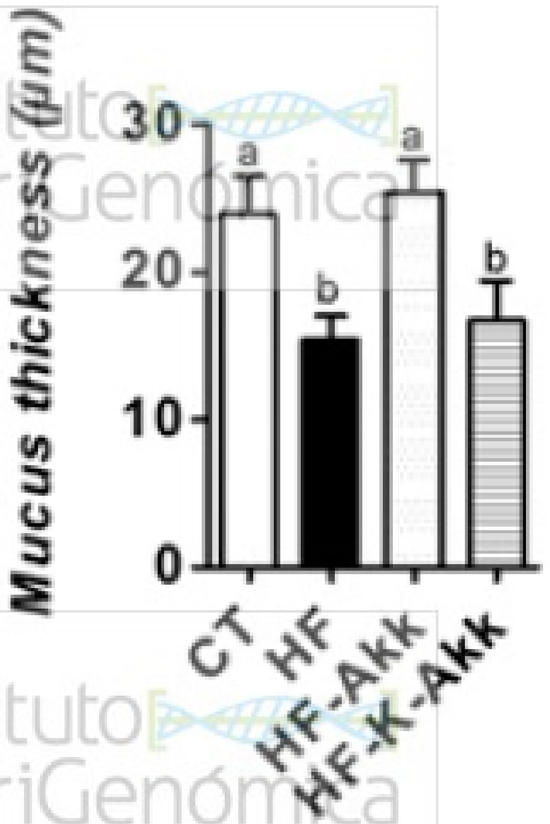
(Everard et al, 2013)
PNAS 111:9066-9071

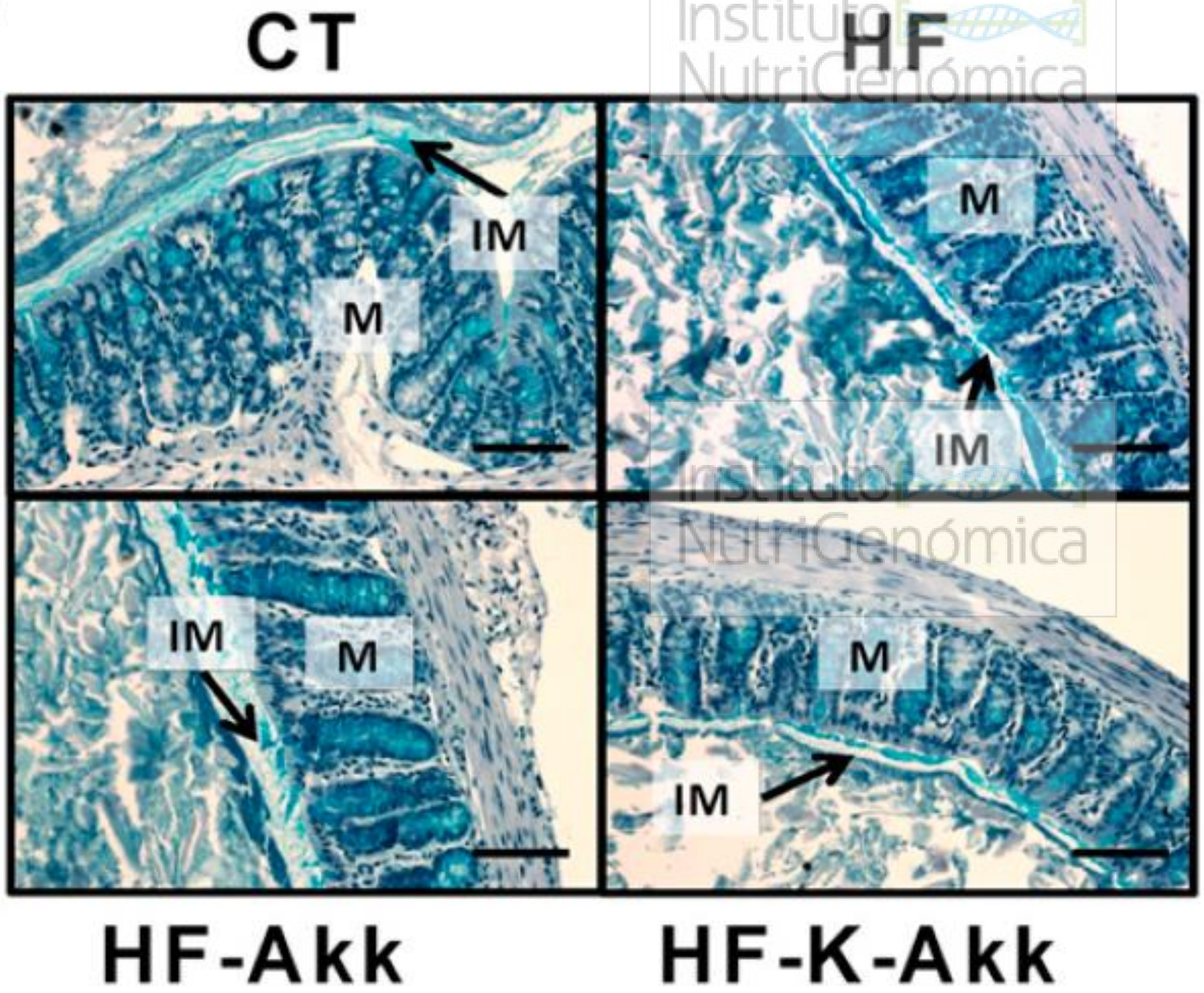


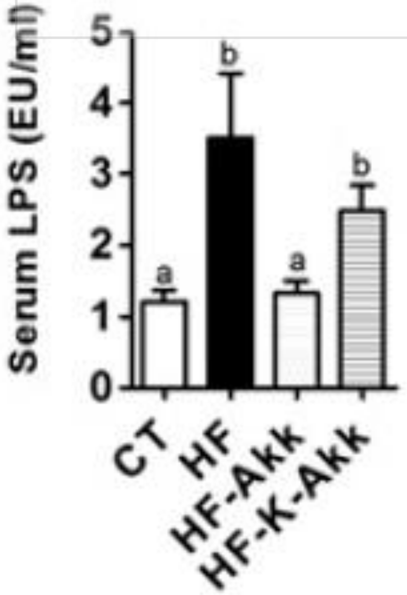


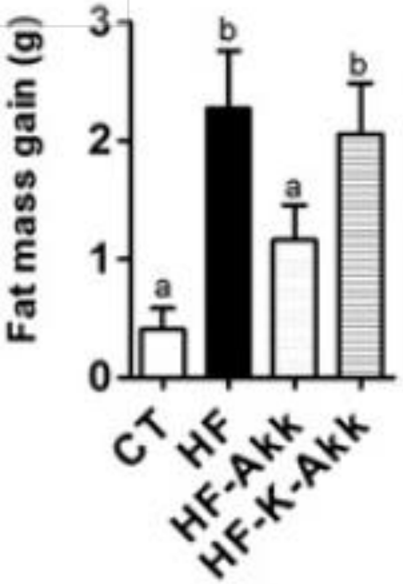





Mucus thickness (μm)
30
20
10
0
a
b
a
b
CT
HF
HF-Akk
HF-K-Akk


CT
HF
IM
M
M
IM
IM
M
IM
M
HF-Akk
HF-K-Akk


Serum LPS (EU/ml)
5
4
3
2
1
0
a
b
a
b
CT
HF
HF-Akk
HF-K-Akk


Fat mass gain (g)
3
2
1
0
a
b
a
b
CT
HF
HF-Akk
HF-K-Akk

Microbiota y síndorme metabólico
- Obesidad e insulinorresistencia -

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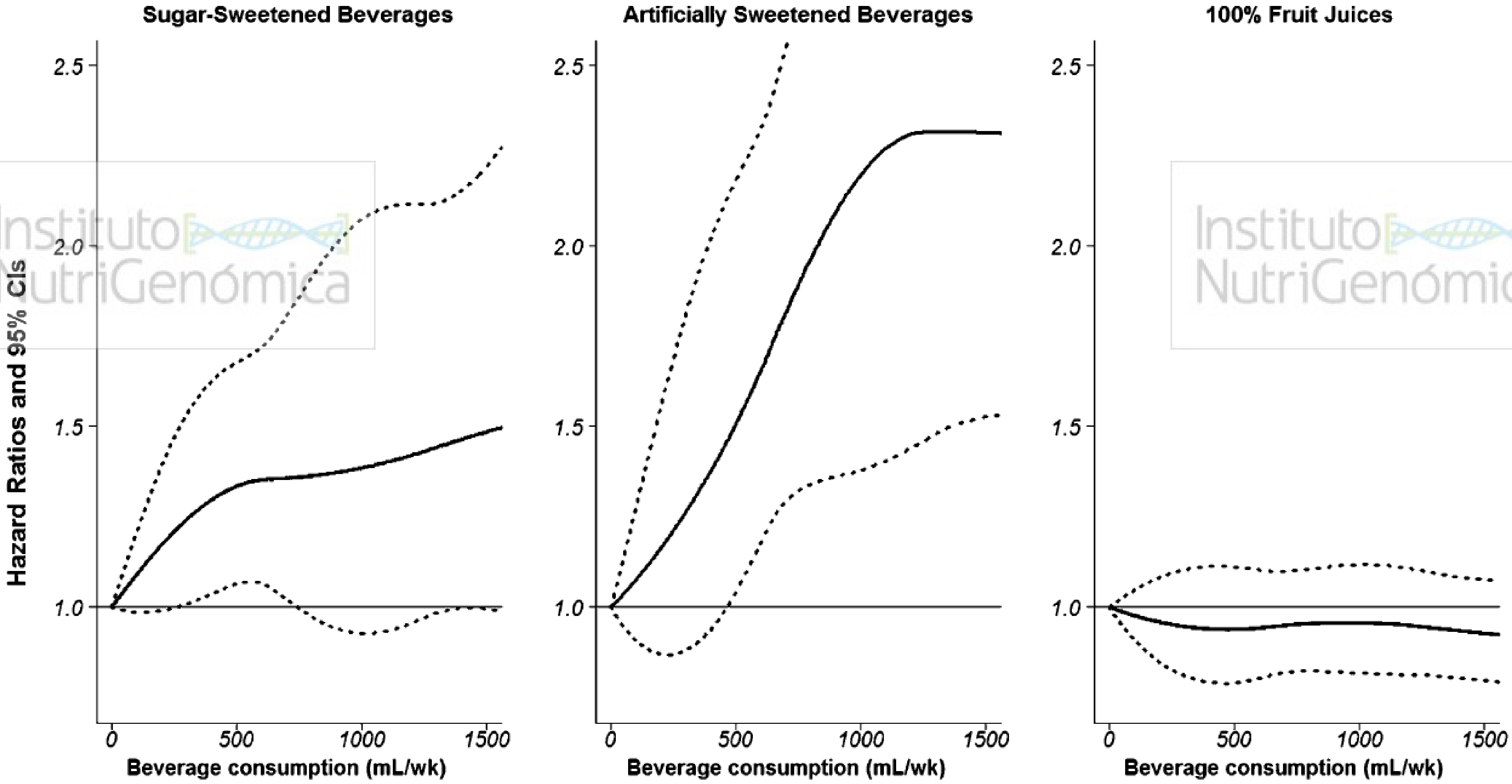
Consumption of artificially and sugar-sweetened beverages and incident type 2 diabetes in the Etude Epidemiologique aupres des femmes de la Mutuelle Generale de l'Education Nationale-European Prospective Investigation into Cancer and Nutrition cohort

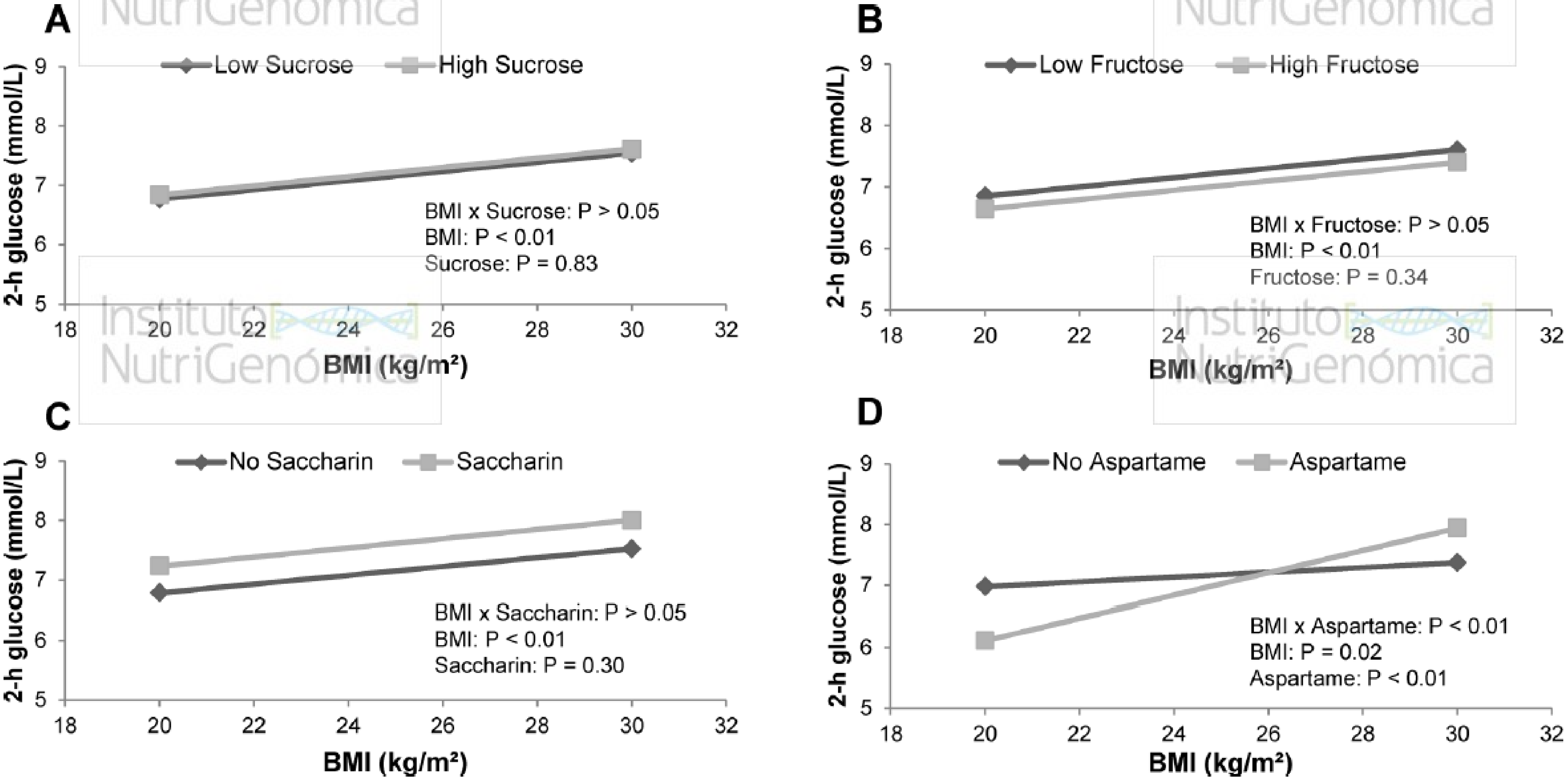
(Fagherazzi et al, 2013)

Am J Clin Nutr 97:517-523



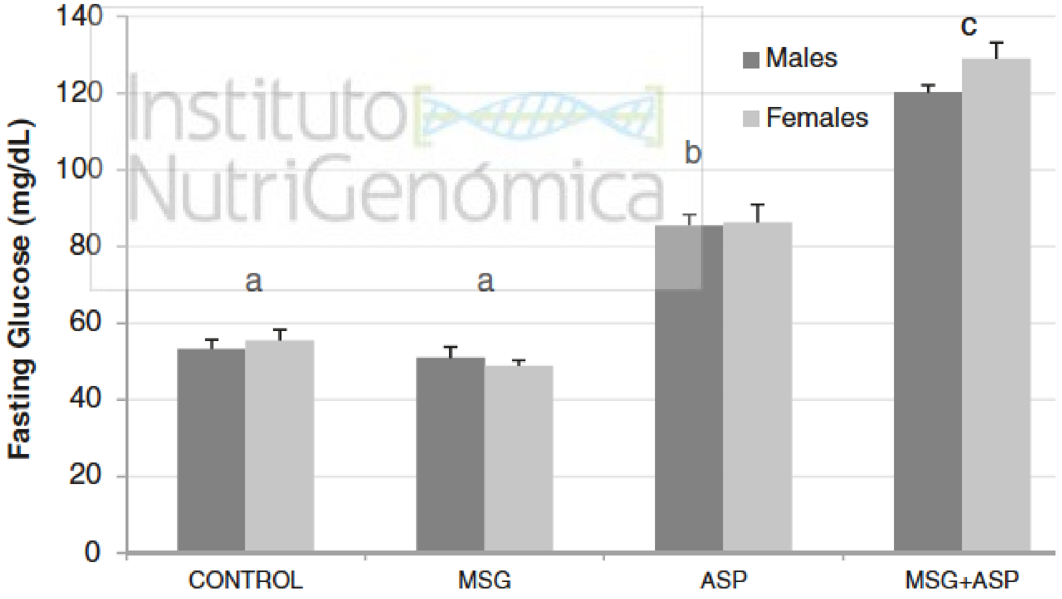
Aspartame intake is associated with greater glucose intolerance in individuals with obesity

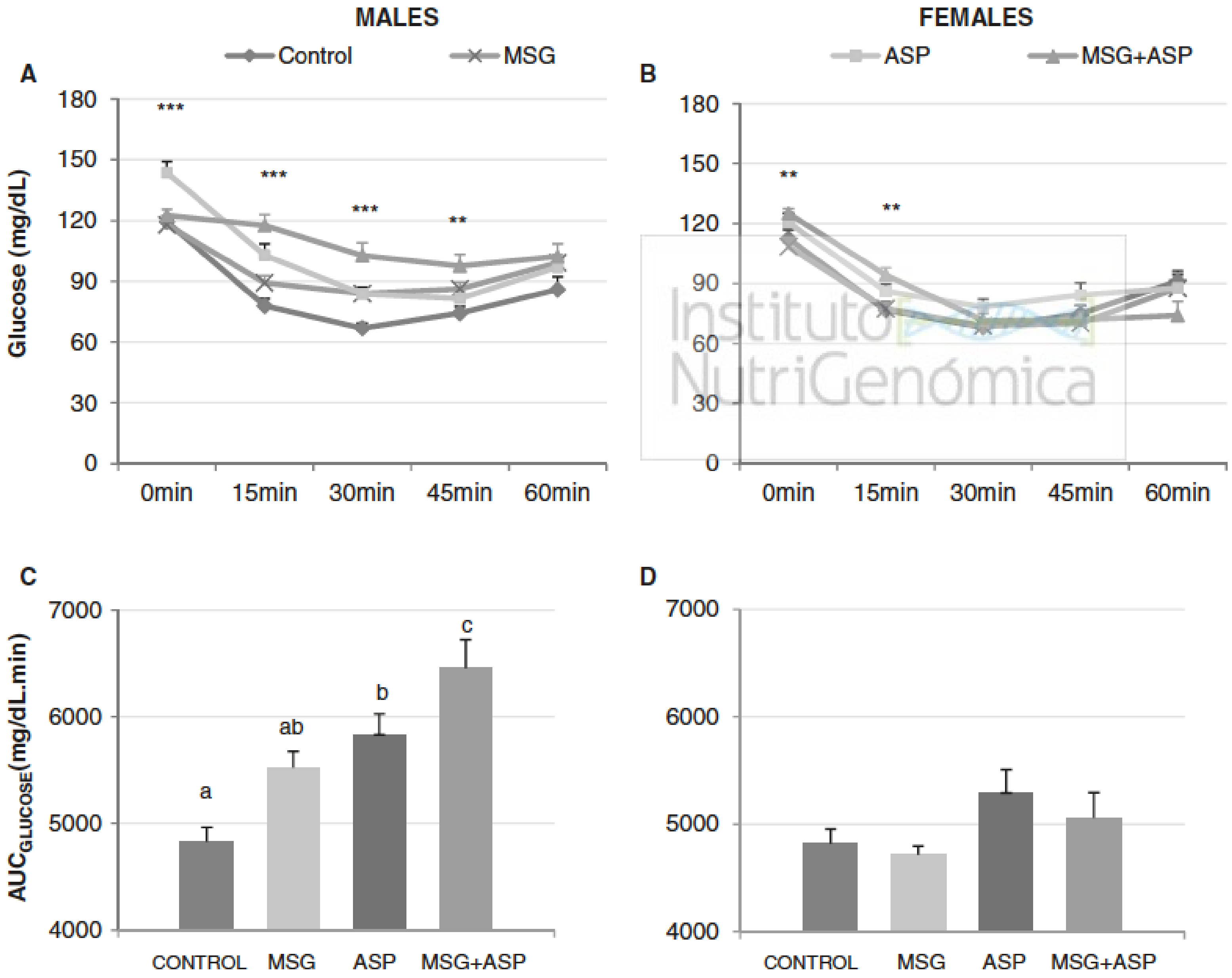
(Kuk & Brown, 2016)
Appl Physiol Nutr Metab 41:795-798



Interactive effects of neonatal exposure to monosodium glutamate and aspartame on glucose homeostasis

(Collison et al, 2012)
Nutr Metab 9:58

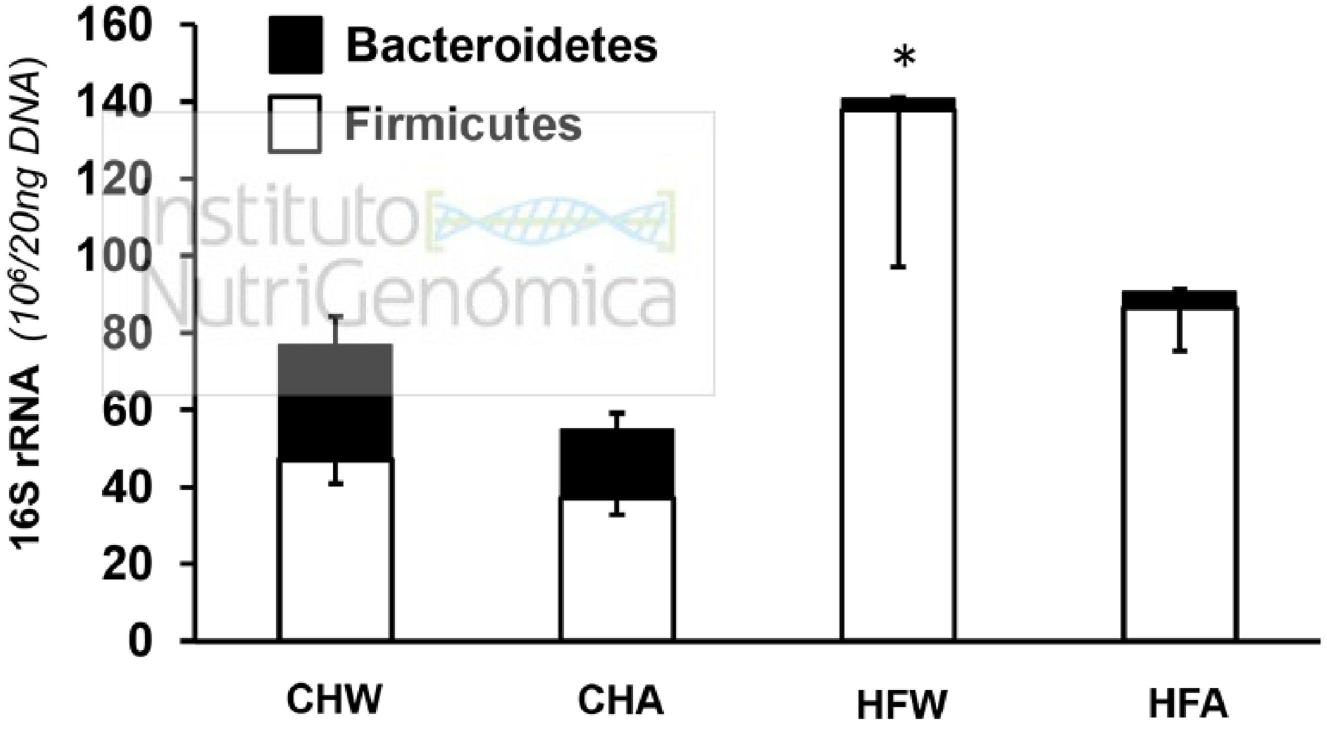


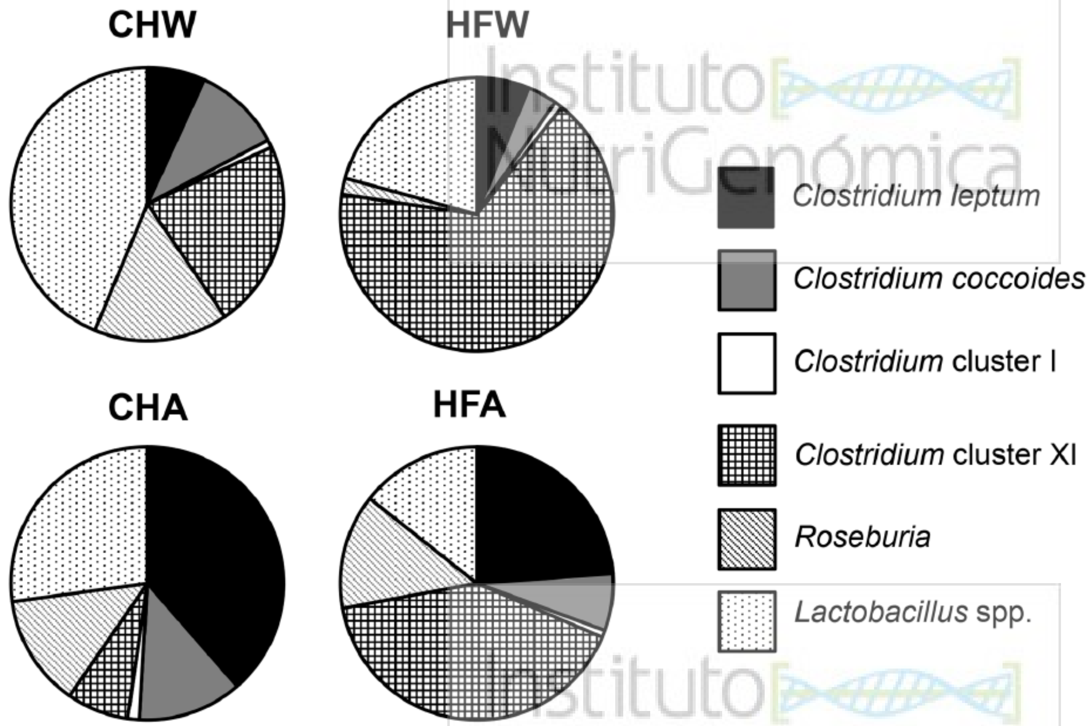


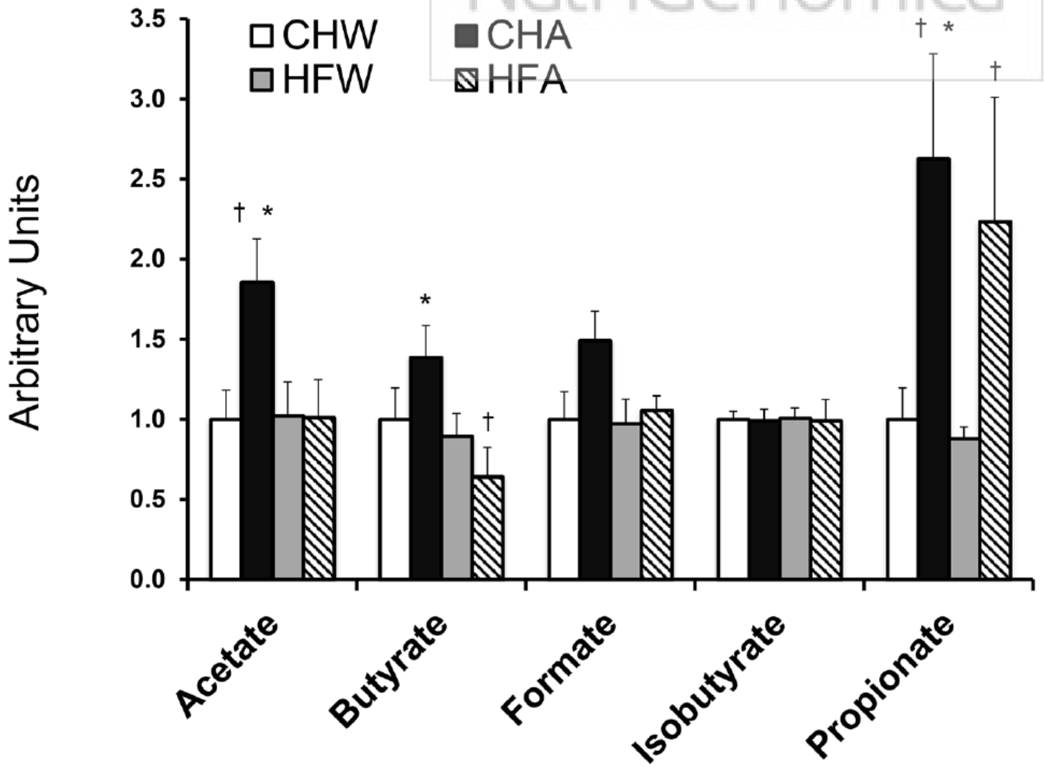
Low-Dose Aspartame Consumption Differentially Affects Gut Microbiota-Host Metabolic Interactions in the Diet-Induced Obese Rat

(Palmnäs et al, 2014)

PLoS One 9:e109841



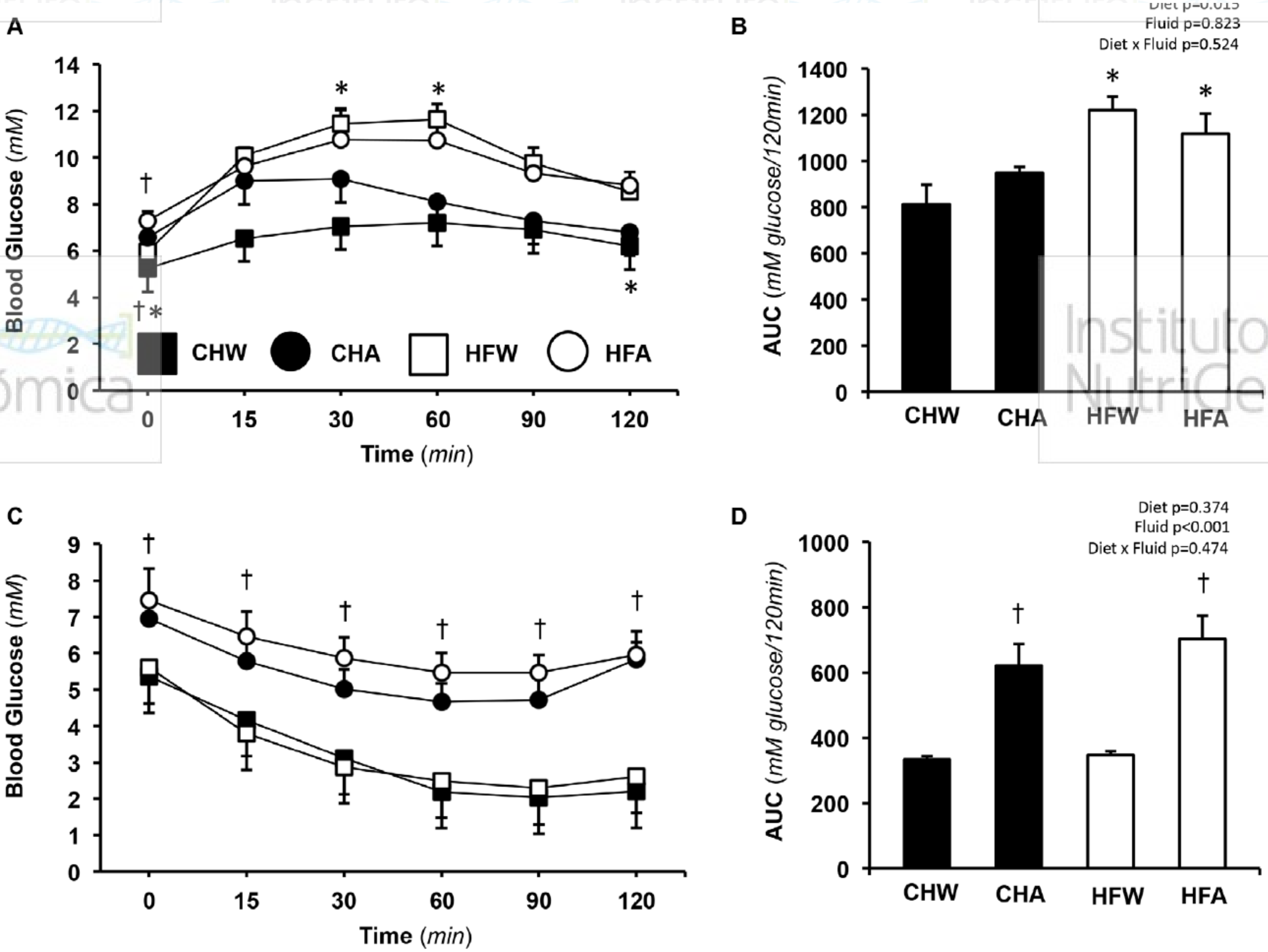




Low-Dose Aspartame Consumption Differentially Affects Gut Microbiota-Host Metabolic Interactions in the Diet-Induced Obese Rat

(Palmnäs et al, 2014)
PLoS One 9:e109841

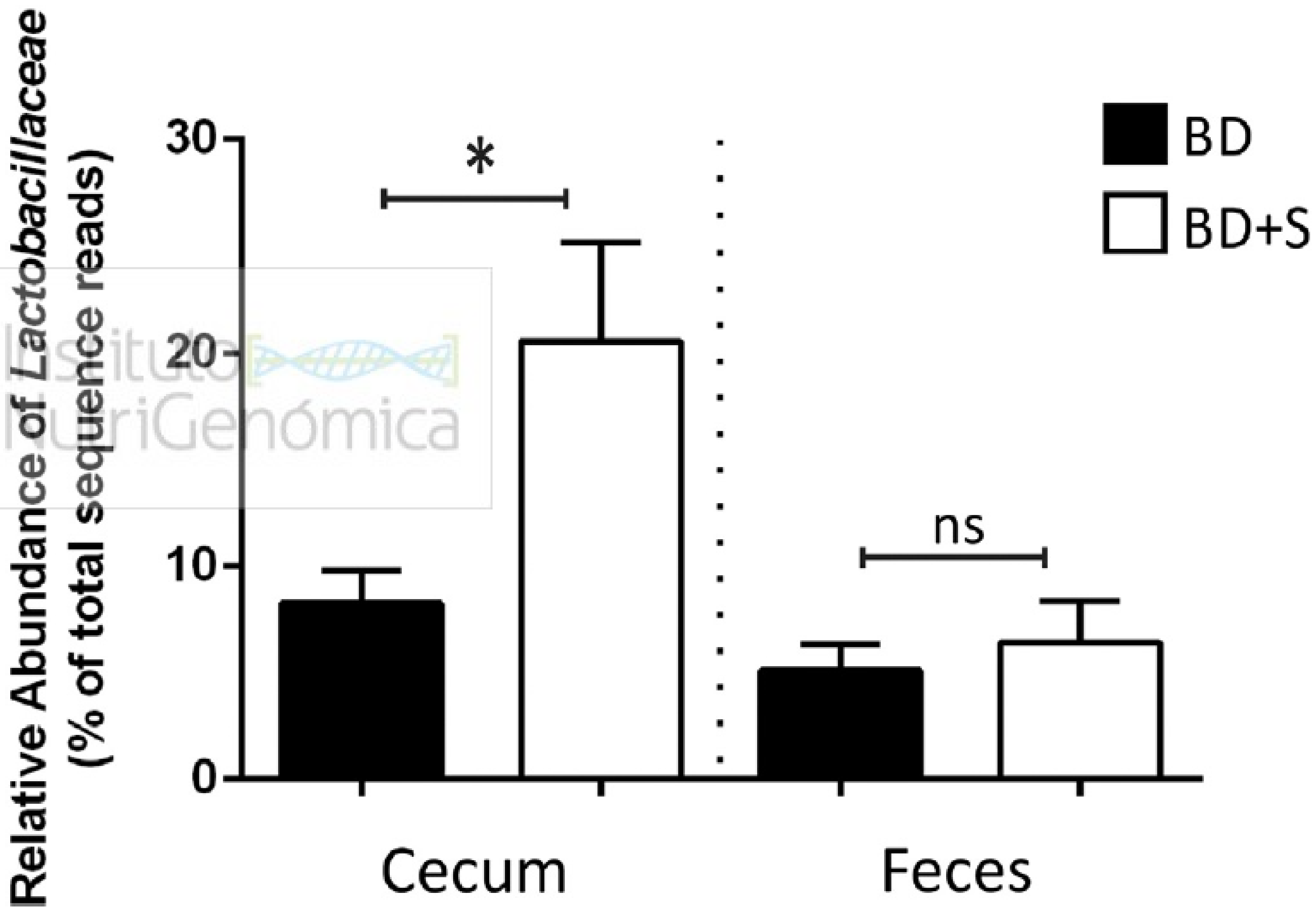
Aspartame



Low calorie sweeteners and gut microbiota

(Daly et al, 2016)

Physiology and behavior.



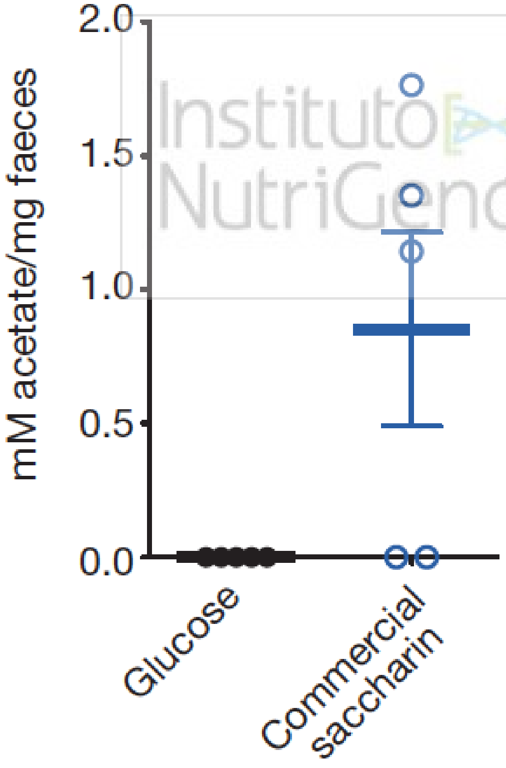
SUCRAM®

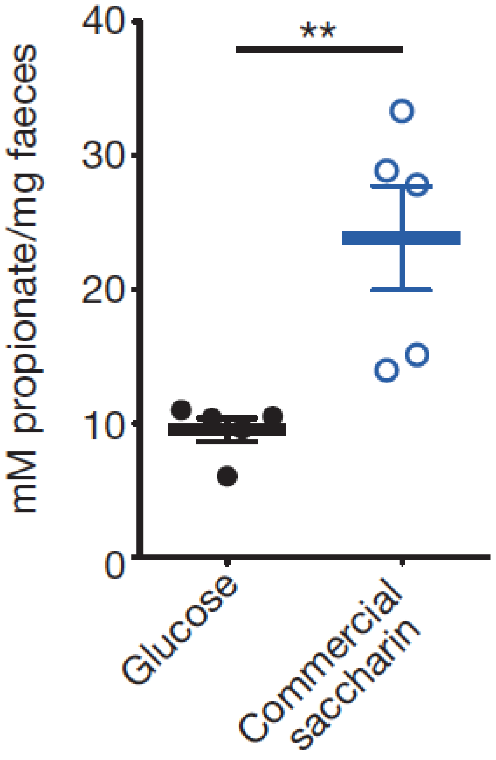
at least 50 parts by weight of a saccharine-type sweetener, at least 0.15 part by weight of glycyrrhizine, neohesperidin dihydrochalcone

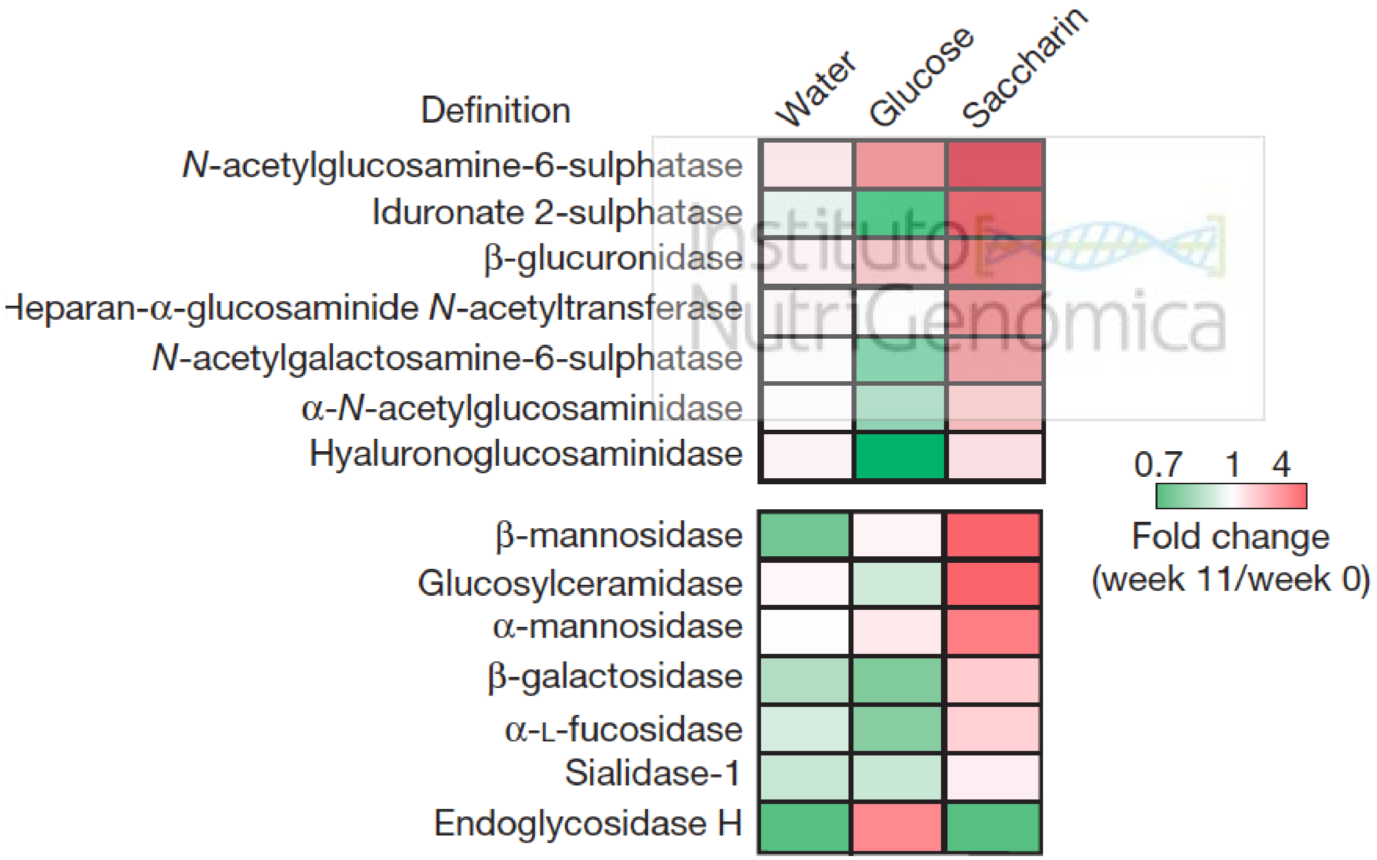
Artificial sweeteners induce glucose intolerance by altering the gut microbiota

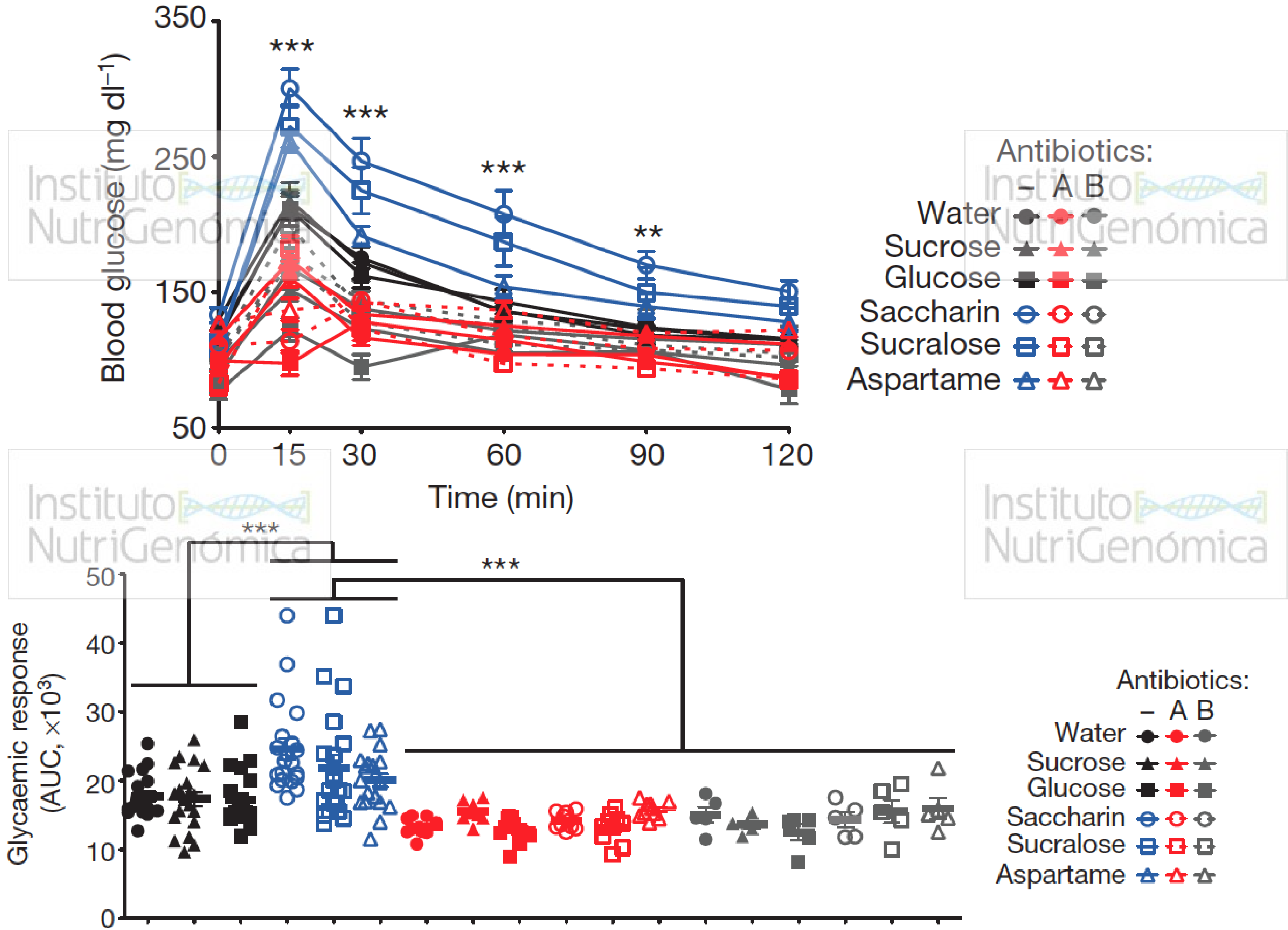
(Suez et al, 2014)
Nature ***514****, 181–186*

Sacarina



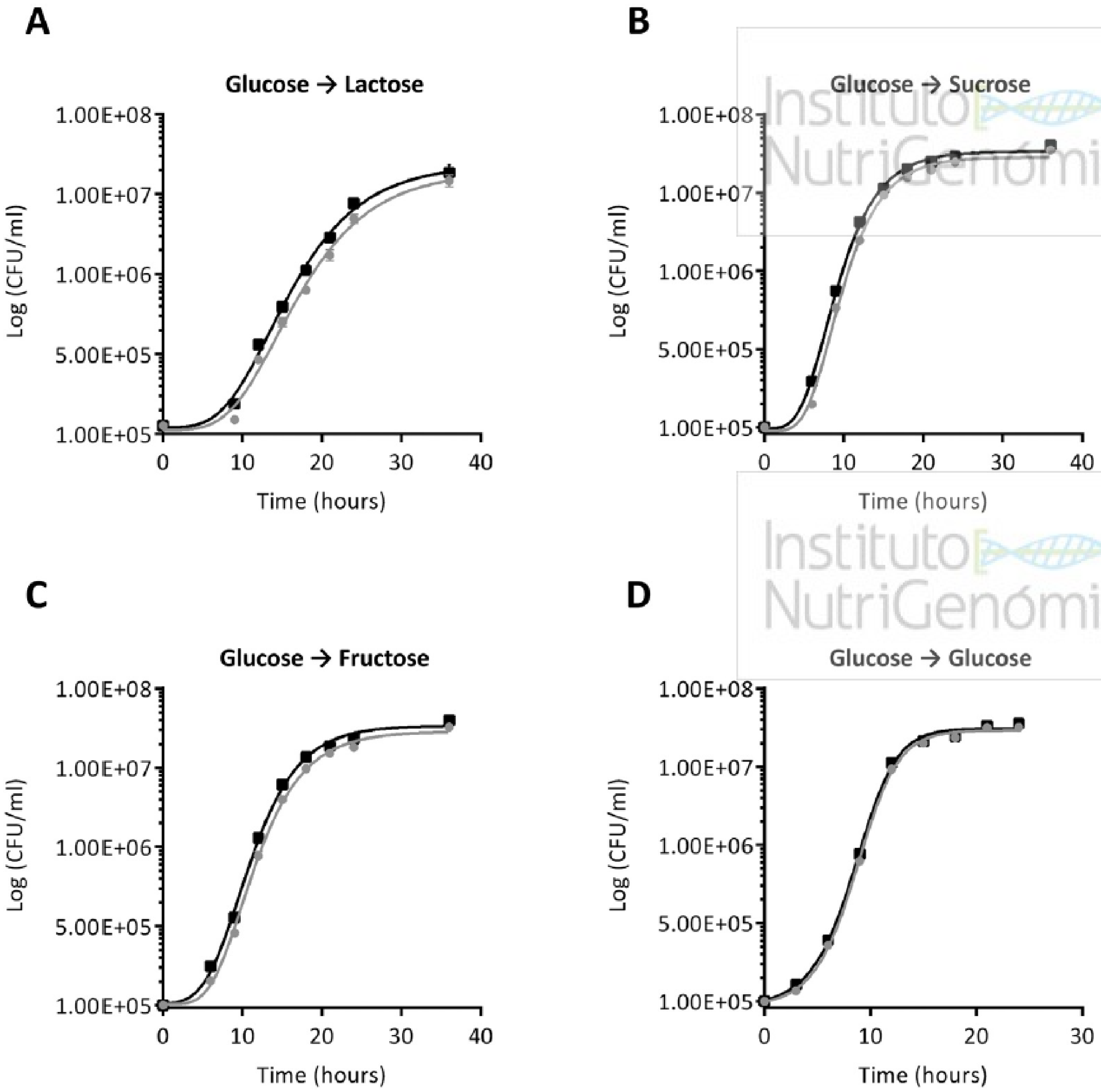





350
250
150
50
Blood glucose (mg dl^{-1})
***
***
***
**
0
15
30
60
90
120
Time (min)
Antibiotics:
– A B
Water
Sucrose
Glucose
Saccharin
Sucralose
Aspartame
***
***
50
40
30
20
10
0
Glycaemic response (AUC, ×10^3)
Antibiotics:
– A B
Water
Sucrose
Glucose
Saccharin
Sucralose
Aspartame

Low calorie sweeteners and gut microbiota

(Daly et al, 2016)
Physiology and behavior.



Conclusiones

- Definitivamente la microbiota colónica tiene una relación en el desarrollo del síndrome metabólico:
  - Utilización de energía derivada de la fracción indigerible
  - Inflamación crónica sub-aguda

- No existe suficiente evidencia que relacione un enterotipo específico con el desarrollo del síndrome metabólico. Parece que es más importante la diversidad

- Existen evidencias de algunos tratamientos nutricionales (e.g. probióticos) para mejorar el síndrome metabólico.